ABSTRACT NUMBER: 0775

A Phase 3, Randomized, Double-Blind, Multicenter, Placebo-Controlled Study of Inebilizumab in IgG4-Related Disease (MITIGATE): Primary Efficacy and Safety Findings

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SESSION INFORMATION

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Session Type: Abstract Session

Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease I

Session Time: 1:00PM-2:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) is a rare, systemic, fibroinflammatory disease characterized by unpredictable and recurring flares, leading to organ damage and decreased quality of life. The role of B cells in the pathophysiology of IgG4-RD and existing clinical experience suggest that B cell depletion may be an effective therapeutic avenue. Inebilizumab (INEB) is a humanized, glycoengineered, CD19-directed, monoclonal antibody that depletes B cells effectively in a targeted manner. **The aim is to evaluate the efficacy and safety** of inebilizumab monotherapy for reducing the risk of flare in adult participants with IgG4-RD.

Methods: The MITIGATE trial (NCT04540497), conducted at 80 sites in 22 countries, enrolled adult

patients who met the ACR/EULAR Classification Criteria for IgG4-RD with a score ≥20. Key eligibility criteria included a history of multiorgan disease and active disease at screening. Participants were stratified based on newly diagnosed vs. recurrent disease. Randomization was 1:1 with INEB 300 mg IV or Placebo (PBO) treatment on Day 1, 15, and Week 26 of the 52 week Randomized Controlled Period (RCP). Corticosteroids were normalized to 20 mg/day prednisone at the time of randomization and were tapered to discontinuation at the end of study Week 8. An IgG4-RD flare was defined as new or worsening signs and symptoms of IgG4-RD activity that met one or more organ-specific flare criteria developed for this study. The primary endpoint was time to first adjudication committee (AC)-determined and investigator-treated IgG4-RD flare during the RCP. Key secondary endpoints included annualized flare rate during the RCP and the proportion of participants achieving flare-free, treatment-free complete remission or corticosteroid-free complete remission at Week 52. Safety was evaluated.

Results: 135 subjects were randomized and received at least one dose of INEB (n=68) or PBO (n=67). Baseline demographics and disease characteristics were generally balanced between those receiving INEB and PBO (**Table 1**).

The primary endpoint was met, with INEB treatment significantly reducing the risk of IgG4-RD flares compared to PBO during RCP (hazard ratio 0.13; 95% CI: 0.06, 0.28; p< 0.0001) (**Figure 1**). The statistically significant treatment effect of INEB compared to PBO was seen for all key secondary endpoints (**Table 2**).

During the RCP, 66 (97.1%) INEB and 66 (98.5%) PBO participants had ≥1 treatment emergent adverse event (TEAE), the most frequent (>10%) were COVID-19 (16 [23.5%] INEB, 13 [19.4%] PBO), lymphopenia (11 [16.2%] INEB, 6 [9.0%] PBO), and UTI (8 [11.8%] INEB, 4 [6.0%] PBO). No subjects died; no SAE occurred in >1 subject. AEs of special interest included infusion related reactions in 3 (4.4%) INEB and 5 (7.5%) PBO and serious and/or opportunistic infections in 6 (8.8%) INEB and 2 (3.0%) PBO. In INEB participants, serious infections included COVID-19, appendicitis, and diverticulitis, and opportunistic infections were herpes zoster.

Conclusion: The MITIGATE trial, the first randomized, double-blind, placebo-controlled study ever conducted in IgG4-RD, establishes the safety and efficacy of CD19-targeted B cell depletion with inebilizumab in IgG4-RD.

Baseline Characteristics Study Population (n=135)	**Placebo (n=67)**	**Inebilizumab (n=68)**
Age, y (mean)	58.2	58.2
Sex		
Female, n (%)	18 (26.9%)	29 (42.6%)
Male, n (%)	49 (73.1%)	39 (57.4%)
Race		
Asian, n (%)	25 (37.3%)	38 (55.9%)
White, n (%)	32 (47.8%)	21 (30.9%)
Other, n (%)	10 (14.9%)	9 (13.2%)
IgG4 Manifestation		
Newly Diagnosed, n (%)	31 (46.3%)	31 (45.6%)
Recurrent, n (%)	36 (53.7%)	37 (54.4%)
Disease duration, y, mean (SD)	2.54 (3.06)	2.64 (3.73)
IgG4-RD Responder Index, Mean (SD)	6.0 (4.0)	5.4 (4.0)
Organs ever affected at time of enrollment		

Organs ever affected at time of enrollment		
2-3 organs affected, n (%)	22 (32.8%)	27 (39.7%)
4-5 organs affected, n (%)	28 (41.8%)	22 (32.3%)
≥6 organs affected, n (%)	17 (25.4%)	19 (27.9%)

