

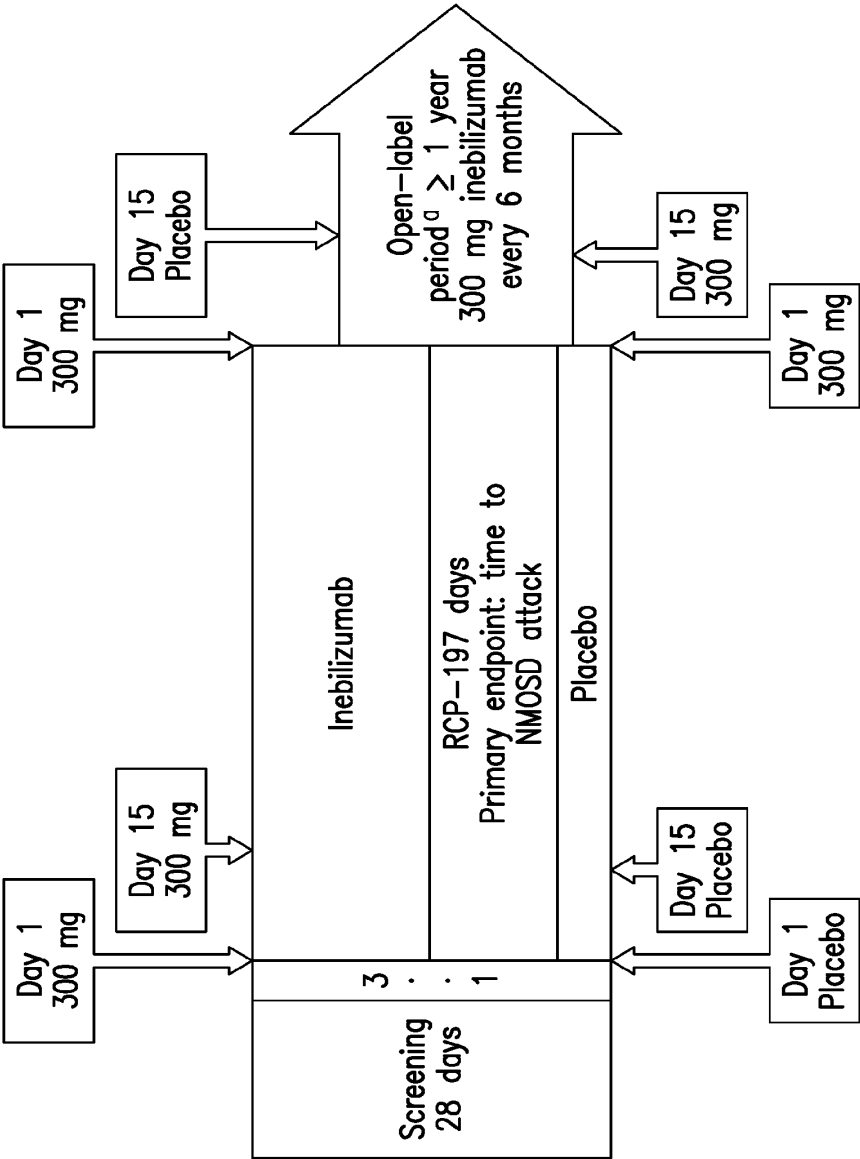


FIG.1A

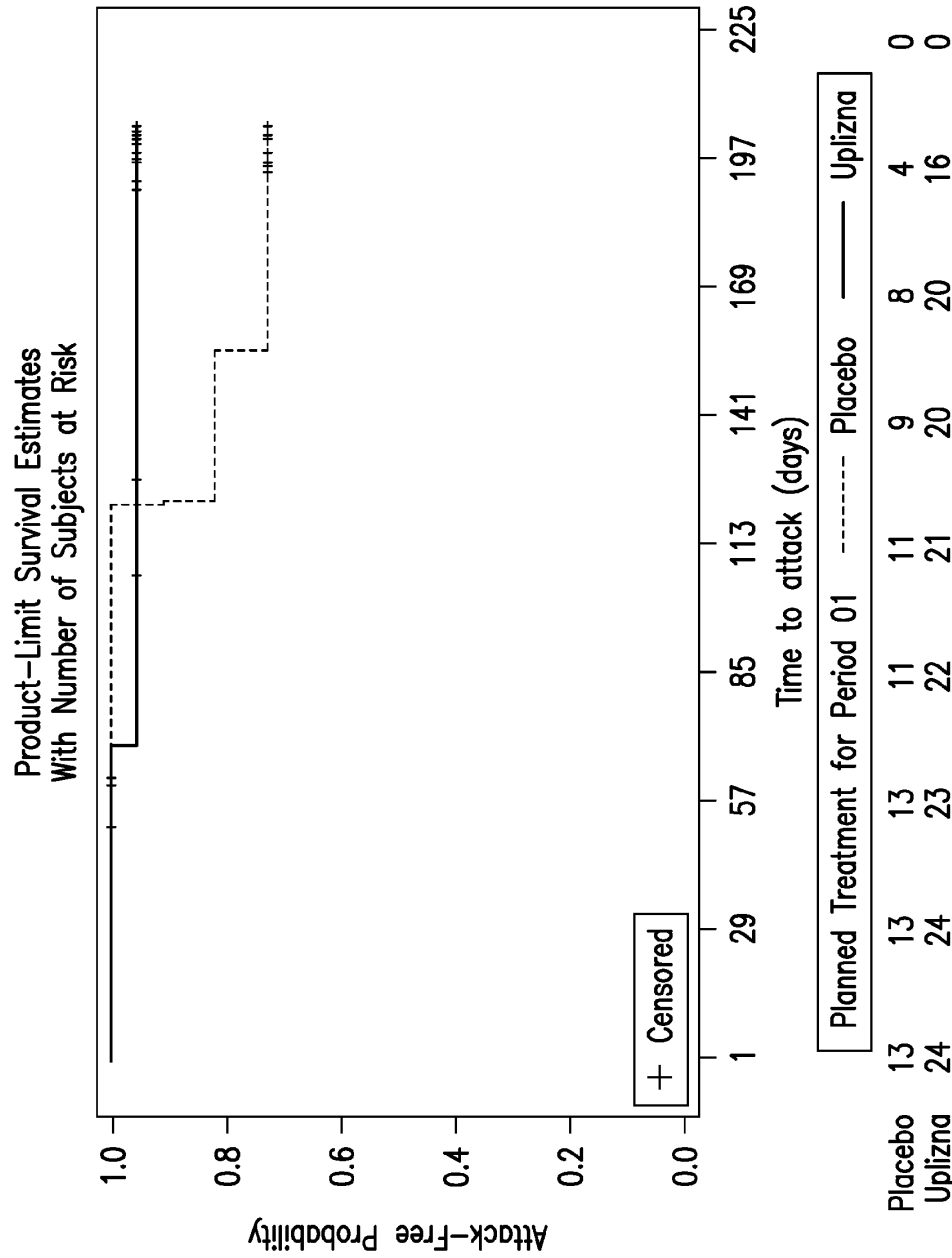


FIG.1B

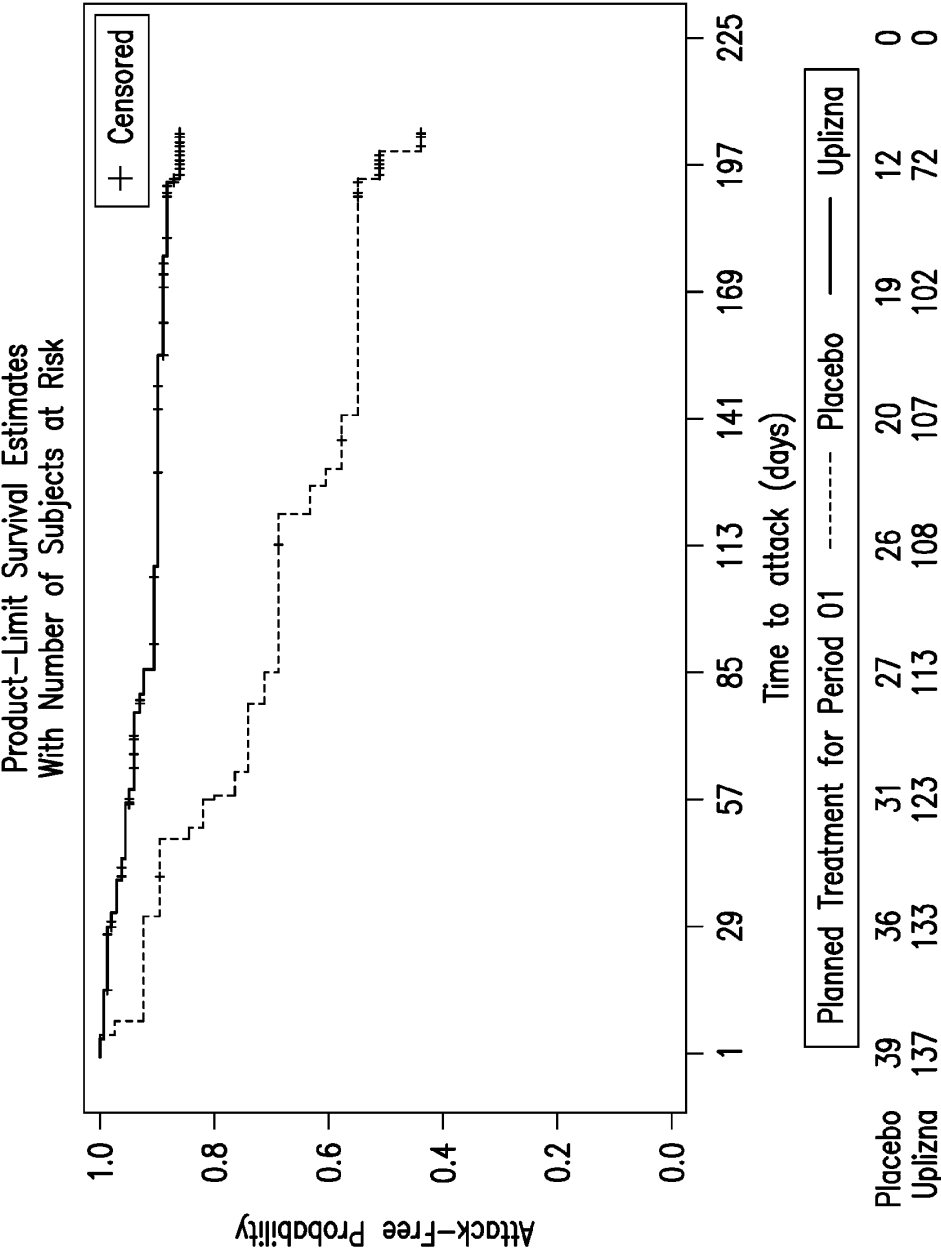


FIG.1C

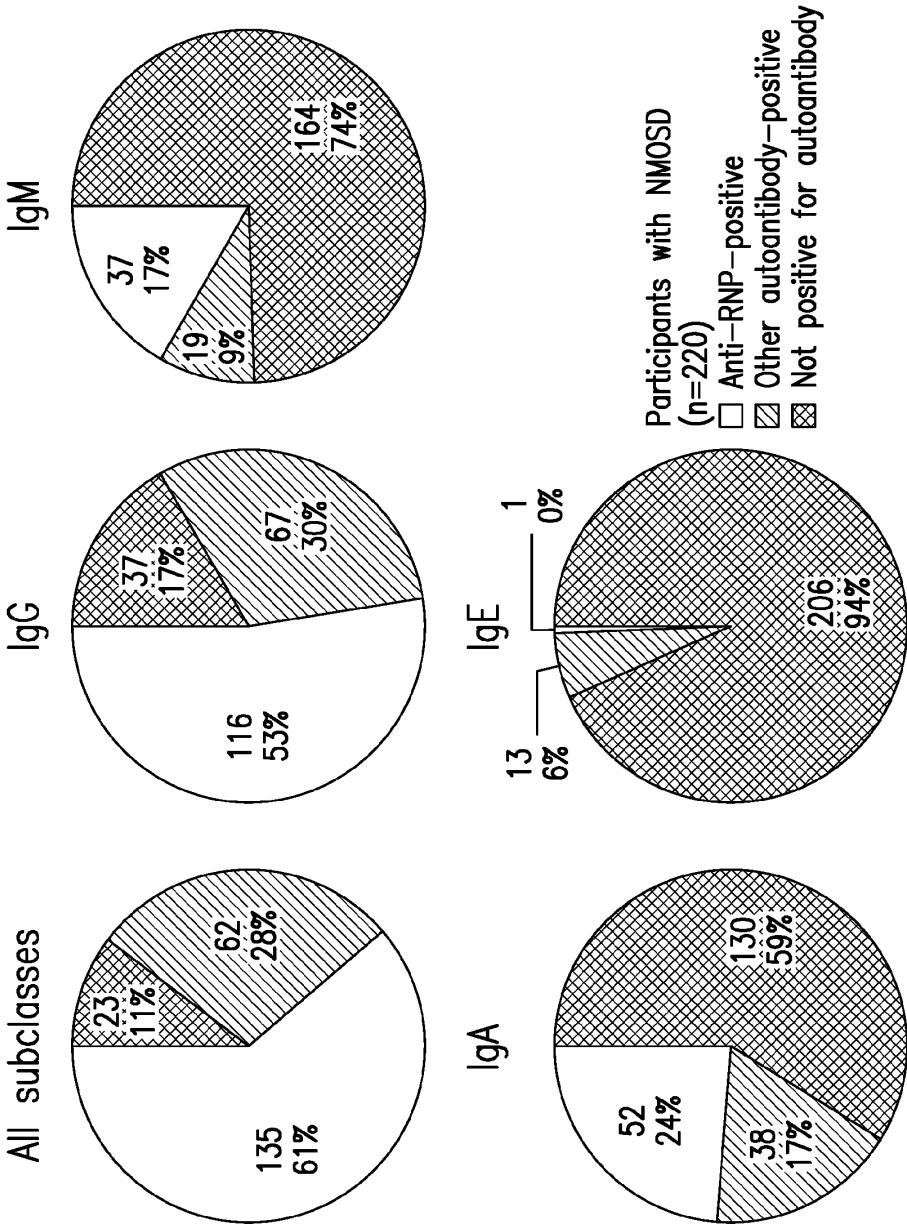
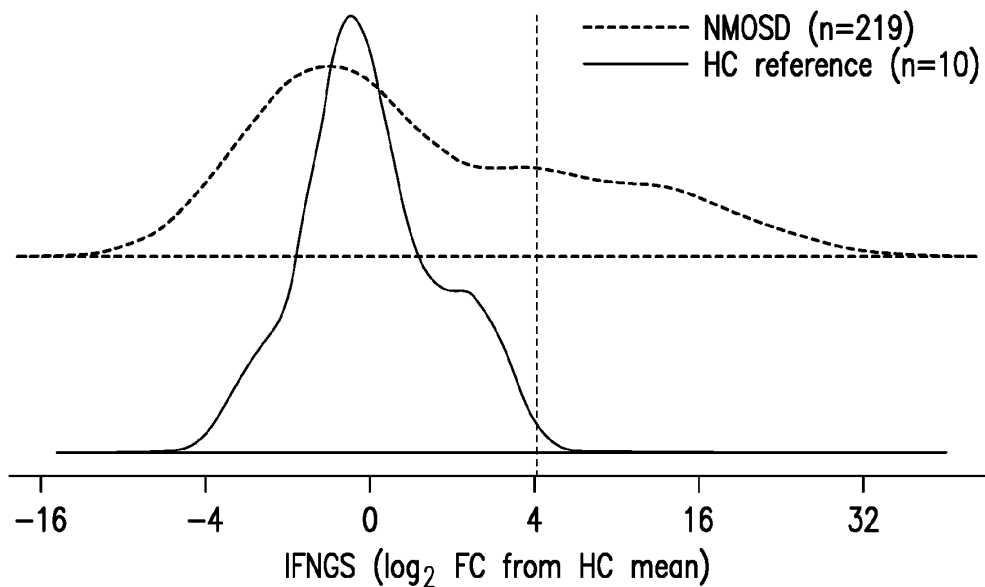


FIG.2A

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* Vertical dashed line indicates > 4-fold change from HC mean. FC, fold change; HC, healthy control; IFNGS, type 1 interferon-inducible gene signature; NMOSD, neuromyelitis optica spectrum disorder.

FIG.2B

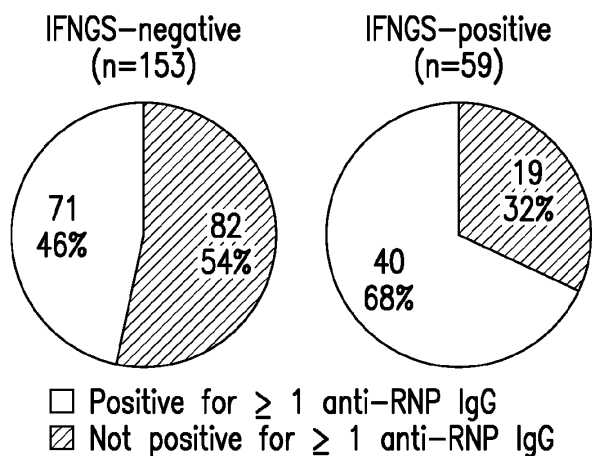
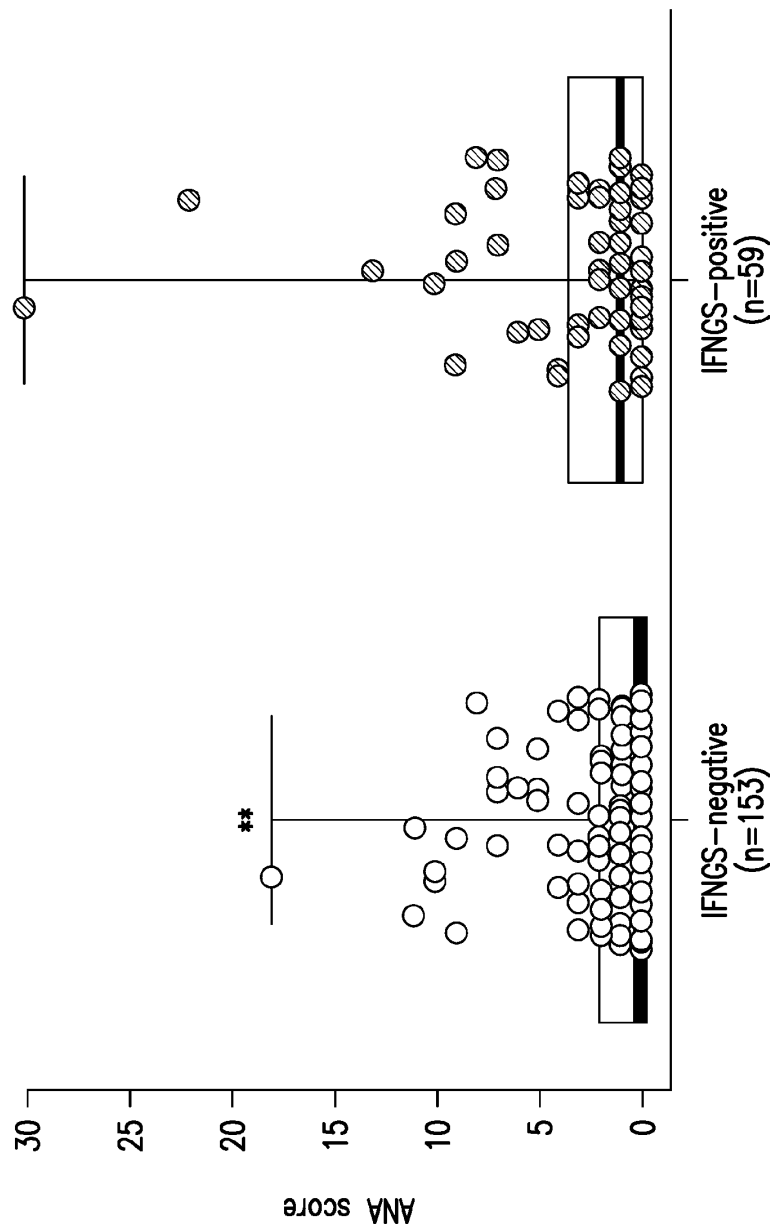
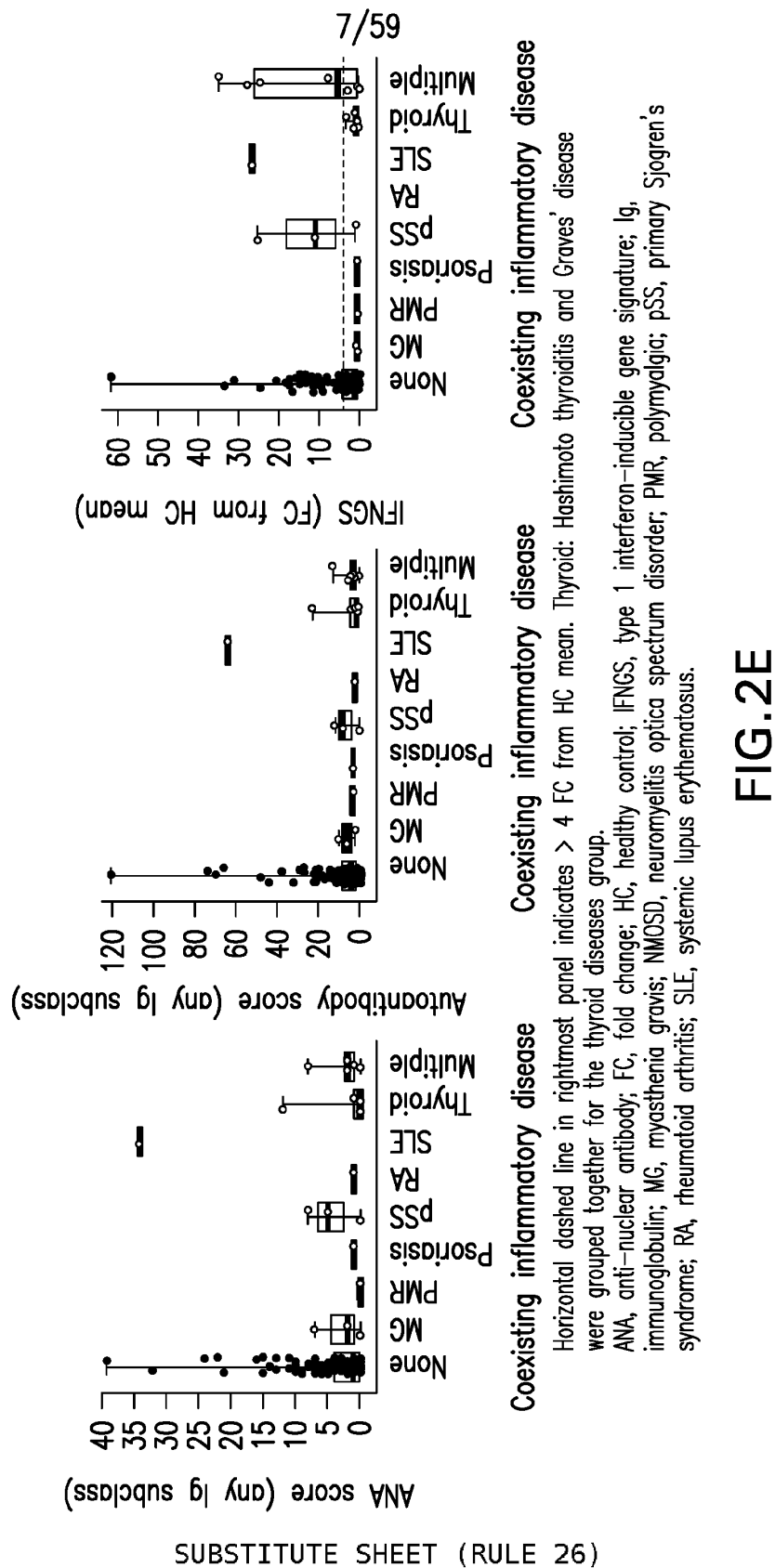


