The Safety And Efficacy Of Inebilizumab In Those With Previous Rituximab Exposure

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Disclosures

M. Levy reports consulting fees from Viela Bio, Alexion and Genentech.

E. Flanagan is a site principal investigator in the N-MOmentum trial funded by MedImmune/Viela Bio. He receives no personal compensation and just receives reimbursement for the research activities related to the trial.

In the past 12 months, Bruce Cree has received personal compensation for consulting from Alexion, Atara, Autobahn, EMD Serono, Novartis, Sanofi, Therini and TG Therapeutics and received research support from Genentech.

D. She, E. Katz and J. Ratchford are employees of Viela Bio.

Background

- The B-cell–depleting agent rituximab (anti-CD20) is commonly used based on empiric data to prevent attacks in patients with neuromyelitis optica spectrum disorder (NMOSD)
- Inebilizumab, which targets and depletes CD19-expressing B cells, received approval from the US Food and Drug Administration for treatment of NMOSD based on primary results from the randomized, placebo-controlled, phase 2/3 N-MOmentum trial[1]
- This post hoc analysis of N-MOmentum assessed inebilizumab efficacy and tolerability in patients previously treated with rituximab

1. Cree BAC, *et al*. *Lancet* 2019;394:1352–63

Study design, methods and objectives

- N-MOmentum was a multicenter, double-blind, randomized, placebo-controlled, phase 2/3 study assessing the efficacy and safety of inebilizumab in patients with NMOSD
  - Patients with NMOSD were randomized 3:1 to inebilizumab or placebo monotherapy for 28 weeks or up to attack occurrence
  - Complete methodology was previously published[1]
- Adjudicated attacks, secondary efficacy outcomes, and treatment-emergent adverse events were assessed by prior rituximab use during a 6-month randomized control period and open-label extension

Objective	**To determine the safety and efficacy of inebilizumab in N-MOmentum trial participants with NMOSD previously treated with rituximab.**

NMOSD, neuromyelitis optica spectrum disorder, OLP; open label period,

1. Cree BAC, *et al*. *Lancet* 2019;394:1352–63.

Table 1. Demographics and Baseline Characteristics of Participants in N-MOmentum With Prior Rituximab Use

Parameter	Randomized control group		Overall (N=17)
	Inebilizumab (n=13)	Placebo (n=4)	
Age, median (IQR), y	47 (32-50)	38 (29-46)	46 (31-49)
Women, n (%)	13 (100)	3 (75)	16 (94)
White or Asian, n (%)	4 (31)	1 (25)	5 (29)
AQP4-IgG seropositive	12 (92)	4 (100)	16 (94)
B-cell count (IQR)	342.6 (181.2-319.3)	198.9 (67.8-330.1)	308.7 (171.8-319.3)
Time between last rituximab dose and first dose of inebilizumab, median (range), y	1.5 (0.8-4.4)	1.3 (0.9-3.1)	1.5 (0.8-4.4)
Rituximab doses, median (range), n	1 (1-11)	1 (1-2)	1 (1-11)
Attack while on rituximab, n (%)	5 (38)	2 (50)	7 (41)
AAR before first dose of inebilizumab (range)	0.728 (0.342-1.886)	0.924 (0.401-1.875)	0.779 (0.342-1.886)

AQP4, aquaporin-4; AAR, annualized attack rate; IgG, immunoglobulin; IQR, interquartile range.

