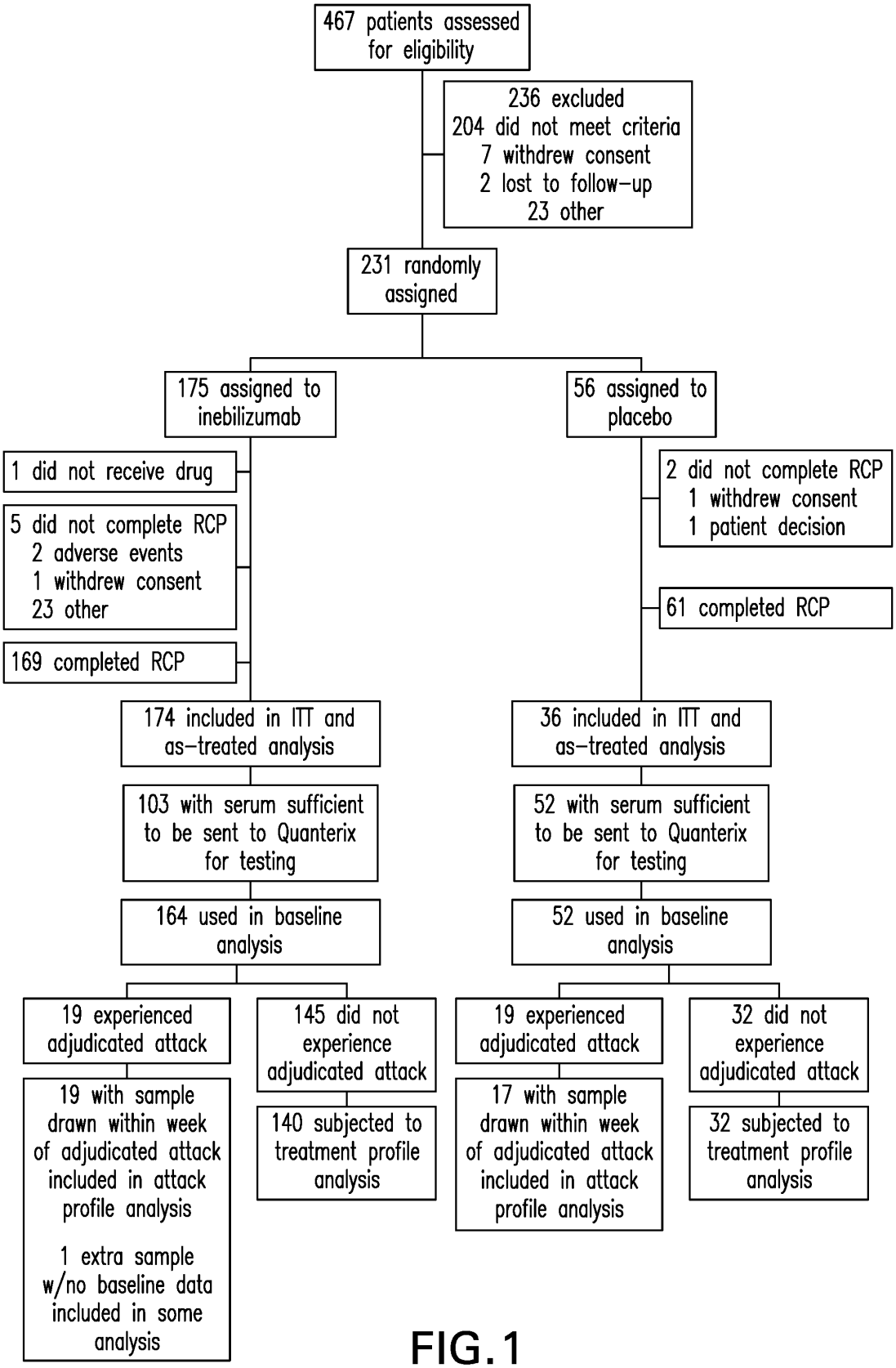

467 patients assessed for eligibility
236 excluded
204 did not meet criteria
7 withdrew consent
2 lost to follow-up
23 other
231 randomly assigned
175 assigned to inebilizumab
56 assigned to placebo
1 did not receive drug
5 did not complete RCP
2 adverse events
1 withdrew consent
23 other
169 completed RCP
2 did not complete RCP
1 withdrew consent
1 patient decision
61 completed RCP
174 included in ITT and as-treated analysis
36 included in ITT and as-treated analysis
103 with serum sufficient to be sent to Quanterix for testing
52 with serum sufficient to be sent to Quanterix for testing
164 used in baseline analysis
52 used in baseline analysis
19 experienced adjudicated attack
145 did not experience adjudicated attack
19 experienced adjudicated attack
32 did not experience adjudicated attack
19 with sample drawn within week of adjudicated attack included in attack profile analysis
1 extra sample w/no baseline data included in some analysis
140 subjected to treatment profile analysis
17 with sample drawn within week of adjudicated attack included in attack profile analysis
32 subjected to treatment profile analysis

FIG. 1

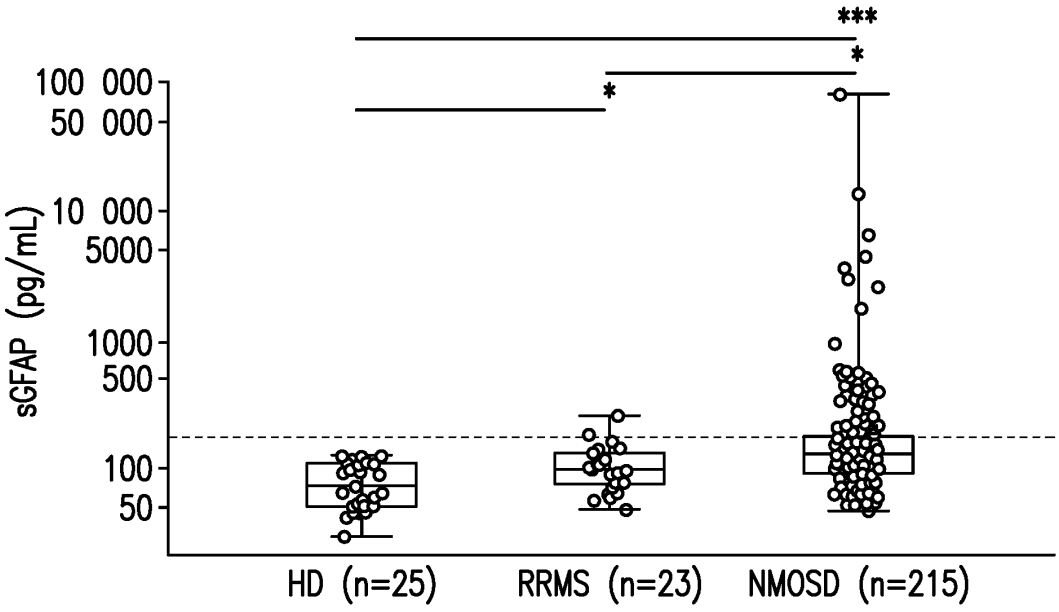

***
*
*
100 000
50 000
10 000
5000
1000
500
100
50
sGFAP (pg/mL)
HD (n=25)
RRMS (n=23)
NMOSD (n=215)

FIG.2A

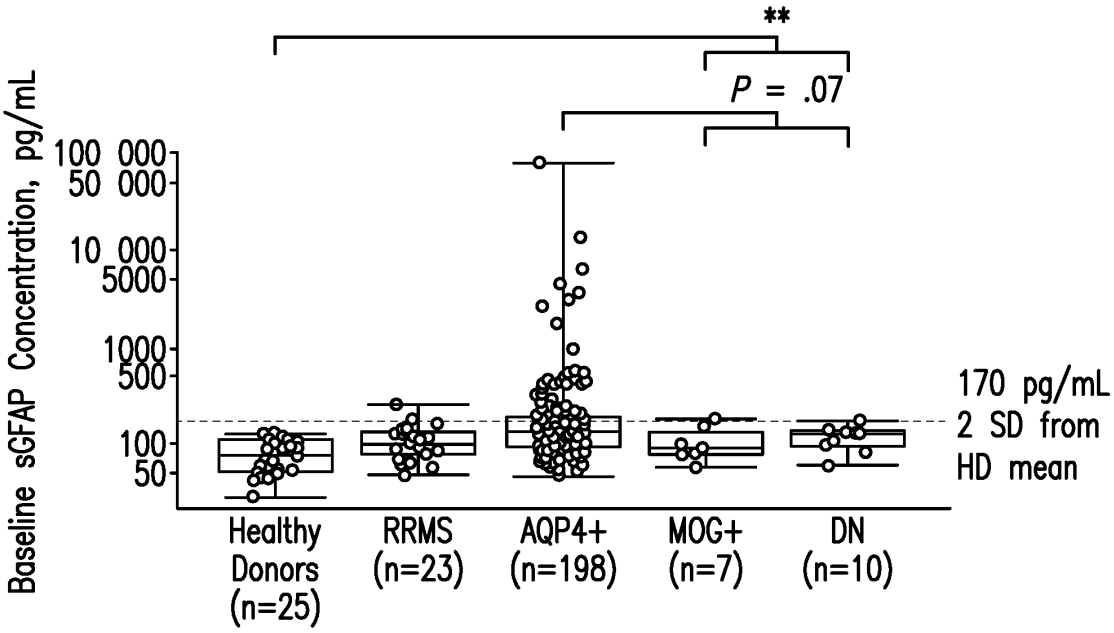

**
P = .07
100 000
50 000
10 000
5000
1000
500
100
50
Baseline sGFAP Concentration, pg/mL
170 pg/mL
2 SD from
HD mean
Healthy Donors (n=25)
RRMS (n=23)
AQP4+ (n=198)
MOG+ (n=7)
DN (n=10)

FIG.2B

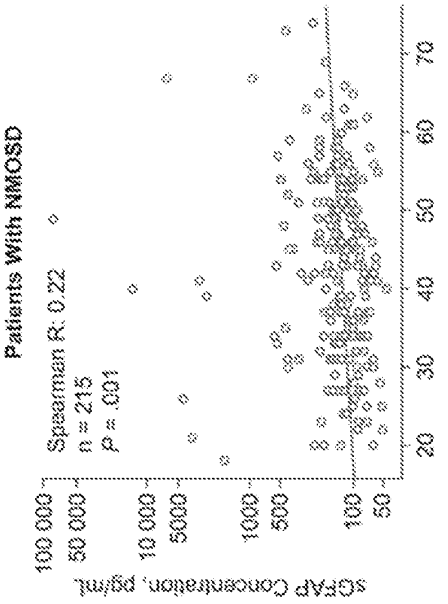

Patients With NMOSD
Spearman R: 0.22
n = 215
P = .001
sGFAP Concentration, pg/mL
100 000
50 000
10 000
5000
1000
500
100
50
20
30
40
50
60
70
Age, y

FIG.3B

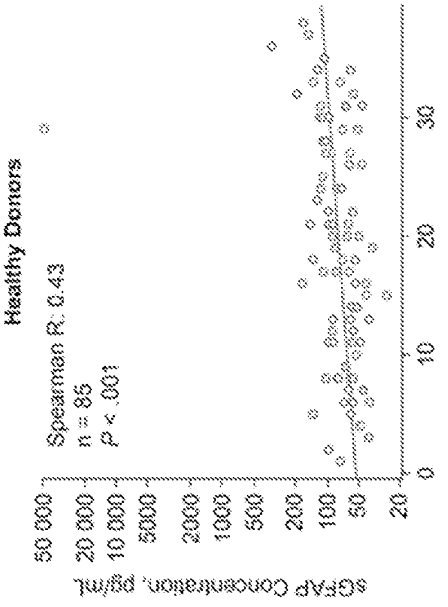

Healthy Donors
Spearman R: 0.43
n = 85
P < .001
sGFAP Concentration, pg/mL
50 000
20 000
10 000
5000
2000
1000
500
200
100
50
20
0
10
20
30
Age, y

FIG.3A

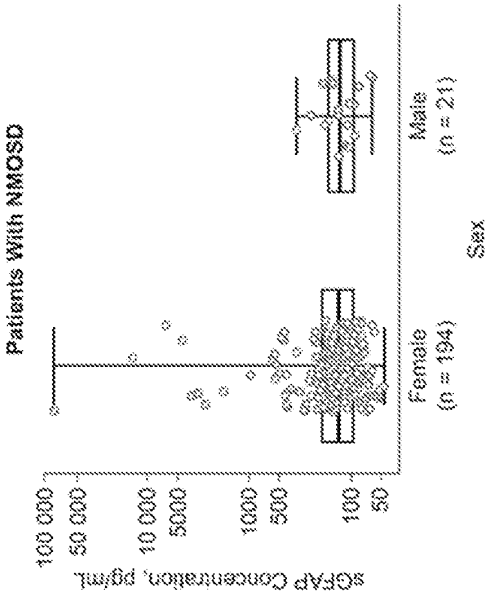

Patients With NMOSD
sGFAP Concentration, pg/mL
100 000
50 000
10 000
5000
1000
500
100
50
Female
(n = 194)
Male
(n = 21)
Sex

FIG.3D

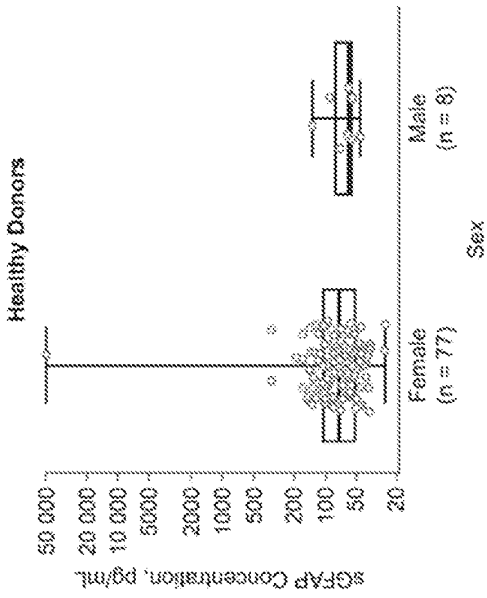

Healthy Donors
sGFAP Concentration, pg/mL
50 000
20 000
10 000
5000
2000
1000
500
200
100
50
20
Female
(n = 77)
Male
(n = 8)
Sex