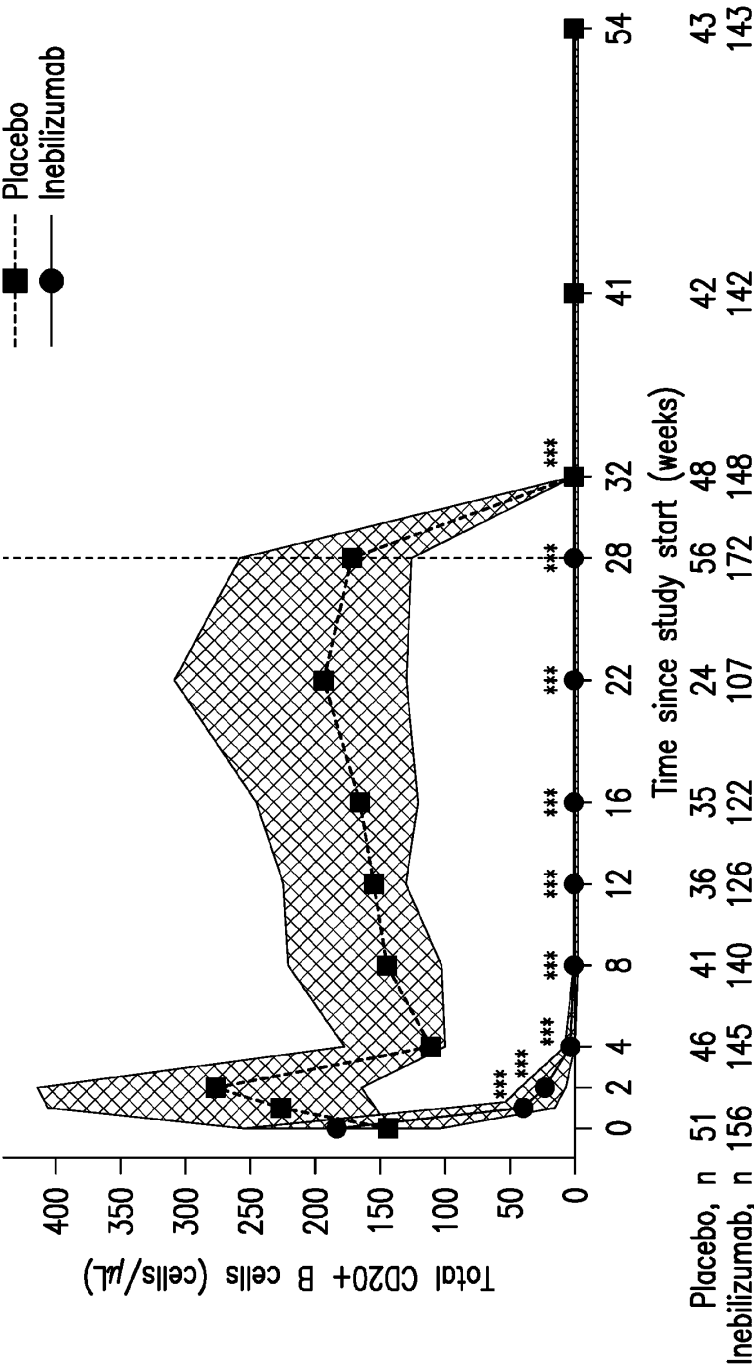
FIG.2C



AUC = 0.63; **p = 0.002.
Statistical significance was assessed using a Mann-Whitney U-test.

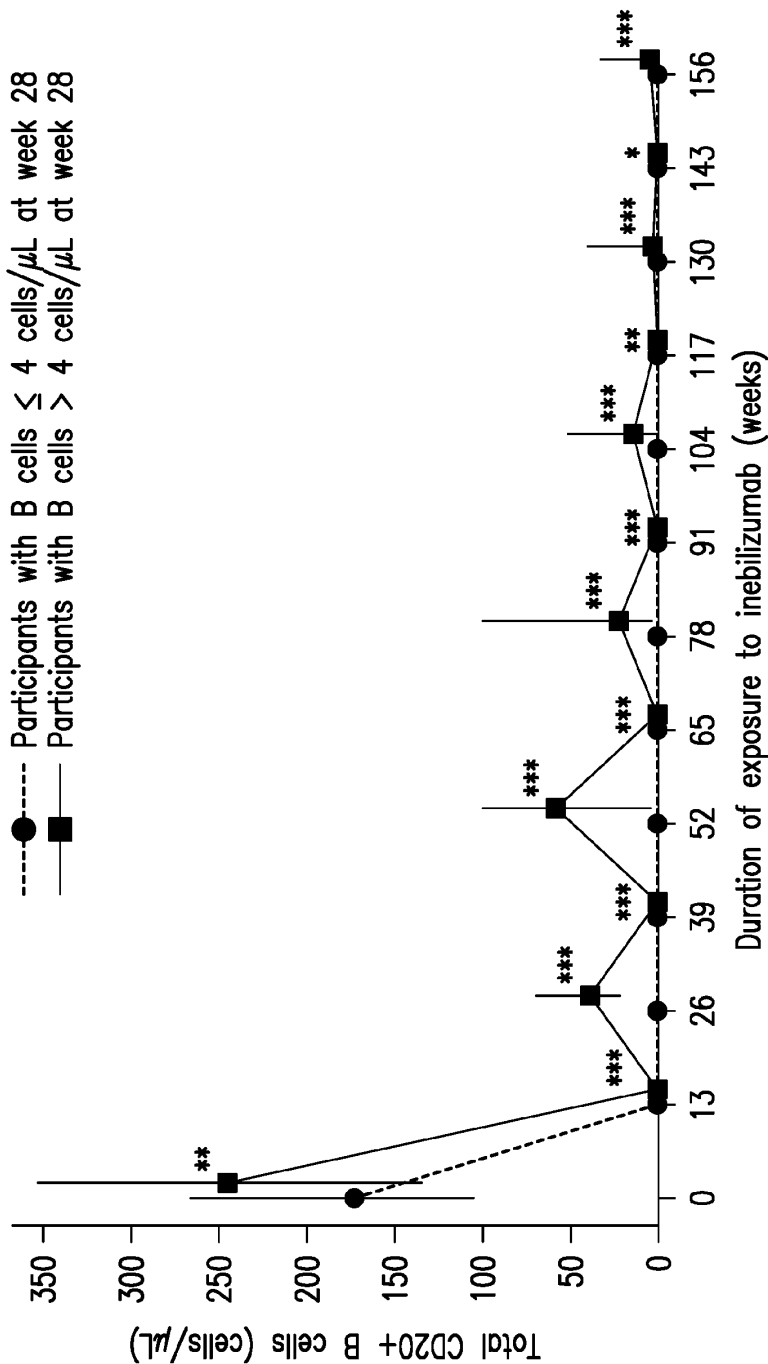
FIG.2D





***p < 0.001.
B cells were enumerated using CD20 as a lineage FACS marker, as bound inebilizumab interferes with the CD19-based FACS assay. Points represent medians. Shaded region represents IQR. LLoQ was 0.2 cells/μL. Vertical dashed line represents the transition into the OLP; the placebo cohort received two inebilizumab doses, whereas the inebilizumab cohort received an additional maintenance dose. FACS, fluorescence-activated cell sorting; IQR, interquartile range; LLoQ, lower limit of quantification; OLP, open-label period.

FIG.3A



* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.
Points represent medians $\pm$ IQR.
B-cell count cut-off point of 4 cells/ μ L was found to be optimal to separate patients with decreased risk of elevated NMOSD activity over the subsequent inebilizumab doses.
IQR, interquartile range; NMOSD, neuromyelitis optica spectrum disorder.

FIG.3B

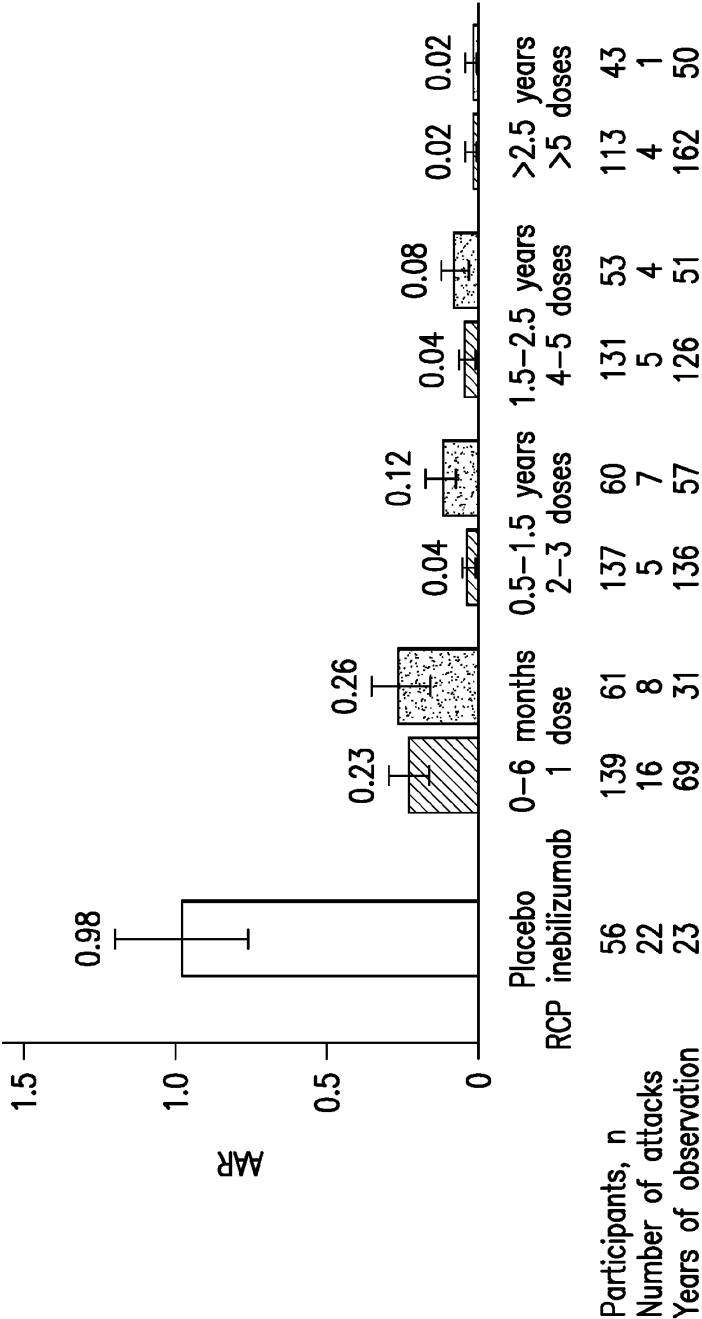


FIG.3C

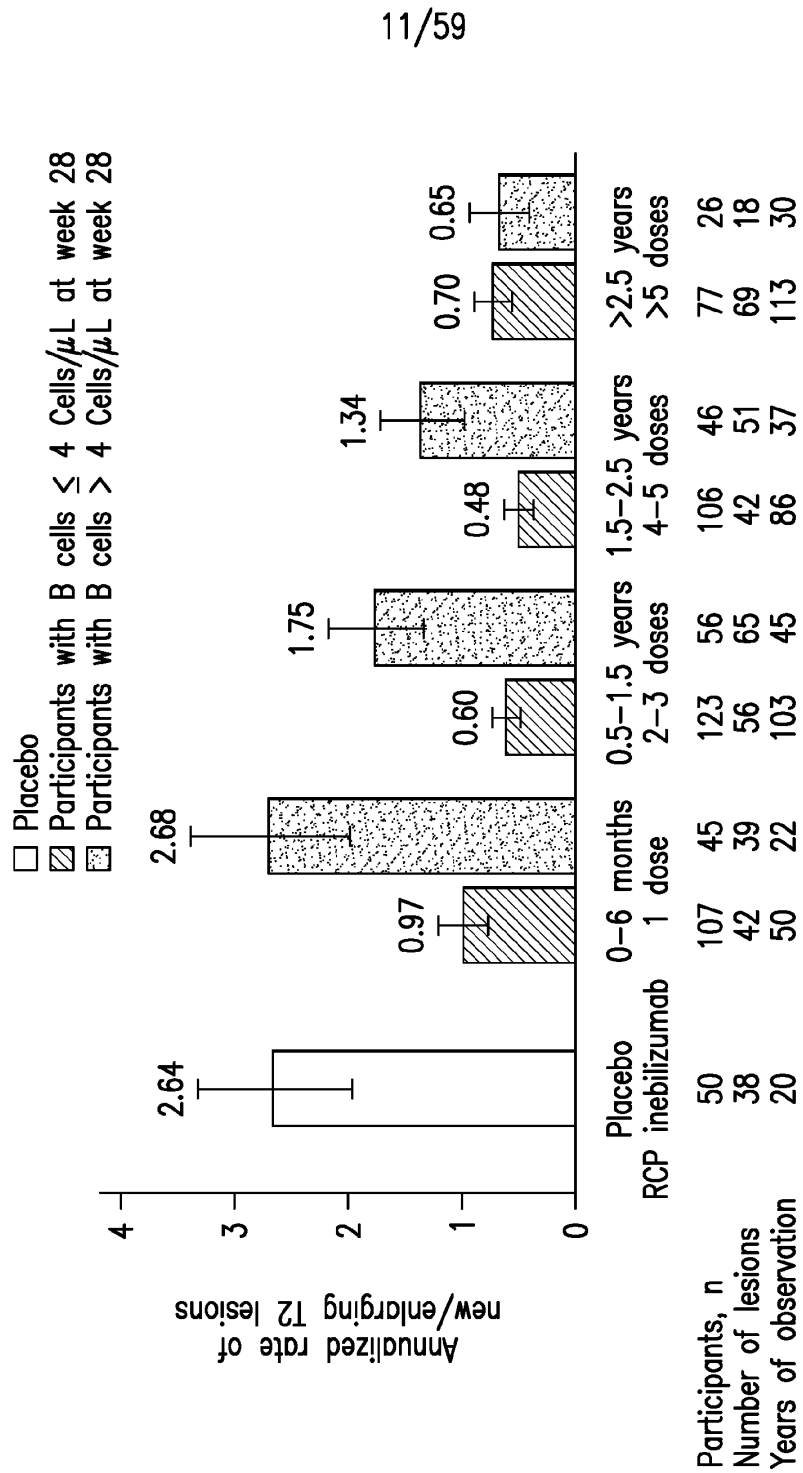


FIG.3D

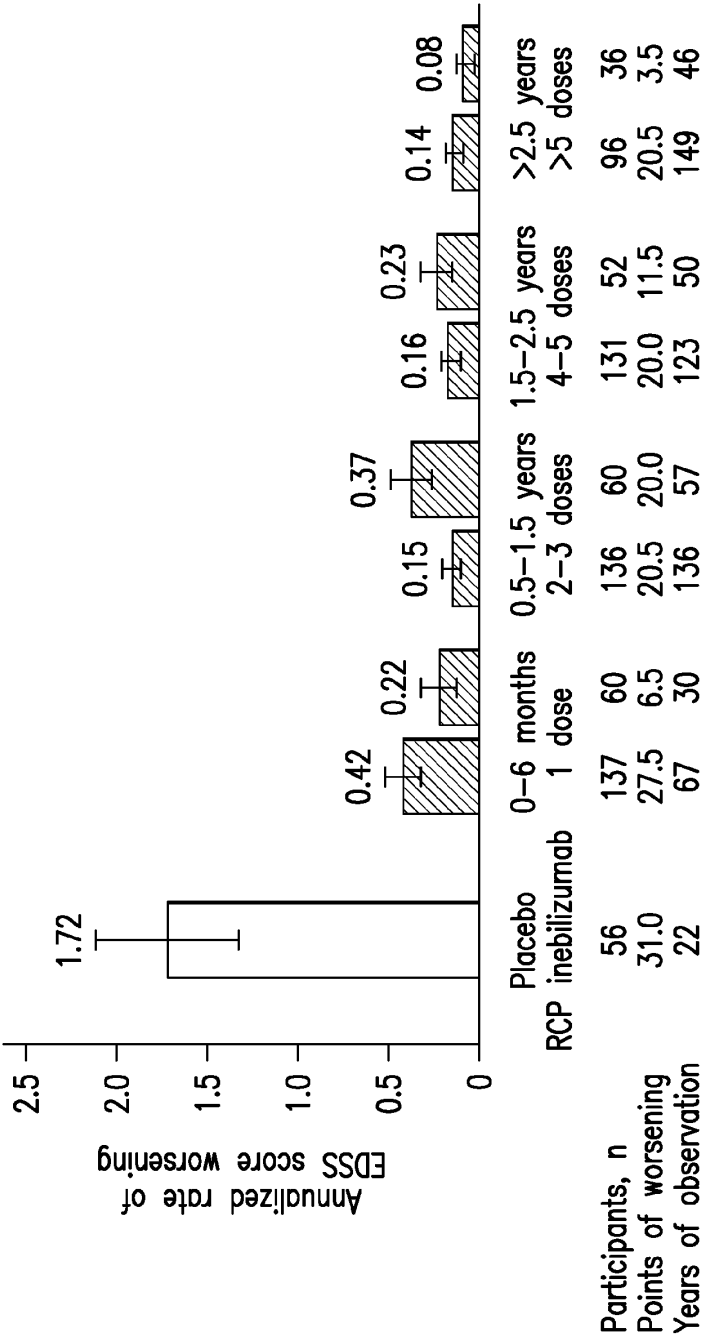


FIG.3E

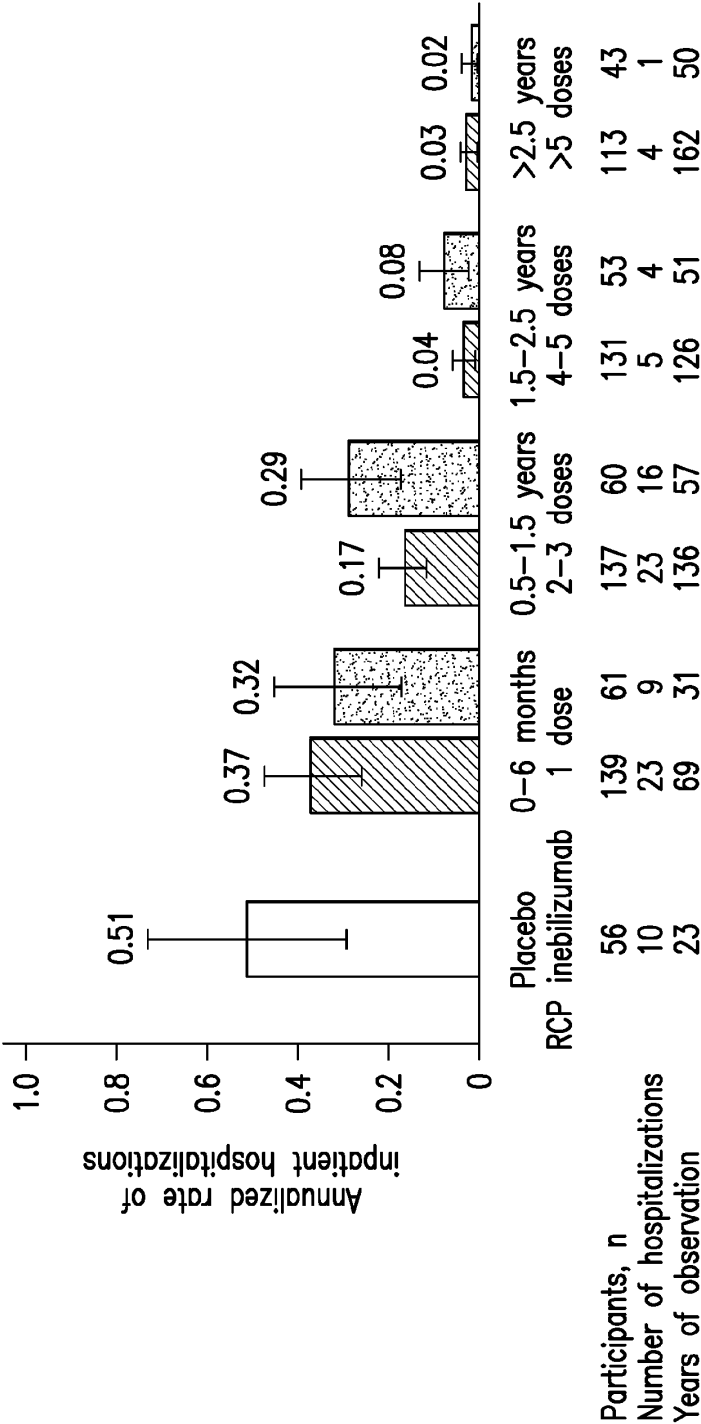


FIG.3F



FIG. 3G

Error bars represent 95% CI estimated by negative binomial regression. AAR, annualized attack rate; CI, confidence interval; NMOSD, neuromyelitis optica spectrum disorder; RCP, randomized controlled period.

