Real world clinical experience from ENABLE, the first Phase 4 observational study for patients with relapsing multiple sclerosis initiating ublituximab

Carrie M Hersh[1], Angel R Chinea[2], Emily Riser[3], Christina Weber[4], Sidarth Dasari[5], Jacqueline Rosenthal[6], Andrew Bouley[7], Diana Andino[8], Matthew C Carraro[9], Jeanie Cote[10], Jean-Raphael Schneider[11], Jonathan Calkwood[12], Sangjin Oh[13], Bhupendra Khatri[14], Jackie Parker[15], Karthik Bodhinathan[15], Peter Sportelli[15], Hari Miskin[15], Edward Fox[15]

[1]Lou Ruvo Center for Brain Health, Cleveland Clinic, Las Vegas, NV; [2]Centro Internacional De Mercadeo, Guaynabo, PR; [3]Alabama Neurology Associates, Birmingham, AL; [4]Colorado MS Center, CO; [5]Advanced Neurology of Colorado, Fort Collins, CO; [6]Shepherd Center, Atlanta, GA; [7]The Elliot Lewis Center, Wellesley, MA; [8]Austin Regional Clinic, Austin, TX; [9]The Charlotte Center for MS, Lake Norman Neurology, Charlotte, NC; [10]Memorial Healthcare, Owosso, MI; [11]MS and Neuromuscular Center of Excellence, Clearwater, FL; [12]Minnesota Center for Multiple Sclerosis, Plymouth, MN; [13]Maryland Center for Neurology and Sleep, Glen Burnie, MD; [14]Center for Neurological Disorders, Milwaukee, WI; [15]TG Therapeutics, Morrisville, NC

BACKGROUND

- Ublituximab is a novel monoclonal antibody that targets a unique epitope of CD20 and is glycoengineered for enhanced antibody-dependent cellular cytotoxicity (ADCC) and enhanced Fcγ-receptor (FcγR) binding relative to all other currently approved anti-CD20 therapies in multiple sclerosis (MS).[1,2,3]
- Ublituximab, approved for treating relapsing multiple sclerosis (RMS) in adults, demonstrated significant clinical benefit vs teriflunomide in two identical phase 3 trials, ULTIMATE I and II. These benefits continued to be observed over 6 years during the open-label extension period.[4,5]
- Ublituximab is administered at lower doses and with shorter infusion times (1-hour infusions after the first infusion) compared with other infused anti-CD20 therapies.[6]
- The first Phase 4 observational study for patients with relapsing multiple sclerosis (RMS) treated with ublituximab, entitled "Evaluating the rEal-world experieNce of patients treated with BRIUMVI® (ublituximAB-xiiy) for RMS, in a Longitudinal rEgistry (ENABLE)" (NCT06433752) is designed to collect valuable real-world clinical evidence on the effectiveness, safety, and tolerability of ublituximab.
- Results from the first interim analysis of the ongoing study are presented here.

METHODS

- ENABLE participants who received at least one dose of ublituximab and any baseline efficacy evaluation as of the data cut-off date of June 30, 2025, were included in the analysis.
- Annualized relapse rate is calculated as cumulative number of relapses/cumulative treatment time. Duration of infusion (in minutes) was defined as duration between infusion start to stop time.
- PROs (TSQM and MSIS) were evaluated by Mixed Model Repeated Measures of the transformed score, and the model includes visit as covariates and an unstructured covariance matrix.

RESULTS

Table 1. Baseline Demographics

Characteristic, Mean ± SD or n(%)	Ublituximab (N=393)
Age (years)	42.9 ± 11.74
Gender, Female, n (%)	296 (75.3%)
Race, n (%)	
White	276 (70.2%)
Black or African-American	79 (20.1%)
Other	34 (8.7%)
Unknown or Not Reported	4 (1.0%)
Ethnicity	
Hispanic or Latino	57 (14.5%)
Not Hispanic or Latino	283 (72.0%)
Unknown or Not Reported	53 (13.5%)
Weight (kg)	86.7 ± 25.6
Height (cm)	168.18 ± 9.54
BMI (kg/m^2)	30.57 ± 8.76
BMI category	
<30 kg/m^2	204 (51.9%)
≥30 kg/m^2	158 (40.2%)
Unknown or Not Reported	31 (7.9%)

Baseline population included as of data cutoff on 30-June-2025; patients are actively enrolling.

- The average age of ENABLE participants (42.9 years) is higher than that of UILTIMATE I and II participants (35.4 years).
- 75.3% of participants were female, a higher proportion than in ULTIMATE I and II (62.9% female).
- 70.2% and 20.1% of participants are White/Caucasian and Black/African-American, respectively. In ULTIMATE I and II, Black/African-American participants were 1.5% of trial population, owing to the majority of sites being in Eastern Europe.
- The number of participants with body mass index (BMI) ≥30 kg/m^2 was 40.2%, which was relatively higher compared to ULTIMATE I/II participants (11.3%).