FIG.3C

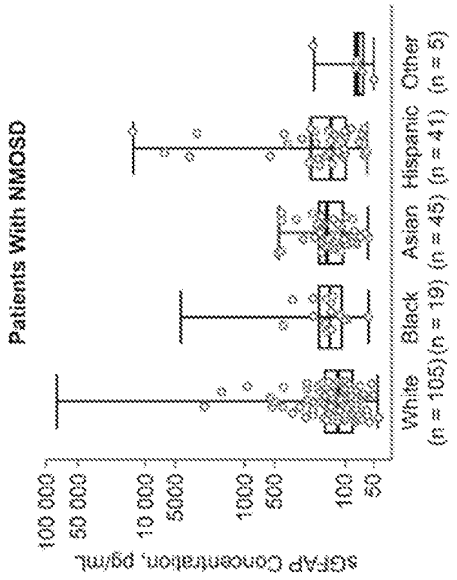

Patients With NMOSD
sGFAP Concentration, pg/mL
100 000
50 000
10 000
5000
1000
500
100
50
White (n = 105)
Black (n = 19)
Asian (n = 46)
Hispanic (n = 41)
Other (n = 5)
Ethnicity

FIG.3F

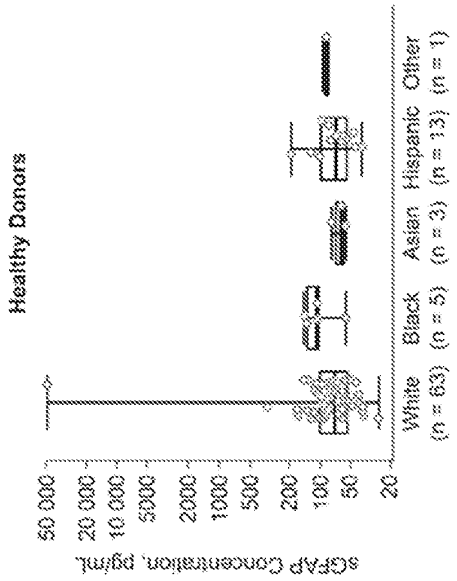

Healthy Donors
sGFAP Concentration, pg/mL
50 000
20 000
10 000
5000
2000
1000
500
200
100
50
20
White (n = 63)
Black (n = 5)
Asian (n = 3)
Hispanic (n = 13)
Other (n = 1)
Ethnicity

FIG.3E

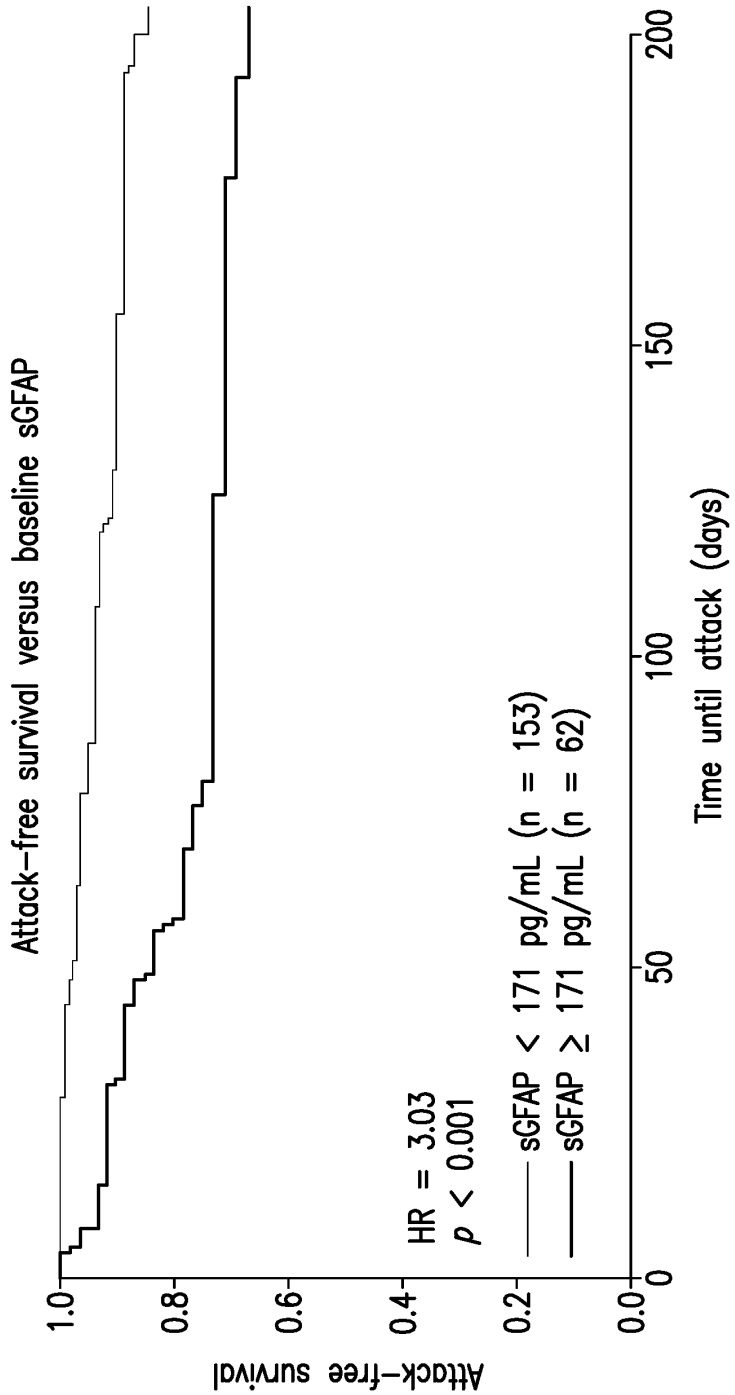
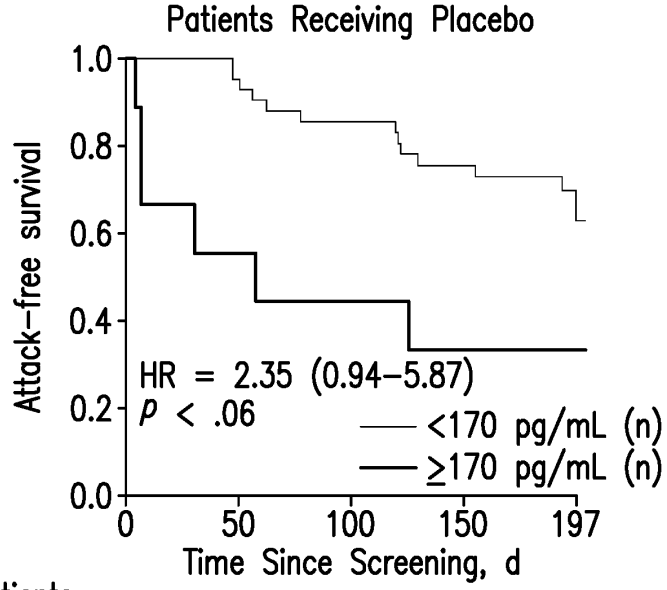
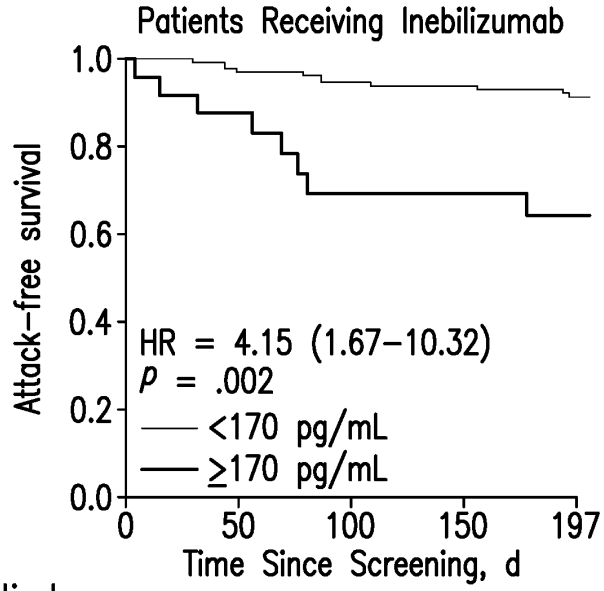

Attack–free survival versus baseline sGFAP
Attack–free survival
1.0
0.8
0.6
0.4
0.2
0.0
0
50
100
150
200
Time until attack (days)
HR = 3.03
p < 0.001
sGFAP < 171 pg/mL (n = 153)
sGFAP ≥ 171 pg/mL (n = 62)

FIG.4A



No. Patients					
<170 pg/mL (n)	35	34	31	25	14
≥170 pg/mL (n)	16	11	8	7	4

FIG.4B



No. Patients					
<170 pg/mL (n)	118	112	104	97	72
≥170 pg/mL (n)	46	39	31	31	20

FIG.4C

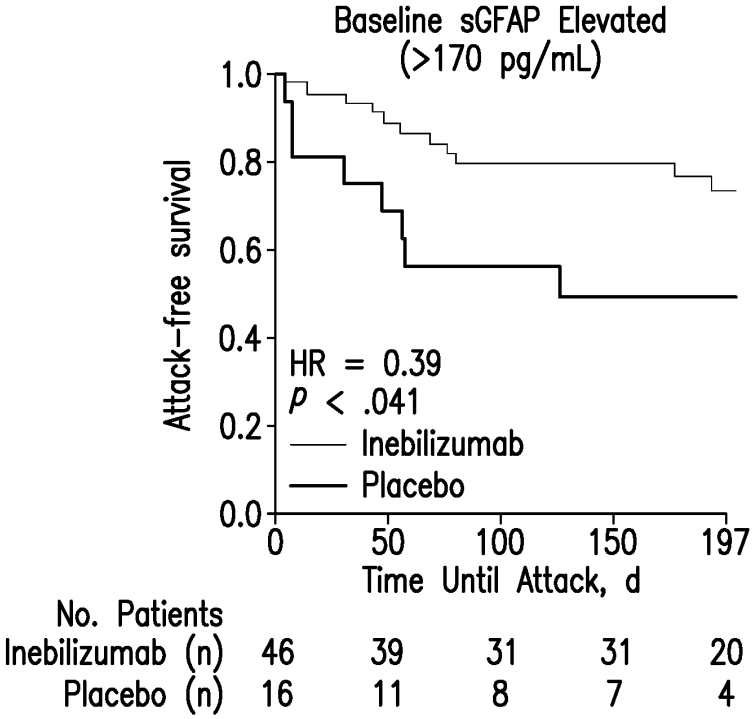

Baseline sGFAP Elevated
(>170 pg/mL)
Attack-free survival
1.0
0.8
0.6
0.4
0.2
0.0
HR = 0.39
p < .041
Inebilizumab
Placebo
0
50
100
150
197
Time Until Attack, d
No. Patients
Inebilizumab (n) 46 39 31 31 20
Placebo (n) 16 11 8 7 4

FIG.4D

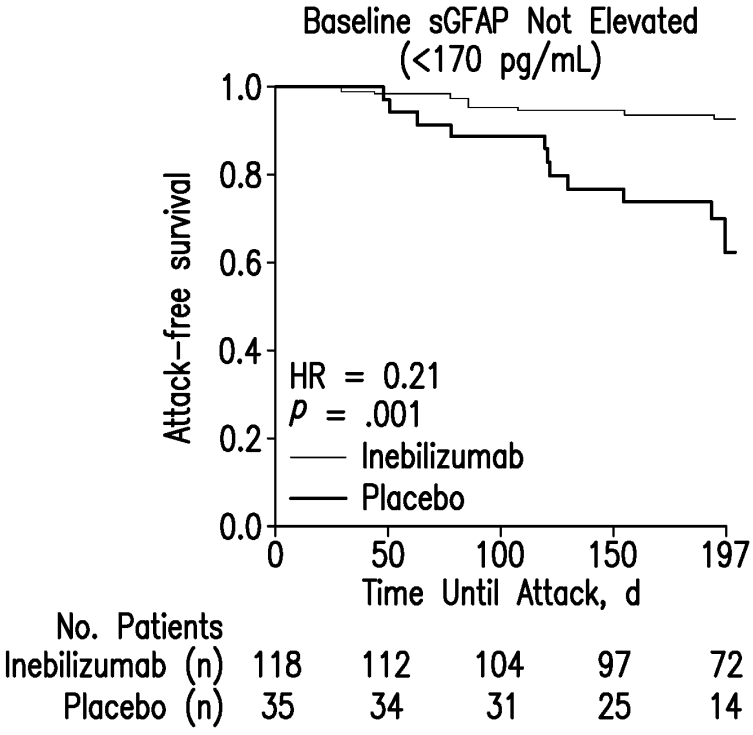

Baseline sGFAP Not Elevated
(<170 pg/mL)
Attack-free survival
1.0
0.8
0.6
0.4
0.2
0.0
HR = 0.21
p = .001
Inebilizumab
Placebo
0
50
100
150
197
Time Until Attack, d
No. Patients
Inebilizumab (n) 118 112 104 97 72
Placebo (n) 35 34 31 25 14