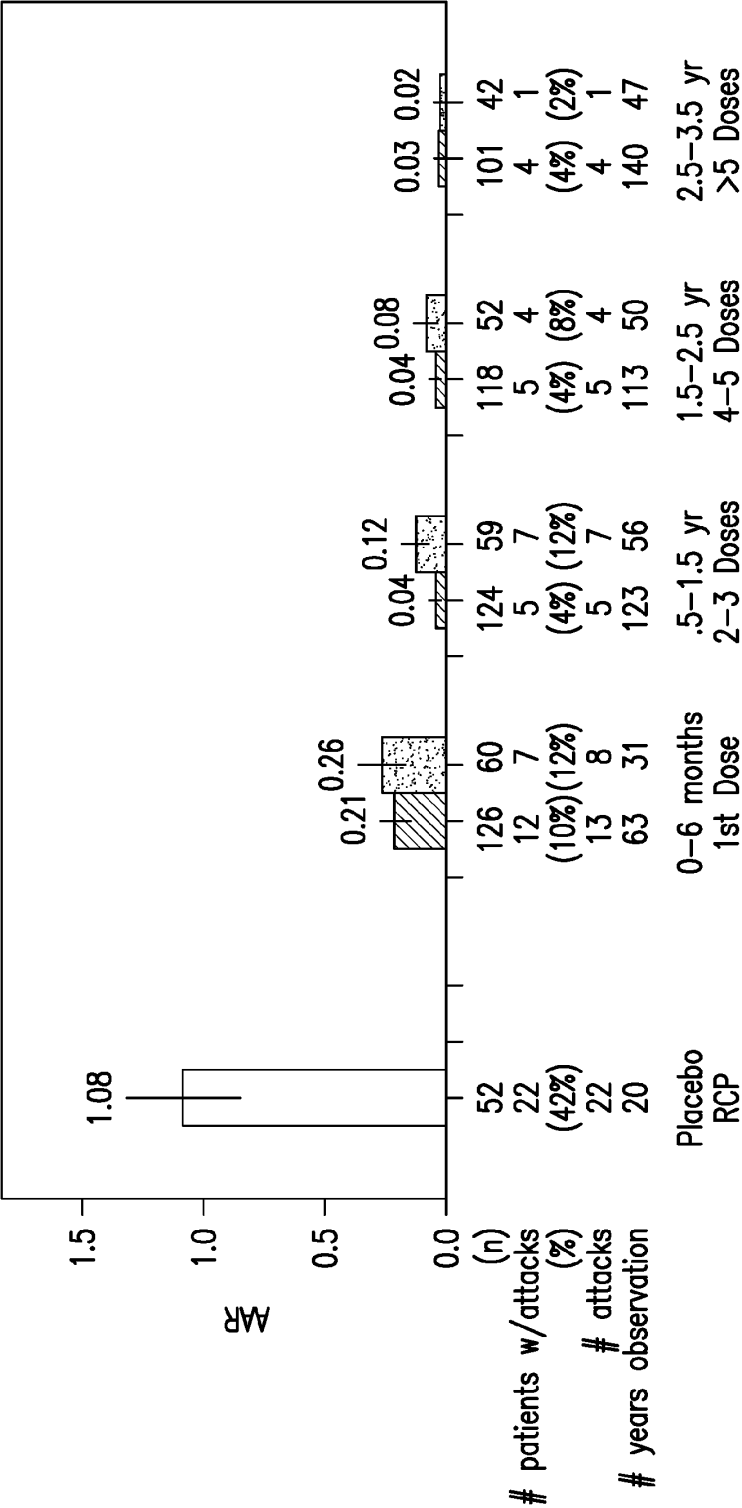


FIG.4A

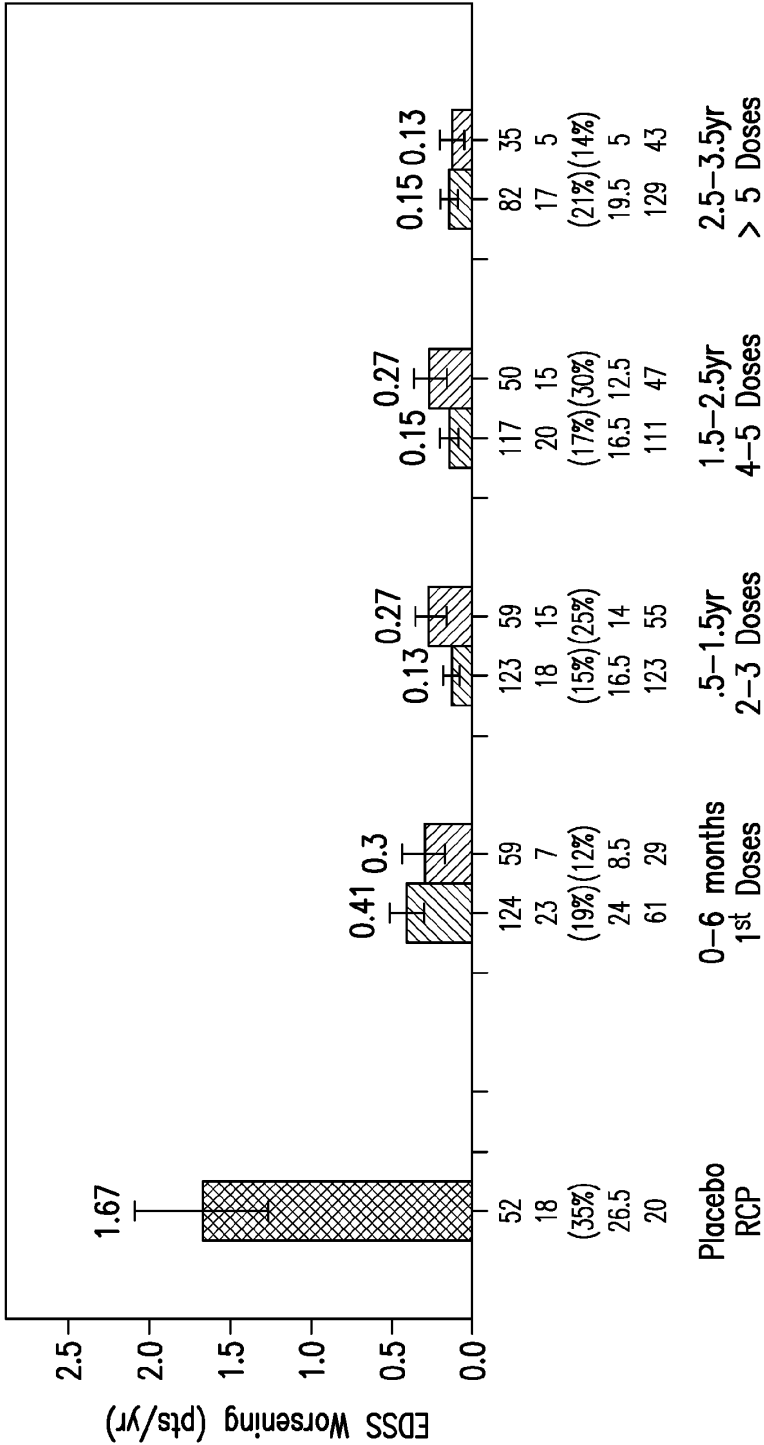


FIG.4B

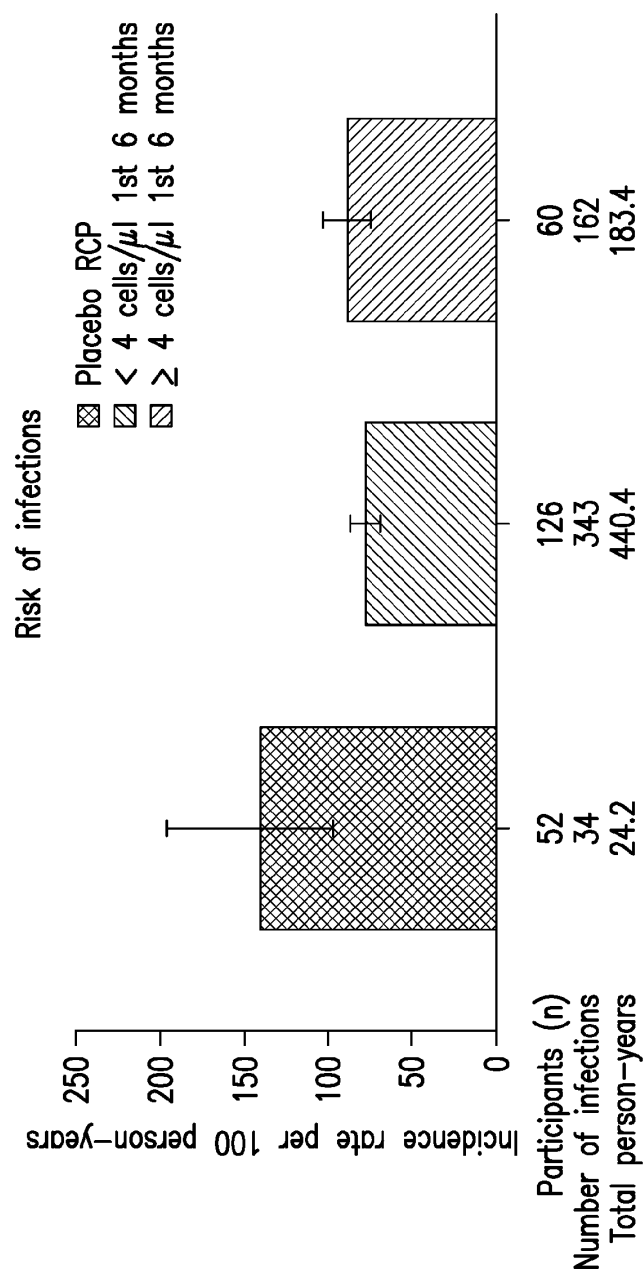


FIG.4C

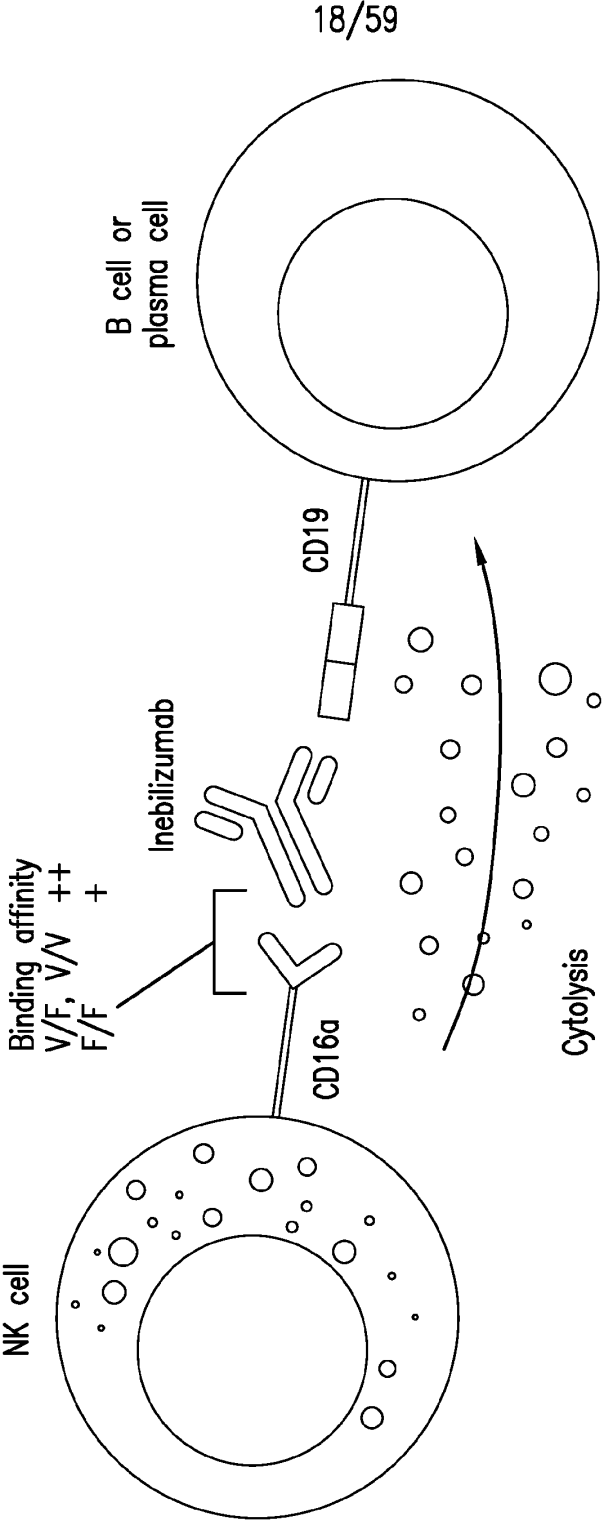
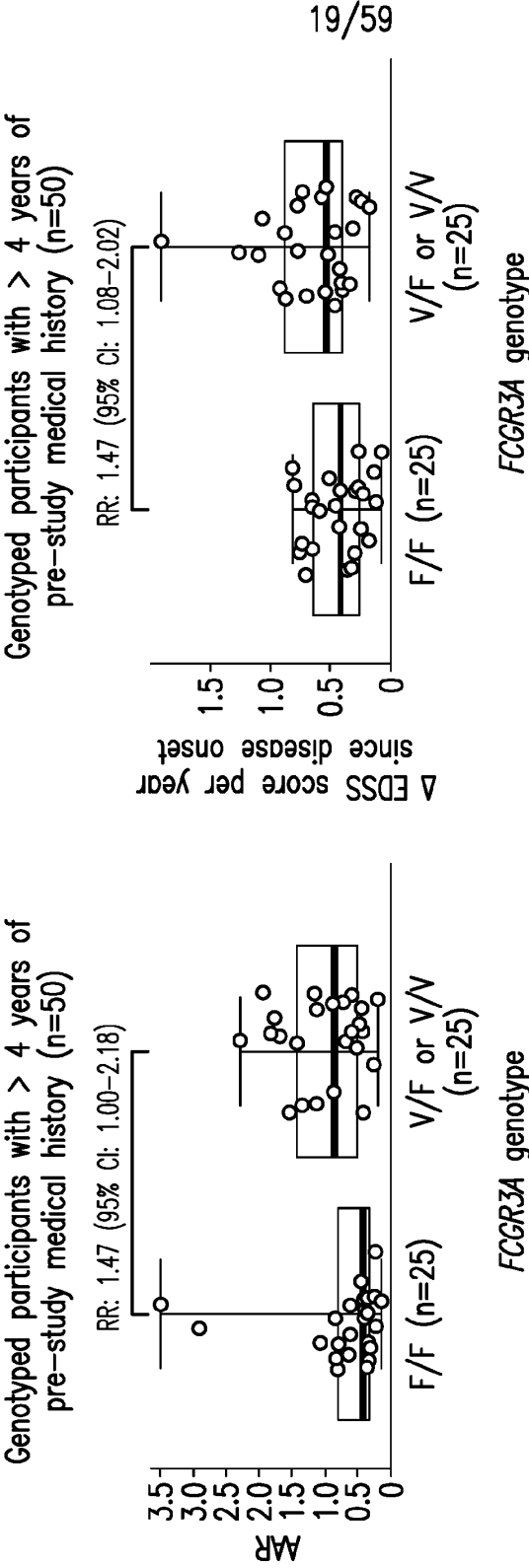


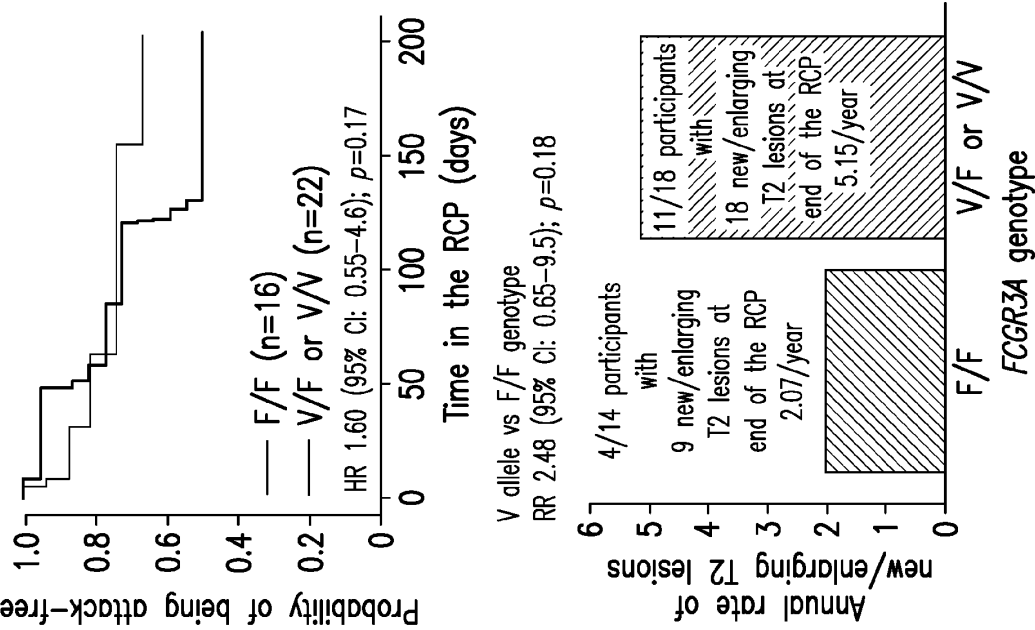
FIG.5A

ADCC, antibody-dependent cell-mediated cytotoxicity; F, phenylalanine; NK, natural killer; V, valine.



Difference in AARs and EDSS score worsening between genotypes assessed using negative binomial regression.
AAR, annualized attack rate; CI, confidence interval; EDSS, Expanded Disability Status Scale; F, phenylalanine; FCGR3A, low-affinity immunoglobulin G Fc region receptor III–A gene; RR, rate ratio; V, valine.

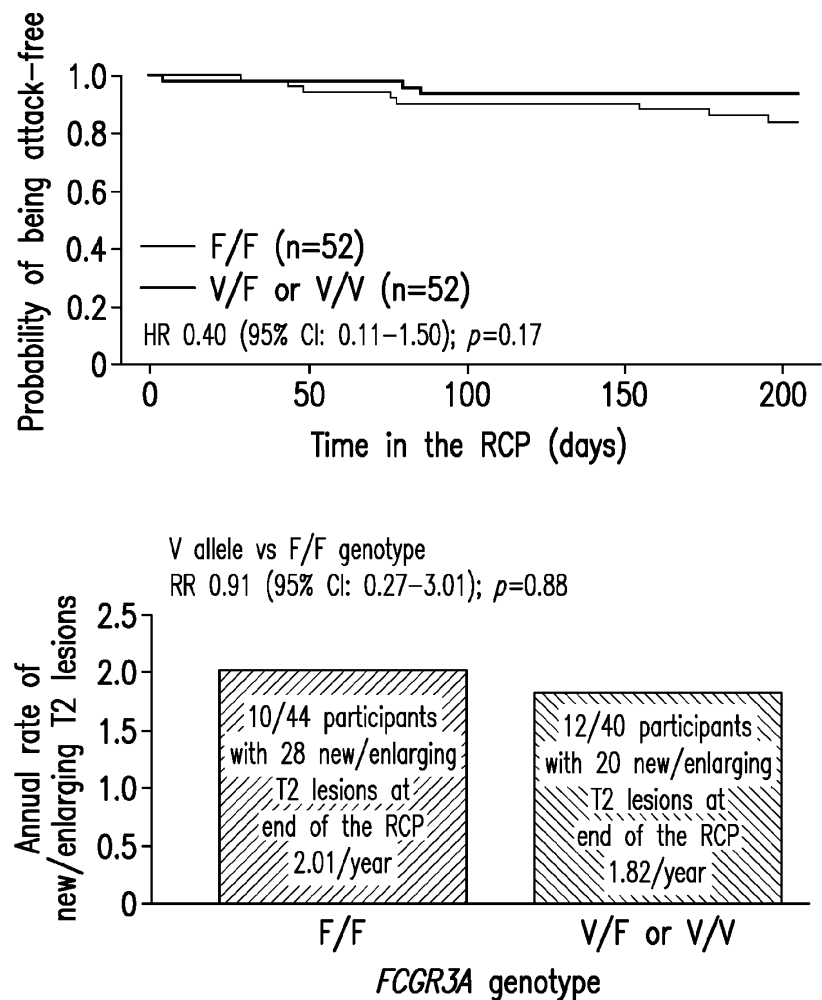
FIG.5B



CI, confidence interval; F, phenylalanine; FCGR3A, low-affinity immunoglobulin G Fc region receptor III–A gene; HR, hazard ratio; RCP, randomized controlled period; RR, rate ratio; V, valine.

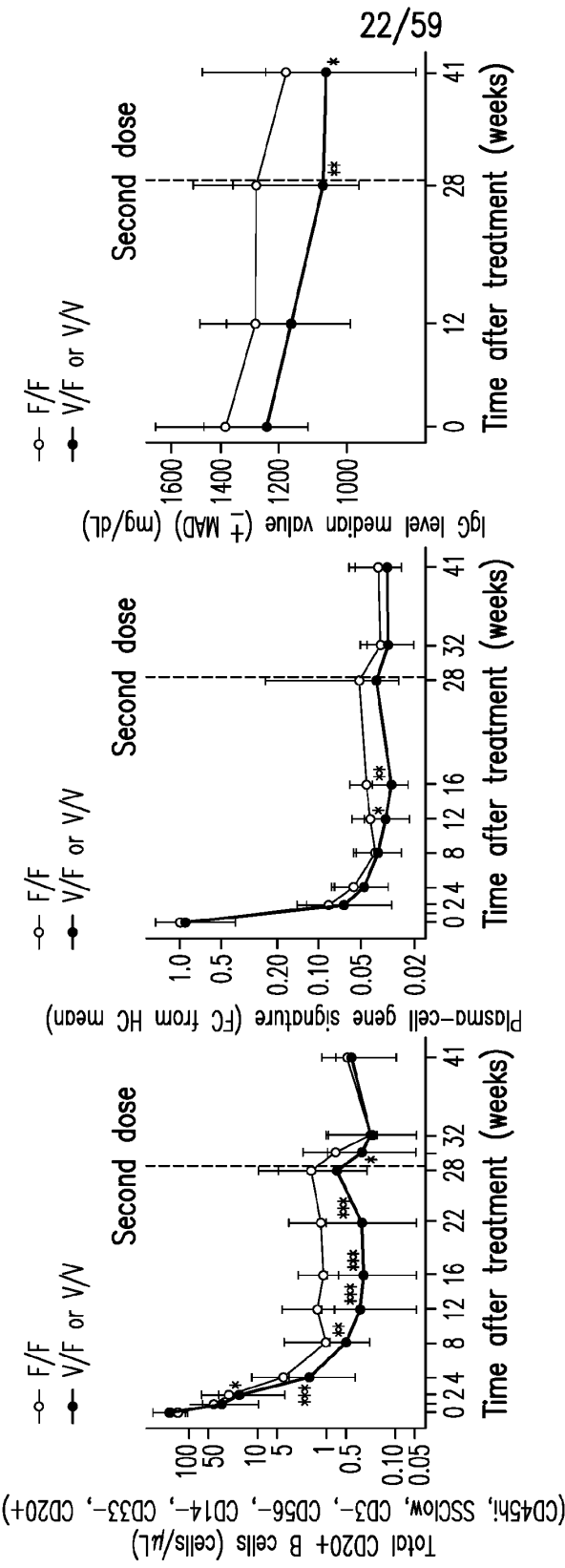
FIG.5C

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CI, confidence interval; F, phenylalanine; FCGR3A, low-affinity immunoglobulin G Fc region receptor III-A gene; HR, hazard ratio; RCP, randomized controlled period; RR, rate ratio; V, valine.

