Safety and Tolerability of a Modified Ublituximab Dosing Regimen: Updates from the ENHANCE Study

Barry Singer,[1] Craig Herrman,[2] Derrick Robertson,[3] Idanis Berrios Morales,[4] Sidarth Dasari,[5] Jonathan Calkwood,[6] Mary Hughes,[7], John Scagnelli,[8] Alise Carlson,[9] Theodore Brown,[10] Lawrence Goldstick,[11] Gabriel Pardo,[12] Sibyl Wray,[13] Michael Sy,[14] Martin Belkin,[15] Ahmed Z. Obeidat,[16] Emily Riser,[17] Peiqing Qian,[18] Salvatore Napoli,[19] Christopher LaGanke,[20] Peter Sportelli,[21] Hari Miskin,[21] Ed Fox,[21] Christopher Rowland,[21] John Foley,[22]

[1]MS Center for Innovations in Care, St. Louis, USA; [2]JWM Neurology, Carmel, USA; [3]University of South Florida, Tampa, USA; [4]University of Massachusetts Medical School, Worcester, USA; [5]Advanced Neurology of Colorado, Fort Collins, USA; [6]Minnesota Center for Multiple Sclerosis, Plymouth, MN, USA, [7]Premier Neurology, Greenville, USA; [8]Raleigh Neurology Associates, Raleigh, USA; [9]Cleveland Clinic Mellen Center, Cleveland, USA; [10]EvergreenHealth, Kirkland, USA, [11]University of Cincinnati, Dayton, USA; [12]Oklahoma Medical Research Foundation, Oklahoma City, USA; [13]Hope Neurology PLLC, Knoxville, USA,[14]University of California, Irvine, Irvine, USA; [15]Michigan Institute for Neurological Disorders (MIND), Farmington Hills, USA; [16]Medical College of Wisconsin, Milwaukee, USA; [17]Alabama Neurology Associates, Birmingham, USA, [18]Swedish Medical Center, Seattle, USA; [19]Neurology Center Of New England, PC, Foxborough, USA; [20]North Central Neurology Associates, Cullman, USA; [21]TG Therapeutics, Inc, Morrisville, USA; [22]Rocky Mountain Multiple Sclerosis, Salt Lake City, USA

BACKGROUND

- Ublituximab is a novel monoclonal antibody that targets a unique epitope of CD20 and is glycoengineered for enhanced antibody-dependent cellular cytotoxicity (ADCC)[1] and enhanced Fcγ-receptor (FcγR) binding relative to all other currently approved anti-CD20 therapies in multiple sclerosis (MS).[1,2,3]
- Ublituximab is approved for adults with relapsing forms of multiple sclerosis (RMS) with an administration schedule of 150 mg dose on Day 1 followed by 450 mg doses on Day 15, Week 24, and subsequently every 24 weeks.
- Consolidating the initial 150 mg and 450 mg doses into a single 600 mg infusion administered on Day 1 may improve patient convenience and create greater efficiency for providers.

METHODS

- ENHANCE is a multi-center, open-label, 48-week study in participants with RMS evaluating modified dosing regimens for ublituximab.
- The study is actively enrolling participants with RMS who are treatment naïve or transitioning from other disease-modifying therapies.
- Recommended premedications included a non-drowsy antihistamine, corticosteroid, and antipyretic at each infusion.
- The Treatment Satisfaction Questionnaire for Medication (TSQM)-9 was administered at Weeks 24 and 48.
- Data is provided herein on all participants who received an initial ublituximab infusion of 600 mg (N=221).