FIG.4E

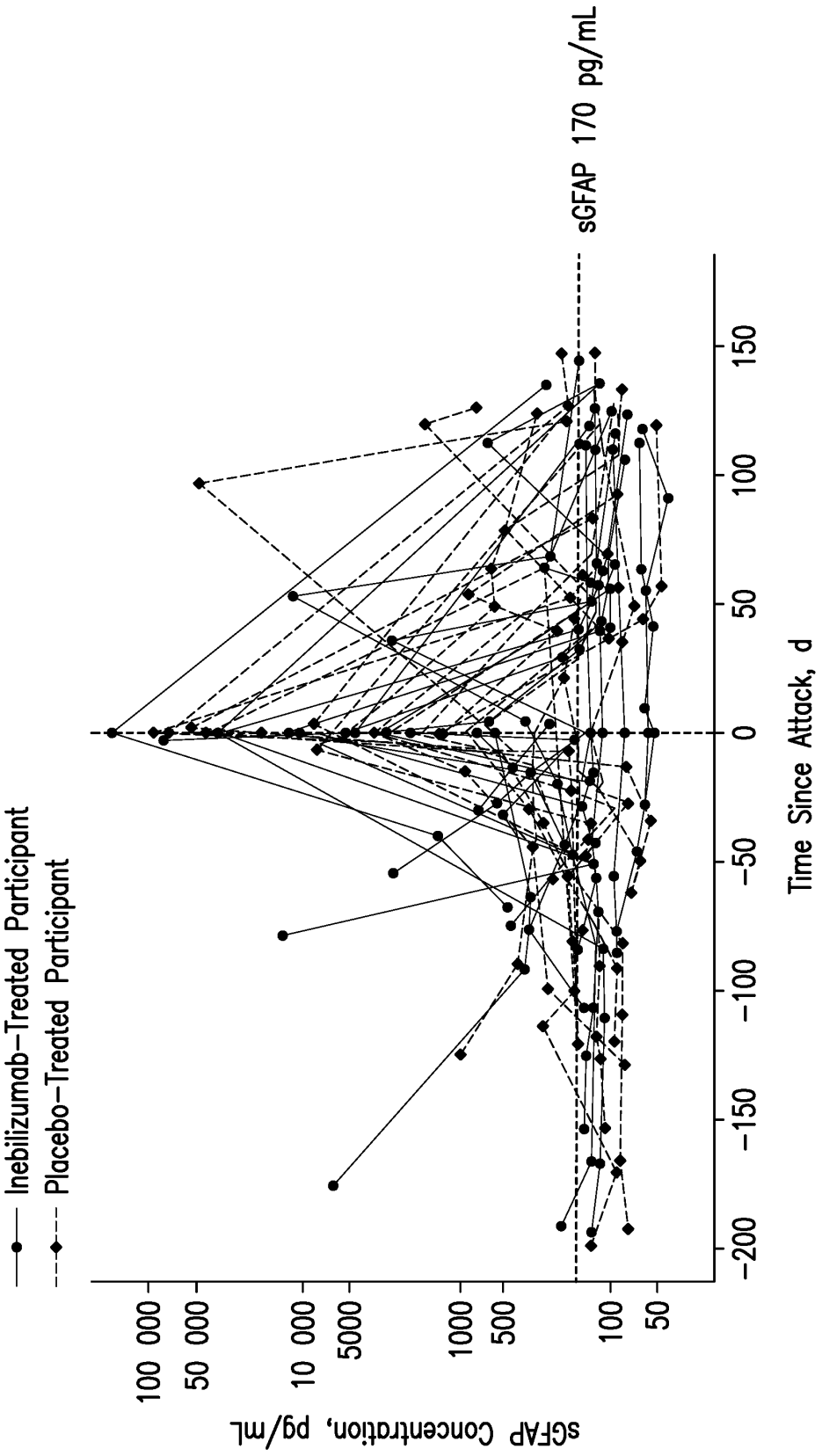

Inebilizumab–Treated Participant
Placebo–Treated Participant
sGFAP 170 pg/mL
sGFAP Concentration, pg/mL
100 000
50 000
10 000
5000
1000
500
100
50
Time Since Attack, d
−200
−150
−100
−50
0
50
100
150

FIG.5A

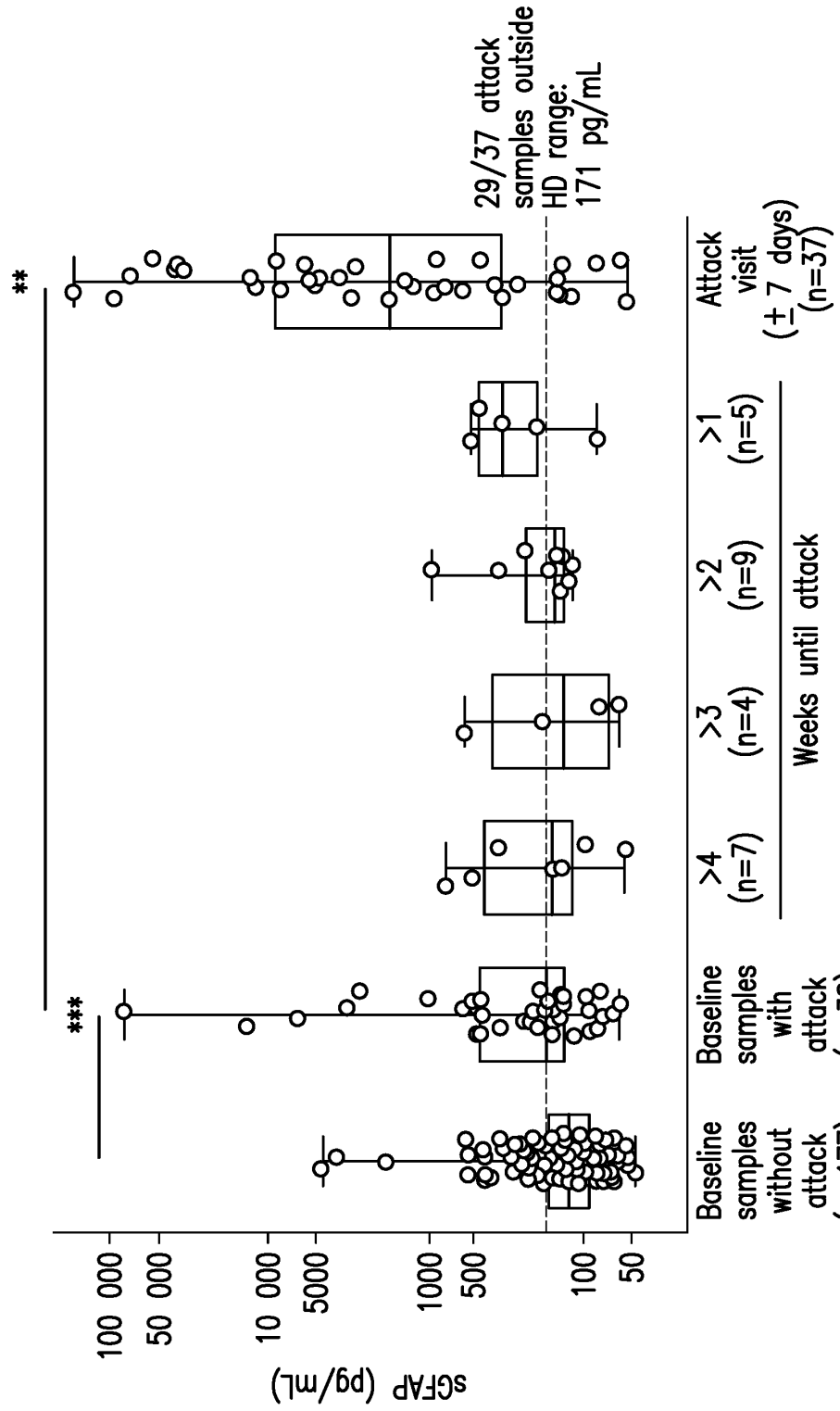

sGFAP (pg/mL)
100 000
50 000
10 000
5000
1000
500
100
50
***
**
29/37 attack samples outside HD range: 171 pg/mL
Baseline samples without attack (n=177)
Baseline samples with attack (n=38)
>4 (n=7)
>3 (n=4)
>2 (n=9)
>1 (n=5)
Attack visit (± 7 days) (n=37)
Weeks until attack

FIG.5B

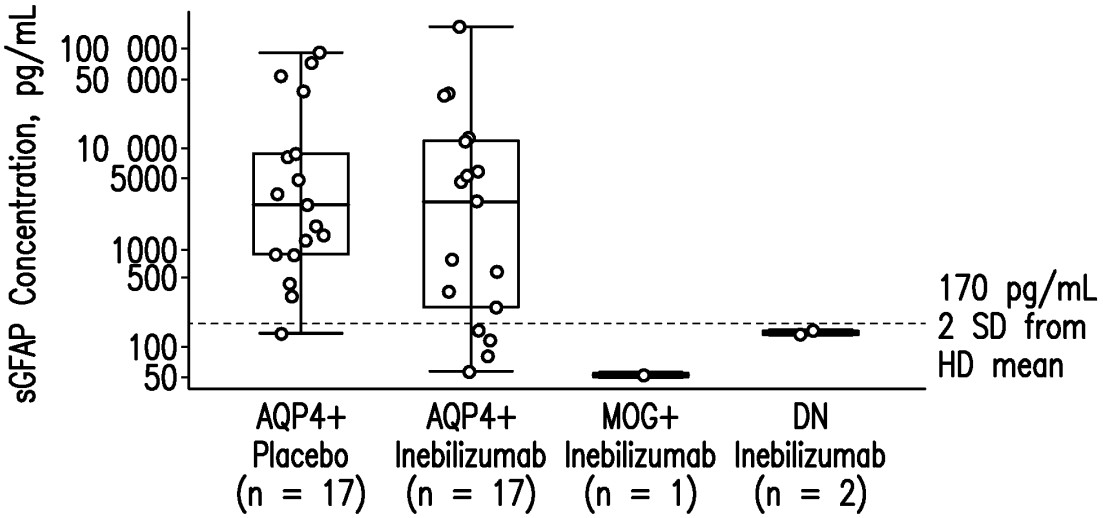

sGFAP Concentration, pg/mL
100 000
50 000
10 000
5000
1000
500
100
50
170 pg/mL
2 SD from
HD mean
AQP4+
Placebo
(n = 17)
AQP4+
Inebilizumab
(n = 17)
MOG+
Inebilizumab
(n = 1)
DN
Inebilizumab
(n = 2)

FIG.5C

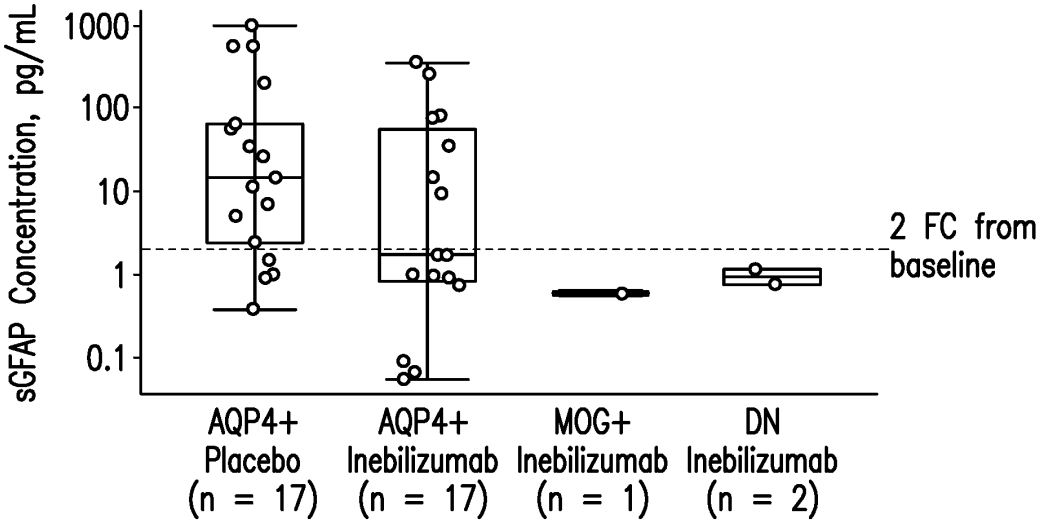

sGFAP Concentration, pg/mL
1000
100
10
1
0.1
2 FC from
baseline
AQP4+
Placebo
(n = 17)
AQP4+
Inebilizumab
(n = 17)
MOG+
Inebilizumab
(n = 1)
DN
Inebilizumab
(n = 2)

FIG.5D

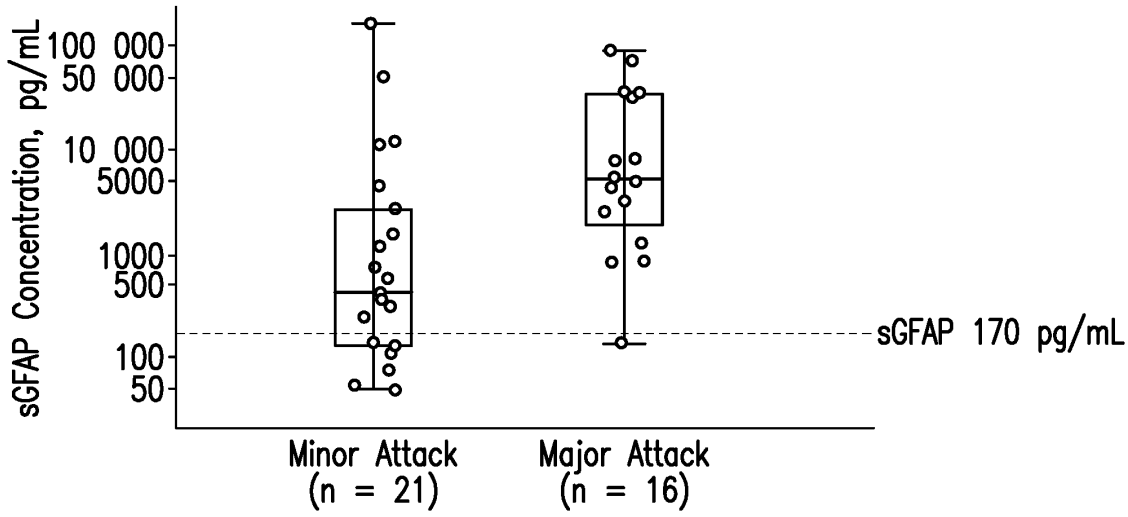

sGFAP Concentration, pg/mL
100 000
50 000
10 000
5000
1000
500
100
50
sGFAP 170 pg/mL
Minor Attack
(n = 21)
Major Attack
(n = 16)

FIG.6A

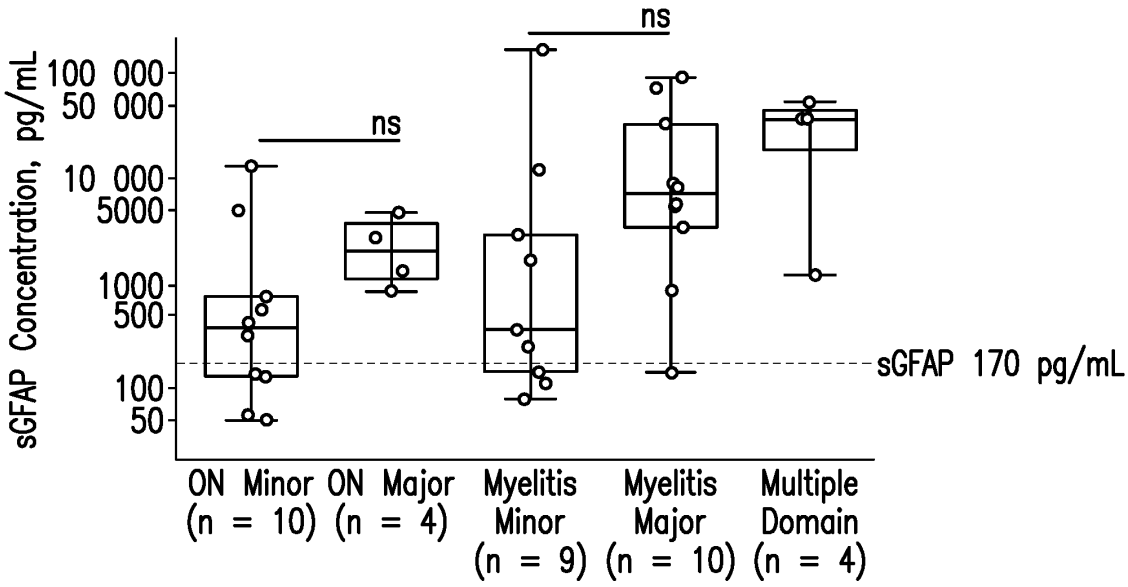

sGFAP Concentration, pg/mL
100 000
50 000
10 000
5000
1000
500
100
50
ns
ns
sGFAP 170 pg/mL
ON Minor
(n = 10)
ON Major
(n = 4)
Myelitis
Minor
(n = 9)
Myelitis
Major
(n = 10)
Multiple
Domain
(n = 4)