FIG.5D



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* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
Statistical significance was assessed using a Mann-Whitney U-test.
F, phenylalanine; FC, fold-change; FCGR3A, low-affinity immunoglobulin G Fc region receptor III-A gene; HC, healthy control; IgG, immunoglobulin G; MAD, median absolute deviation; V, valine

FIG.5E

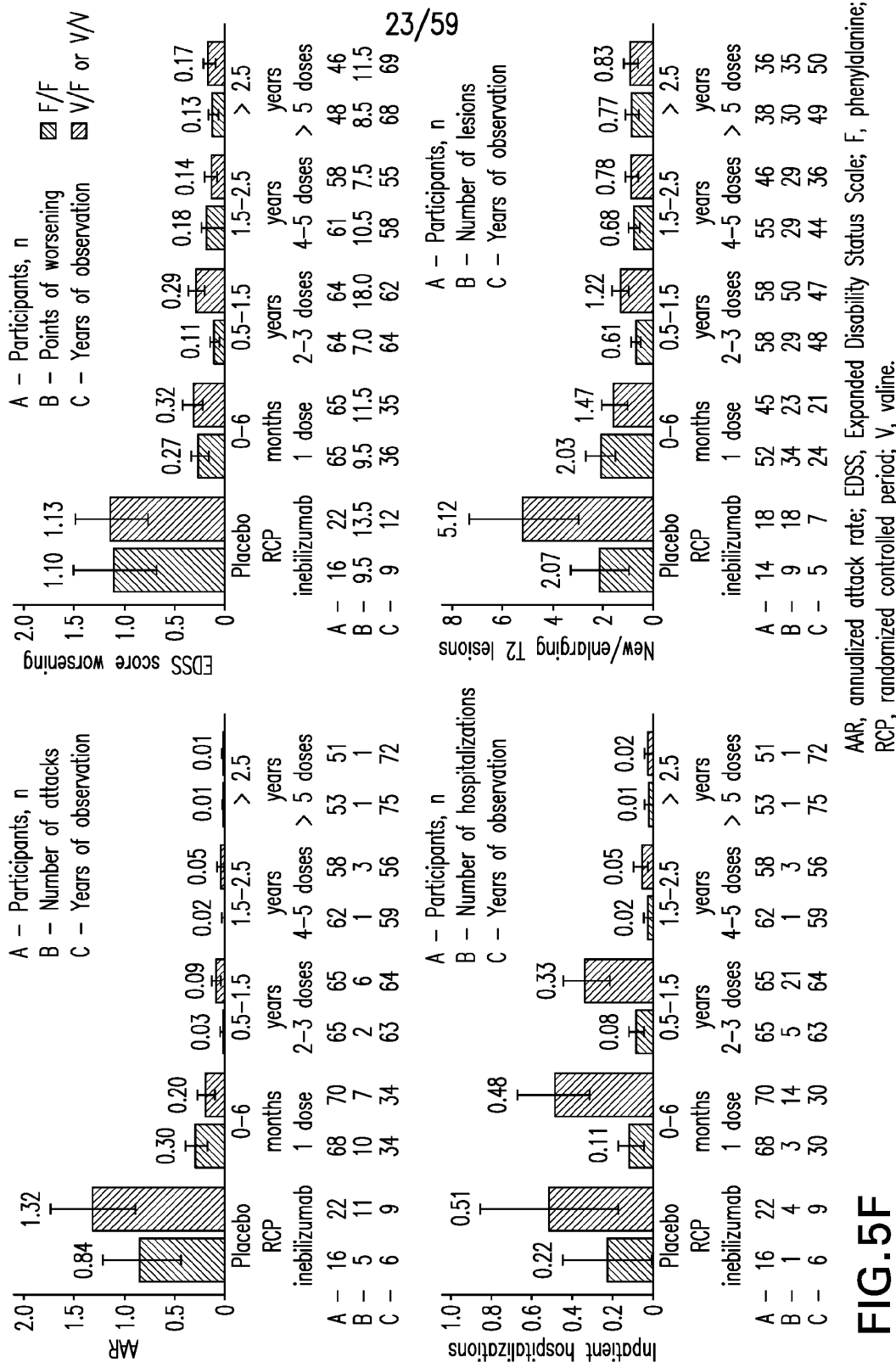


FIG.5F

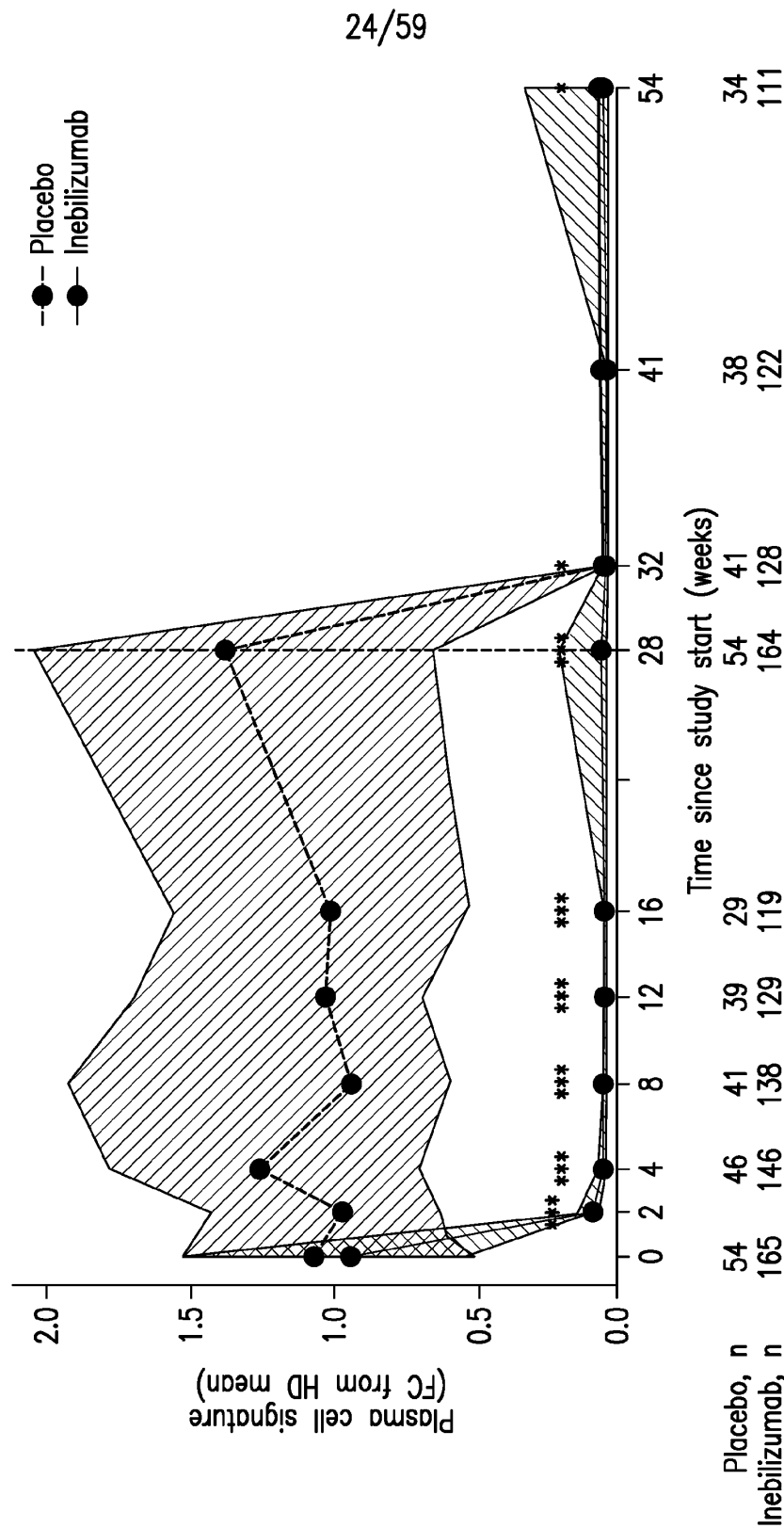


FIG.6A

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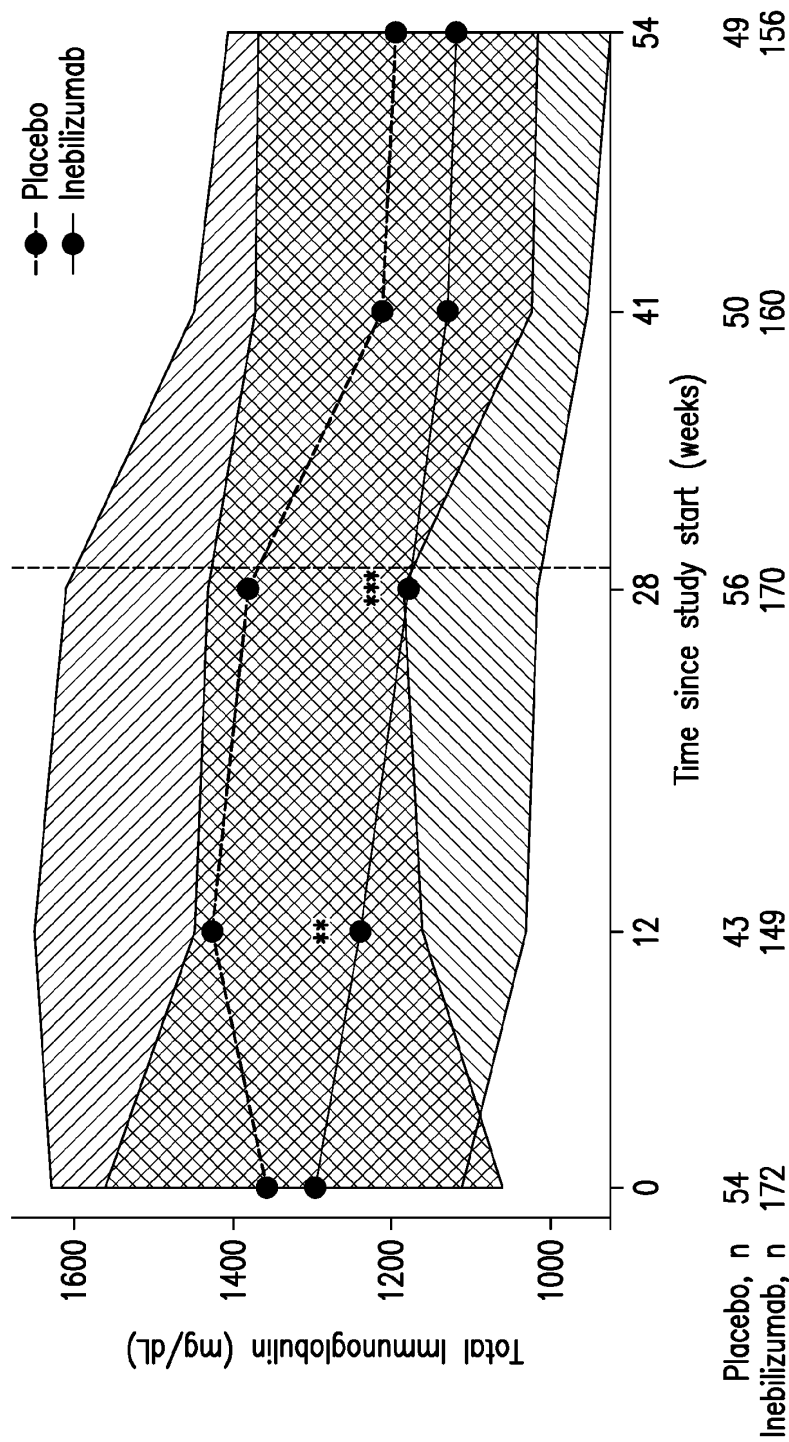


FIG.6B

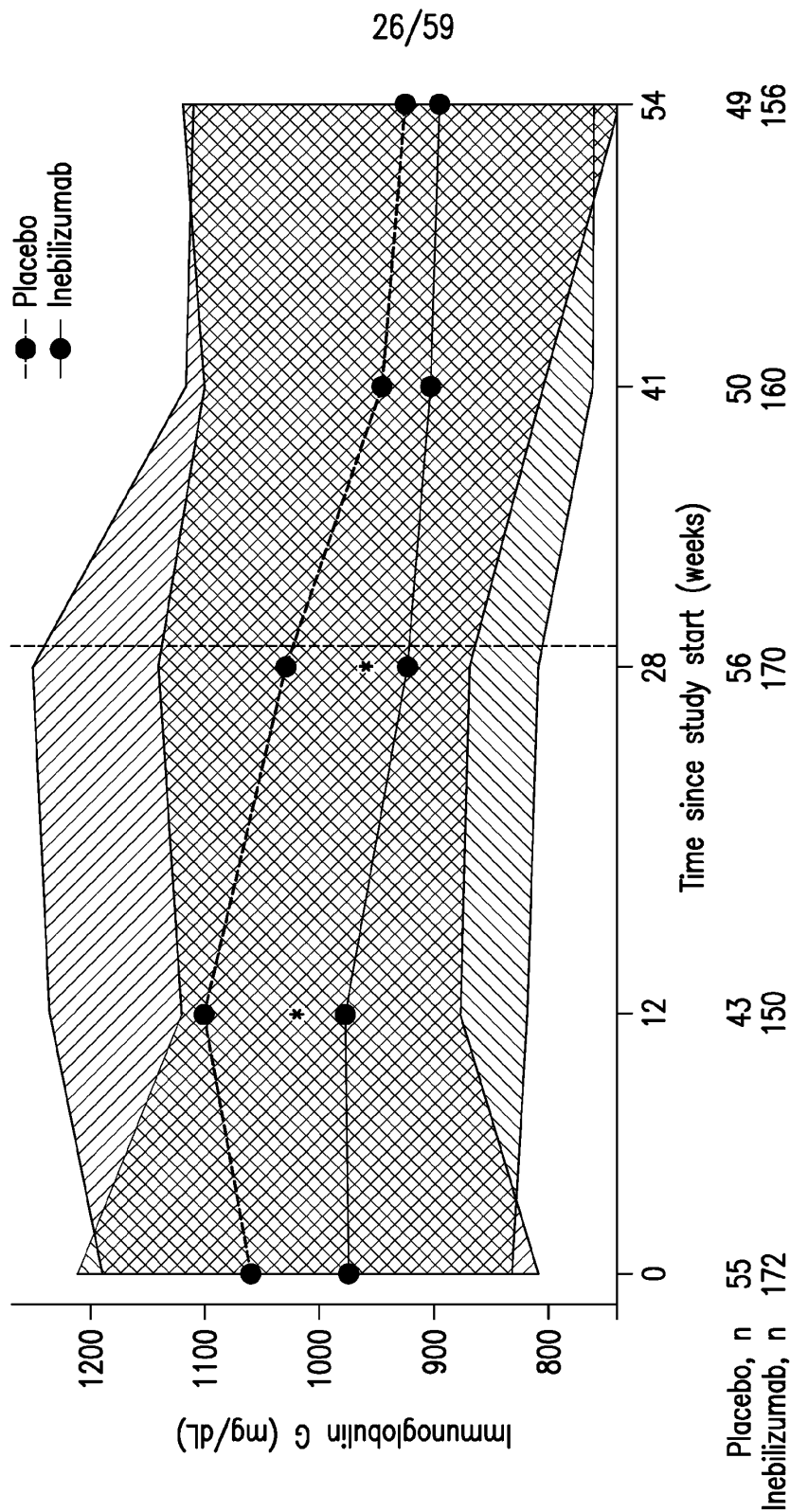


FIG.6C

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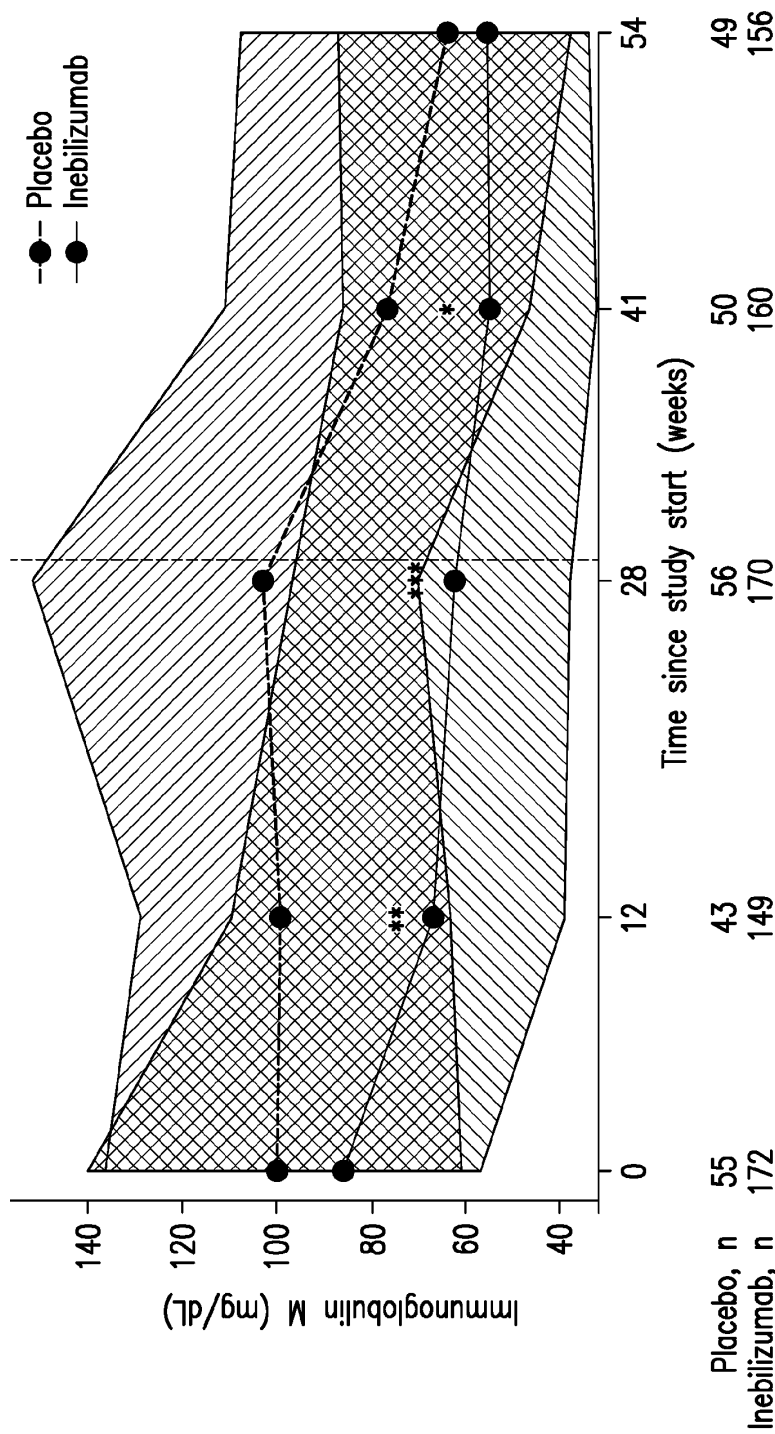


FIG.6D

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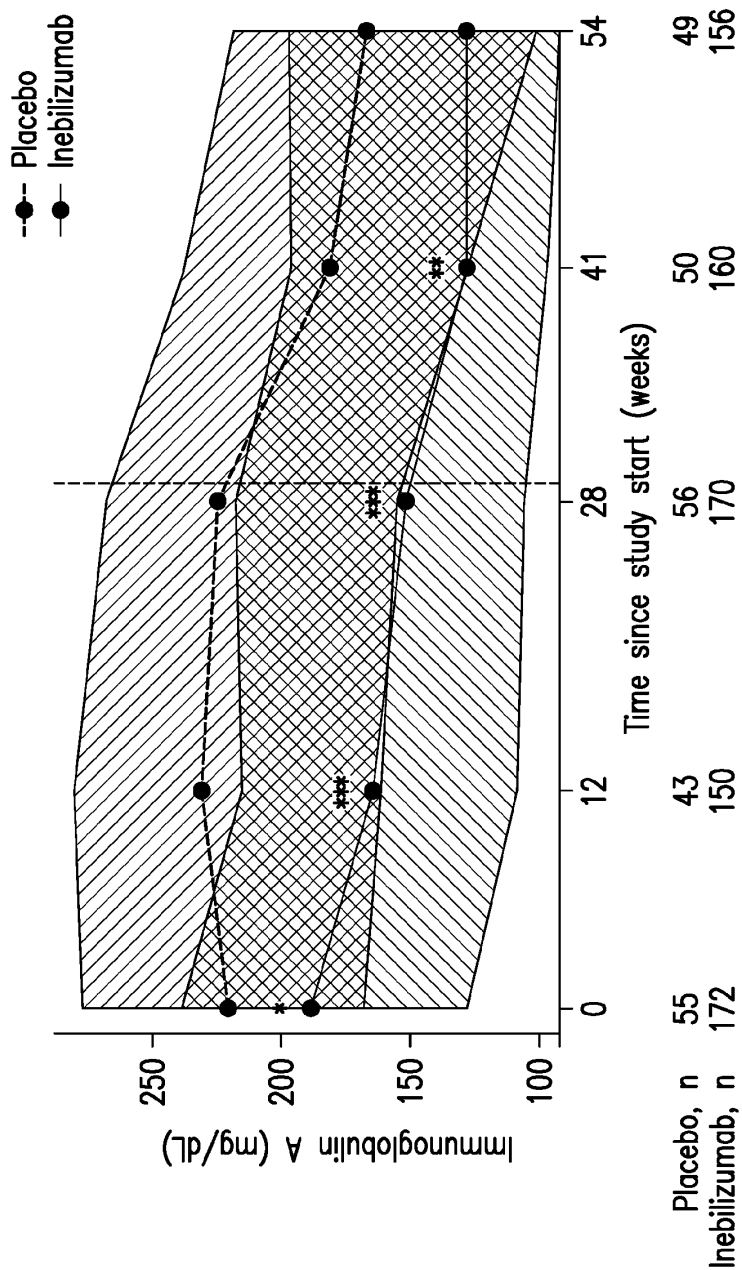