RESULTS

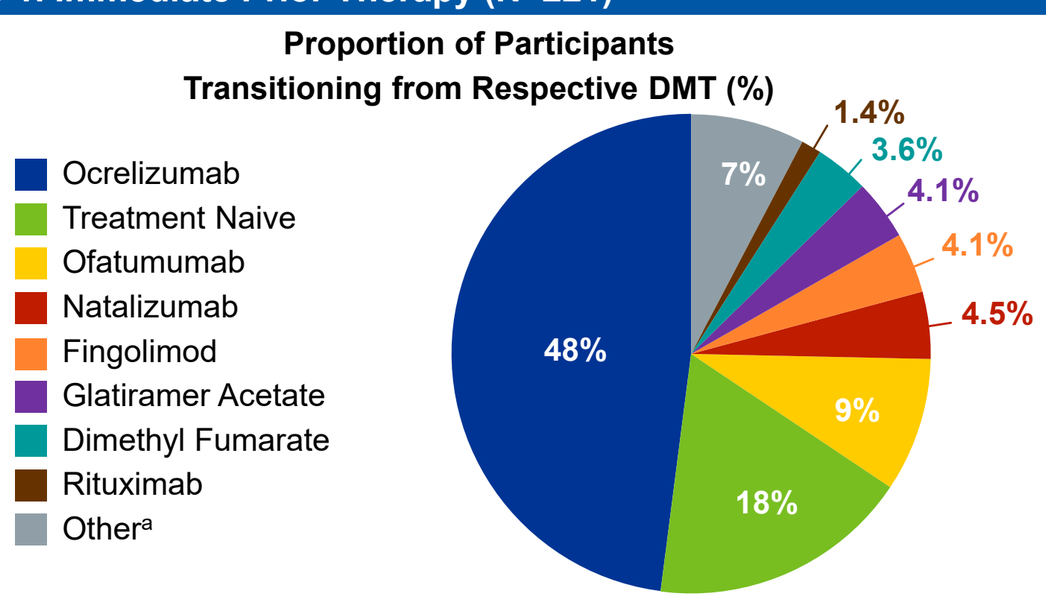
Population Baseline Characteristics and Most Recent DMT

Table 1. Baseline Characteristics

Characteristic	Overall N = 221
B-cell count, median (IQR)	44 (1, 211)
Treatment naïve, n (%)	40 (18%)
Transitioned from anti-CD20, n (%)	129 (58%)
Transitioned from other DMT, n (%)	52 (24%)
Age, years, median (IQR)	44 (36, 52)
Female, n (%)	158 (71%)
Race, n (%)	
White	175 (79%)
Black or African American	35 (16%)
Other	6 (2.7%)
Asian	3 (1.4%)
American Indian or Alaska Native	2 (0.9%)
Years since MS diagnosis, median (IQR)	8 (3, 14)
Relapses in prior 2 years, median (IQR)	0 (0, 1)

Data cut-off: June 27, 2025; IQR: Interquartile range, DMT: disease-modifying treatment

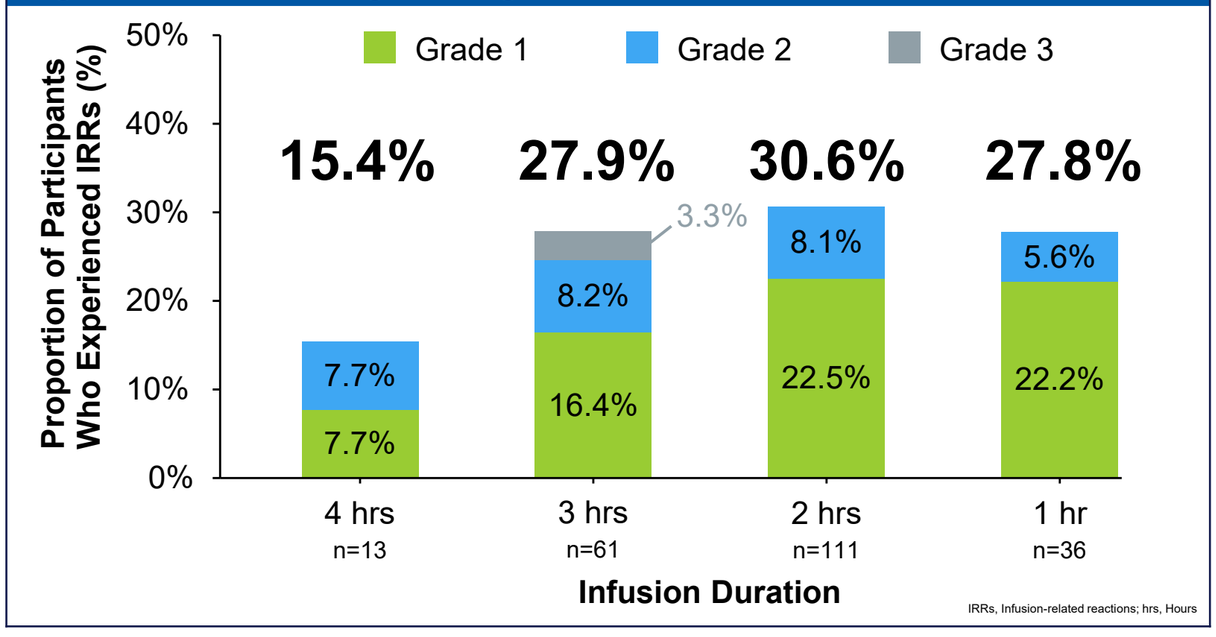
Figure 1. Immediate Prior Therapy (N=221)