FIG.6B

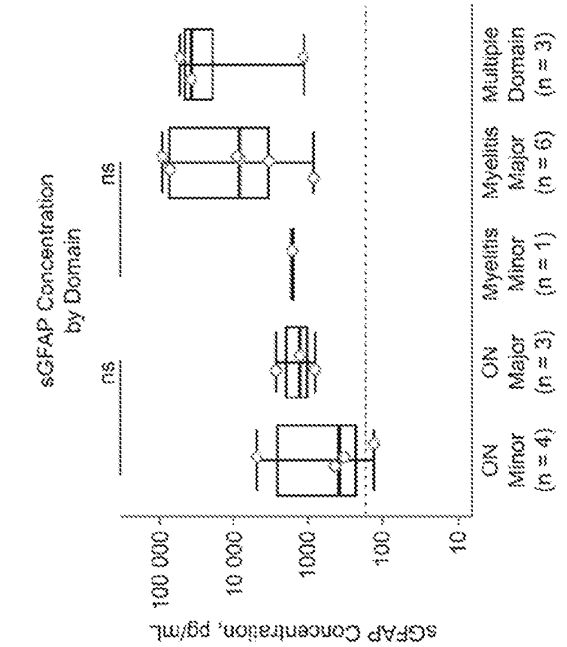

sGFAP Concentration by Domain
ns
ns
sGFAP Concentration, pg/mL
100 000
10 000
1000
100
10
ON Minor (n = 4)
ON Major (n = 3)
Myelitis Minor (n = 1)
Myelitis Major (n = 6)
Multiple Domain (n = 3)

FIG.7B

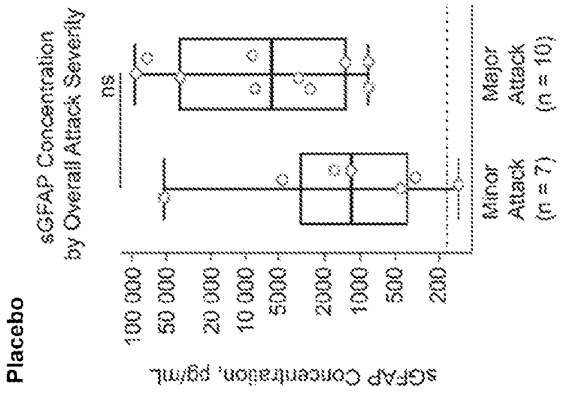

Placebo
sGFAP Concentration by Overall Attack Severity
ns
sGFAP Concentration, pg/mL
100 000
50 000
20 000
10 000
5000
2000
1000
500
200
Minor Attack (n = 7)
Major Attack (n = 10)

FIG.7A

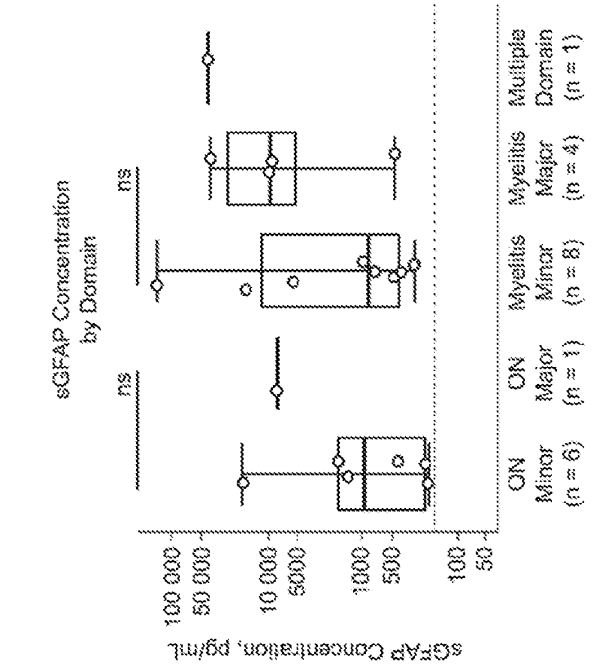

sGFAP Concentration by Domain
ns
ns
sGFAP Concentration, pg/mL
100 000
50 000
10 000
5000
1000
500
100
50
ON Minor (n = 6)
ON Major (n = 1)
Myelitis Minor (n = 8)
Myelitis Major (n = 4)
Multiple Domain (n = 1)

FIG.7D

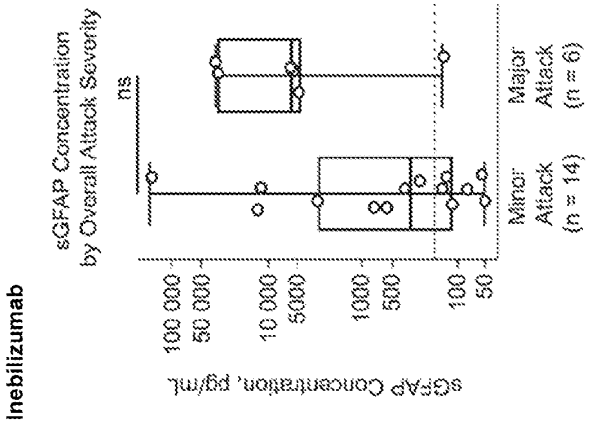

Inebilizumab
sGFAP Concentration by Overall Attack Severity
ns
sGFAP Concentration, pg/mL
100 000
50 000
10 000
5000
1000
500
100
50
Minor Attack (n = 14)
Major Attack (n = 6)

FIG.7C

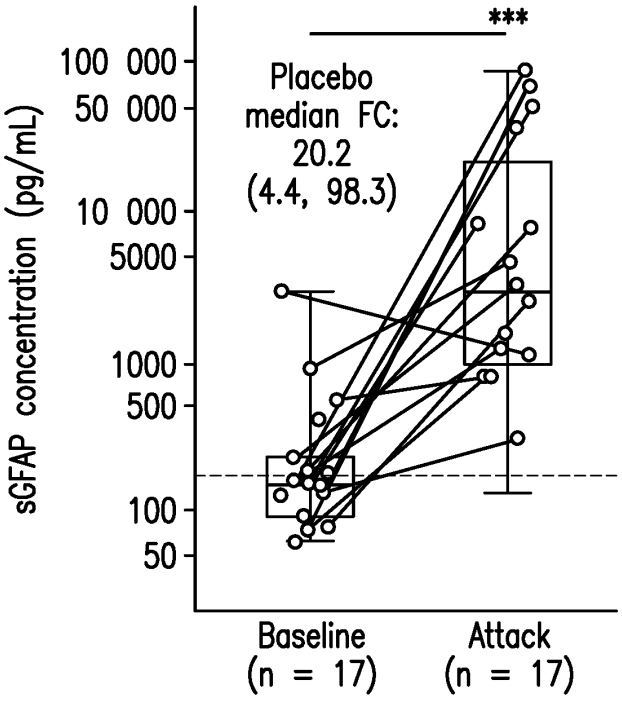

***
Placebo
median FC:
20.2
(4.4, 98.3)
sGFAP concentration (pg/mL)
100 000
50 000
10 000
5000
1000
500
100
50
Baseline
(n = 17)
Attack
(n = 17)

FIG.8A

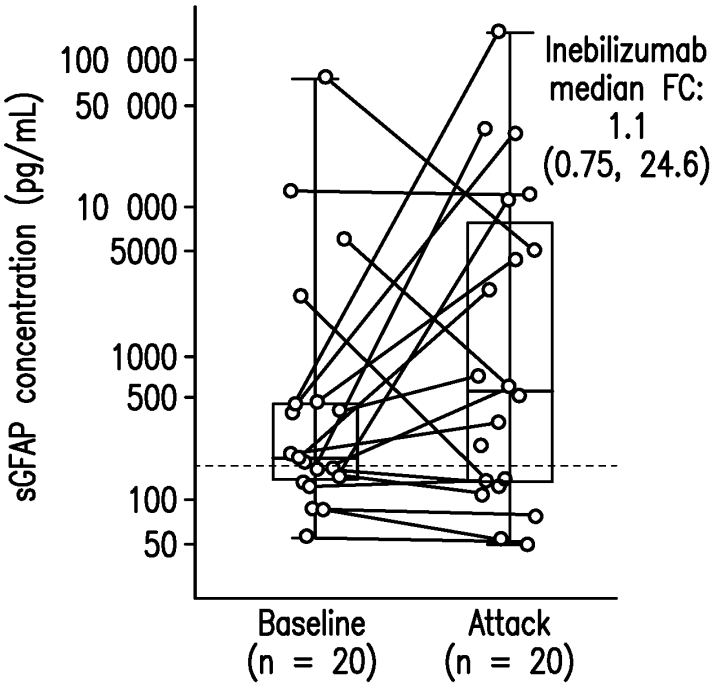

Inebilizumab
median FC:
1.1
(0.75, 24.6)
sGFAP concentration (pg/mL)
100 000
50 000
10 000
5000
1000
500
100
50
Baseline
(n = 20)
Attack
(n = 20)

FIG.8B

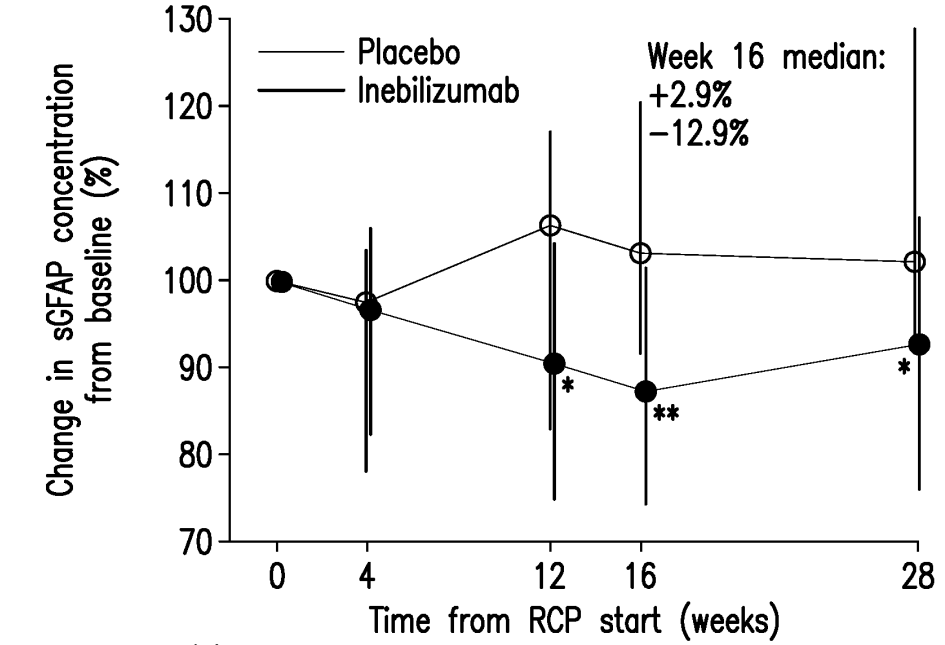

Placebo
Inebilizumab
Week 16 median:
+2.9%
−12.9%
Change in sGFAP concentration from baseline (%)
130
120
110
100
90
80
70
*
**
*
0
4
12
16
28
Time from RCP start (weeks)
Placebo (n) 32 31 30 27 25
Inebilizumab (n) 145 134 134 124 116

FIG.8C

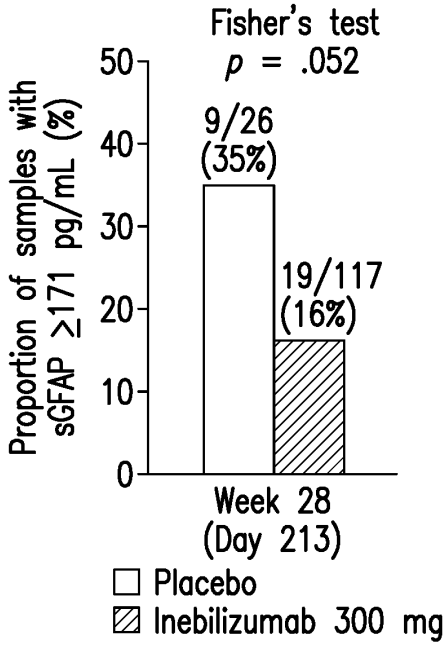

Fisher's test
p = .052
Proportion of samples with sGFAP ≥171 pg/mL (%)
50
40
30
20
10
0
9/26
(35%)
19/117
(16%)
Week 28
(Day 213)
Placebo
Inebilizumab 300 mg

