Randomized, Double-Blind Evaluation of a Consolidated Ublituximab Initial Dosing Regimen Versus Conventional Ublituximab Regimen

Derrick Robertson[1], Krzysztof Selmaj[2], Elzbieta Jasinska[3], Robert Bonek[4], Craig Hermann[5], Monika Adamczyk-Sowa[6], Lawrence Goldstick[7], Alise Carlson[8], Jonathan Calkwood[9], Ewa Krzystanek[10], Emily Riser[11], Chris LaGanke[12], Sidarth Dasari[13], Theodore Brown[14], Janusz Zbrojkiewicz[15], Jan Ilkowski[16], Hari Miskin[17], Peter Sportelli[17], Edward Fox[17], Christopher Rowland[17], John Foley[18]

[1]University of South Florida, Tampa, United States, [2]Centrum Neurologii, Łódź, Poland [3]Wrocław University of Science and Technology, Wrocław, Poland, [4]Neurocentrum, Bydgoszcz, Poland, [5]JWM Neurology, Indianapolis, United States, [6]Samodzielny Publiczny Szpital Kliniczny Nr 1, Oddział Neurologii, Zabrze, Poland, [7]University of Cincinnati, Dayton, United States, [8]Cleveland Clinic Mellen Center, Cleveland, United States, [9]Minnesota Center for Multiple Sclerosis, Plymouth, United States, [10]Department of Neurology, Faculty of Health Sciences in Katowice, Medical University of Silesia, Katowice, Poland, [11]Alabama Neurology Associates, Birmingham, United States, [12]North Central Neurology Associates, Cullman, United States, [13]Advanced Neurology of Colorado, Fort Collins, United States, [14]EvergreenHealth, Kirkland, United States, [15]NEURO-MEDIC Sp. z o.o., Katowice, Poland, [16]NZOZ Neuro-KardIlkowski i Partnerzy, Poznan, Poland, [17]TG Therapeutics, Inc, Morrisville, United States, [18]Rocky Mountain MS Center, Salt Lake City, United States

CONCLUSIONS

- Consolidating the Day 1 (150 mg) and Day 15 (450 mg) infusions into a single 600 mg dose resulted in bioequivalent pharmacokinetic exposure.
- IRRs in both regimens were lower than those reported in the ULTIMATE studies, with no Grade 3 or higher IRRs occurring in any participant.
- The consolidated regimen rapidly induced and maintained robust B-cell depletion to the same extent as the conventional regimen.
- 100% of participants treated with the consolidated regimen had no T1 Gd+ lesions at Week 24 and were relapse-free throughout the study.
- The consolidated regimen offers equivalent exposure with a favorable benefit-risk profile, providing an additional treatment option for patients and HCPs.

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.

ACKNOWLDGEMENTS:
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.

DISCLOSURES:

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. KS has received honoraria for speaking, consulting, and serving on advisory boards for Merck, Novartis, Roche, Biogen, Celgene, BMS, and TG Therapeutics. EJ has received honoraria from Novartis, Merck, Roche, and Neuroxpharm and participated in a steering committee for Novartis. RB has nothing to disclose. CH has received research support from Genentech, Merck, and Novartis. MAS has nothing to disclose. 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. 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. 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. EK has nothing to disclose. ER has received speaker fees from TG Therapeutics and received research support from TG Therapeutics, Alexion, Genentech, Novartis, Sanofi, and Corvitas. CL has served as a consultant for Acorda Therapeutics, Bayer, Biogen Idec, Cephalon, EMD Serono, Genzyme, Novartis, Pfizer, Questcor, Strativa, Teva, and UCB. SD is a speaker for TG Therapeutics. TB has received research grants from BMS, Genentech, TG therapeutics. He has also received consulting fees from Genentech and Cycle Pharma. JZ has nothing to disclose. JI has nothing to disclose. HM, PS, EF, and CR are employees of TG Therapeutics, Inc. 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.