FIG.6E

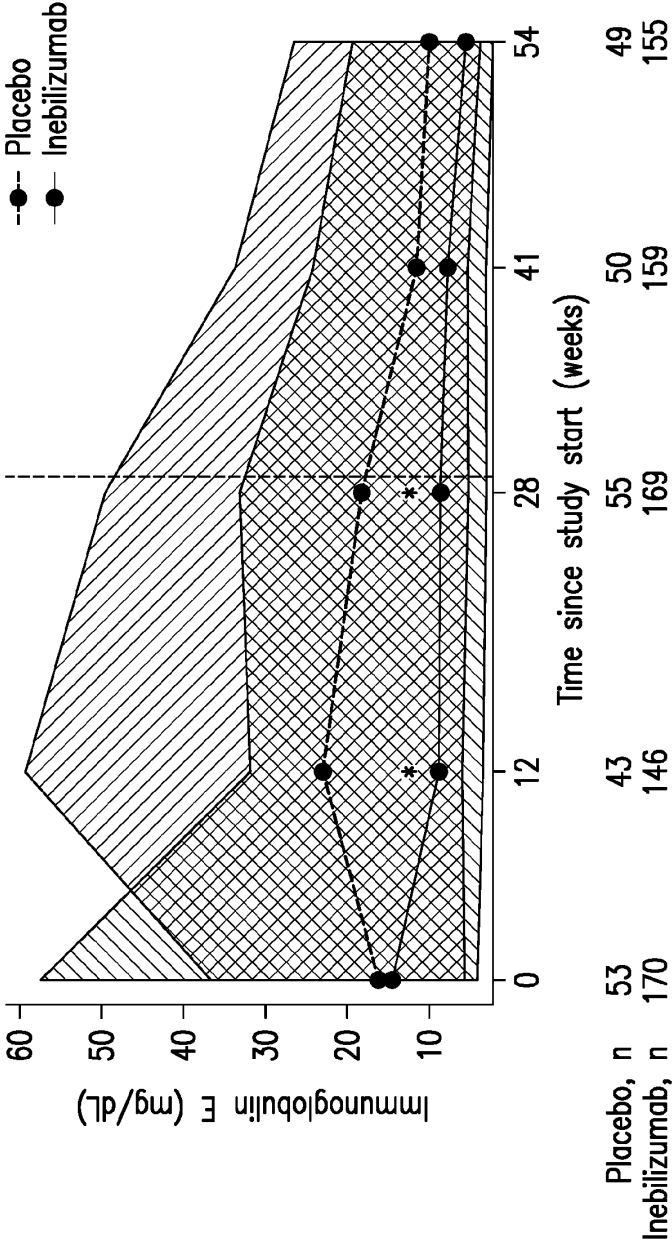


FIG.6F

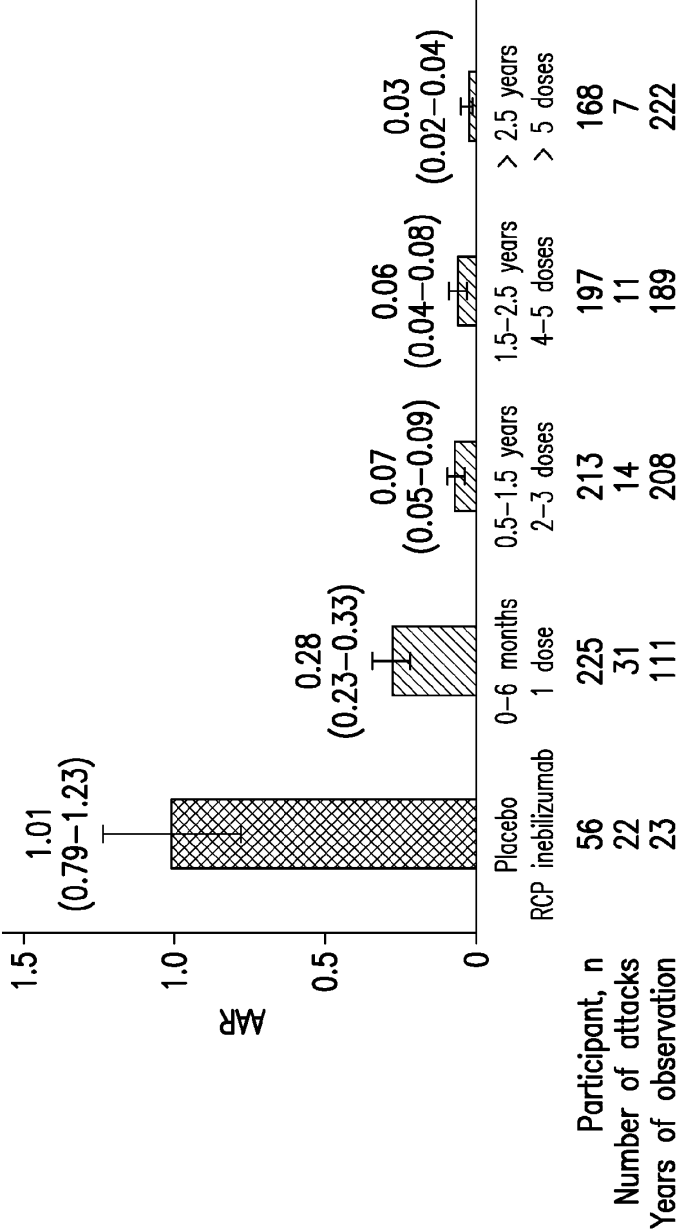


FIG.7A

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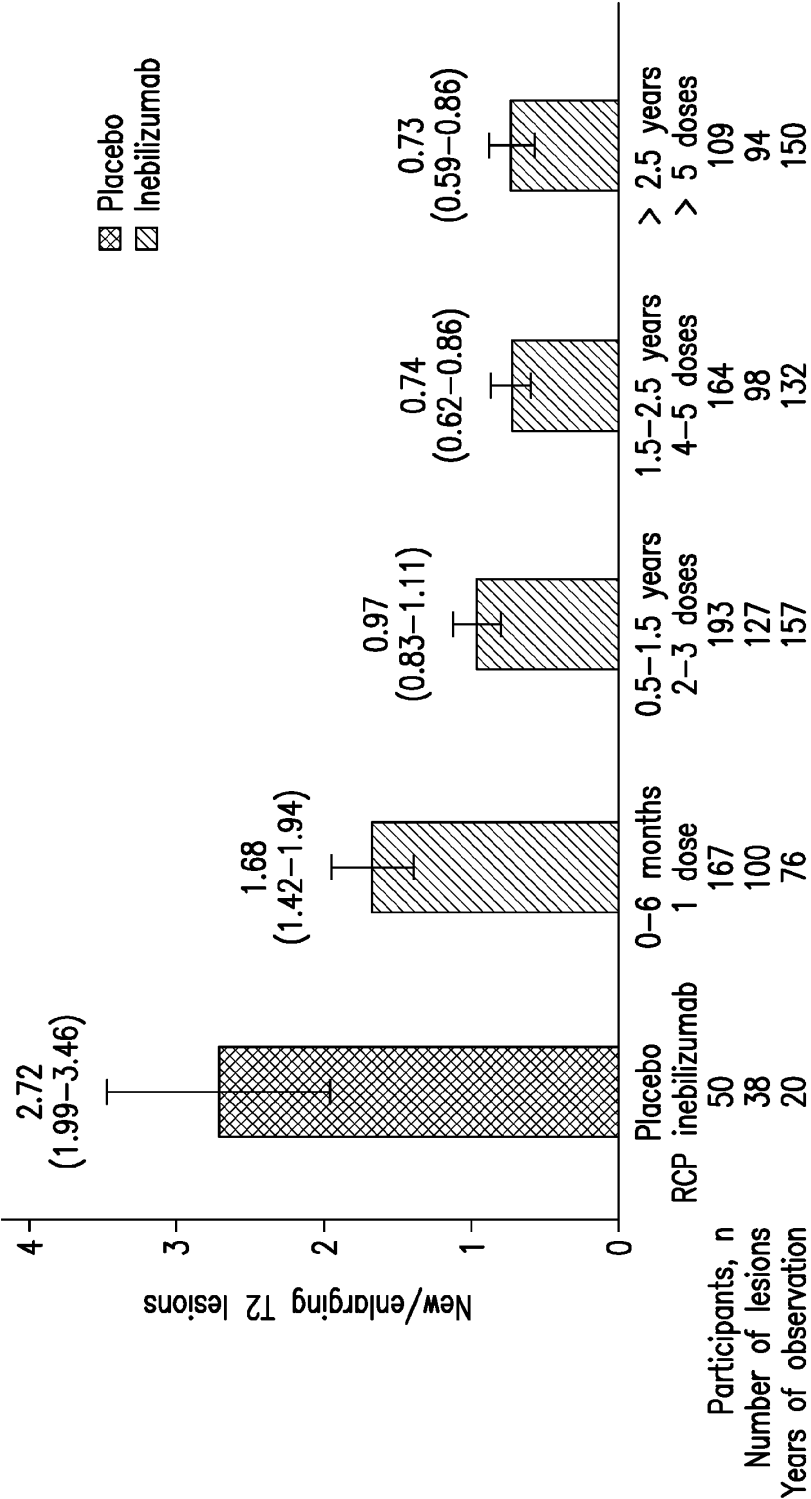


FIG.7B

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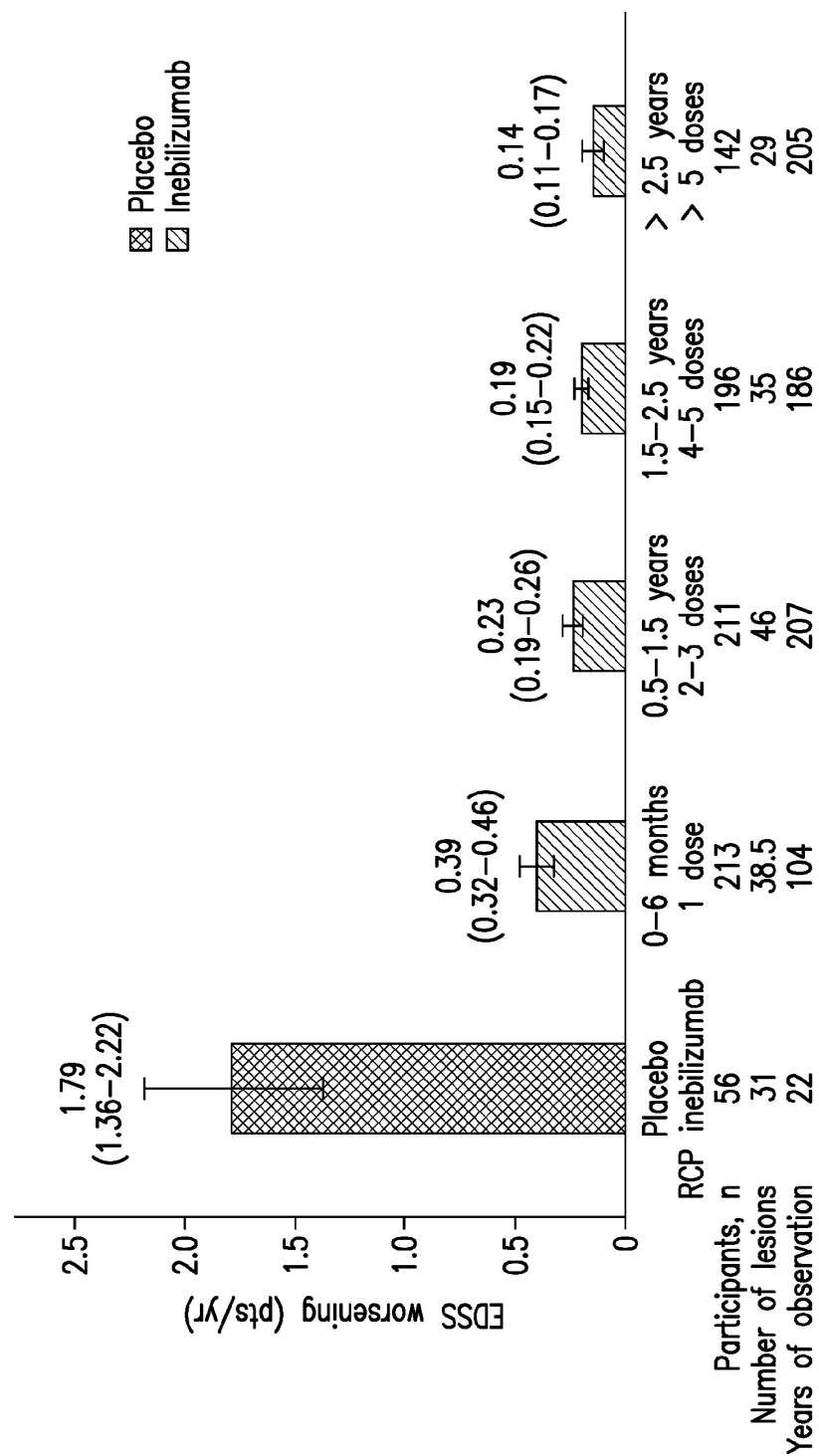
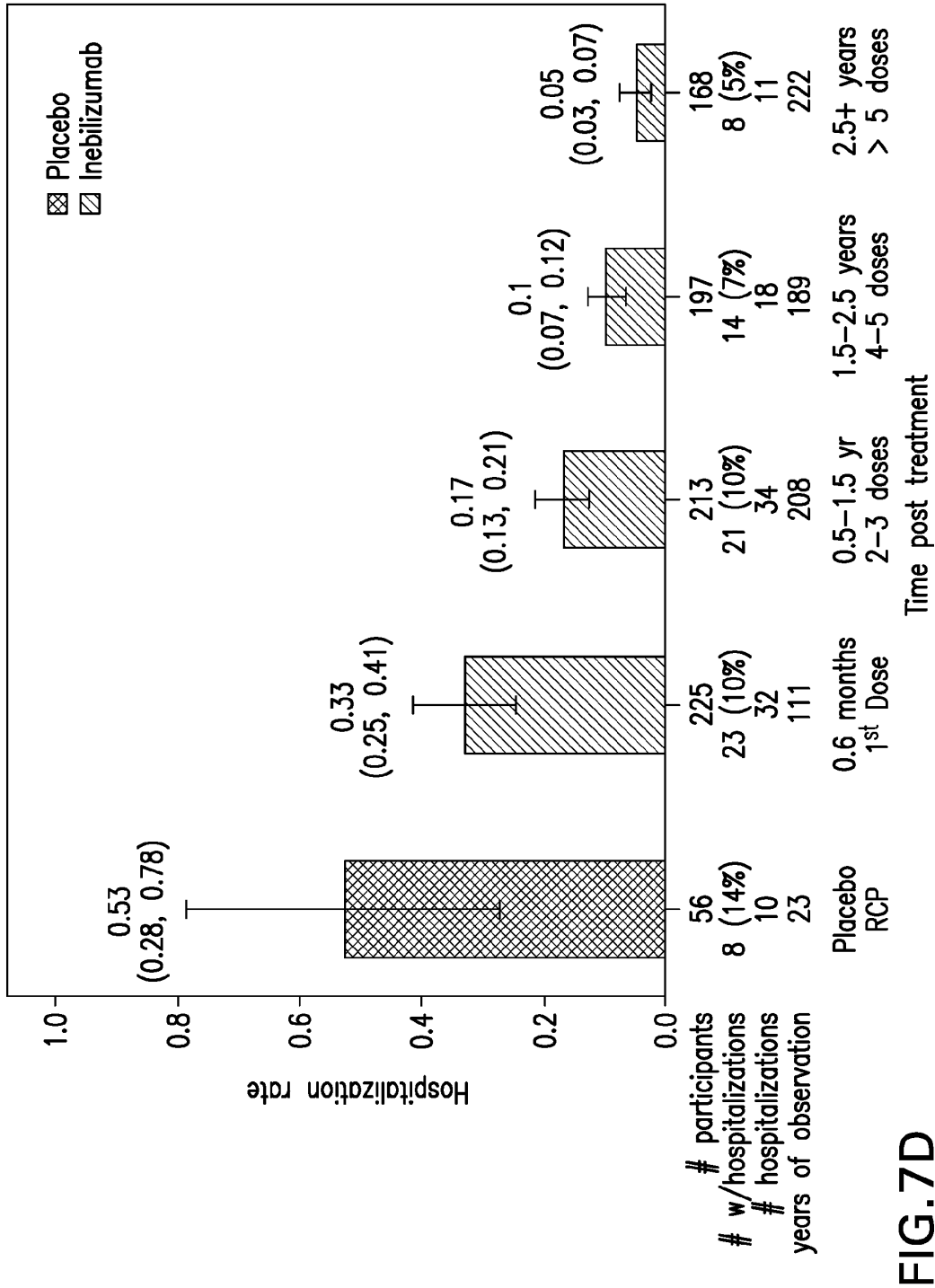