FIG.8D

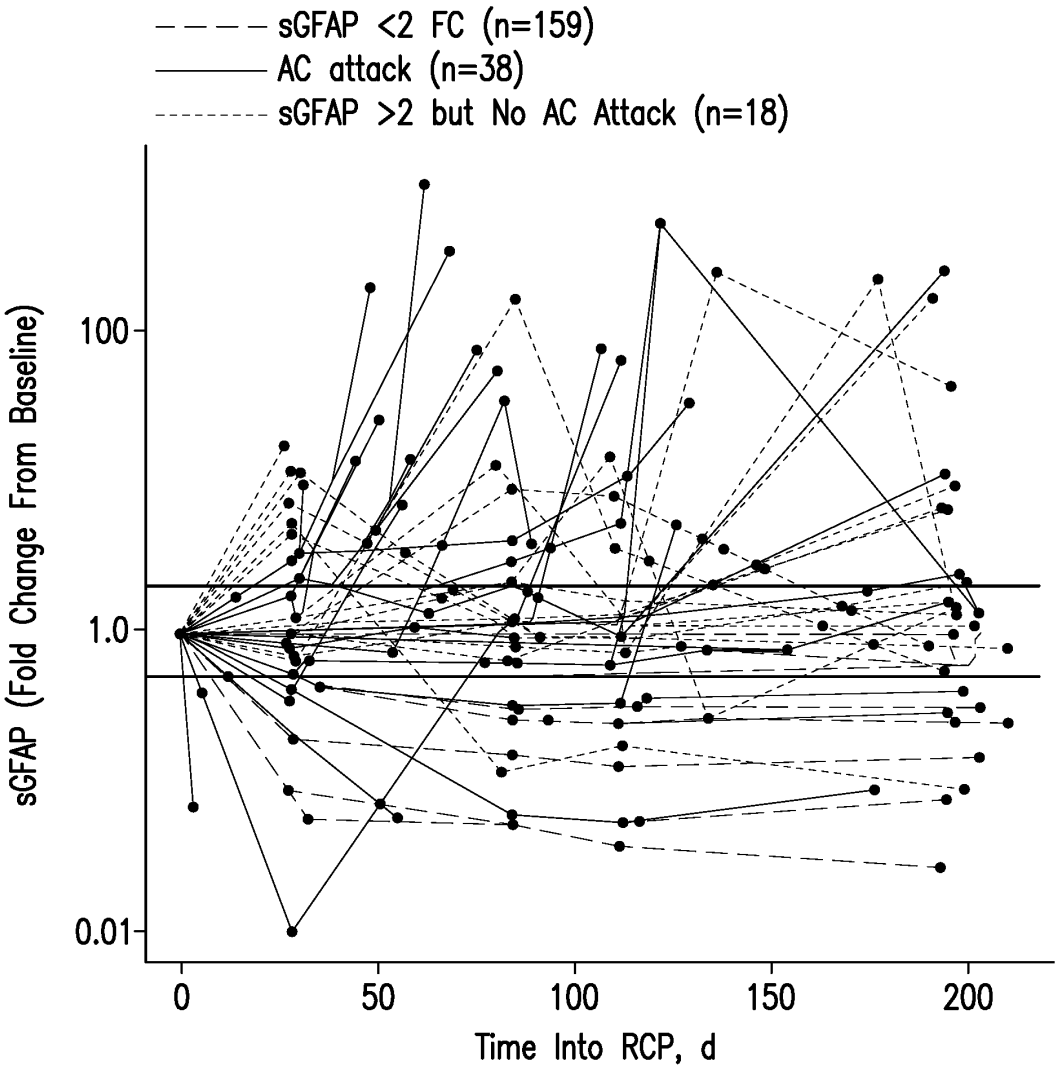

sGFAP <2 FC (n=159)
AC attack (n=38)
sGFAP >2 but No AC Attack (n=18)
sGFAP (Fold Change From Baseline)
100
1.0
0.01
0
50
100
150
200
Time Into RCP, d

FIG.9A

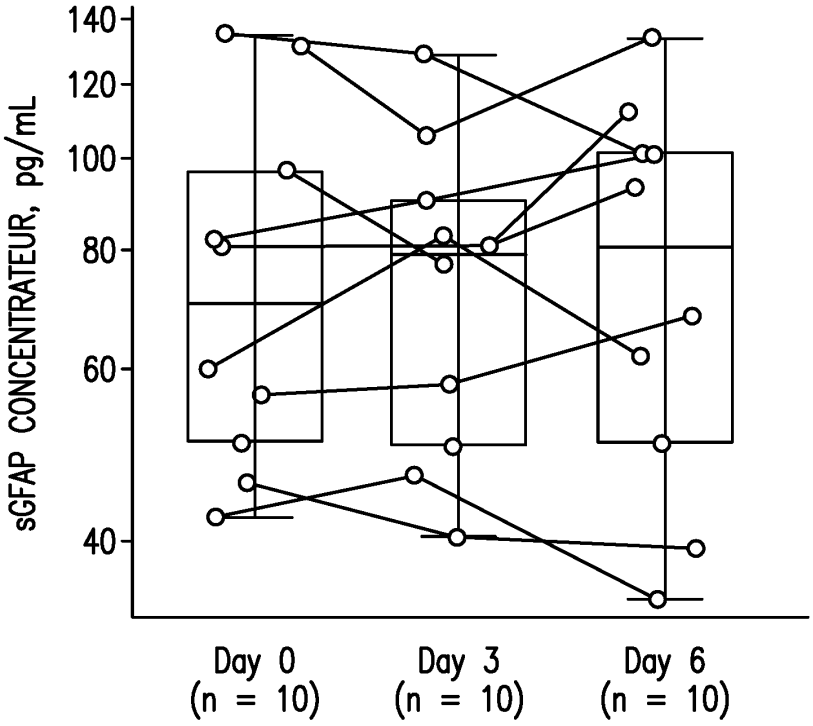

140
120
100
80
60
40
sGFAP CONCENTRATEUR, pg/mL
Day 0
(n = 10)
Day 3
(n = 10)
Day 6
(n = 10)

FIG.9B

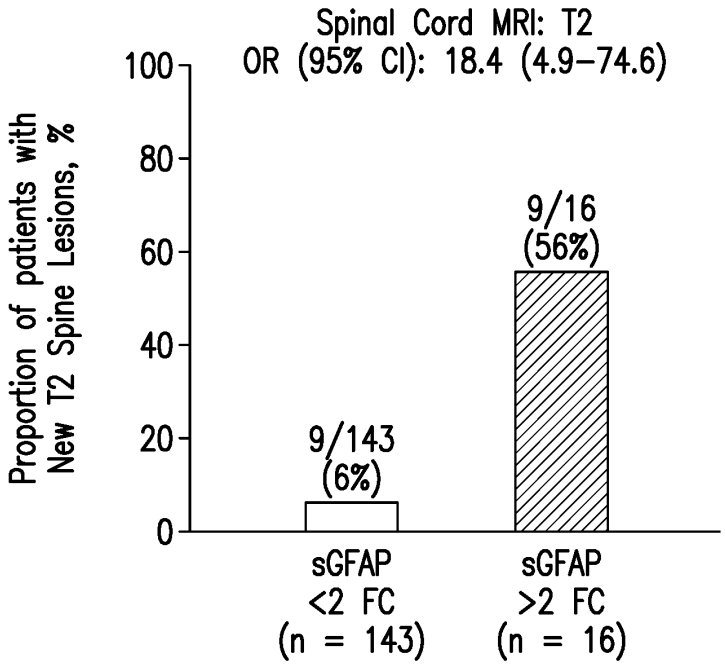


FIG.9C

19/36

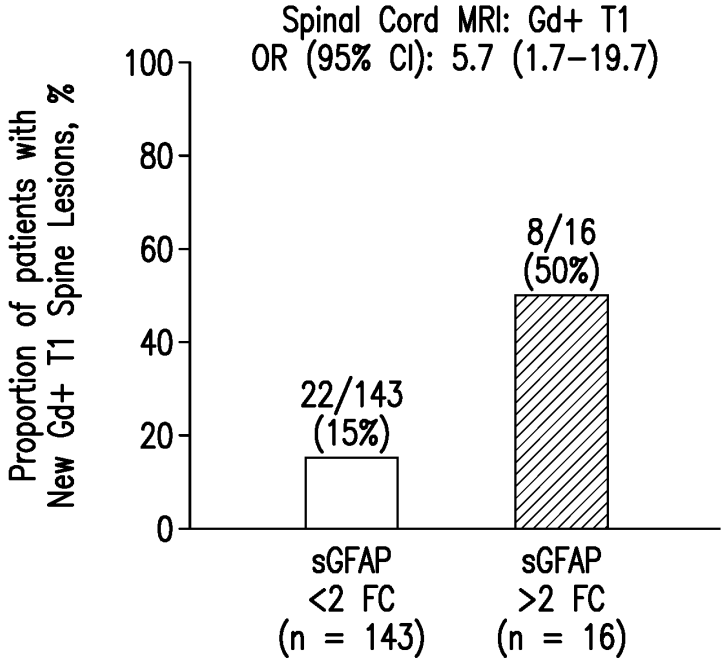


FIG.9D

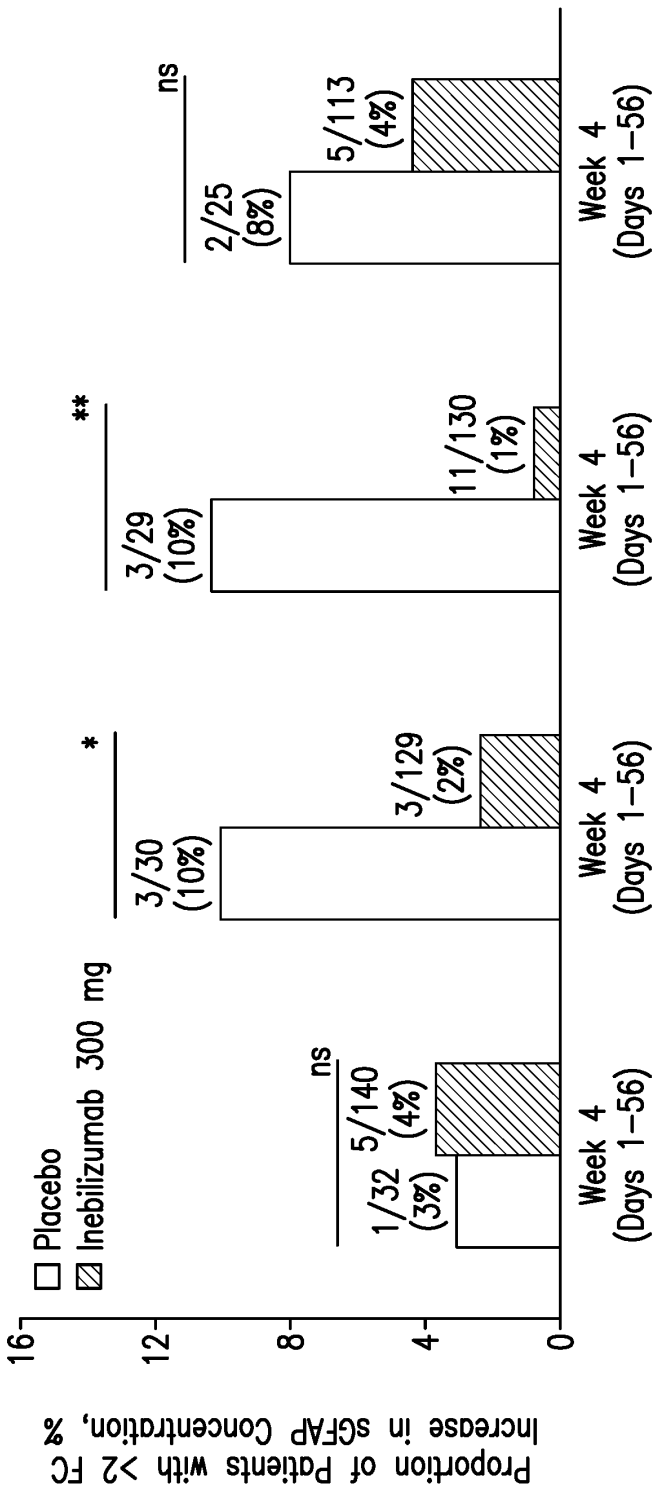

Proportion of Patients with ≥2 FC Increase in sGFAP Concentration, %
16
12
8
4
0
Placebo
Inebilizumab 300 mg
ns
1/32 (3%)
5/140 (4%)
Week 4 (Days 1–56)
*
3/30 (10%)
3/129 (2%)
Week 4 (Days 1–56)
**
3/29 (10%)
11/130 (1%)
Week 4 (Days 1–56)
ns
2/25 (8%)
5/113 (4%)
Week 4 (Days 1–56)
Time From RCP Start, w

FIG.9E

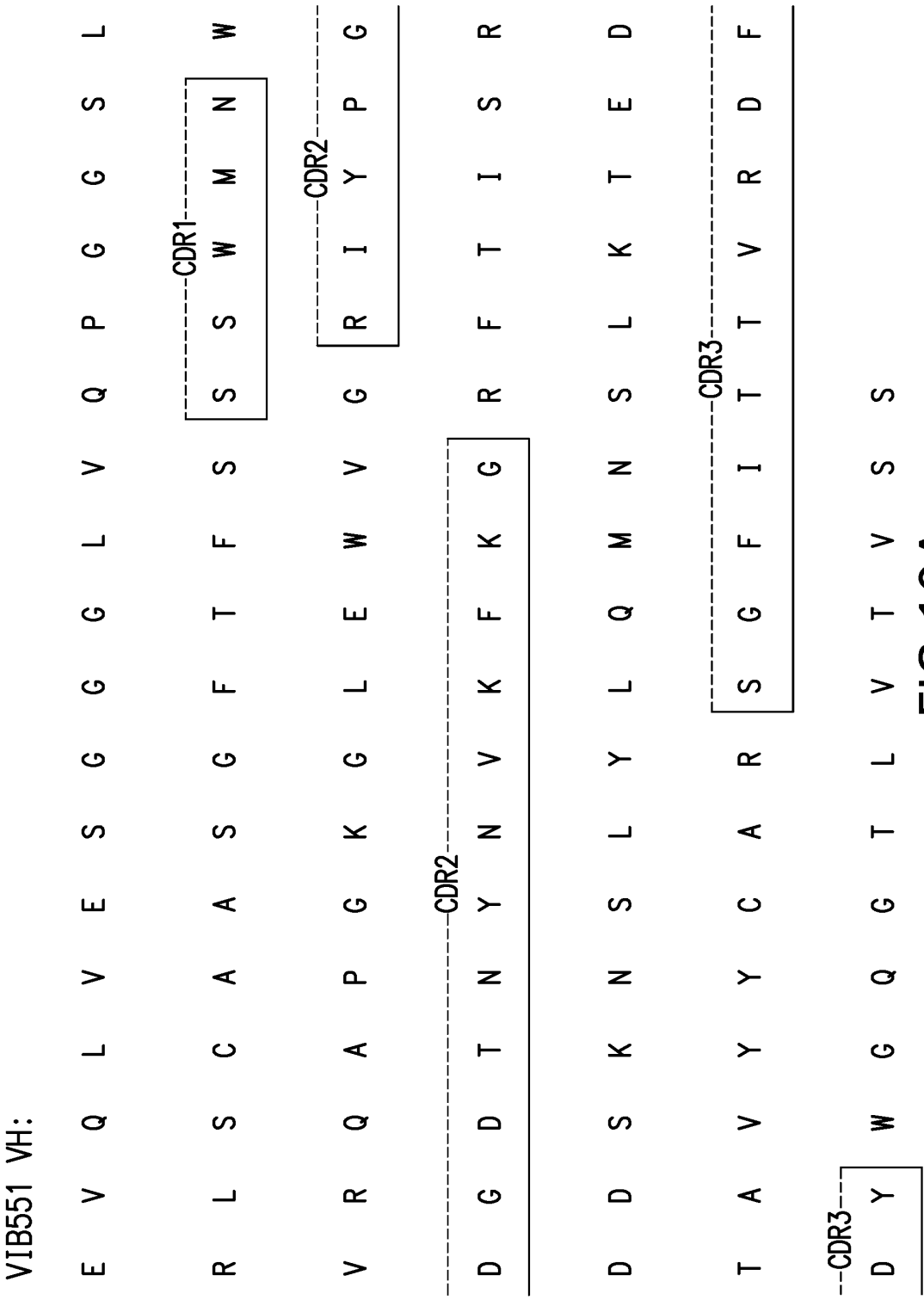

VIB551 VH:
E V Q L V E S G G G L V Q P G G S L
R L S C A A S G F T F S S S W M N W
V R Q A P G K G L E W V G R I Y P G
D G D T N Y N V K F K G R F T I S R
D D S K N S L Y L Q M N S L K T E D
T A V Y Y C A R S G F I T T V R D F
D Y W G Q G T L V T V S S
CDR1
CDR2
CDR2
CDR3
CDR3