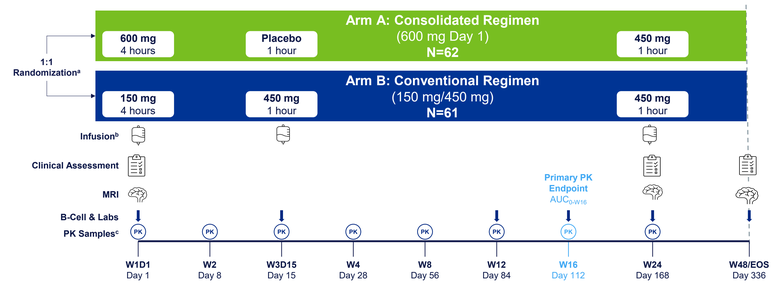
BACKGROUND

- 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.

SCHEMA

ELIGIBILITY

- RMS diagnosis
- Age: 18-65
- Treatment naive or previously treated with a DMT
- EDSS score ≤5.5



a) Randomization was stratified by region (USA vs Poland), sex, and weight
b) Recommended premedications included a non-drowsy antihistamine, corticosteroid, and antipyretic at each infusion
c) PK sampling: W1D1 and D15 pre-dose, end of infusion, and 1 h post-EOI; W2, W4, W8, W12, W16 anytime; W24 pre-dose.
Unscheduled relapse visits may occur as clinically indicated.
AUC: area under the serum concentration–time curve, D: day, EOS: end of study, MRI: magnetic resonance imaging, PK: pharmacokinetic, W: week

RESULTS

Table 1. Demographics

Characteristic Mean ± SD or n (%)	Consolidated Regimen N=62	Conventional Regimen N=61
Poland	33 (53.2)	33 (54.1)
Treatment Naïve	13 (21.0)	24 (39.3)
Transitioned from Anti-CD20	37 (59.7)	25 (41.0)
Depleted[a]	27 (43.5)	18 (29.5)
Age, years	42.2 ± 11.67	39.3 ± 10.47
Female	47 (75.8)	45 (73.8)
Race		
White	53 (85.5)	57 (93.4)
Black or African American	8 (12.9)	4 (6.6)
Other	1 (1.6)	-
BMI, kg/m^2	28.4 ± 6.6	28.4 ± 7.5

a) Depleted defined as B-cell count <10 cells/μL
Data cut-off: 24 March 2026; BMI: body mass index, SD: standard deviation

- No clinically meaningful differences in baseline characteristics between the regimens.

Table 2. Disease History

Characteristic Mean ± SD or n (%)	Consolidated Regimen N=62	Conventional Regimen N=61
Years Since Diagnosis	8.7 ± 8.4	5.3 ± 5.5
Months Since Last Relapse	52.0 ± 47.8	33.5 ± 36.3
Relapses in the Last 2 Years		
0	42 (67.7)	28 (45.9)
1	16 (25.8)	25 (41.0)
2	2 (3.2)	7 (11.5)
3	1 (1.6)	1 (1.6)
4	1 (1.6)	-
Relapses in the Last 2 Years	0.4 ± 0.78	0.7 ± 0.74
Baseline EDSS	2.7 ± 1.2	2.5 ± 1.1
Baseline Gd-Enhancing Lesions		
0	56 (90.3)	53 (86.9)
≥1	5 (8.1)	8 (13.1)

Gd: gadolinium, SD: standard deviation

RESULTS, CONT.

Figure 1. Pharmacokinetics

Administration of ublituximab IV either as 600 mg on Day 1 or 150 mg on Day 1 followed by 450 mg on Day 15 led to **bioequivalent** exposure during the first 16 weeks of the ENHANCE study