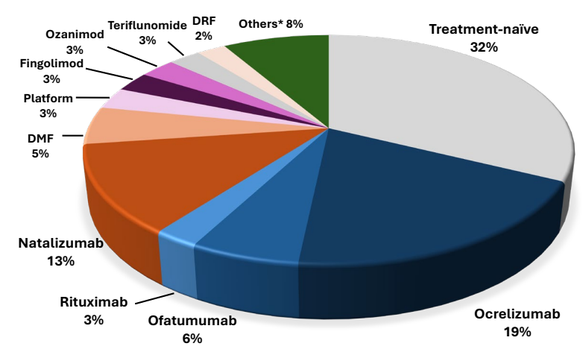
Table 2. Baseline Disease History

Characteristic, Mean ± SD or n (%)	Ublituximab, (N=393)
Time since first MS Symptoms (years)	8.62 ± 9.02
Number of relapses in the 2 years prior to screening	0.6 ± 0.85
Number of relapses in the 2 years prior to screening, n(%)	
0	177 (45.0%)
1	109 (27.7%)
2	29 (7.4%)
≥3	9 (2.3%)
Unknown or Not Reported	69 (17.6)
Number of baseline Gadolinium (Gd)-enhancing lesions	1.5 ± 6.75
Number of baseline Gadolinium (Gd+) lesions, n (%)	
0	216 (55.0%)
≥1	62 (15.8%)
Unknown or Not Reported	115 (29.3%)
Number of New or Enlarging T2 hyperintense Lesions (compared to previous MRI scan)	1.7 ± 5.46
Number of New or Enlarging T2 Hyperintense Lesions, n (%)	
0	187 (47.6%)
≥1	79 (20.1%)
Unknown or Not Reported	127 (32.3%)

Baseline population included as of data cutoff on 30-June-2025; patients are actively enrolling.

- ENABLE participants had slightly longer duration since onset of MS symptoms (8.62 years) vs ULTIMATE I and II (~7.4 years).
- Most of the participants either had one relapse (27.7%) or were relapse-free (45.0%) in the 2 years prior to screening.
- At baseline, 55% of participants starting ublituximab had no Gadolinium (Gd)-enhancing lesions which was in line with ULTIMATE I and II (~53%).

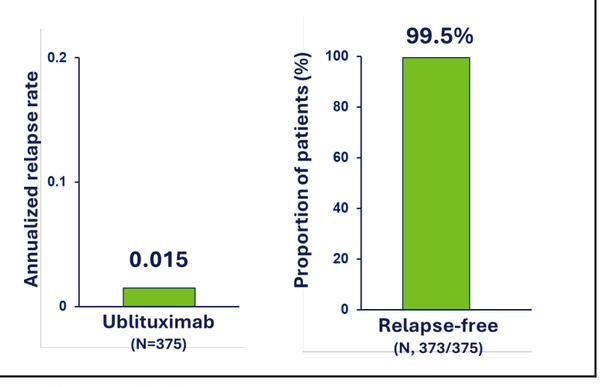
Figure 1. Prior DMT treatment history for MS patients starting ublituximab on ENABLE



Data cutoff: 30-June-2025. *The category "Others" includes missing input from n=21 (5.3%). Listed DMTs are immediately prior to start of ublituximab

- Majority of patients (32%) were treatment-naïve at the start of ENABLE
- A large proportion of patients (28%) transitioned to ublituximab from a B-cell therapy- ocrelizumab, ofatumumab or rituximab

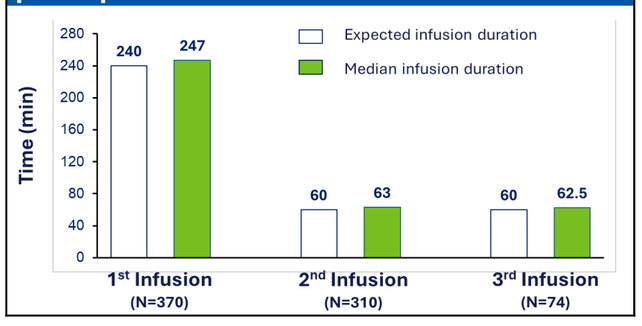
Figure 2. Summary of on-treatment relapses and ARR



Data cutoff: 01-July-2025. The relapse analysis based on participants with at least one dose of ublituximab and any post-baseline efficacy evaluation. Annualized relapse rate is calculated as cumulative number of relapses/cumulative treatment time.