FIG.10A

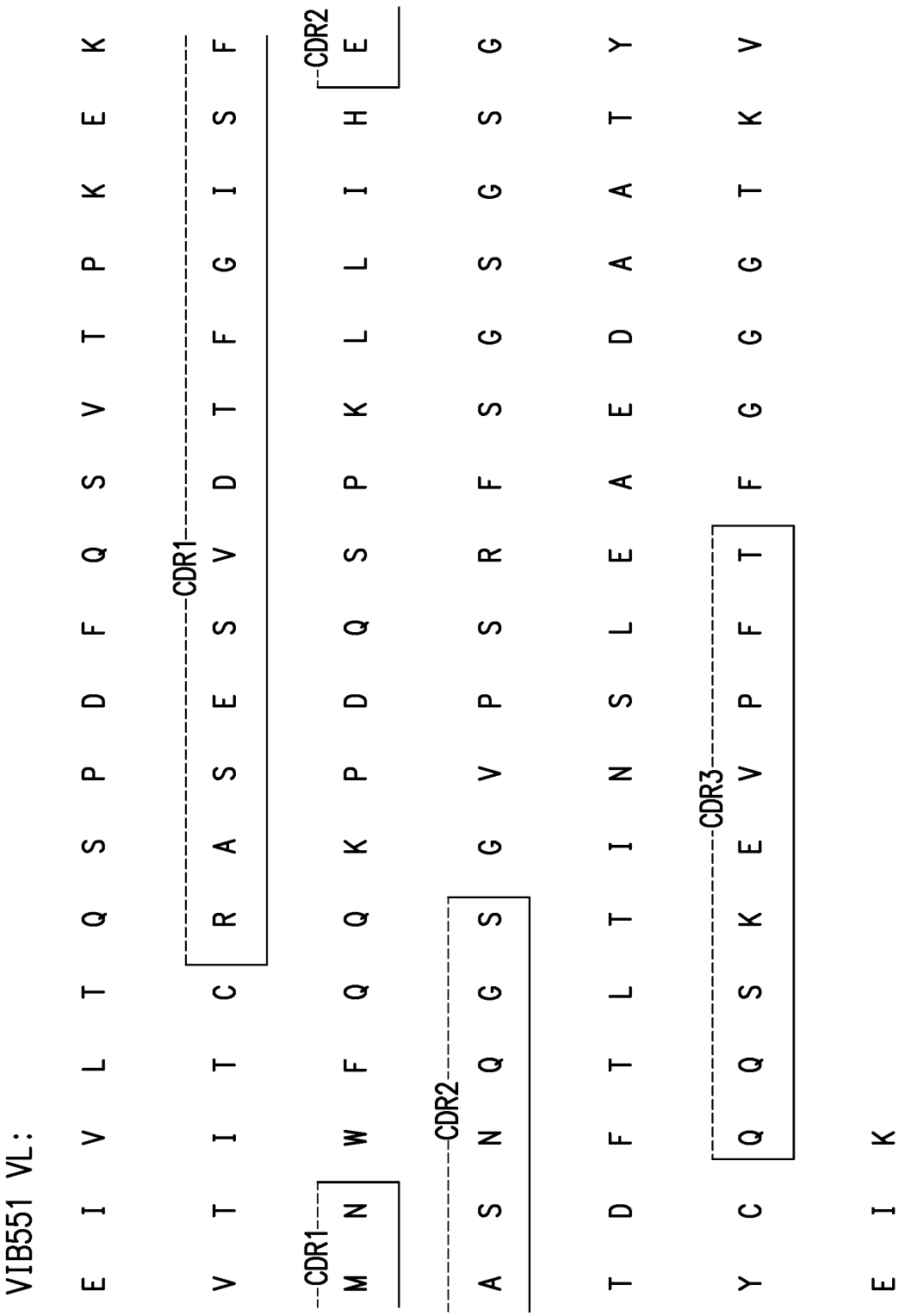

VIB551 VL:
E I V L T Q S P D F Q S V T P K E K
V T I T C R A S E S V D T F G I S F
M N W F Q Q K P D Q S P K L L I H E
A S N Q G S G V P S R F S G S G S G
T D F T L T I N S L E A E D A A T Y
Y C Q Q S K E V P F T F G G G T K V
E I K
CDR1
CDR2
CDR1
CDR2
CDR3

FIG.10B

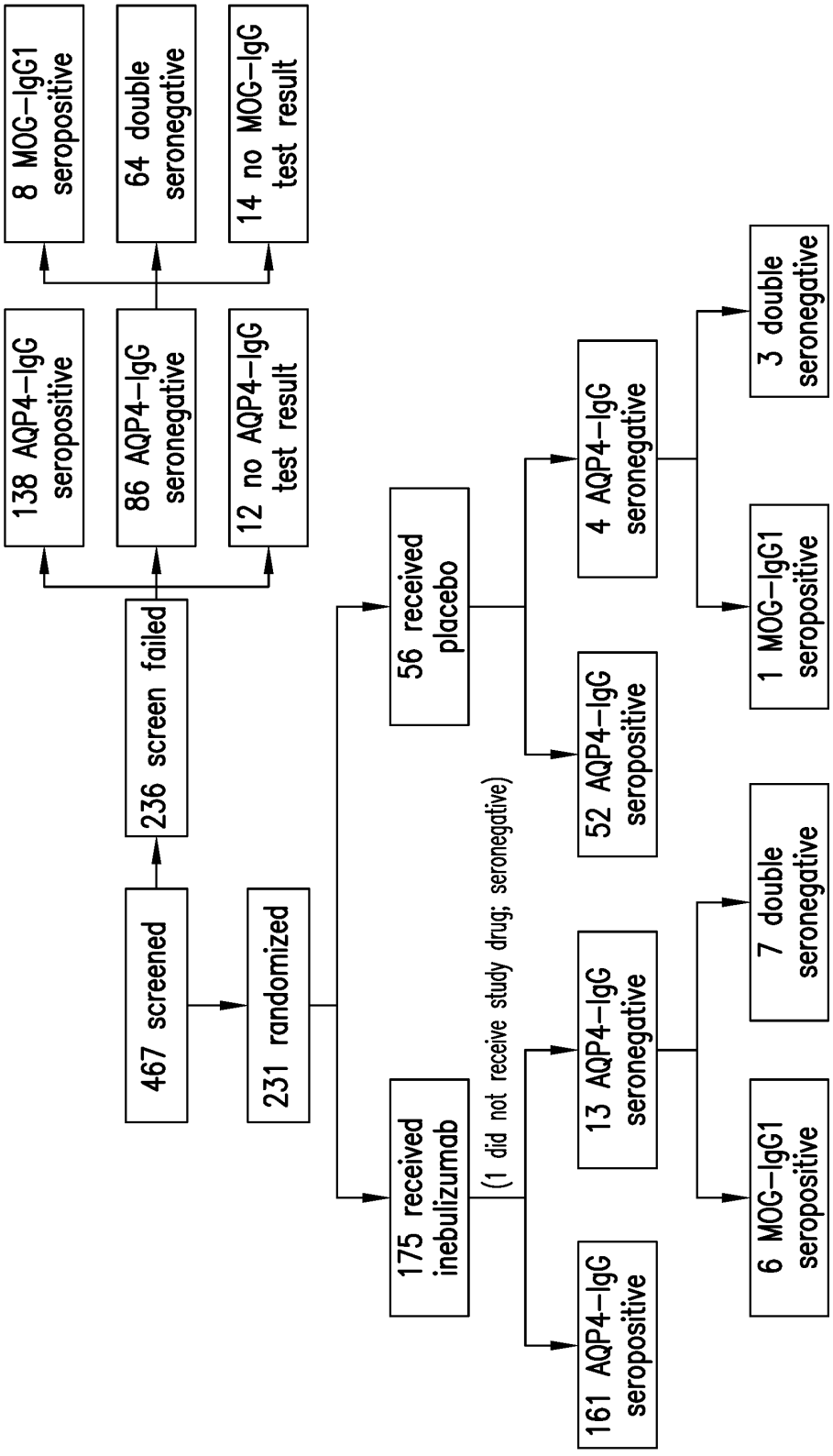

467 screened
236 screen failed
231 randomized
138 AQP4–IgG seropositive
86 AQP4–IgG seronegative
12 no AQP4–IgG test result
8 MOG–IgG1 seropositive
64 double seronegative
14 no MOG–IgG test result
56 received placebo
175 received inebulizumab
(1 did not receive study drug; seronegative)
4 AQP4–IgG seronegative
52 AQP4–IgG seropositive
3 double seronegative
1 MOG–IgG1 seropositive
13 AQP4–IgG seronegative
161 AQP4–IgG seropositive
7 double seronegative
6 MOG–IgG1 seropositive

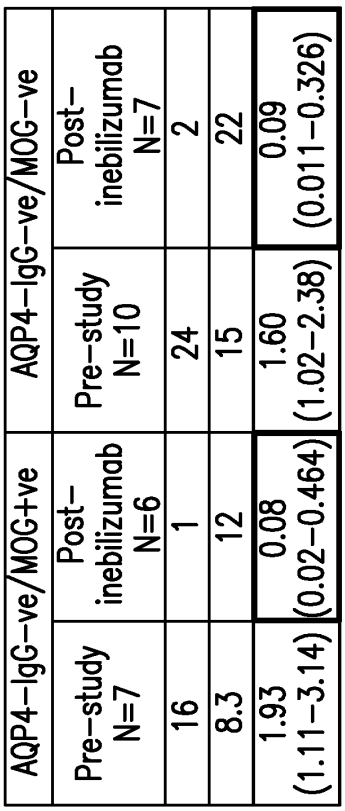
FIG.11A

		AQP4–IgG seropositive (n=213)	AQP4–IgG seronegative (n=17)
Age, years	Mean (SD)	43.0 (12.3)	41.7 (10.6)
	Median (range)	43.0 (18–74)	43.0 (22–56)
Sex	Female	200 (93.9%)	9 (52.9%)
	Male	13 (6.1%)	8 (61.5%)
Race	American Indian or Alaskan Native	16 (7.5%)	3 (17.6%)
	Asian	45 (21.1%)	2 (11.8%)
	Black or African American	19 (8.9%)	1 (5.9%)
	White	110 (51.6%)	10 (58.8%)
	Other	22 (10.3%)	1 (5.9%)
	Multiple categories checked	1 (0.5%)	0 (0%)
Ethnicity	Hispanic or Latino	40 (18.8%)	3 (17.6%)
Disease duration, years	Mean (SD)	2.59 (3.42)	1.23 (1.43)
	Median (range)	1.13 (0.1–22.2)	0.87 (0.2–5.5)
Type of most recent attack	Optic neuritis	96 (45.1%)	10 (58.8%)
	Myelitis	126 (59.2%)	7 (41.2%)
	Brain or brainstem	14 (6.6%)	4 (23.5%)
Gadolinium–enhancing lesions	Mean (SD)	1.1 (1.1)	0.6 (0.9)
	Median (range)	1.0 (0–5)	0.0 (0–3)
EDSS score	Mean (SD)	2.9 (2.5)	4.3 (3.1)
	Median (range)	2.0 (1–7)	5.0 (1–7)

FIG. 11B

	AQP4 Seronegative N = 17	
Primary Endpoint	Placebo N=4	Inebilizumab N=13
# of patients with an AC-determined attack	0	3 (23.1%)

FIG.12



	AQP4–IgG–ve	
	Pre–study N=17	Post–inebilizumab N=13
Number of attacks*	40	3
Patient years	23	34.2
AAR (95% CI)	1.72 (1.23–2.33)	0.09 (0.02–0.26)

	AQP4–IgG–ve/MOG+ve		AQP4–IgG–ve/MOG–ve	
	Pre–study N=7	Post–inebilizumab N=6	Pre–study N=10	Post–inebilizumab N=7
	16	1	24	2
	8.3	12	15	22
	1.93 (1.11–3.14)	0.08 (0.02–0.464)	1.60 (1.02–2.38)	0.09 (0.011–0.326)

* AC–determined attacks post–inebilizumab

FIG.13

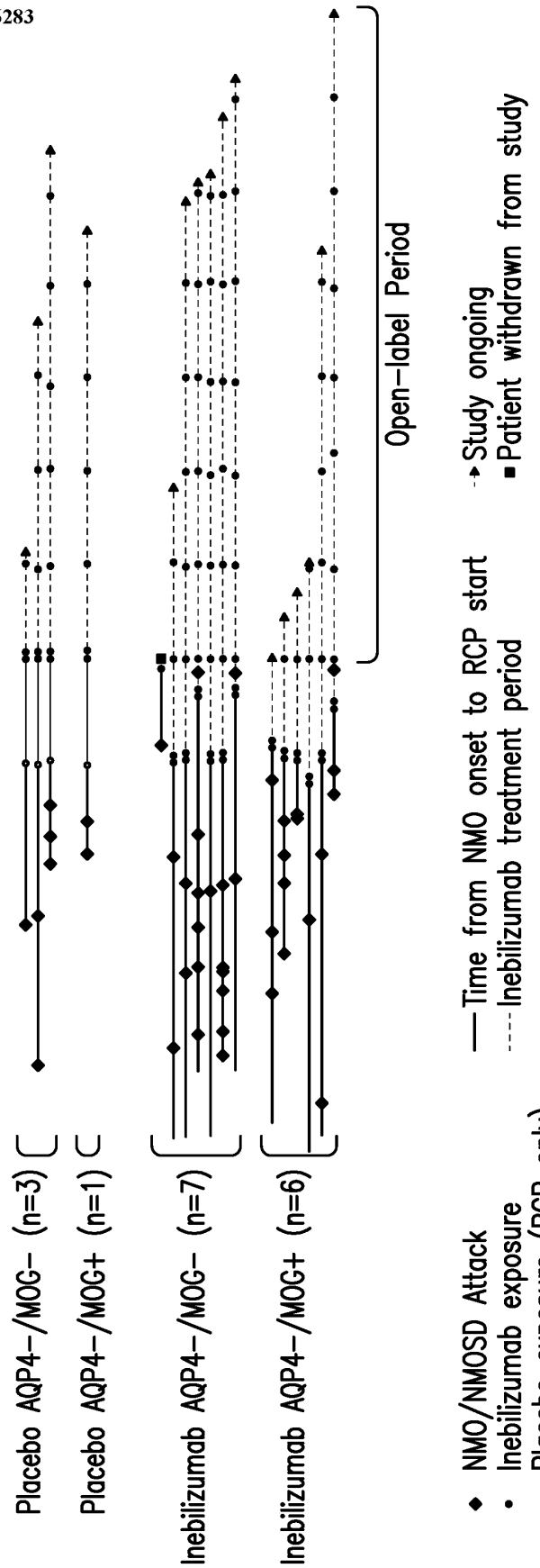

Placebo AQP4−/MOG− (n=3)
Placebo AQP4−/MOG+ (n=1)
Inebilizumab AQP4−/MOG− (n=7)
Inebilizumab AQP4−/MOG+ (n=6)
Open−label Period
Time from NMO onset to RCP start
Inebilizumab treatment period
Study ongoing
Patient withdrawn from study
NMO/NMOSD Attack
Inebilizumab exposure
Placebo exposure (RCP only)