[a]Teriflunomide (n=5), Diroximel Fumarate (n=4), Siponimod (n=2), Interferon Beta-1a (n=1), Mycophenolate Mofetil (n=1), Orelabrutinib (n=1), Ozanimod (n=1), Peginterferon Beta-1a (n=1)

Infusion Tolerability Experience

Figure 2. IRRs During 600 mg Initial Infusions



IRRs, Infusion-related reactions; hrs, Hours

- IRR Symptoms Reported in >3 Participants
  - Throat irritation 9.0%
  - Headache 4.5%
  - Flushing 2.7%
  - Nausea 2.3%
  - Fatigue 1.8%
- 90% of infusions were completed without interruption or slowing.
- IRRs were generally self-limiting; 12% received supportive medication for IRRs, primarily diphenhydramine.
- All IRRs resolved completely.

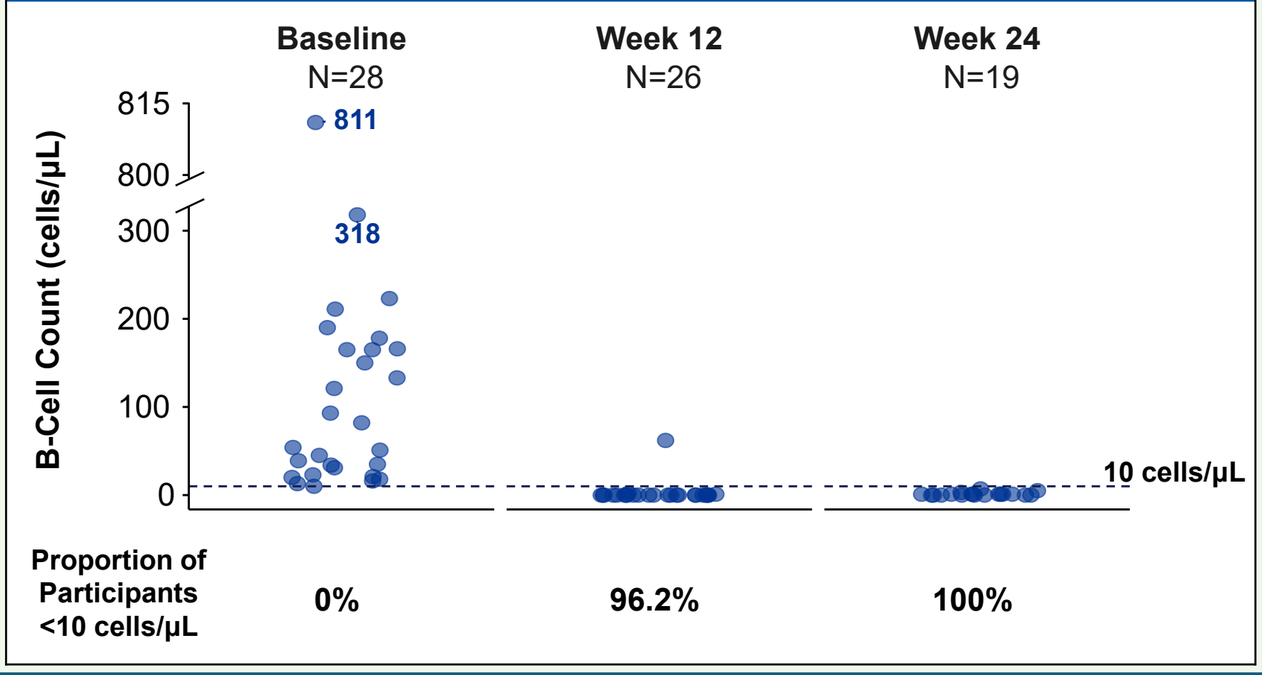
Subgroup Analysis of Ocrelizumab Switches