FIG. 7C



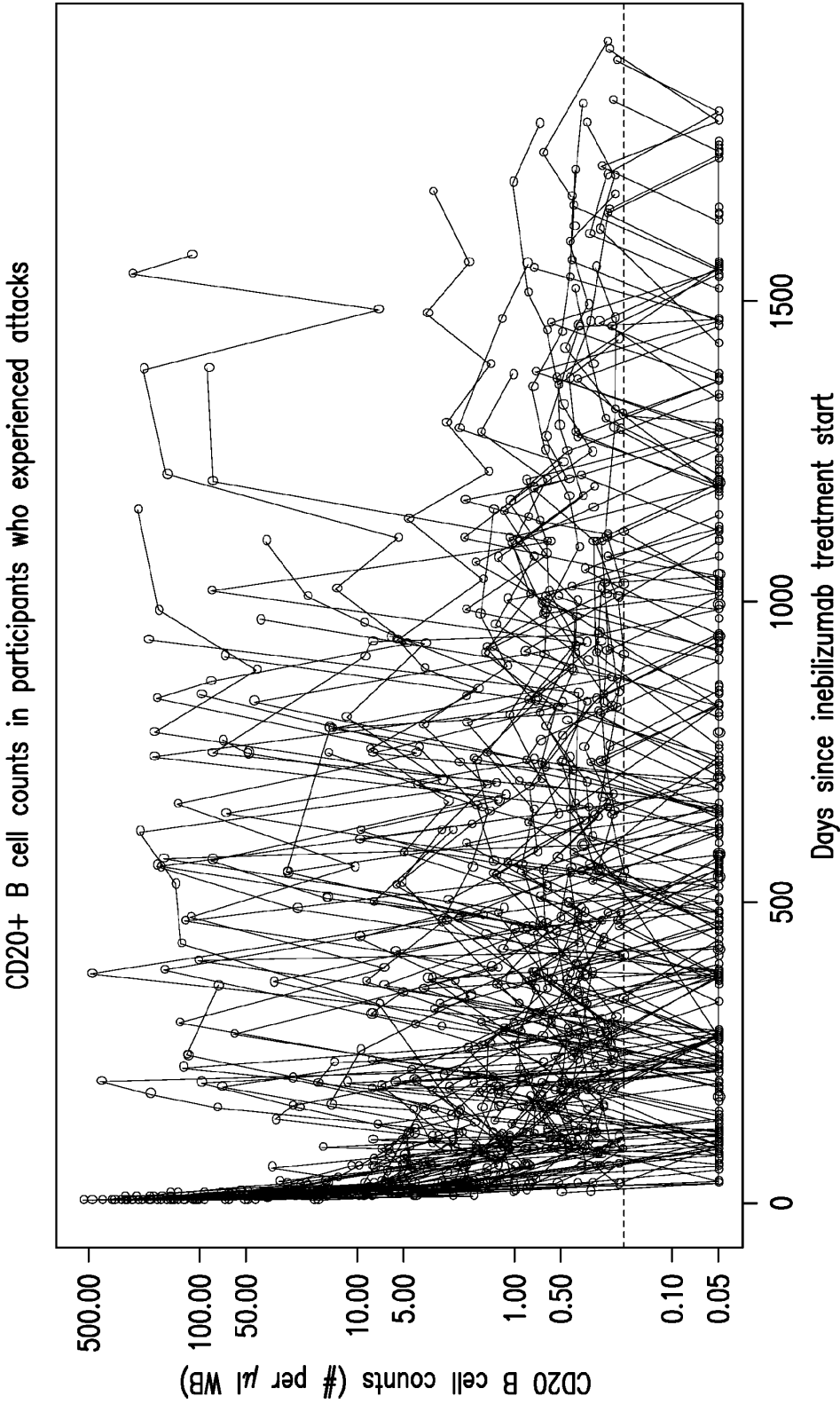


FIG.8A

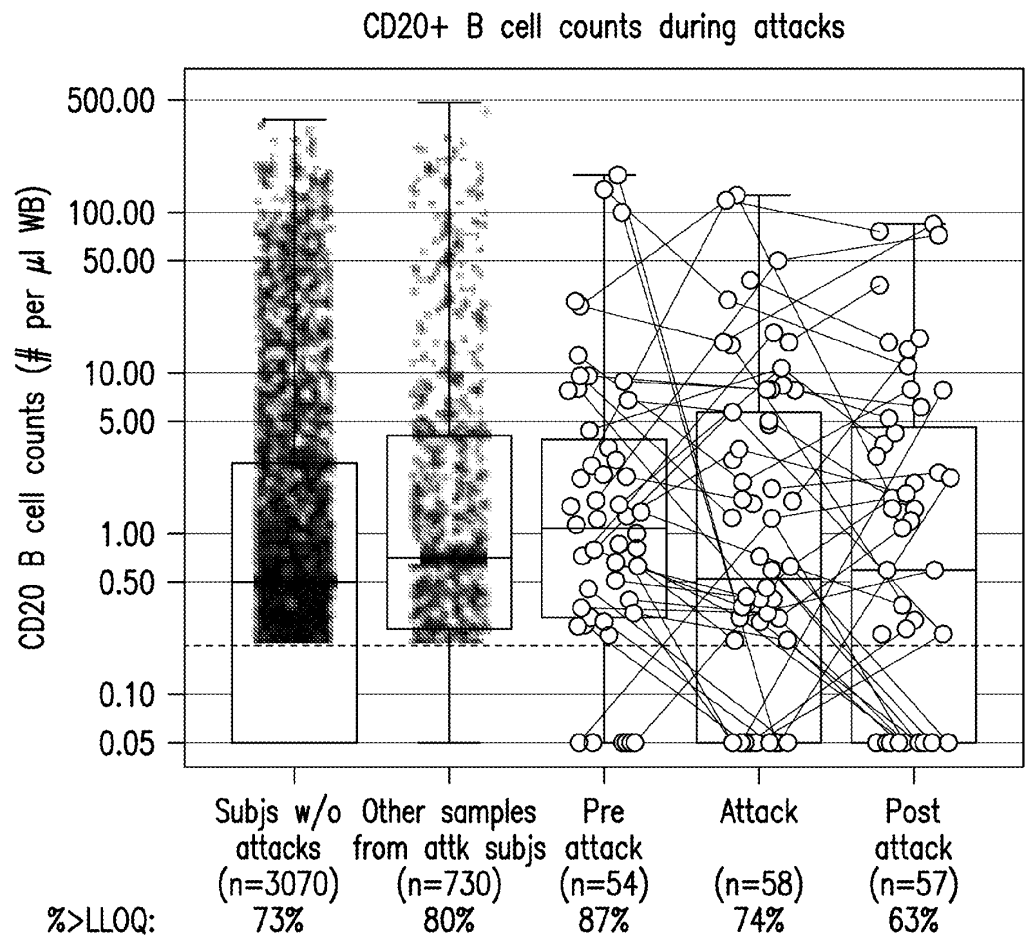


FIG.8B

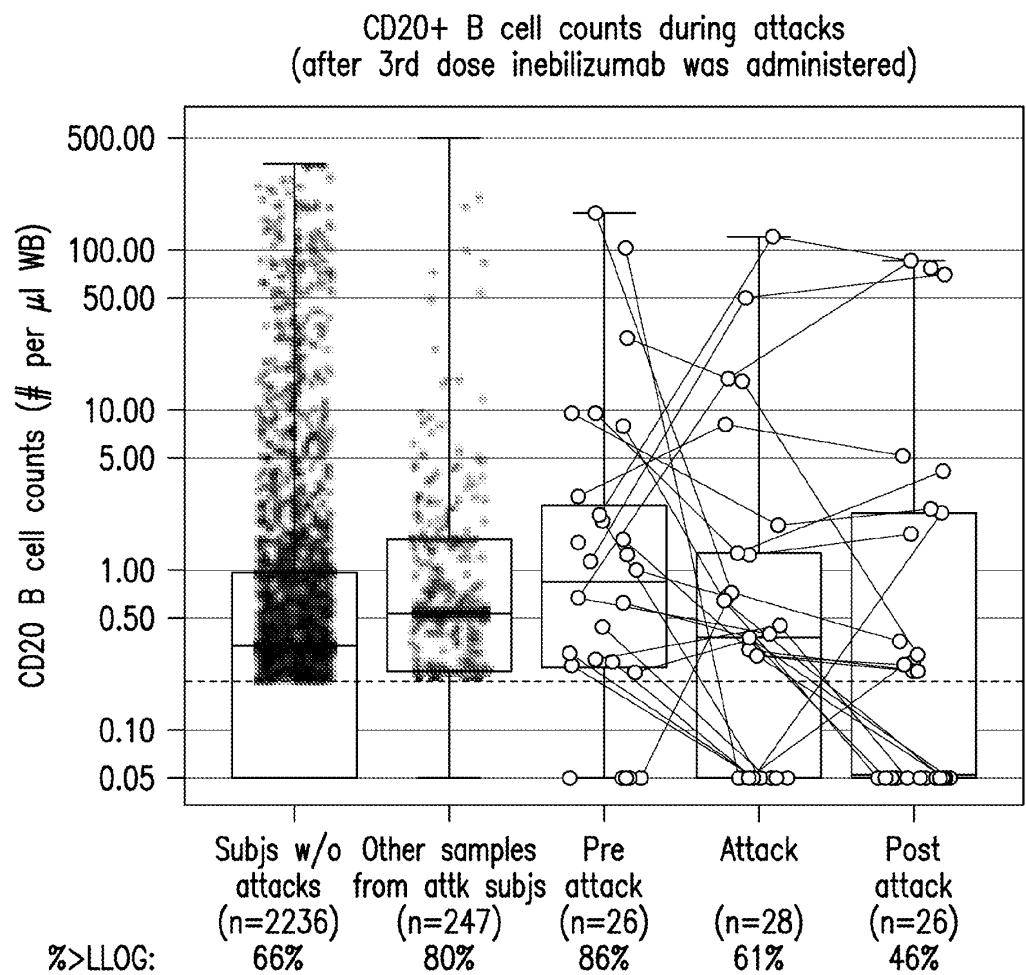
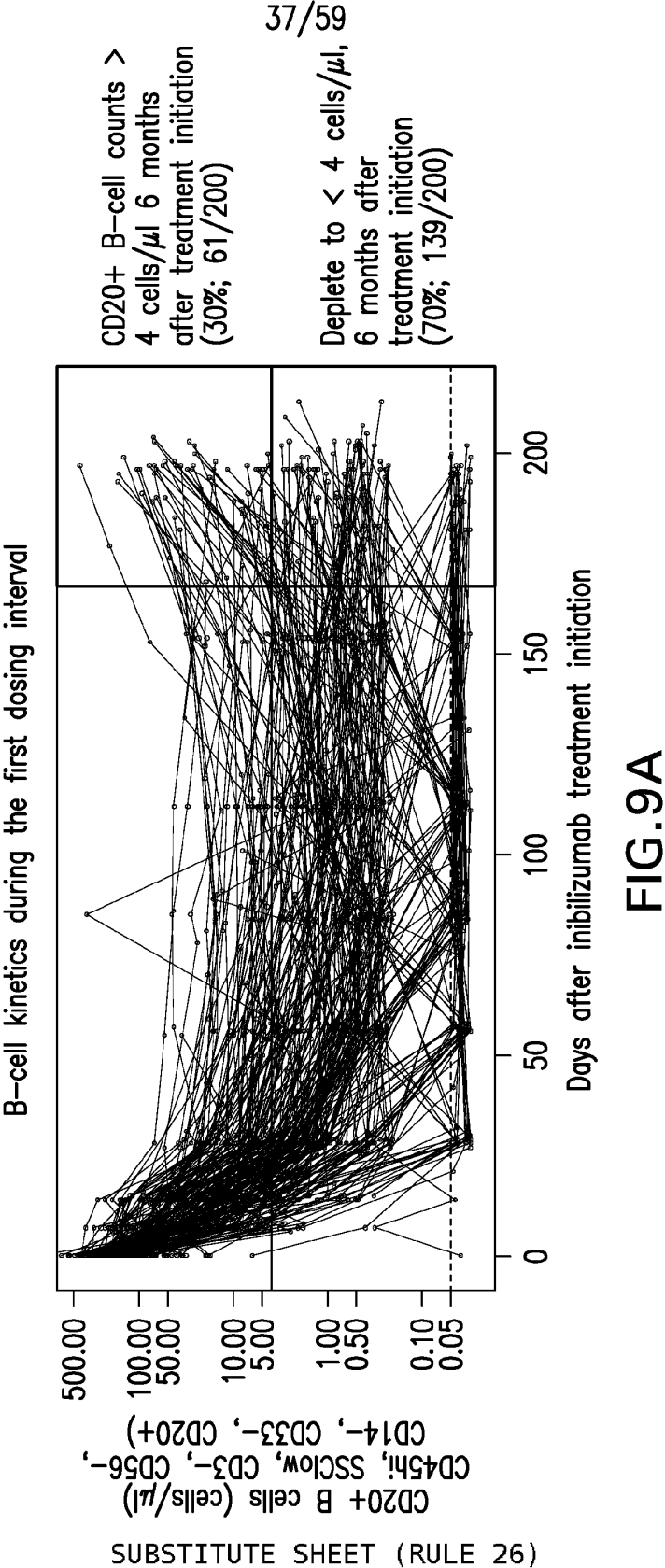
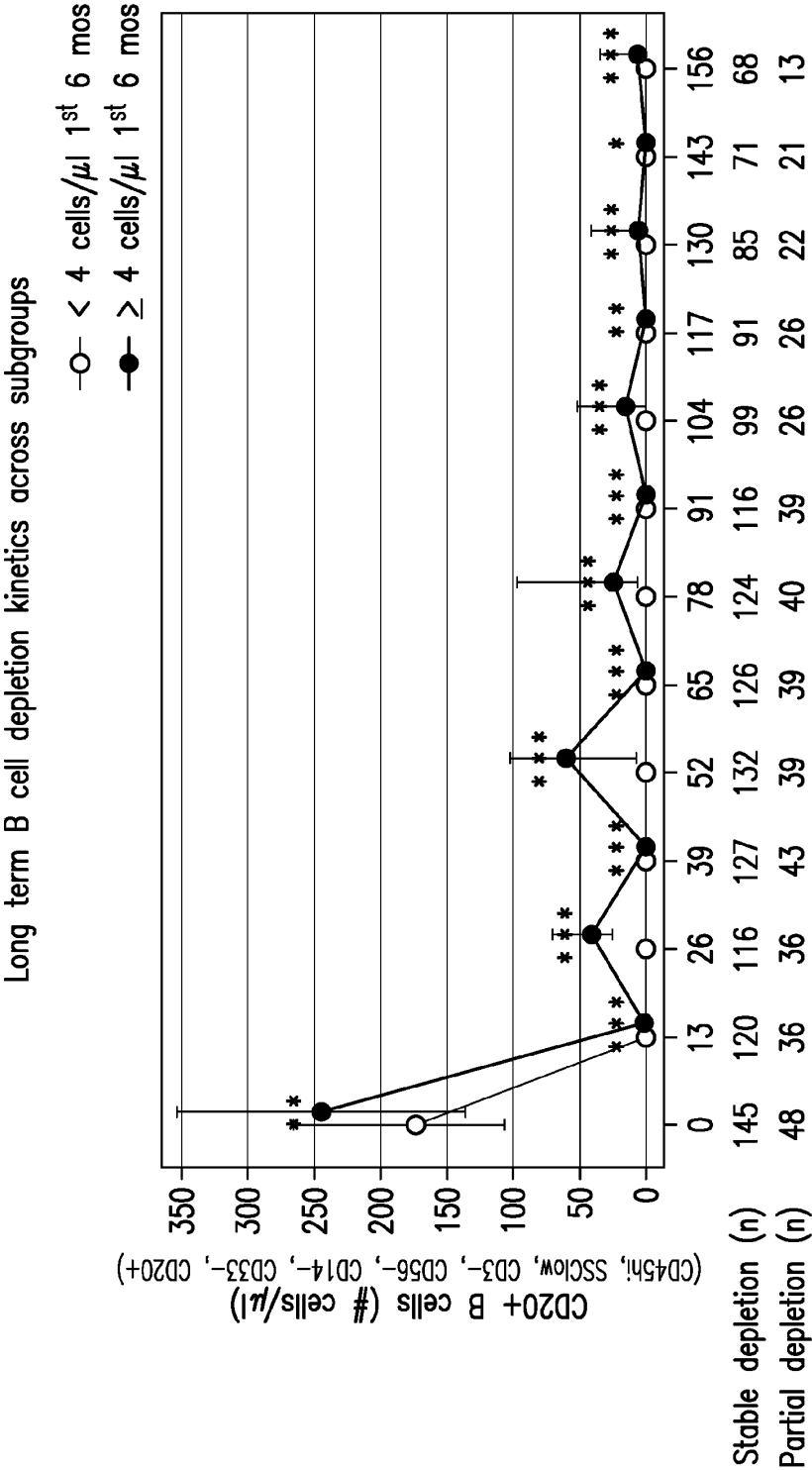


FIG.8C





(*p<0.05, **p<0.01, ***p<0.001, Mann–Whitney U Test)

FIG.9B

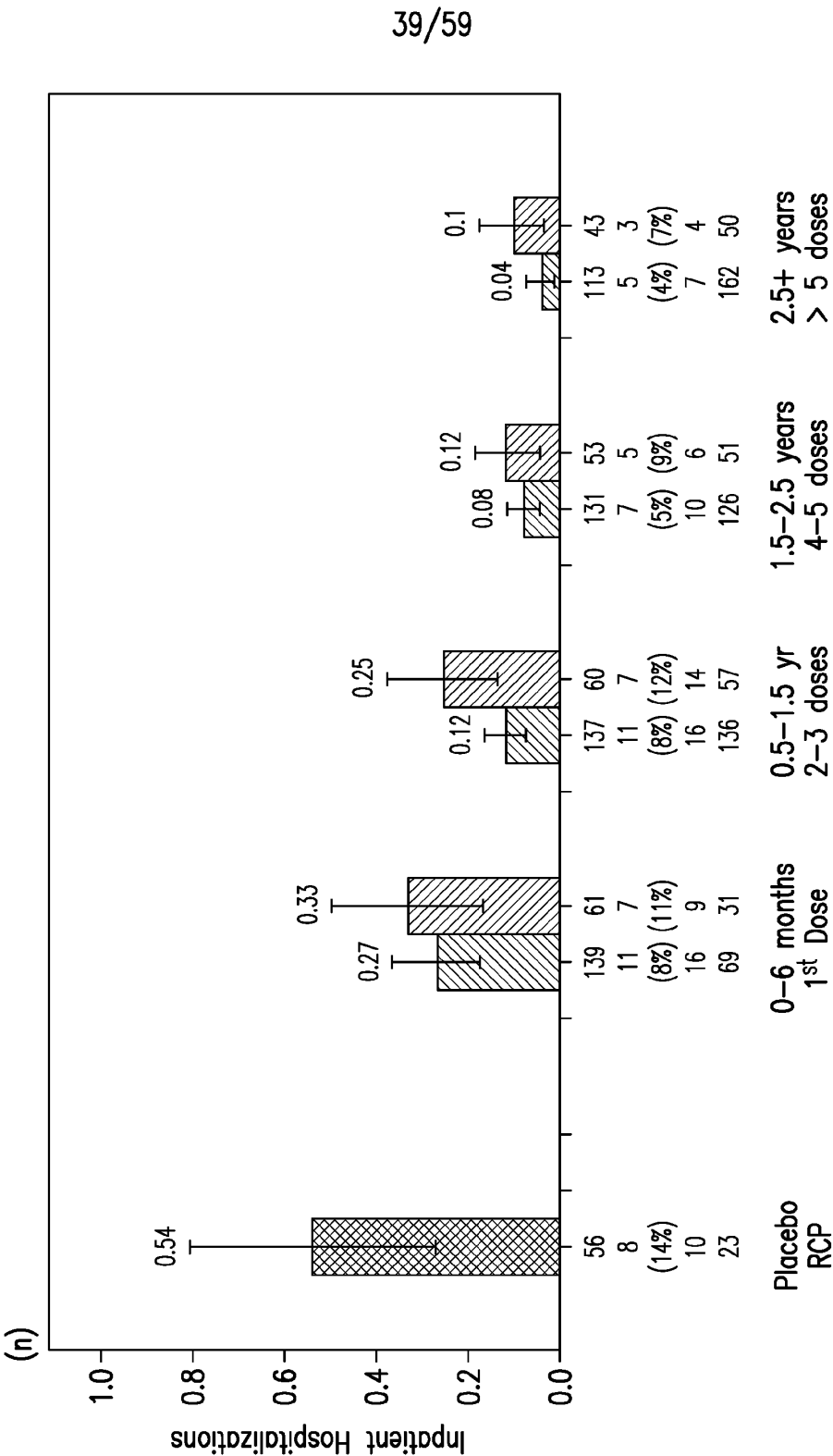


FIG.10

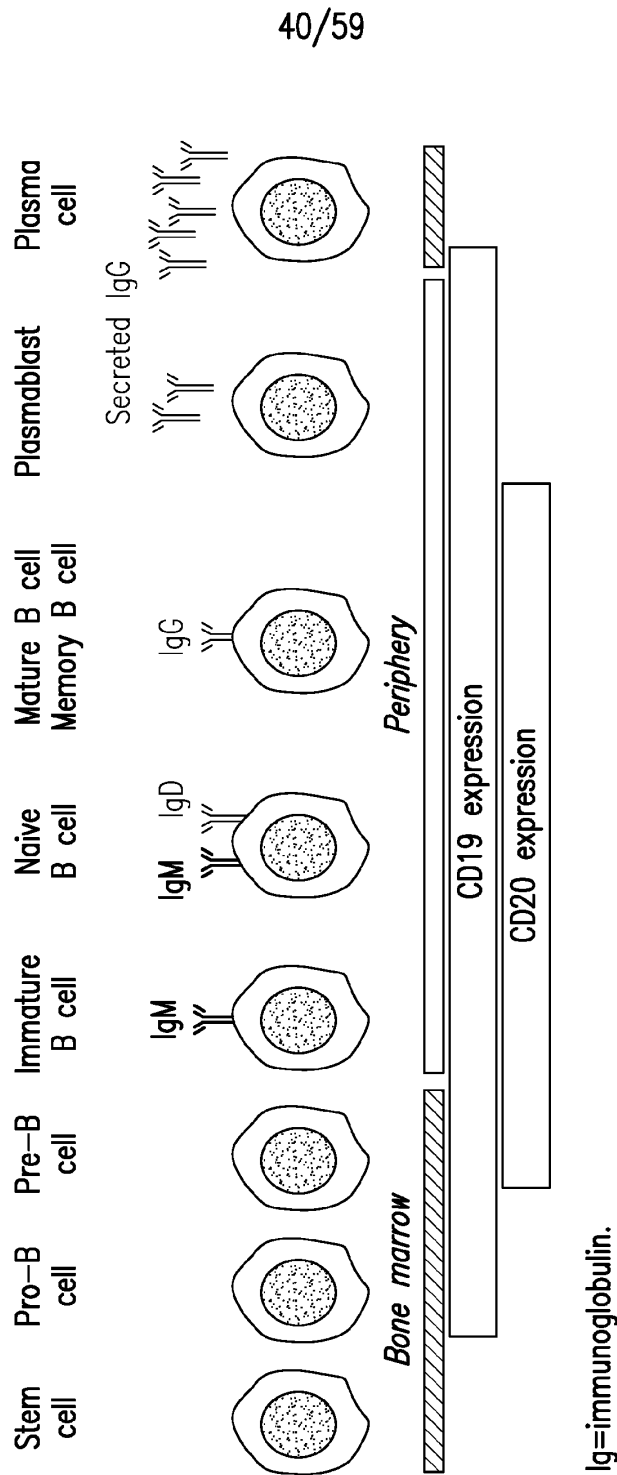


FIG.11

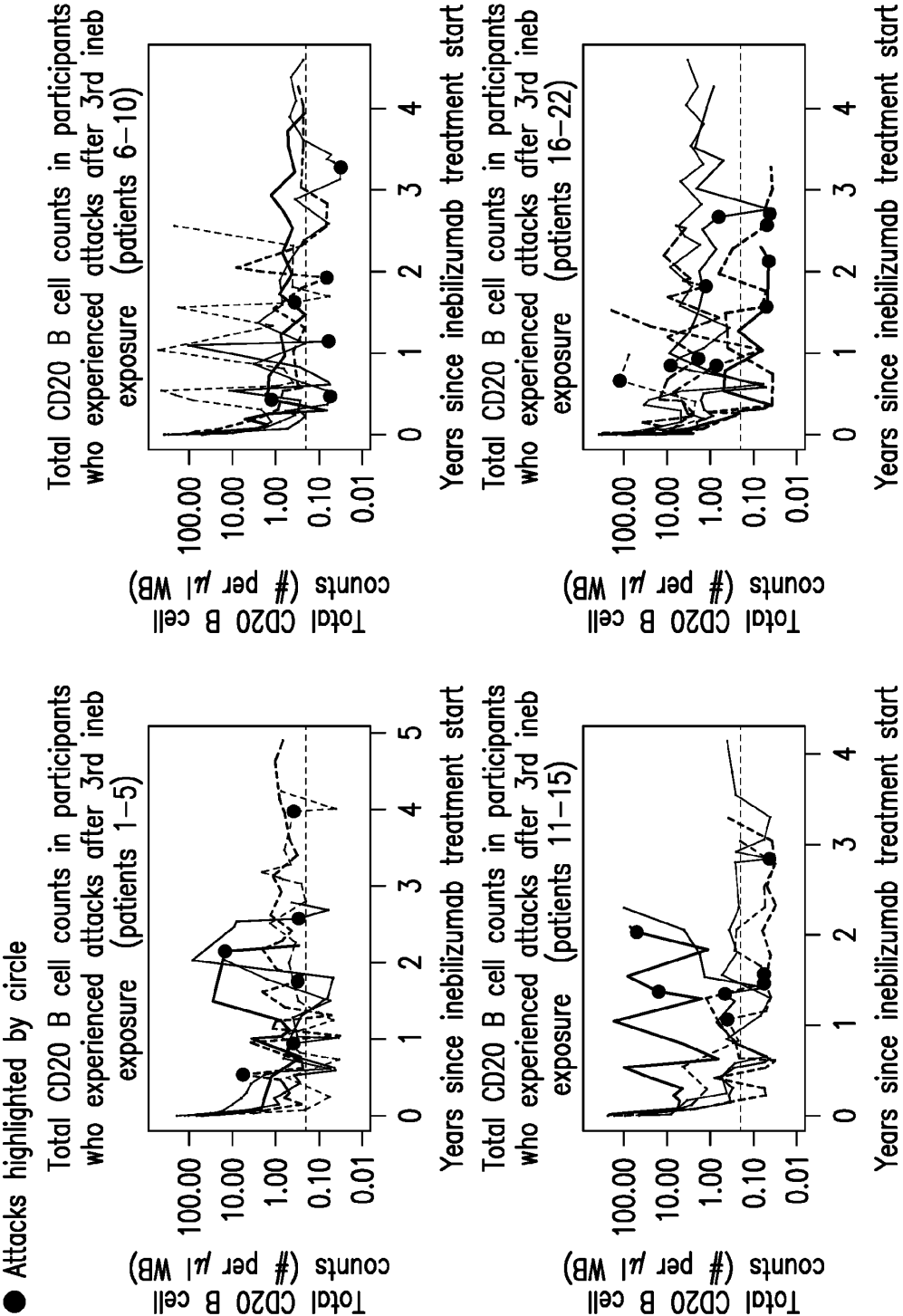


FIG.12A

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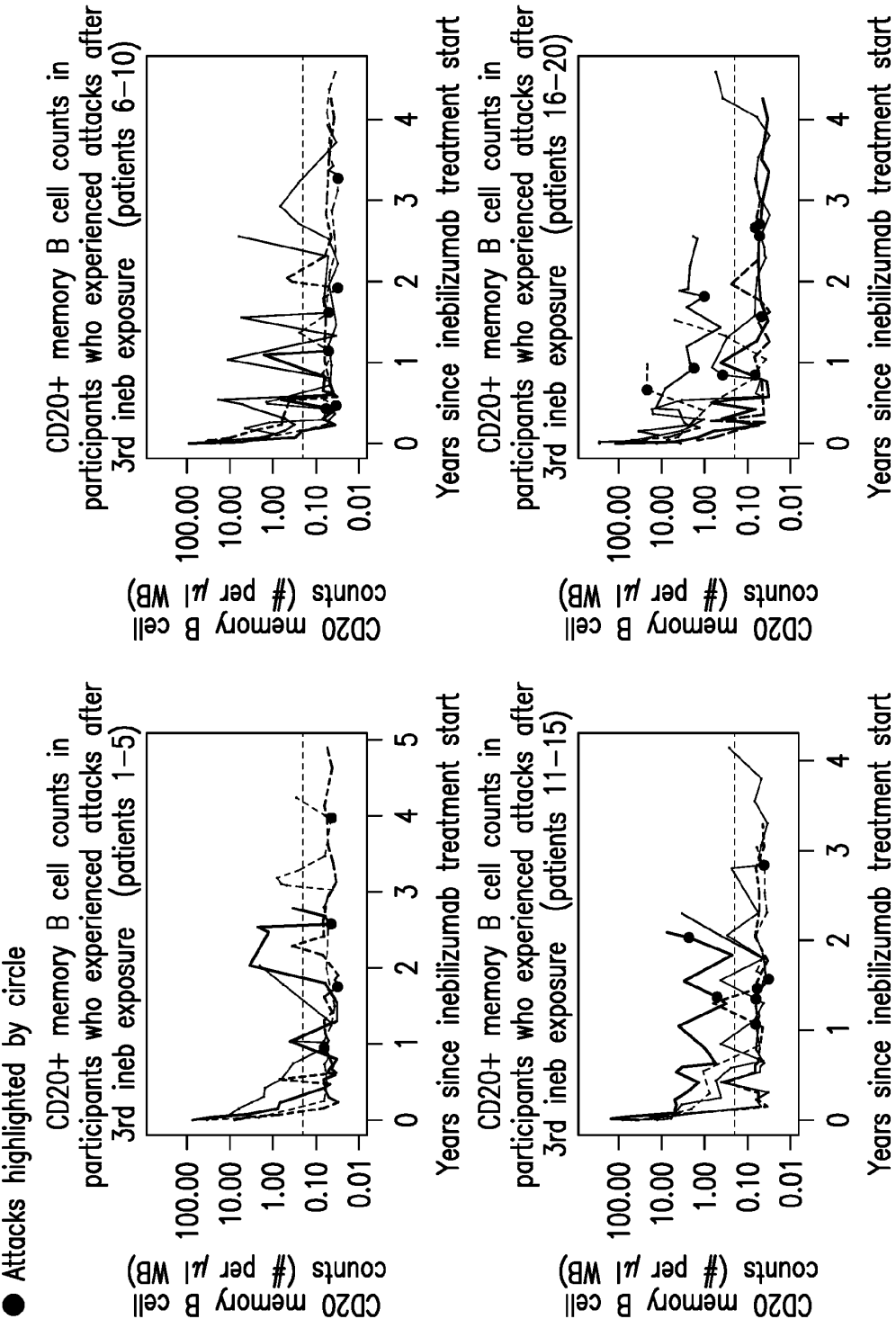


FIG.12B

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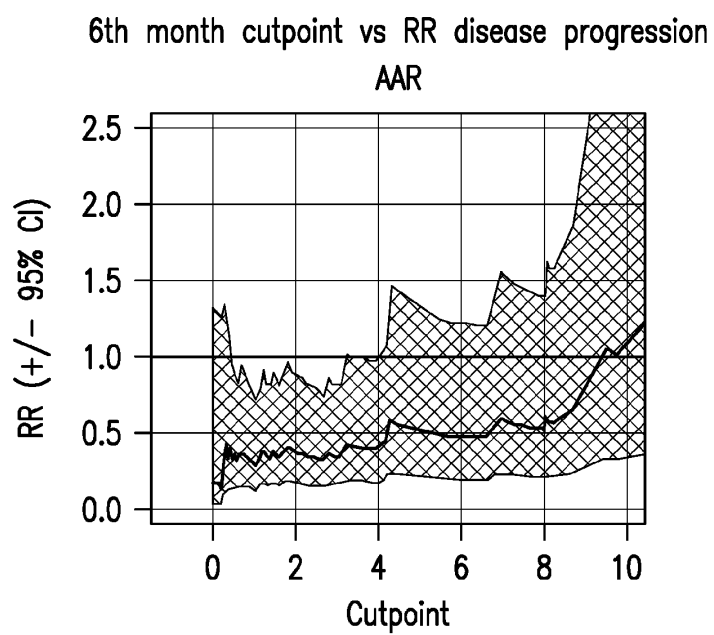