FIG.14

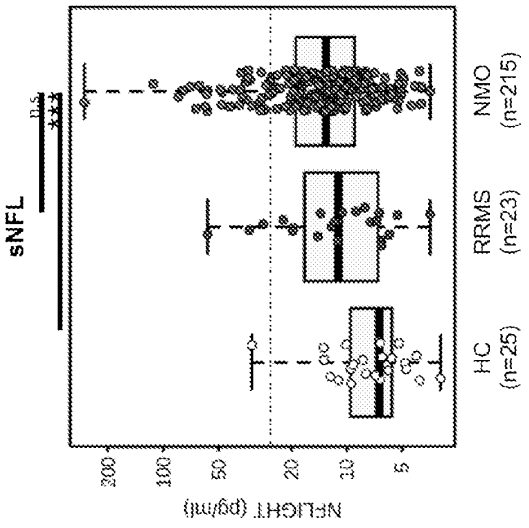


FIG.15B

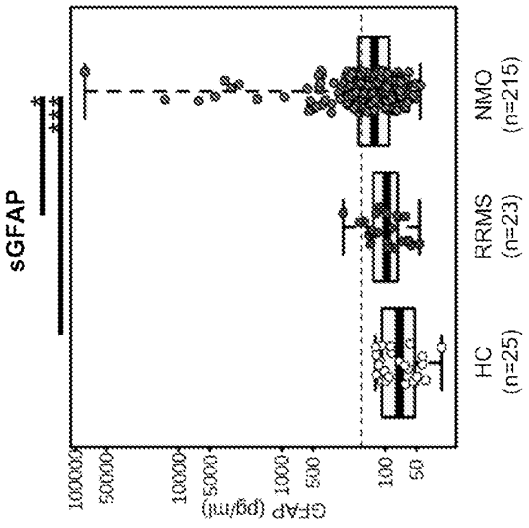


FIG.15A

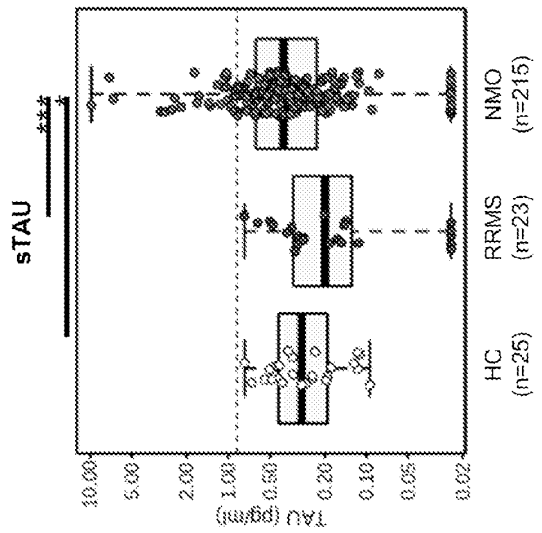


FIG.15D

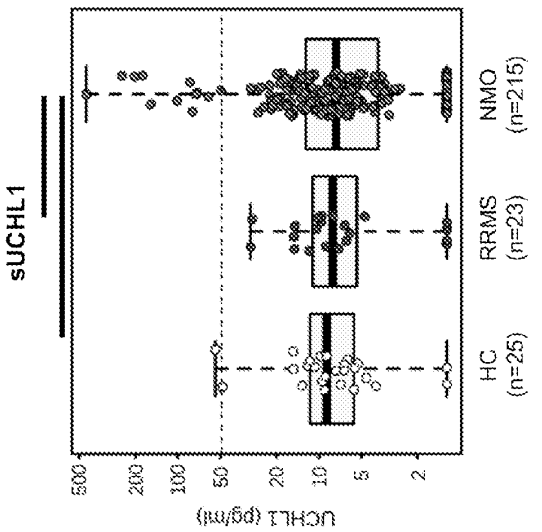
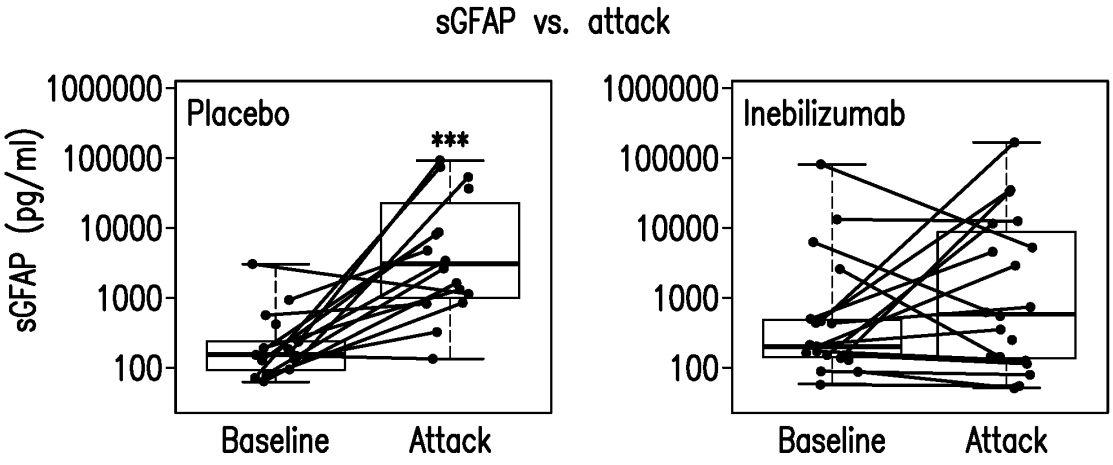
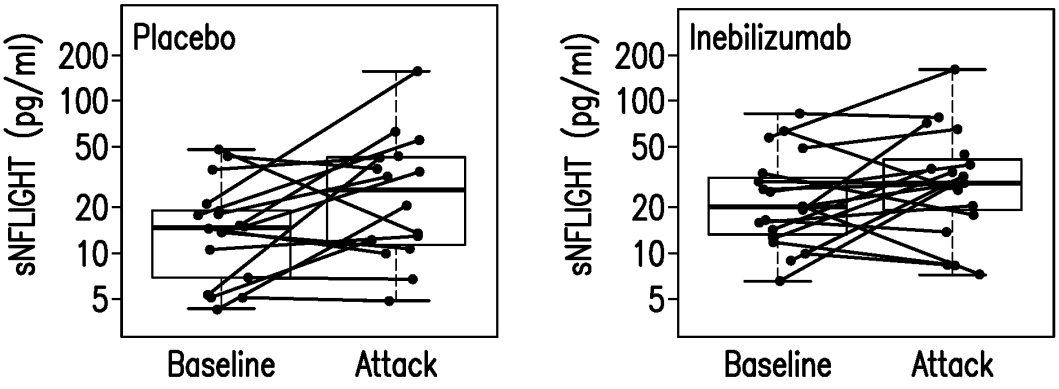


FIG.15C



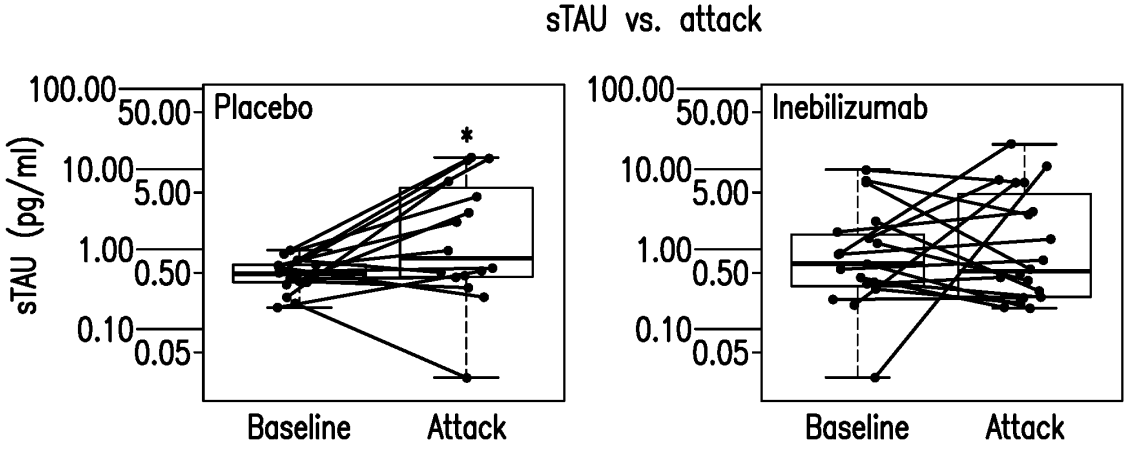
Median FC change from baseline in sGFAP:
Inebilizumab: 1.11 (0.75, 24.6); Placebo: 20.2 (4.4, 98)
Mann–Whitney p–value = 0.037

FIG.16A



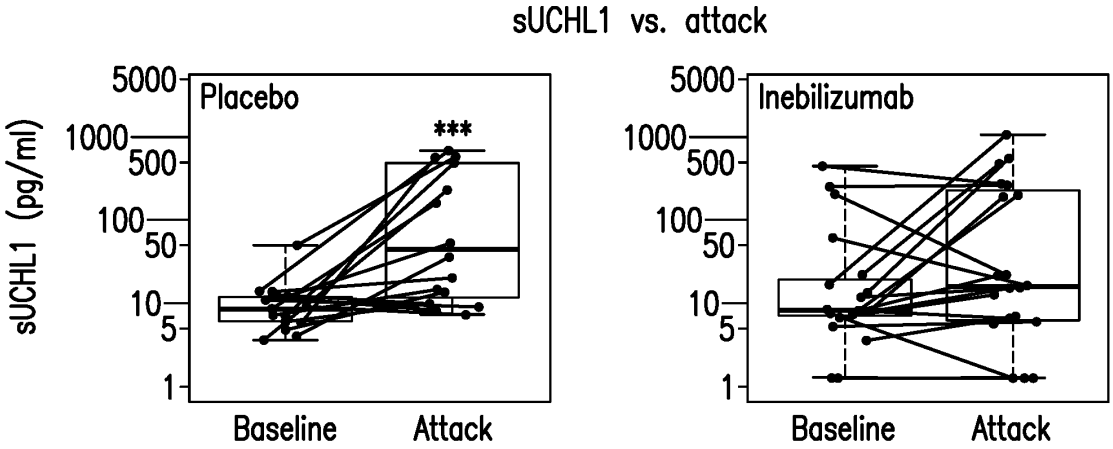
Median FC change from baseline in sNFL:
Inebilizumab: 1.30 (0.84, 2.14); Placebo: 1.49 (0.93, 3.37)
Mann–Whitney p–value = 0.40

FIG.16B



Median FC change from baseline in sTAU:
Inebilizumab: 1.09 (0.40, 3.7); Placebo: 2.19 (0.96, 9.46)
Mann–Whitney p–value = 0.23

FIG.16C



Median FC change from baseline in sUCHL1:
Inebilizumab: 1.85 (0.89, 23); Placebo: 6.70 (1.59, 52.4)
Mann–Whitney p–value = 0.12