Table 2. Participants Who Switched from Ocrelizumab

B-Cell Depletion Status	Non-Depleted (≥10 cells/µL) N=28	Depleted (<10 cells/µL) N=78	Overall N=106
B-cell count at baseline, median (IQR)	68 (27, 166)	1 (0, 1)	1 (0, 13)
BMI (kg/m^2), median (IQR)	34 (31, 41)	29 (25, 35)	32 (25, 36)
Race			
White	18 (64%)	67 (86%)	85 (80%)
Black or African American	8 (29%)	8 (10%)	16 (15%)
Other	1 (3.6%)	2 (2.6%)	3 (2.8%)
American Indian or Alaska Native	1 (3.6%)	1 (1.3%)	2 (1.9%)
Age, median (IQR)	43 (33, 53)	47 (40, 55)	45 (39, 55)
# of prior anti-CD20 infusions, median (IQR)	6 (4, 9)	9 (6, 13)	9 (5, 12)
Years of prior anti-CD20 treatment, median (IQR)	2.0 (1.3, 3.6)	4.5 (2.7, 6.2)	3.8 (2.1, 5.9)
Months since last anti-CD20 dose, median (IQR)	9 (6, 12)	6 (6, 7)	6 (6, 7)
Duration of last anti-CD20 infusion (minutes), median (IQR)	150 (122, 210)	132 (120, 240)	135 (120, 228)
Experienced wearing-off on prior anti-CD20	***8 (29%)***	***53 (68%)***	***61 (58%)***

- A greater proportion of participants with B cells ≥10 cells/µL at baseline were Black or African American, had a higher body mass index (BMI), and were younger compared to those who were B-cell depleted (<10 cells/µL) at baseline. Notably, the median time since last infusion was longer among these participants than those who were in a depleted state (<10 cells/µL) prior to initiating ublituximab (Table 2).
- Among participants with Week 24 data available at cutoff, 100% remained depleted following a single ublituximab infusion of 600 mg (Figure 4).