FIG.13A

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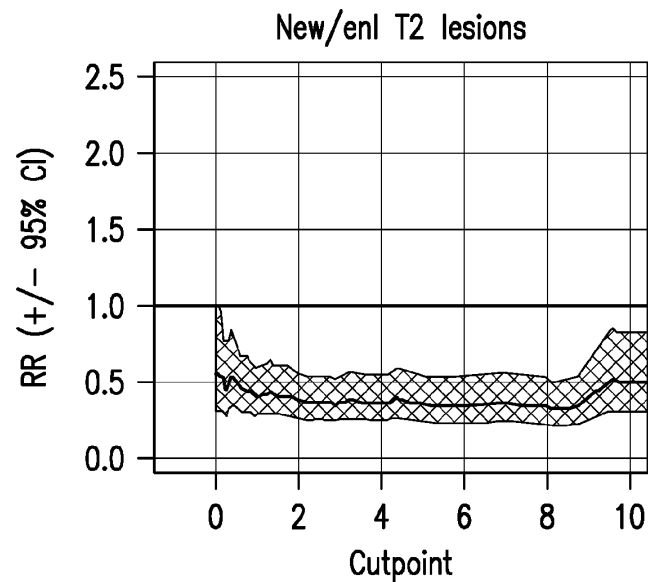


FIG.13B

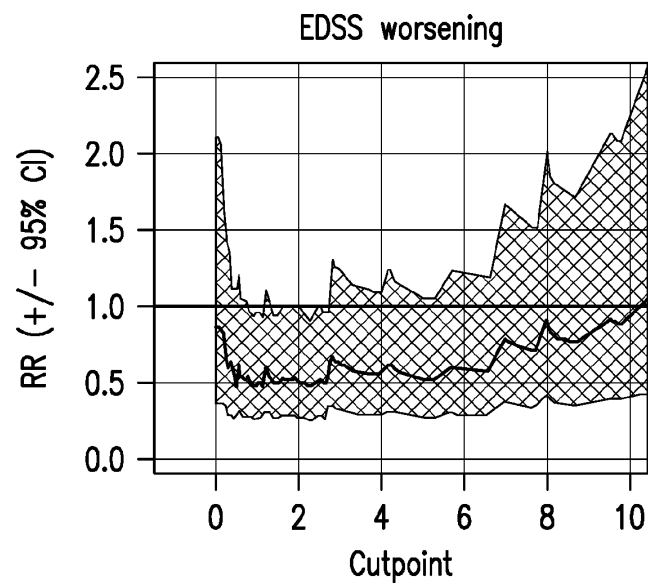


FIG.13C

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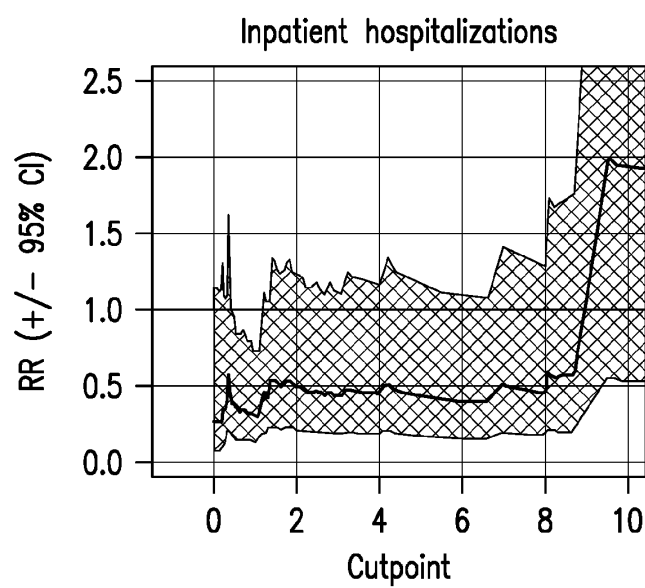


FIG. 13D

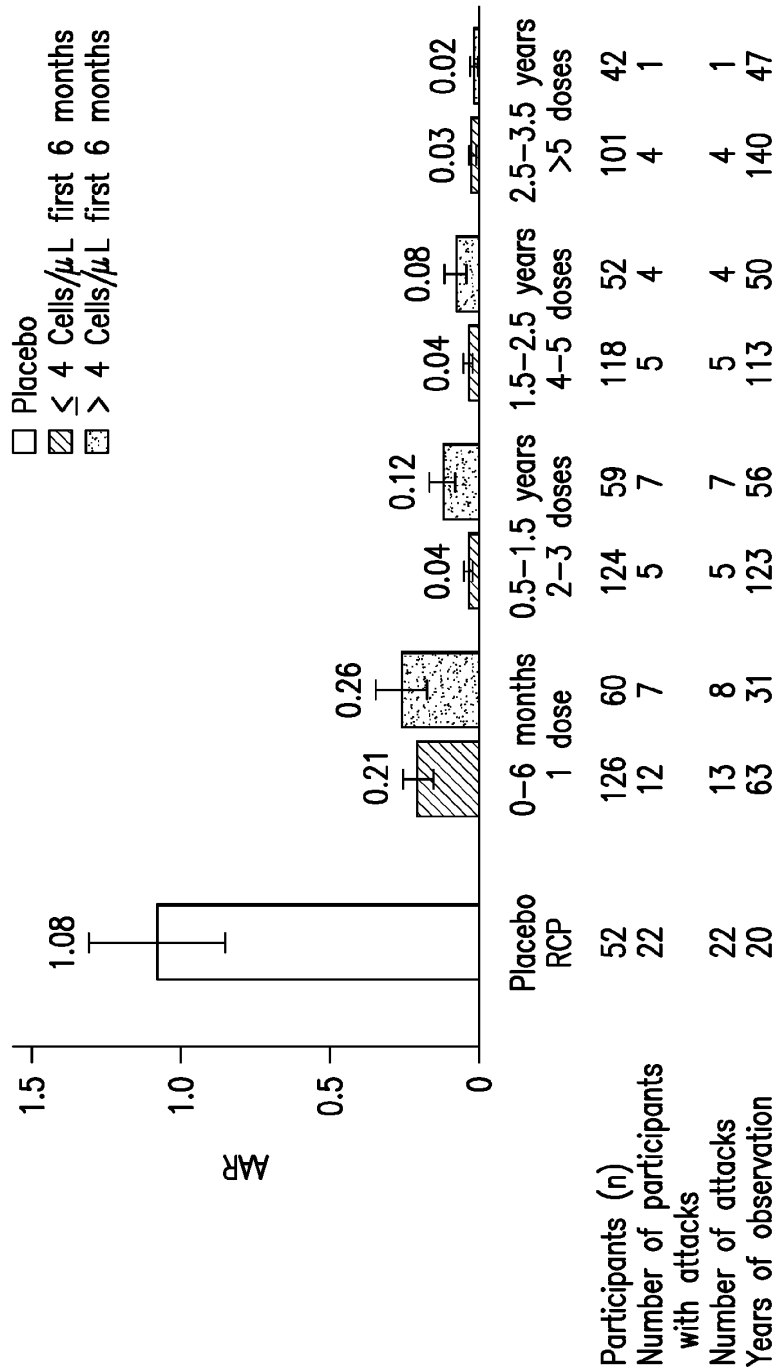


FIG. 14A

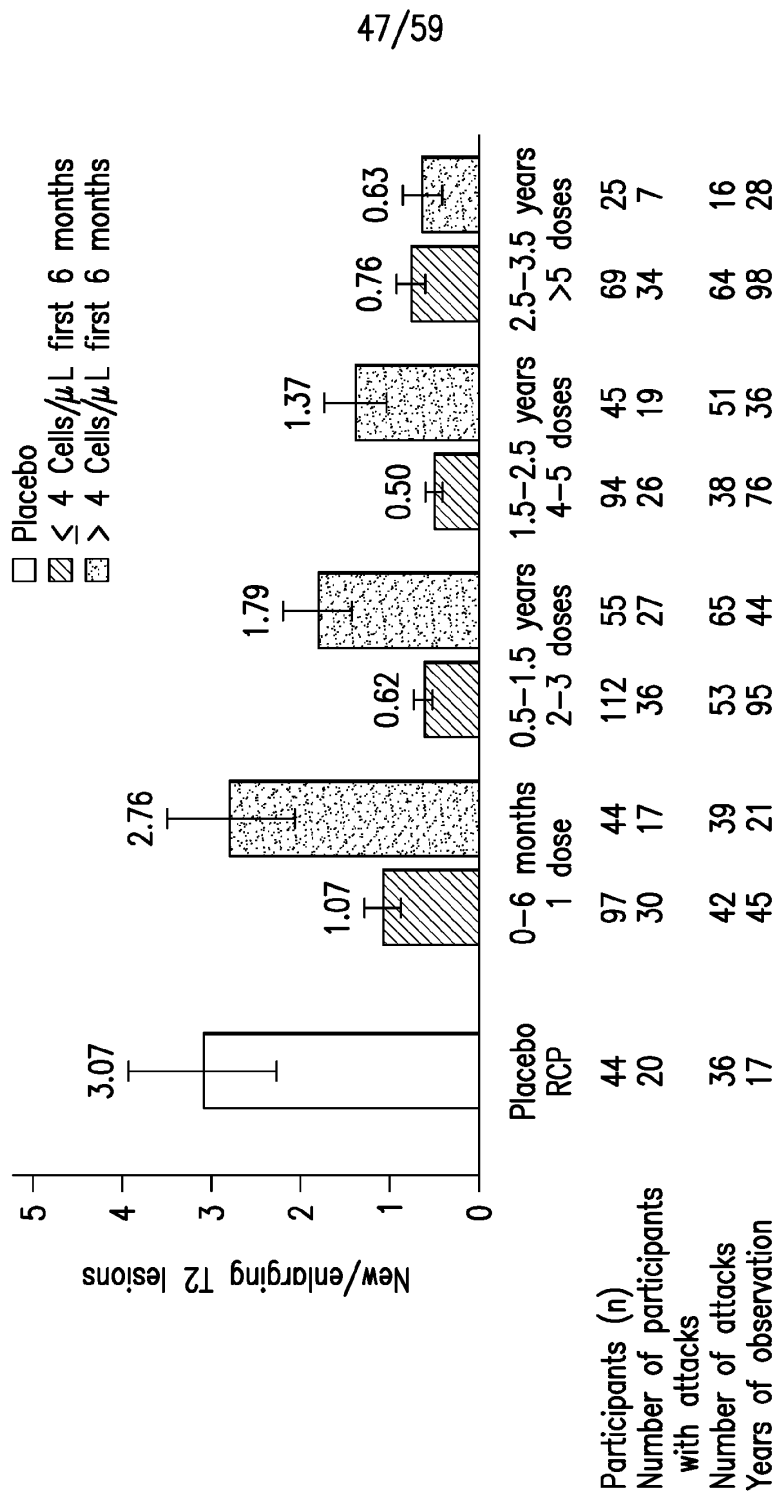


FIG.14B

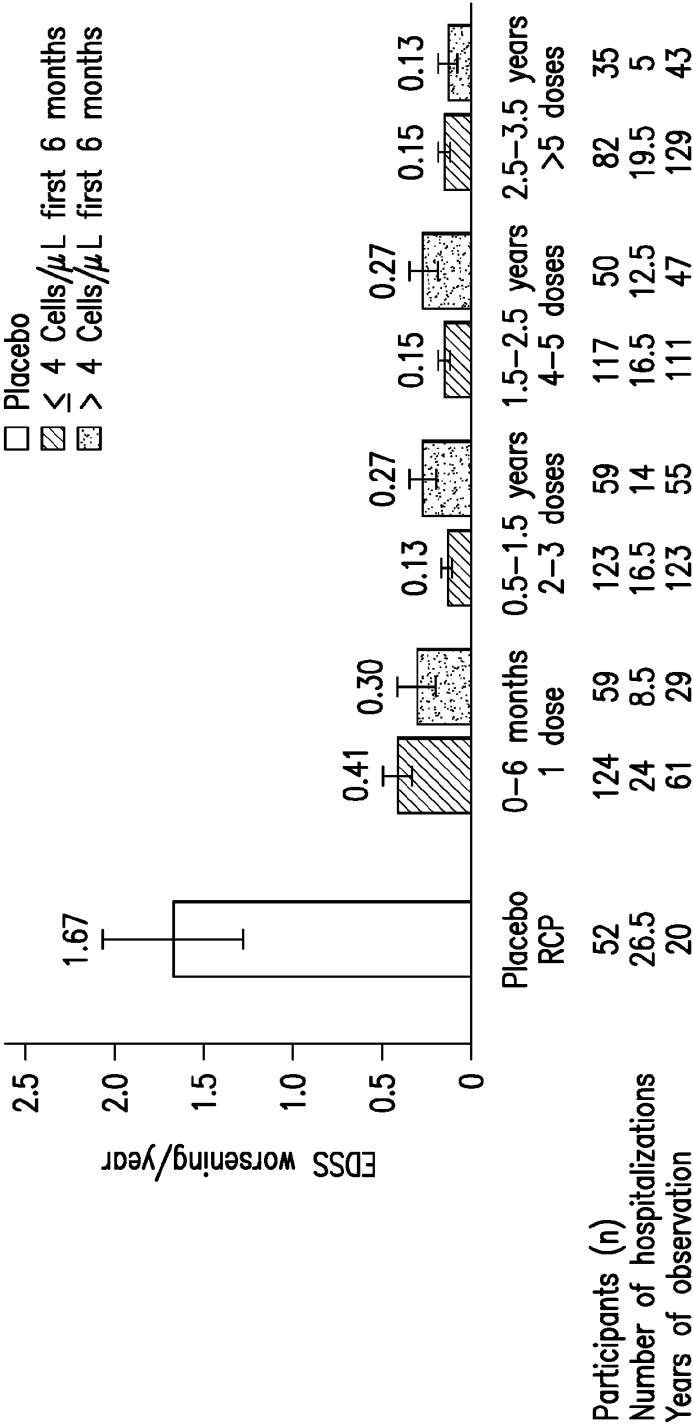


FIG.14C

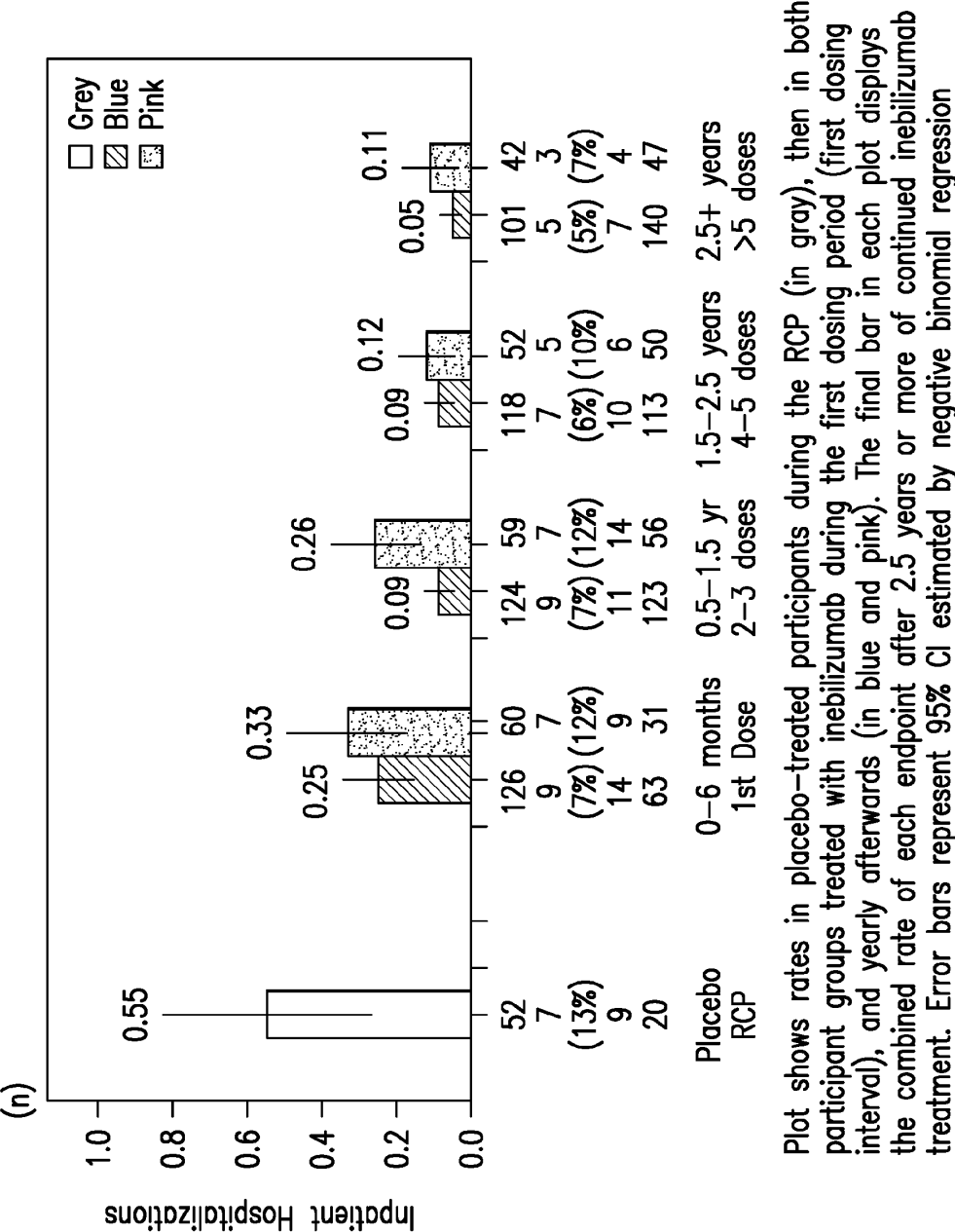


FIG.14D

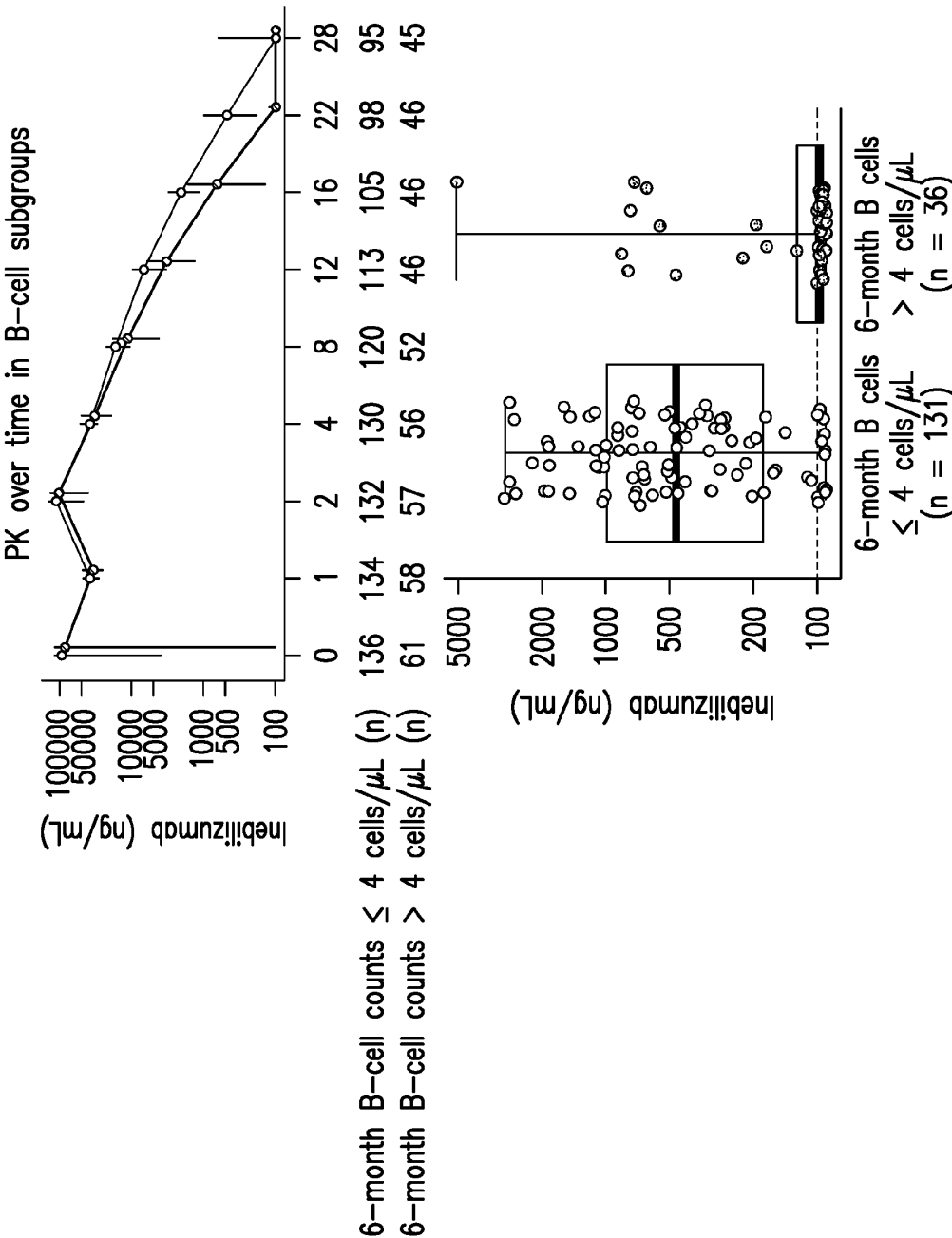


FIG.15

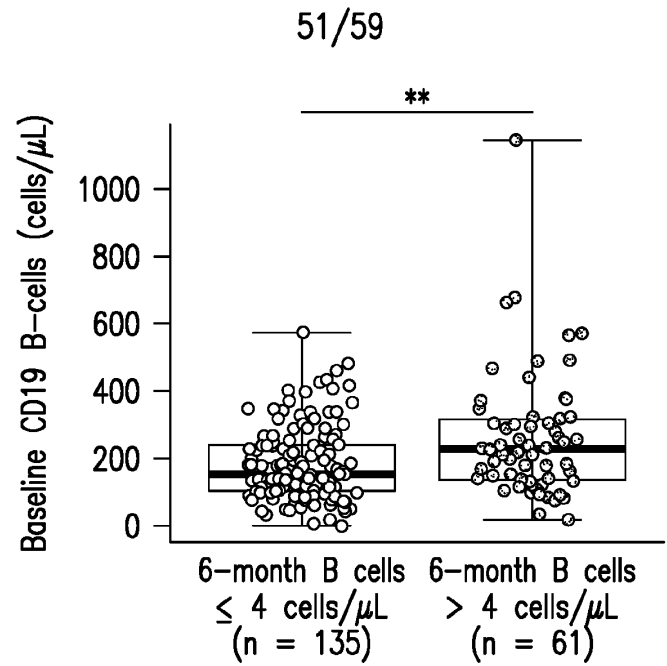


FIG.16A

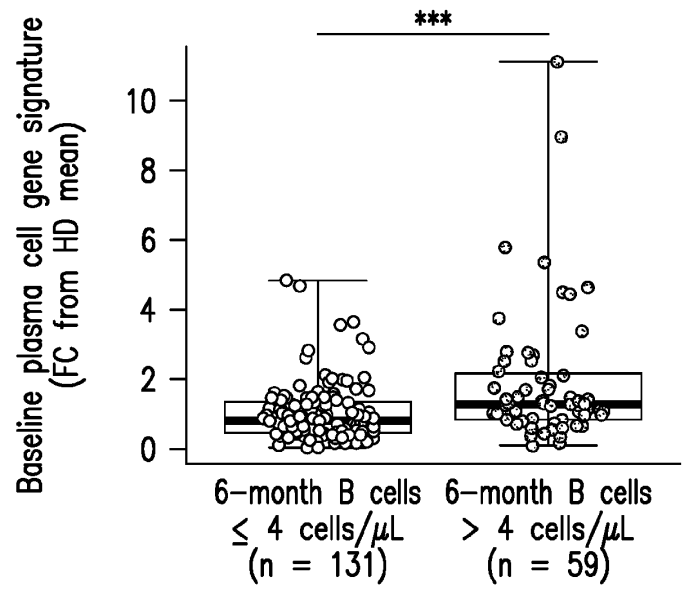


FIG.16B

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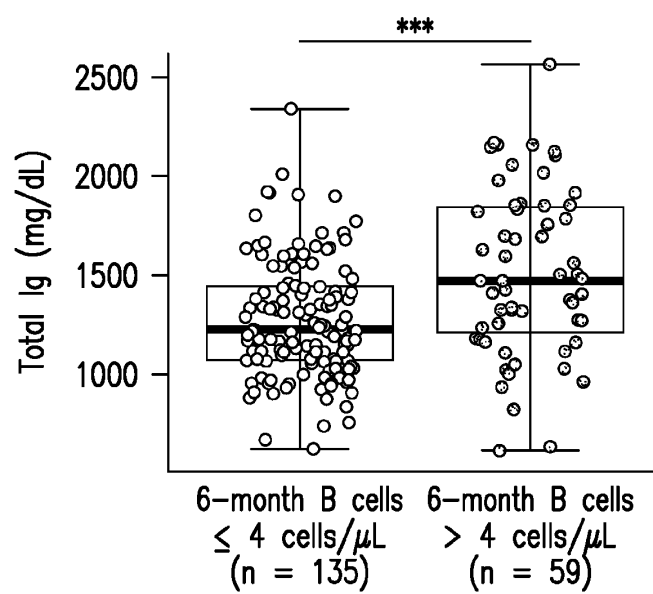