FIG.16D

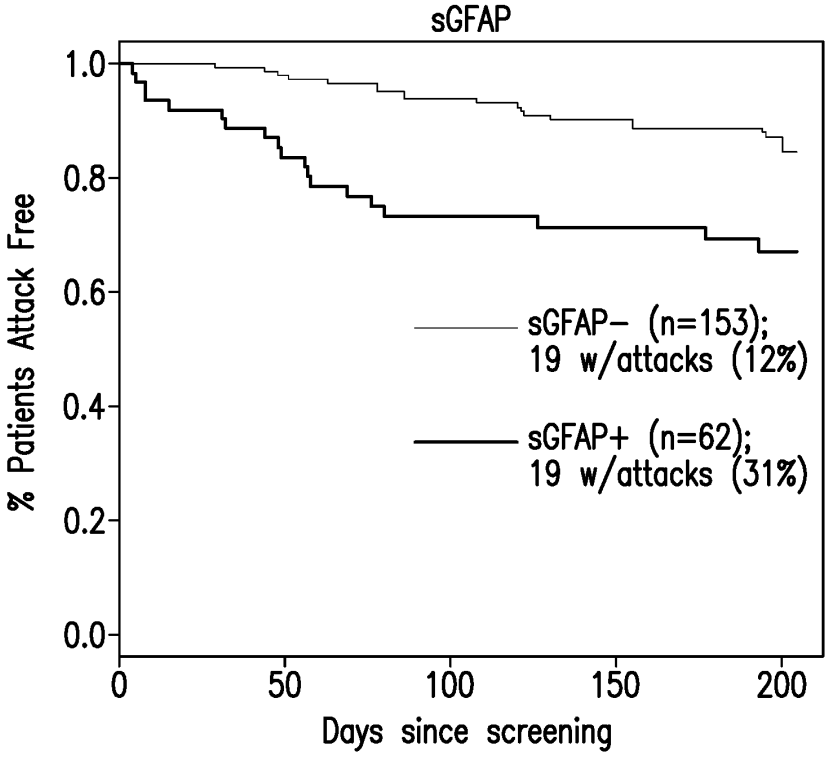


FIG.17A

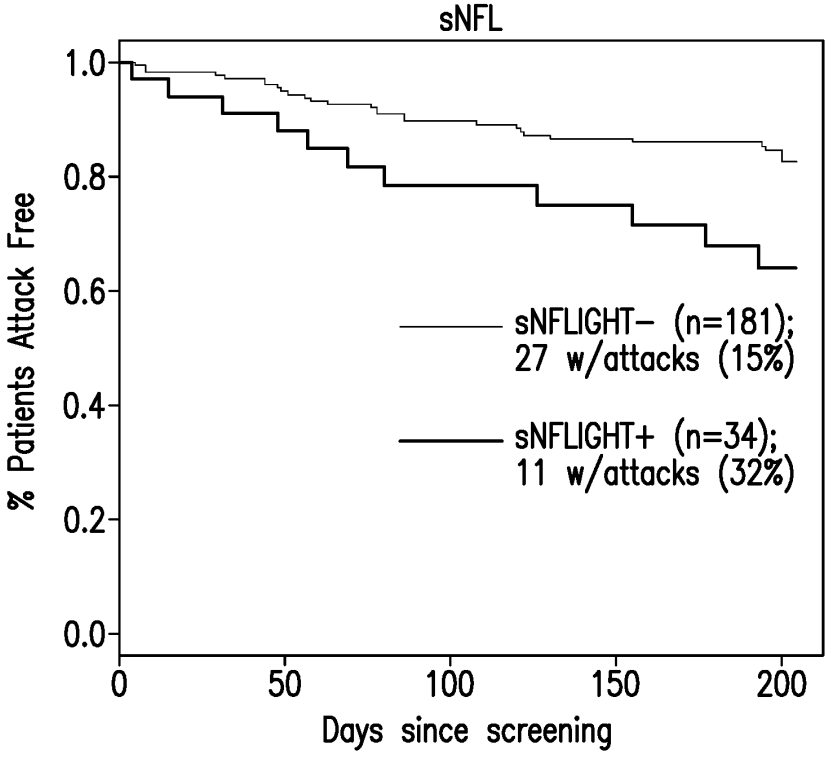


FIG.17B

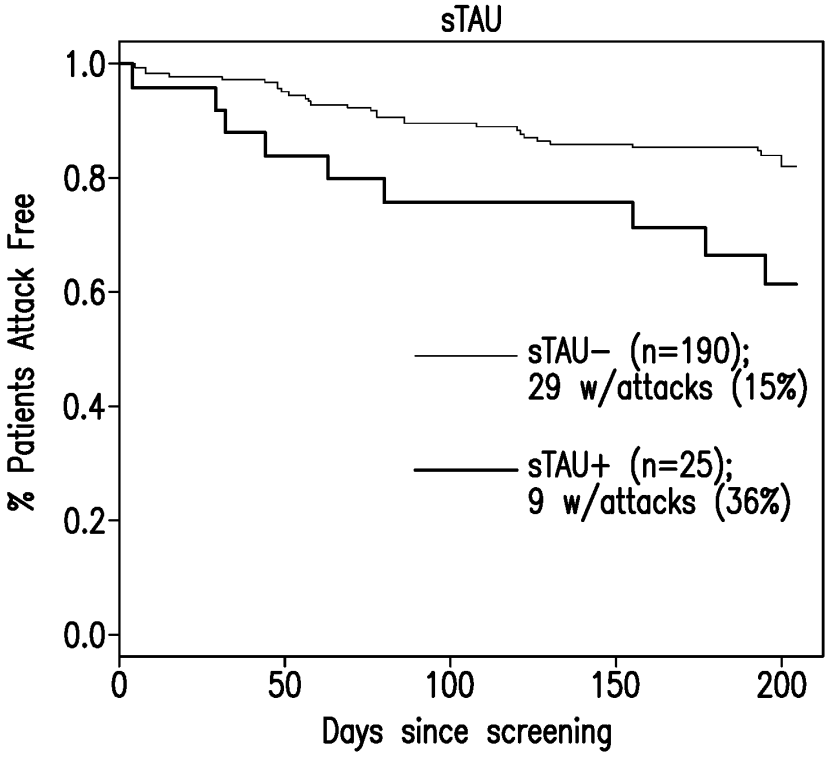


FIG.17C

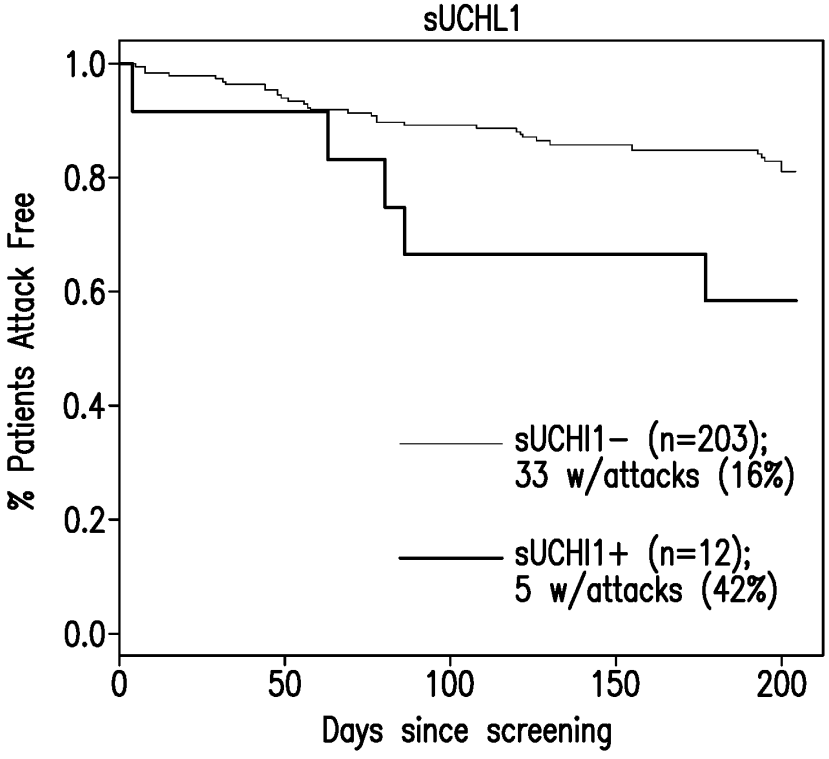


FIG.17D

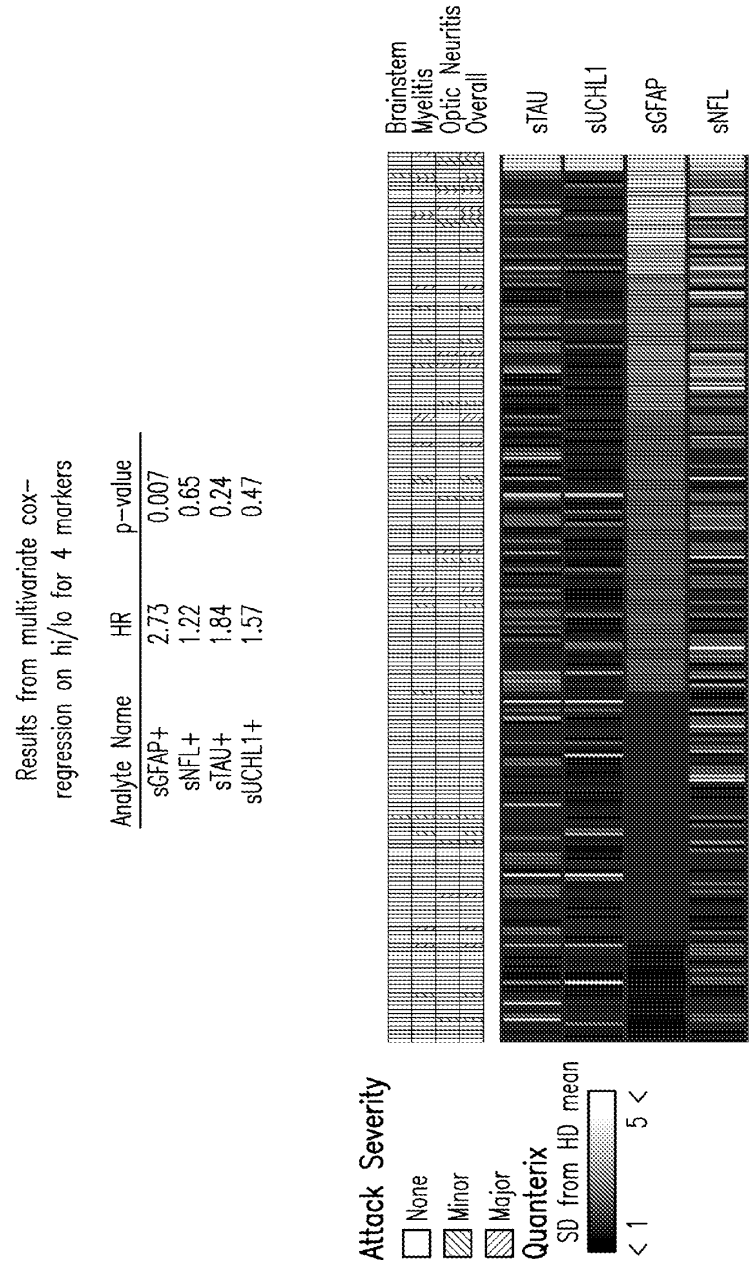

Results from multivariate cox-regression on hi/lo for 4 markers
Analyte Name HR p-value
sGFAP+ 2.73 0.007
sNFL+ 1.22 0.65
sTAU+ 1.84 0.24
sUCHL1+ 1.57 0.47
Brainstem
Myelitis
Optic Neuritis
Overall
sTAU
sUCHL1
sGFAP
sNFL
Attack Severity
None
Minor
Major
Quanterix
SD from HD mean
< 1
5 <

FIG.18

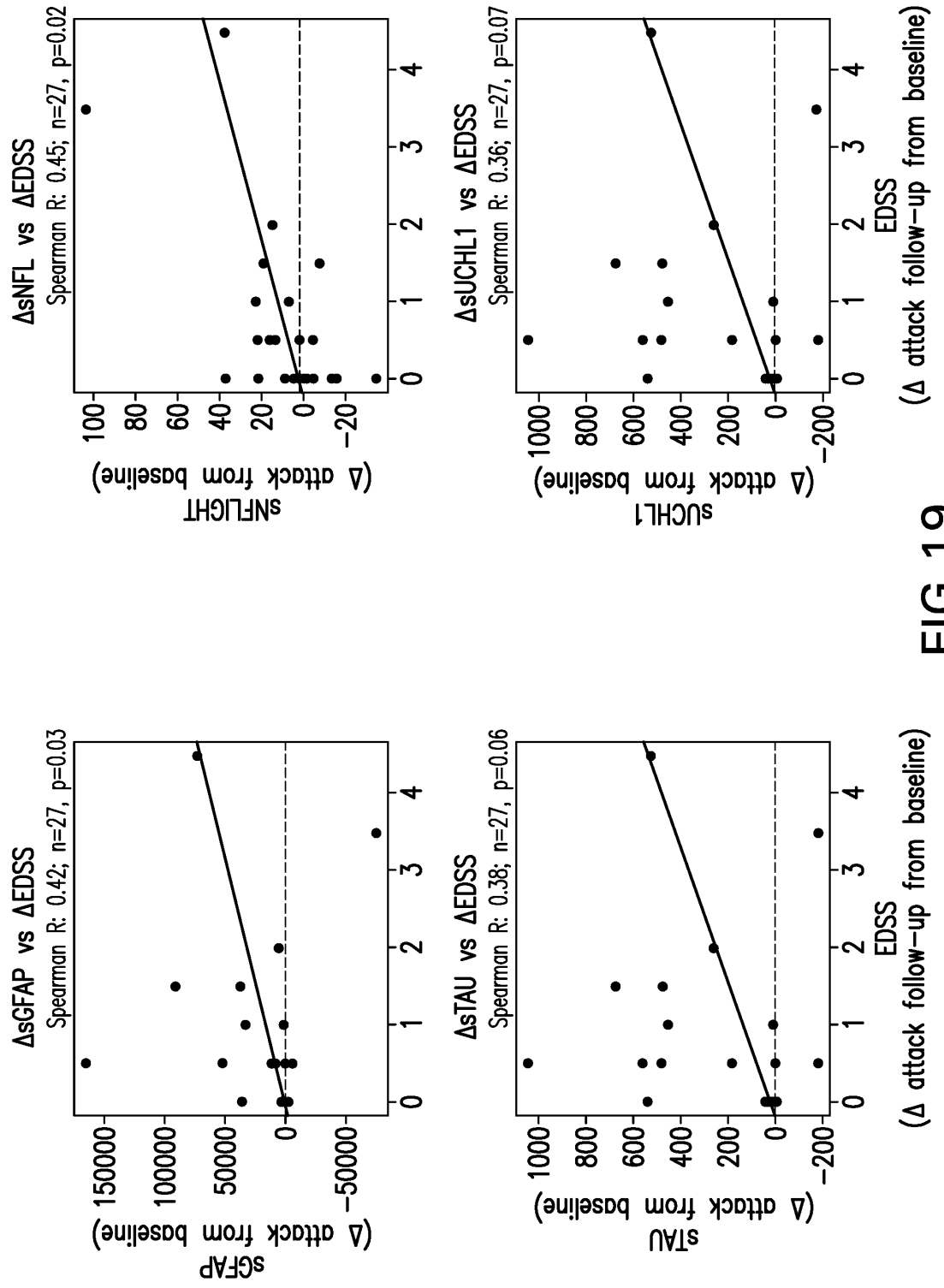

ΔsNFL vs ΔEDSS
Spearman R: 0.45; n=27, p=0.02
sNFLIGHT
(Δ attack from baseline)
ΔsUCHL1 vs ΔEDSS
Spearman R: 0.36; n=27, p=0.07
sUCHL1
(Δ attack from baseline)
ΔsGFAP vs ΔEDSS
Spearman R: 0.42; n=27, p=0.03
sGFAP
(Δ attack from baseline)
ΔsTAU vs ΔEDSS
Spearman R: 0.38; n=27, p=0.06
sTAU
(Δ attack from baseline)
EDSS
(Δ attack follow-up from baseline)

FIG.19

4-way multiple regression on change in quanterix measurements vs change in EDSS:

- multiple R-squared, 0.47
- adjusted R-squared, 0.37
- p-value, 0.008
- T-tests on individual coefficients:

Analyte name	Estimate (95% CI)*	p-value
sGFAP	0.00 (−0.003,0.003)	0.96
sNFL	2.9 (1.0,4.8)	0.006
sTAU	3.5 (−15.4,22.5)	0.70
sUCHL1	0.02 (−0.3,0.4)	0.89

*coefficient estimates reflect change in EDSS per 100 pg/ml change in quanterix measurement

FIG.19 (Continued)