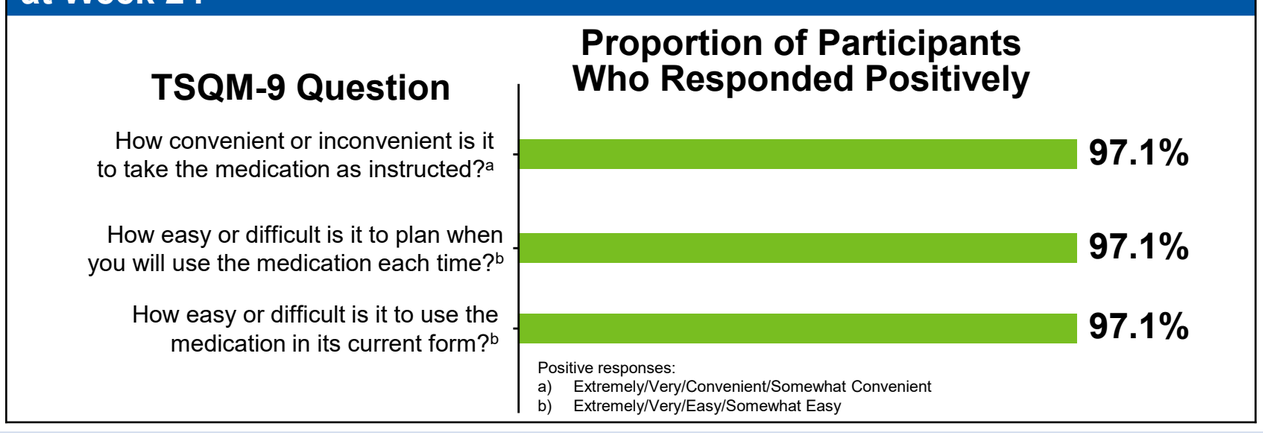
Figure 4. B-Cell Distribution in Ocrelizumab Participants Who Were Not Depleted Upon Initiating Ublituximab



Treatment Satisfaction

- Among participants who reached Week 24 by data cutoff date (N=108), 97.1% reported that 600 mg infusions were convenient and easy to use.

Figure 3. TSQM-9 Evaluation of Convenience and Ease of Use at Week 24



CONCLUSIONS

- Consolidating Day 1 (150 mg) and Day 15 (450 mg) infusions into a single 600 mg dose was well-tolerated across each duration evaluated.
- The 4-hour infusion was associated with the lowest IRR rate and was selected as the duration to be evaluated in a label-enabling trial design.
- 600 mg infusions resulted in high levels of patient satisfaction on the dimensions of convenience and ease of use.
- Ublituximab maintained B-cell depletion among participants who transitioned from ocrelizumab in a non-depleted state.
- The ENHANCE study is ongoing with initial 600 mg infusions being evaluated in a double-blinded, randomized cohort compared to standard dosing.

ACKNOWLEDGMENTS: The authors thank the participants and their families for their contributions in the ENHANCE Study and Victoria Findlen for editorial support. The ENHANCE study is sponsored by TG Therapeutics.

REFERENCES:
1. Steinman L, et al. N Engl J Med. 2022;387(8):704-714.
2. Cree BAC, et al. Presented at 2024 ECTRIMS Meeting, September 18-20, 2024, Copenhagen, DK P324
3. Babiker HM, et al. Expert Opin Investig Drugs. 2018;27(4):407-412.