FIG.16C

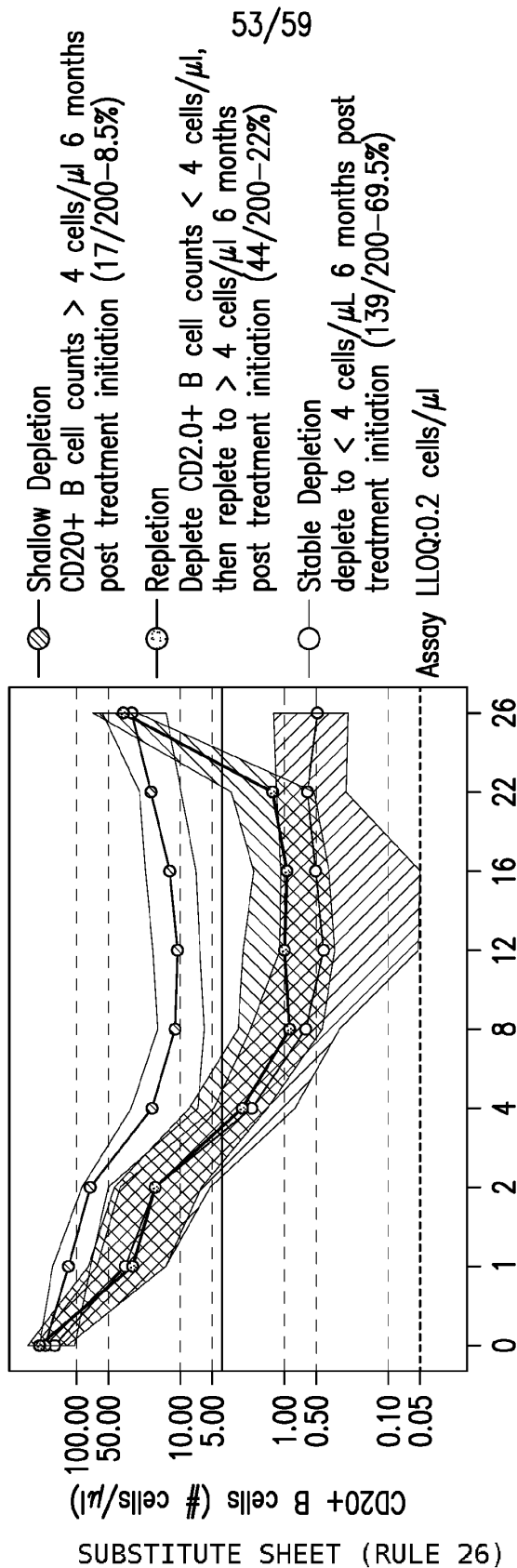


FIG.17A

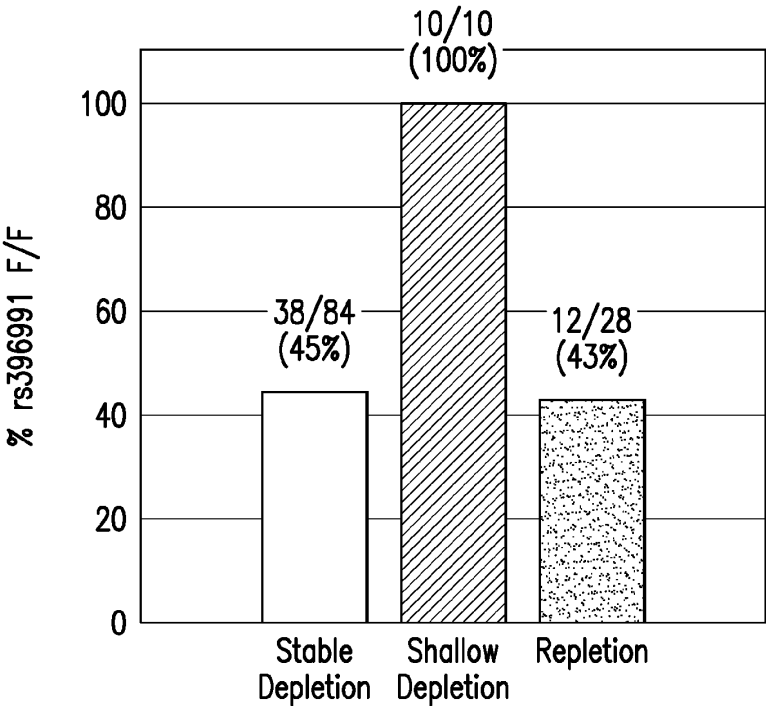


FIG.17B

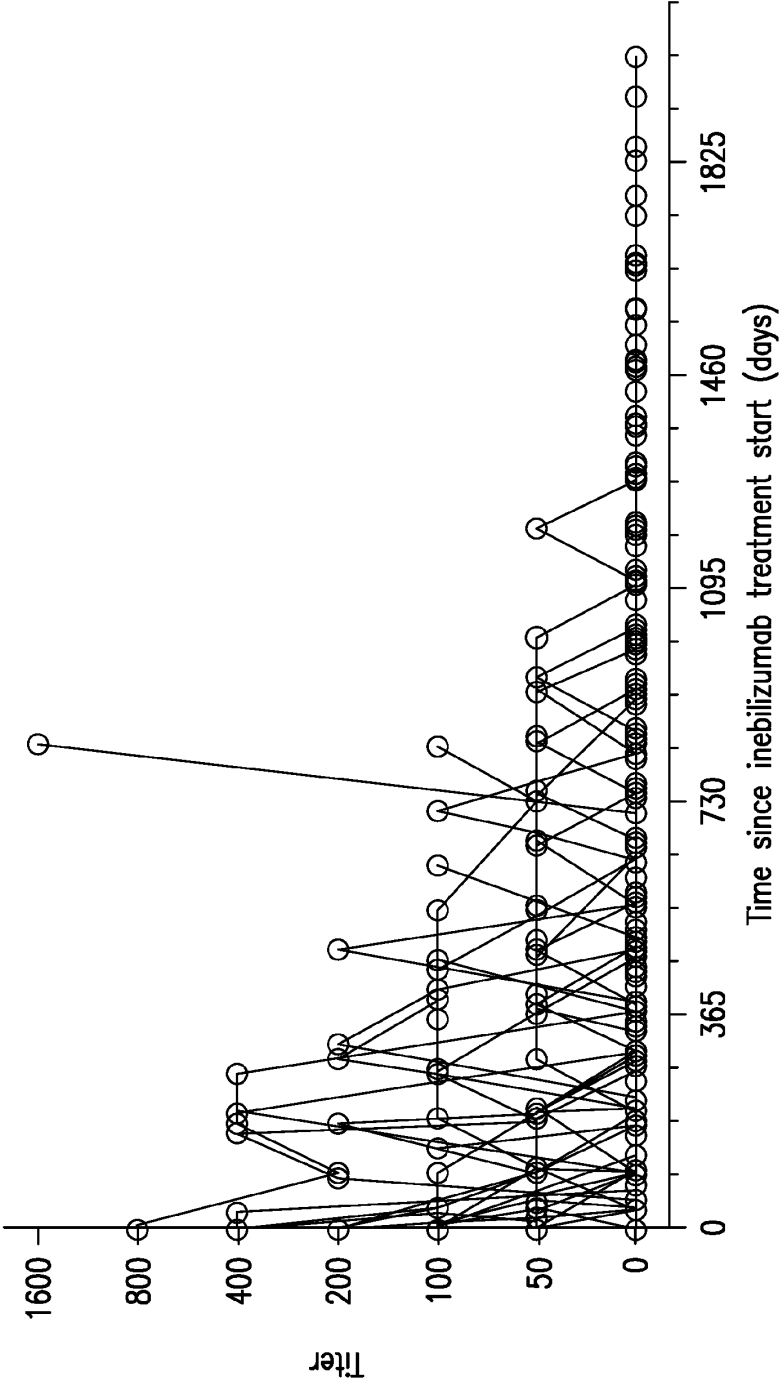


FIG.18A

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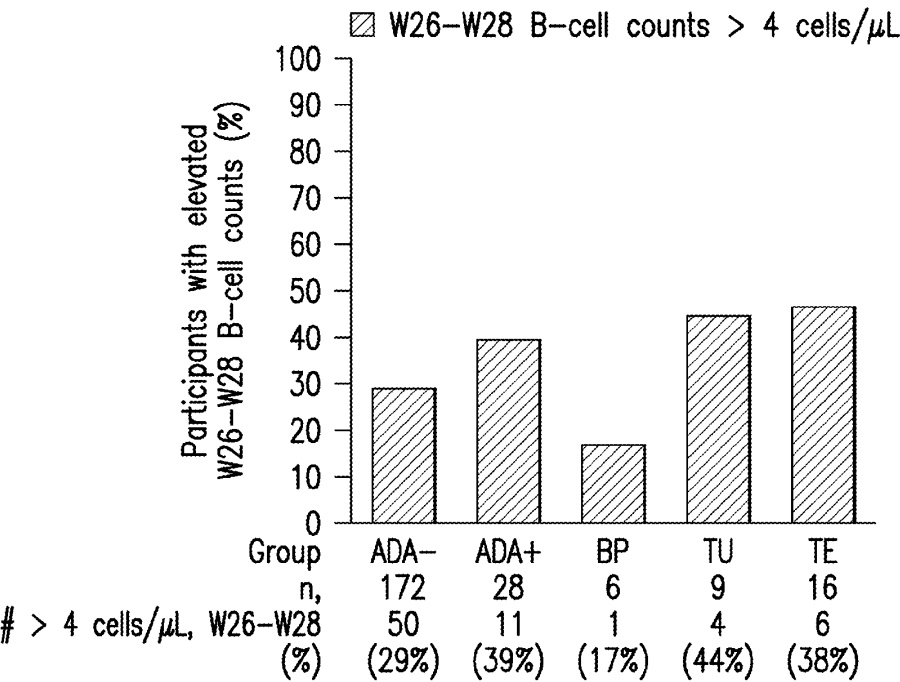


FIG.18B

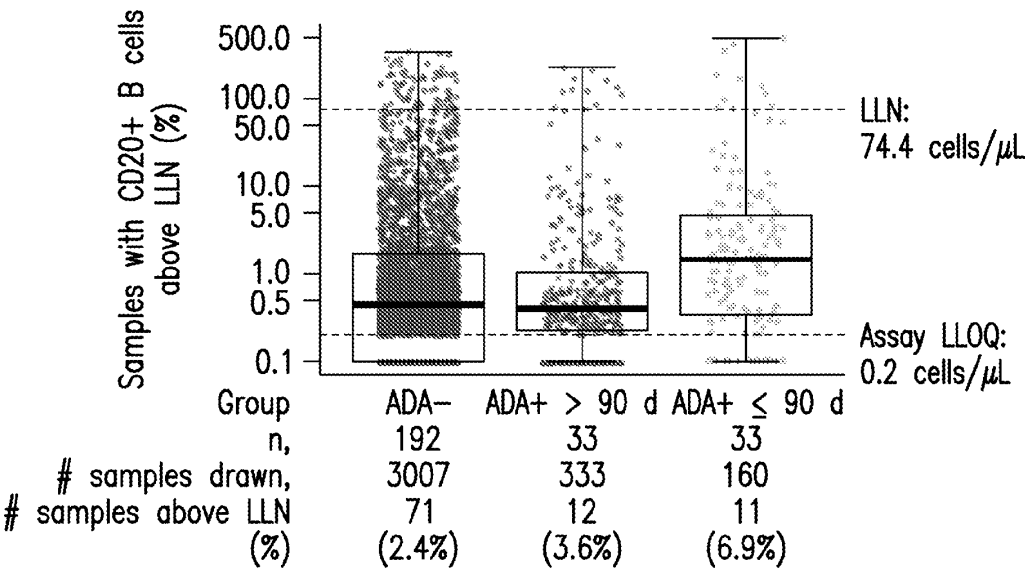
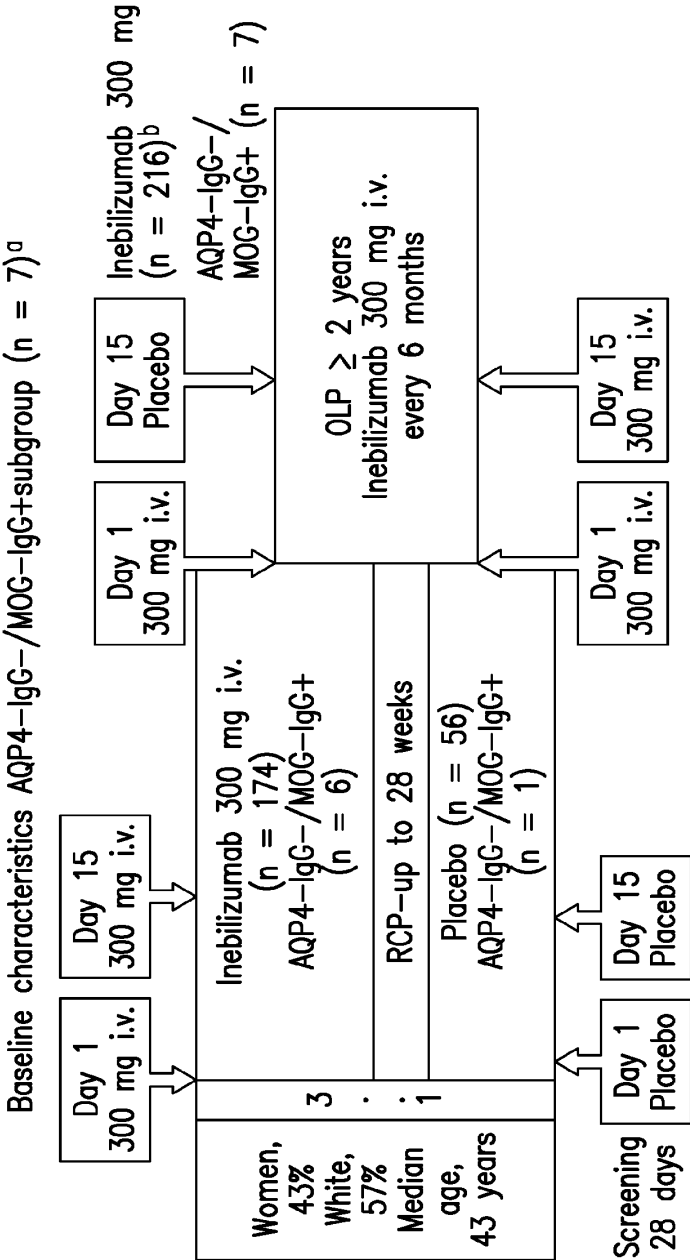


FIG.18C



^a Of 231 subjects randomized in the study, 17 (7.4%) were AQP4-IgG-, and 7 of these subjects (41%) were MOG-IgG+.

^b n = 165 from inebilizumab arm plus n = 51 from the placebo arm in the RCP.

Subjects received study drug according to their randomized allocation on days 1 and 15 of the RCP. To preserve masking in the OLP, those randomized to inebilizumab received inebilizumab on day 1 and placebo on day 15, and those randomized to placebo received inebilizumab on both days 1 and 15. Thereafter all subjects received inebilizumab every 26 weeks.

AQP4, aquaporin-4; Ig, immunoglobulin; i.v. intravenous; MOG, myelin oligodendrocyte glycoprotein; OLP, open-label period; RCP, randomized controlled period.

FIG.19A

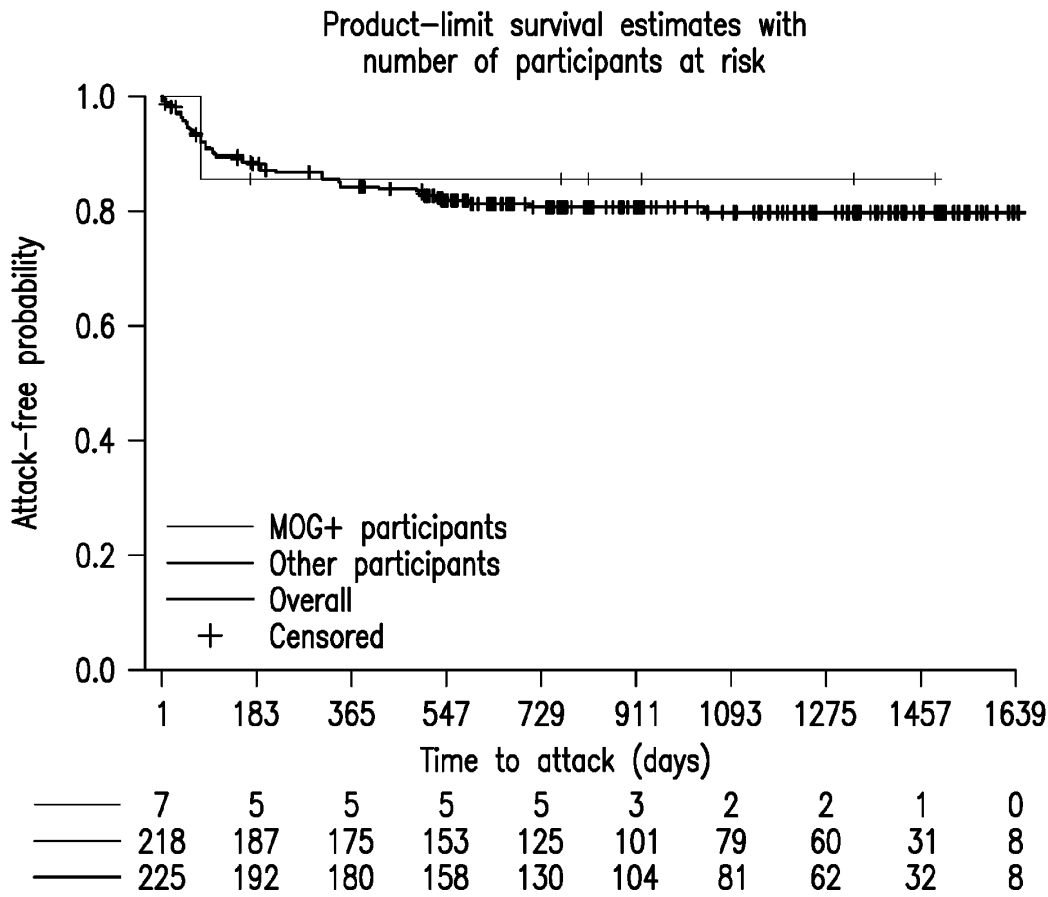
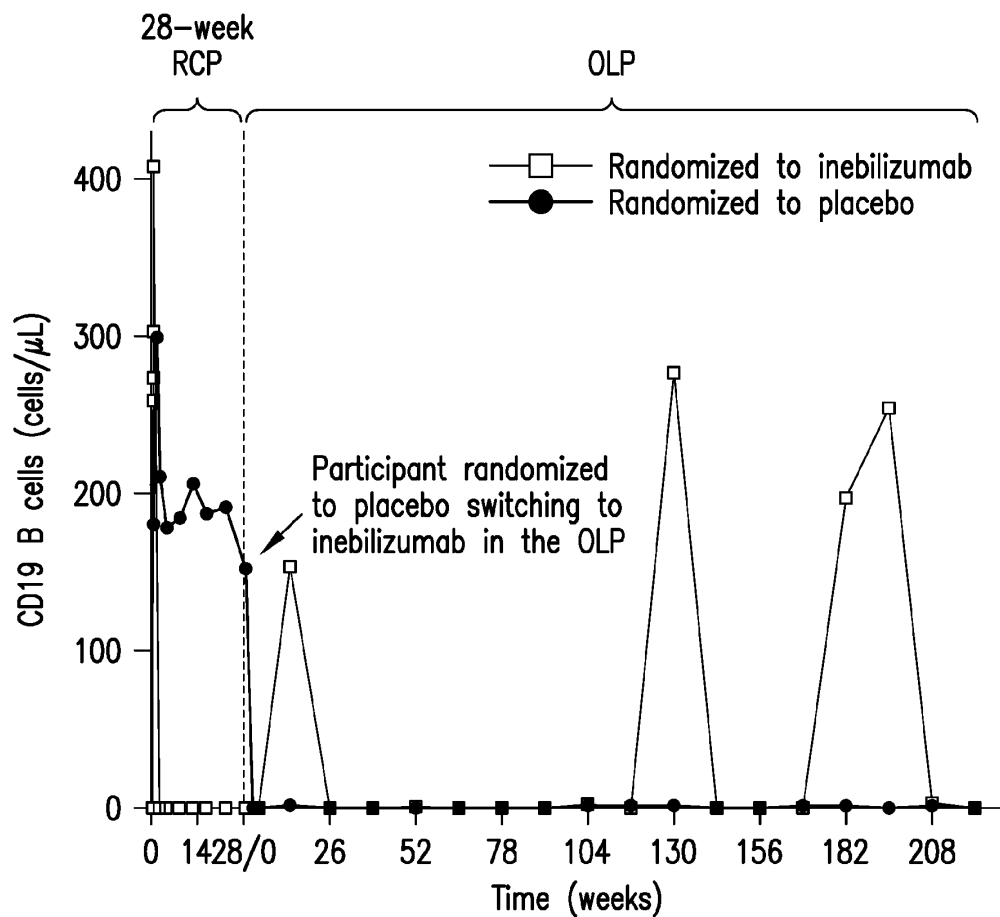


FIG.19B



Inebilizumab 300 mg was administered on days 1, 15 and 197 and every 26 weeks thereafter to those randomized to inebilizumab who continued in the OLP. Those randomized to placebo who continued in the OLP received inebilizumab on days 197 and 211 and every 26 weeks thereafter.

AQP4, aquaporin-4; Ig, immunoglobulin; MOG, myelin oligodendrocyte glycoprotein; OLP, open-label period; RCP, randomized controlled period

FIG. 19C