Figure 1. Attack History for N-MOmentum Participants with Prior Rituximab Usage

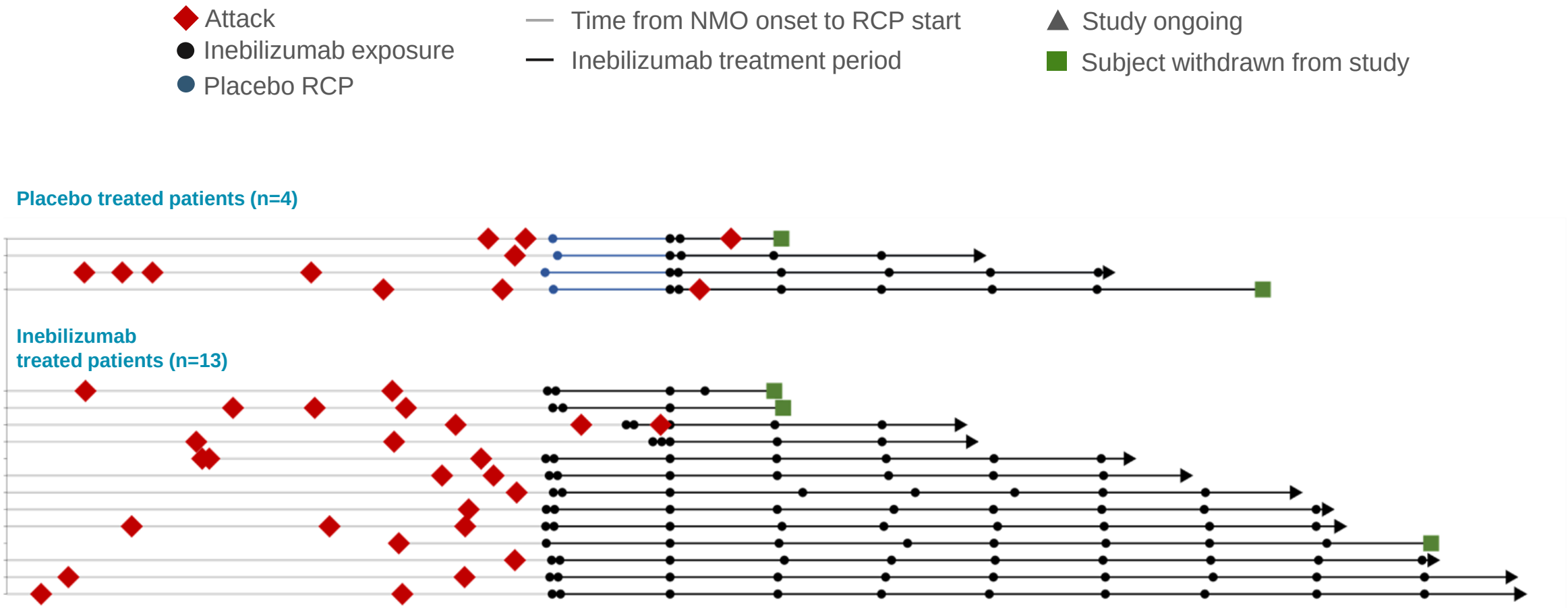
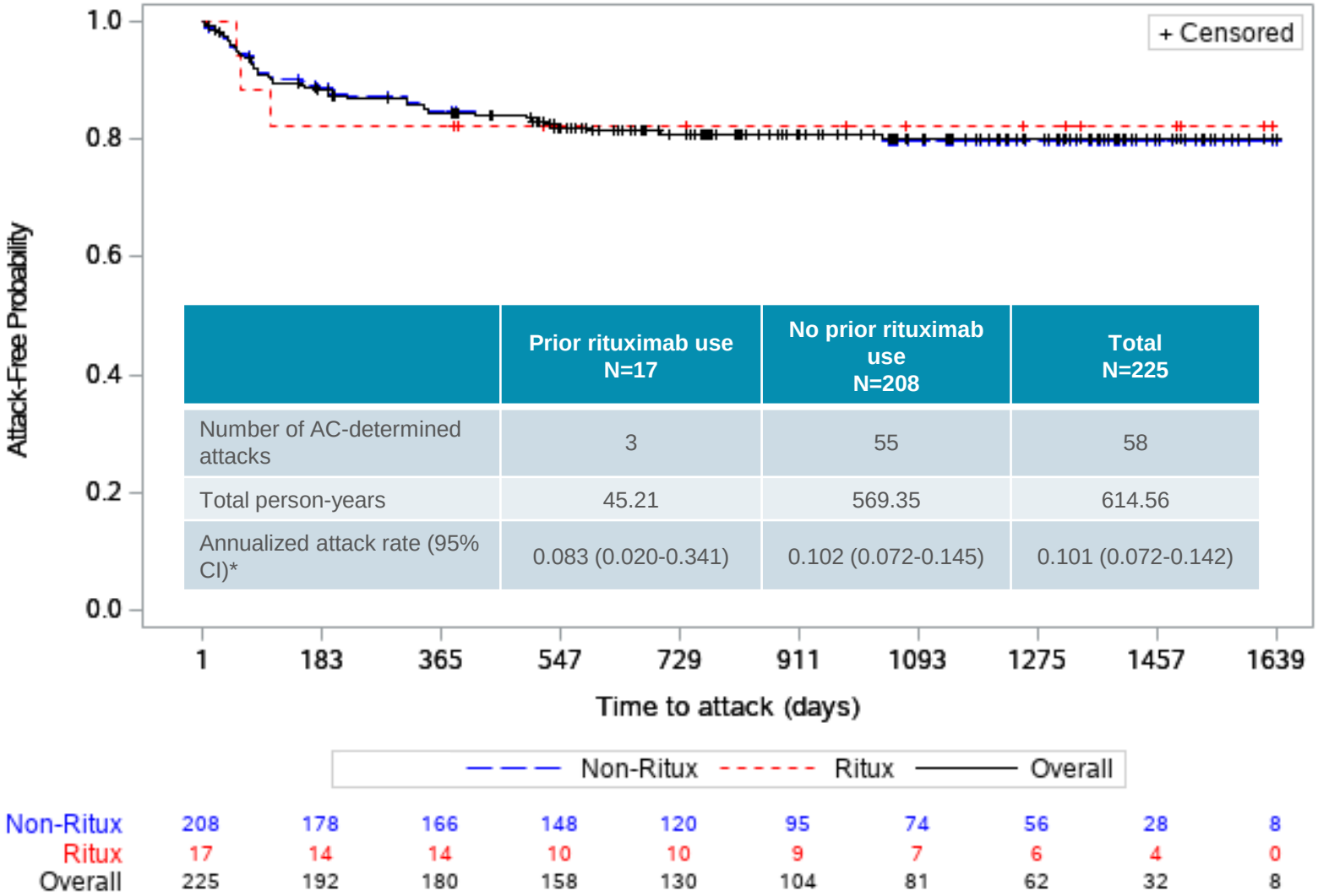