P1699

BS has received research grant support from AbbVie, Biogen, Bristol Myers Squibb, Greenwich Biosciences, Novartis, Sanofi and TG Therapeutics and consulting and/or speaking fees from Alexion, Biogen, Bristol Myers Squibb, Cigna, Cycle, EMD Serono, Genentech, Horizon, Janssen, Novartis, Octave Bioscience, Roche, Sandoz, Sanofi and TG Therapeutics.CH has received research support from Genentech, Merck, and Novartis. DR has received grant support from Anokion, Atara Biotherapeutics, Biogen, CorEvitas, EMD Serono, Genentech, GW Pharmaceuticals, Janssen, Novartis, PCORI, PRIME CME, Sanofi, and TG Therapeutics; has received consulting fees from Alexion, Biogen, Bristol Myers Squibb, EMD Serono, Genentech, Greenwich Biosciences, Horizon, Janssen, Mallinckrodt, Novartis, Sanofi, and TG Therapeutics; has received honoraria or speaker fees from Alexion, Biogen, Bristol Myers Squibb, EMD Serono, Genentech, Horizon, Janssen, PRIME CME, Sanofi and TG Therapeutics. IBM has nothing to disclose. SD is a speaker for TG Therapeutics. JC has received honorarium or financial support for promotional speaking, advisory board services and funding for research from TG Therapeutics, AstraZeneca, Biogen, Genentech, Octave Bio, Sanofi and Zenas BioPharma. MH has nothing to disclose. JS has received honorarium for speaking activities from TG Therapeutics, Biogen, Idec, and Novartis Pharmaceuticals and as an advisory board member for Sanofi. AC reports research support from Genentech and Biogen, has served on scientific advisory boards for Sanofi, Novartis, and TG Therapeutics, and has served as a consultant to Vigil Neuro, Icometrix, and Ionis. TB has received research grants from Merck. LG has served as a speaker or consultant for Biogen, Bristol Myers Squibb, Eli Lilly, EMD Serono, Modern, Roche-Genentech, Sanofi-Genzyme and TG Therapeutics and has received research support from Biogen, Eli Lilly, EMD Serono, Moderna Roche-Genentech, Sanofi-Genzyme and TG Therapeutics. GP has received research grants (to the institution) from Biogen, EMD Serono, Roche/Genentech, Sanofi Genzyme, Novartis, Amgen, Abbvie, TG Therapeutics, and BMS; consultant and/or speaker bureau for Biogen, EMD Serono, Roche/Genentech, Sanofi Genzyme, Novartis, Janssen, BMS, TG Therapeutics, Horizon Therapeutics, Alexion Pharmaceuticals, PRIME Education, and MSAA. SW has received compensation for serving on a Scientific Advisory or Data Safety Monitoring board for for Biogen, Bristol Myers Squibb/Celgene, EMD Serono, Novartis, Roche/Genentech, and Sanofi/Genzyme; and has received compensation for serving on a Speakers Bureau for Biogen, Bristol Myers Squibb, EMD Serono, Roche/Genentech, and Sanofi/Genzyme. The institution of Dr. Wray has received research support from Biogen, Hope, Bristol Myers Squibb/Celgene, Novartis, Roche/Genentech, Sanofi/Genzyme, and TG Therapeutics. MS has consulted with Genentech/Roche, Amgen, Novartis, TG therapeutics, Amgen, and Octave Bioscience, received speaker fees from Alexion, and has clinical research contracts with Genentech/Roche, TG Therapeutics, Sanofi, Novartis, and BMS. MB has received speaker fees from Alexion, Biogen, EMD Serono, Sanofi, Bristol Myers Squibb, Horizon, Genentech, TG Therapeutics. Received Consulting fees from Genentech, Biogen, EMD Serono, Sanofi Horizon. AZO has received speaker fees from Alexion, Amgen, Biogen, Bristol Myers Squibb, EMD Serono, Sanofi-Genzyme, TG Therapeutics, as well as consulted with Alexion, Amgen, AstraZeneca, Banner Life Sciences, Biogen, Bristol Myers Squibb, EMD Serono, Genentech, Merck, Novartis, Roche, Sanofi-Genzyme, TG Therapeutics. ER has received speaker fees from TG Therapeutics and received research support from TG Therapeutics, Alexion, Genentech, Novartis, Sanofi, and Corvitas. PQ has received speaking and consulting honoraria from Biogen, BMS, Sanofi, Genentech, Viela Bio, and TG Therapeutics. SN has received compensation for serving as a Consultant for Biogen, Genentech, Genzyme, Bristol Myers, Serono. He has received compensation for serving on a Speakers Bureau for Biogen, Bristol Myers, Serono, Genzyme, and received compensation for serving as an Expert Witness for vaccine injury. CL has served as a consultant for Acorda Therapeutics, Bayer, Biogen Idec, Cephalon, EMD Serono, Genzyme, Novartis, Pfizer, Questcor, Strativa, Teva, and UCB. PS, HM, EF, and CR are employed by TG Therapeutics. JF has been as consultant for Octave Biosciences; been on advisory panels for Biogen, TG Therapeutics, Horizon Therapeutics, and Sandoz; received research funding from Biogen, IMStem, Genentech, and TG Therapeutics.

Presented at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) | Barcelona, Spain | September 24-26, 2025