	Consolidated Regimen (600 mg Day 1) N=62	Conventional Regimen (150 mg/450 mg) N=61	GMR 600 mg vs 150 mg/450 mg (90% CI)[b]
AUC over the first 16 weeks (AUC_{0-W16})[a]	2199.93 μg/mL*day	2191.86 μg/mL*day	**1.0137** (0.9280 – 1.1073) ← Primary Endpoint

a) Estimated mean exposure for AUC.
b) GMR of consolidated regimen versus conventional regimen and associated 90% CI was calculated retaining up to 4 decimal places. The BE of 600 mg ublituximab IV infusion to the conventional IV regimen was established if the 90% CI of the AUC_{0-W16} GMR was within the range of 0.8000 to 1.2500.
AUC: area under the serum concentration–time curve, BE: bioequivalence, CI: confidence interval, C_{max}: maximum serum concentration, GMR: geometric mean ratio, IV: intravenous

Table 3. Safety Overview

n (%)	Consolidated Regimen N=62	Conventional Regimen N=61b
AEs	49 (79.0)	51 (83.6)
IRRs	13 (21.0)	18 (29.5)
Infections[a]	26 (41.9)	28 (45.9)
SAEs[b]	2 (3.2)	1 (1.6)
Fatal AEs	0	0

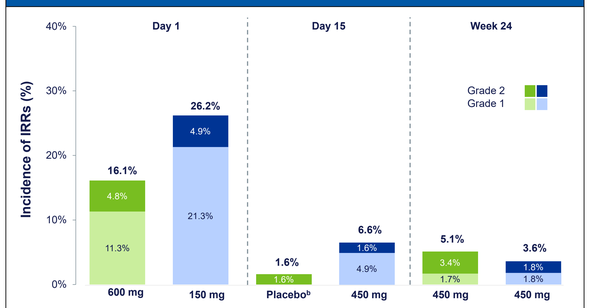
a) Infections reported in >5% of participants in either arm were urinary tract infection, upper respiratory tract infection, nasopharyngitis, oral herpes
b) SAEs in the consolidated regimen were thoracic vertebral fracture (not related) and prostate cancer (not related) in one participant each, and in the conventional regimen were pneumonia mycoplasmal (possible) in one participant
AEs: adverse events, IRRs: infusion related reactions, SAEs: serious adverse events

- The safety profile of consolidated regimen was consistent with the conventional regimen.
- No AEs were fatal or led to discontinuation.

Figure 3. B-Cell Depletion

- Both regimens rapidly induced B-cell depletion and maintained depletion over 24 weeks.

Figure 2. IRRs

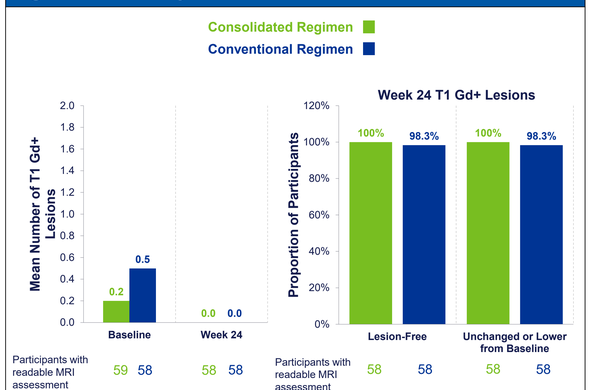


a) Modification defined as interruption or slowing due to IRRs. Percentage calculated out of total number of infusions administered on Day 1 and Day 15 for each regimen.
b) One participant who received a placebo infusion on Day 15 experienced a Grade 2 IRR that completely resolved.

Across Day 1 and Day 15 Infusions:

- No statistical difference in IRR rates between regimens.
- 98.4% of infusions were **completed without modification**[a] in both regimens.
- All infusions were ultimately completed.
- Fewer participants in consolidated regimen required supportive medication for the management of IRRs (6.5% vs 11.5%).
- No IRRs were Grade 3 or 4, serious, or led to treatment discontinuation.
- All IRRs resolved without sequelae.

Figure 4. Efficacy



One participant in the conventional regimen had a T1 Gd+ lesion at Week 24, which was an increase from baseline.

- **97.5%** (116/119) of participants were relapse-free across both regimens.
- Change from baseline in EDSS at Week 24 was similar in the two regimens.

Presented at the 10th Joint ACTRIMS-ECTRIMS Meeting | 21-23 October 2026 | Toronto, Canada | P1419