Table 1: Demographics and Baseline Characteristics

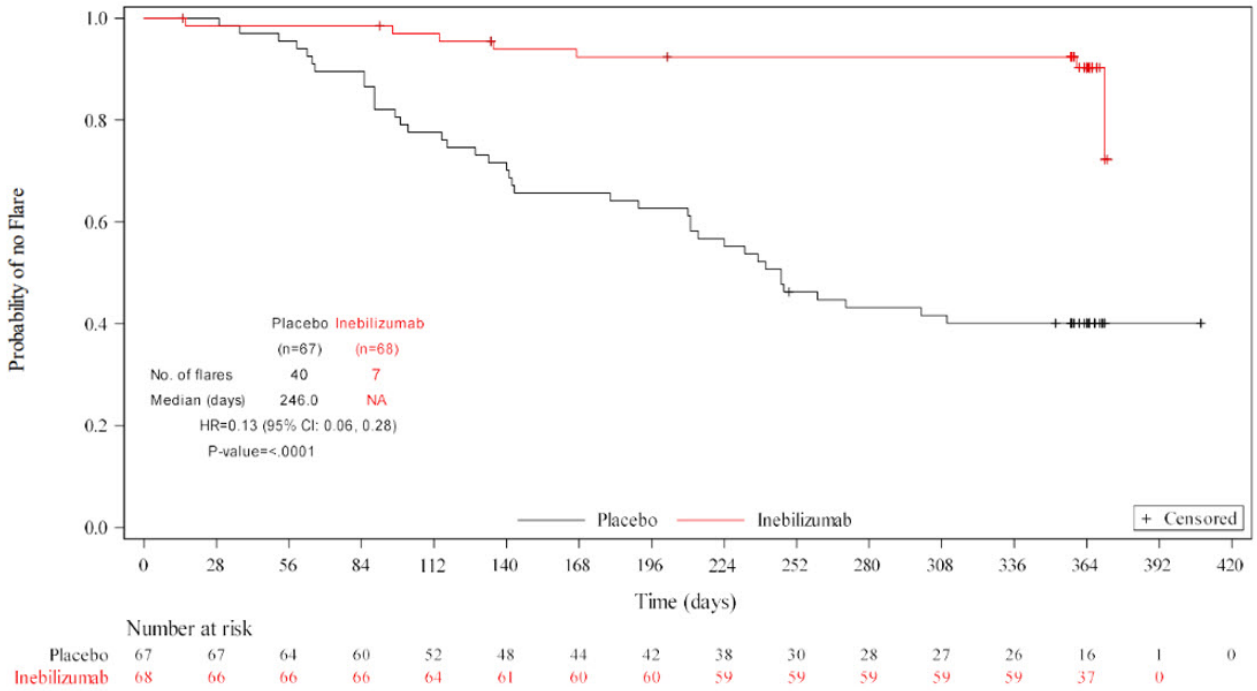

Figure 1: Kaplan Meier Plot for Primary Endpoint

Endpoint	PBO n=67	INEB n=68	P value (PBO vs INEB)
Annualized Flare Rate	0.71	0.10	
Rate Ratio (95% CI)		0.14 (0.06, 0.31)	<0.0001
Flare-free, treatment-free complete remission* at Week 52, n (%)	15 (22.4%)	39 (57.4%)	
Odds ratio (95% CI)		4.68 (2.21, 9.91)	<0.0001
Flare-free, corticosteroid-free complete remission** at Week 52, n (%)	15 (22.4%)	40 (58.8%)	
Odds ratio (95% CI)		4.96 (2.34, 10.52)	<0.0001

*Flare-free, treatment-free complete remission is defined as the absence of evident disease activity at week 52; defined as an IgG4-RD Responder Index score of 0 or determination by the investigator that no disease activity is present on the basis of physical, laboratory, pathology, or other evidence), no AC-determined flare during the RCP of the trial, and no treatment for flare or disease control beyond the protocol required prednisone taper.

** Flare-free, corticosteroid-free complete remission is defined as the absence of evident disease activity at week 52; defined as an IgG4-RD Responder Index score of 0 or determination by the investigator that no disease activity is present on the basis of physical, laboratory, pathology, or other evidence), no AC-determined flare during the RCP of the trial, and no corticosteroid treatment for flare or disease control beyond the protocol required prednisone taper.

Table 2: Key Secondary Endpoints for participants receiving INEB and PBO at Week 52

Disclosures: J. Stone: Amgen, 1, 2, 6, 7, Argenx, 2, Bristol-Myers Squibb(BMS), 5, Novartis, 2, 6, Sanofi, 2, Zenas, 2; **E. Culver**: Amgen Inc., 2, 12, MITIGATE Committee Member; **A. Khosroshahi**: Amgen Inc., 2, 12, MITIGATE Committee Member, Sanofi, 2, 12, Advisory board participant, Viela Bio, 2, 12, Advisory board participant; **W. Zhang**: Amgen Inc., 2, 12, MITIGATE Committee Member; **E. Della Torre**: Amgen Inc., 2, 12, MITIGATE Committee Member; **K. Okazaki**: Amgen Inc., 12, MITIGATE Committee Member; **Y. Tanaka**: AbbVie, 6, Asahi-kasei, 6, Astellas, 6, AstraZeneca, 6, Boehringer Ingelheim, 5, 6, Chugai, 5, 6, Daiichi Sankyo, 6, Eisai, 6, Gilead, 6, GSK, 6, Lilly, 6, Pfizer, 6, Taisho, 5, 6, UCB, 6; **M. Löhr**: Amgen Inc., 12, MITIGATE Committee Member; **N. Schleinitz**: Amgen Inc., 2, 12, MITIGATE Committee Member; **L. Dong**: Amgen Inc., 12, MITIGATE Committee Member; **H. Umehara**: Amgen Inc., 12, MITIGATE Committee Member; **M. Lanzillotta**: Amgen Inc., 12, MITIGATE Committee Member; **Z. Wallace**: Amgen Inc., 2, 12, MITIGATE Committee Member; **M. Ebbo**: Amgen Inc., 12, MITIGATE Committee Member; **G. Webster**: Amgen Inc., 12, MITIGATE Committee Member; **F. Martinez Valle**: Amgen Inc., 12, MITIGATE Committee Member; **M. Nayar**: Amgen Inc., 12, MITIGATE Committee Member; **V. Rebours**: Amgen Inc., 12, MITIGATE Committee Member; **C. Perugino**: Amgen Inc., 2, 12, MITIGATE Committee Member; **X. Dong**: Amgen Inc., 3, 11; **Y. Wu**: Amgen Inc., 3, 11; **N. Rampal**: Amgen Inc., 3, 11; **D. Cimbora**: Amgen Inc., 3, 11.

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