Figure 2. Attack-free Probability Stratified by Prior Rituximab Use



	Prior rituximab use N=17	No prior rituximab use N=208	Total N=225
Number of AC-determined attacks	3	55	58
Total person-years	45.21	569.35	614.56
Annualized attack rate (95% CI)*	0.083 (0.020-0.341)	0.102 (0.072-0.145)	0.101 (0.072-0.142)

Table 2. TEAEs, Serious TEAEs, and TEAEs of Special Interest After Receiving Inebilizumab

Event, n (%)	Prior rituximab use (n=17)	No prior use of rituximab (n=208)
TEAE		
Any	17 (100)	190 (91)
Related to inebilizumab	9 (53)	79 (38)
Leading to treatment discontinuation	1 (6)	6 (3)
Grade ≥3	5 (29)	46 (22)
Serious	6 (35)	38 (18)
Serious and related to inebilizumab	2 (12)	9 (4)
Death	0	2 (1)
TEAE of special interest		
Any	16 (94)	157 (76)
Infusion-related reaction	2 (12)	25 (12)
Anaphylactic reaction	0	0
Hypersensitivity	1 (6)	2 (1)
Infections	16 (94)	146 (70)
Hepatic function abnormality	1 (6)	14 (7)
Cytopenia	1 (6)	12 (6)
Opportunistic infections	0	2 (1)
Confirmed PML	0	0

PML, progressive multifocal leukoencephalopathy; TEAE, treatment-emergent adverse event.

Results Summary

- Seventeen subjects enrolled in N-MOmentum (7.4%) had previous rituximab treatment
  - The median time between the last rituximab use and randomization was 1.5 years
  - Three of the 17 participants had attacks on inebilizumab, one during the RCP and two in the open label phase
- Compared with the rest of the inebilizumab treated group, prior rituximab exposure did not impact efficacy
  - The AAR for those with and without prior rituximab exposure was .083 and .102, respectively
  - Seven of 17 patients entered the study as rituximab ‘failures’, defined as having an NMOSD attack while on (or within 6 months) of the last dose of rituximab. None of the 7 failures had an adjudicated attack after receiving inebilizumab (mean follow-up 2.6 years)
  - Adverse events of interest in this group included infusion reaction (2), infections (16), and cytopenia (1)
  - No opportunistic infections occurred (data not shown)

RCP: randomized controlled period; AAR: annualized attack rate; NMOSD: neuromyelitis optica spectrum disorder.

Conclusions

- Although the numbers are small, these data suggest that previous rituximab exposure does not affect inebilizumab efficacy in patients with NMOSD out to approximately 4 years
- A slightly higher rate of infections was observed among those with prior rituximab therapy when compared to those with any inebilizumab exposure

NMOSD: neuromyelitis optica spectrum disorder.