- On-treatment Annualized relapse rate was 0.015, with cumulative treatment time of 132.4 subject-years
- On-treatment relapses were rare, and 99.5% of participants reported no relapses during treatment with ublituximab

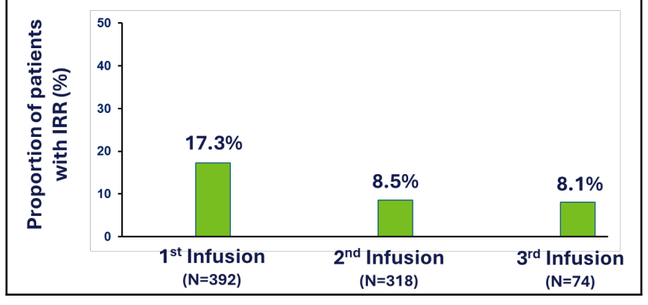
Figure 3. Infusion times in ublituximab-treated participants from ENABLE



Data cutoff: 30-June-2025. Duration of infusion (minutes) was defined as time recorded between start and stop of the IV infusion

- Most infusions were completed within the specified time. The median infusion duration (in mins) was 247, 63, and 62.5 for the first, second and third infusion.

Figure 4. Infusion-related reactions in ublituximab-treated participants from ENABLE



Data cutoff: 30-June-2025. IRR= Infusion-related reaction. Events assessed as IRRs by the treating physician.

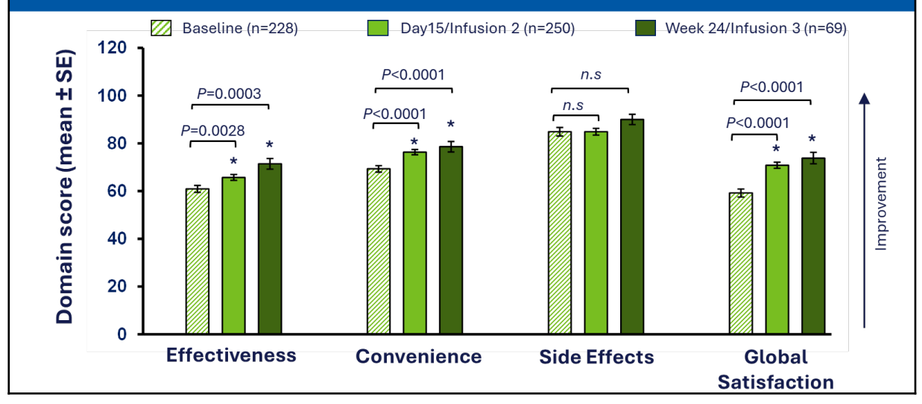
- IRRs were most frequently observed at first infusion (17.3% of participants). IRRs decreased in frequency during second and third infusions (8.5% and 8.1%, respectively)
- None of the IRRs were serious (or ≥ Grade 3) in nature. All IRRs were Grade 1 or Grade 2 and resolved completely
- Premedications included corticosteroid (methylprednisolone, 88.5%), antipyretic (paracetamol, 79.8%), and antihistamines (diphenhydramine 77.6%, and cetirizine 12.8%)

Table 3. Adverse events with an incidence of at least 1% for BRIUMVI

Event	Ublituximab, (n=393) n (%)
Any treatment emergent adverse event (TEAE)	113 (28.8)
Infusion-related reaction	76 (19.3)
Headache	9 (2.3)
Fatigue	6 (1.5)
Urinary tract infection	6 (1.5)
Insomnia	4 (1.0)
Nausea	4 (1.0)

Data cutoff: 30-June-2025.

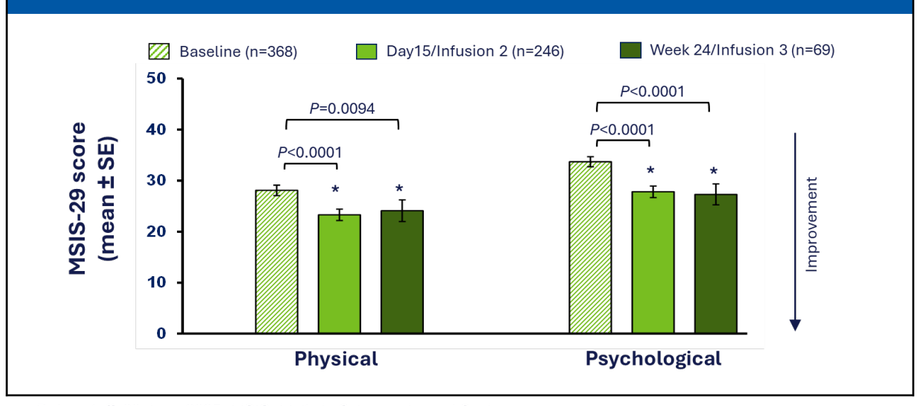
Figure 5. Patient-reported satisfaction with ublituximab treatment



Data cutoff: 30-June-2025. TSQM=Treatment Satisfaction Questionnaire for Medication; n.s=not significant
MMRM (Mixed Model Repeated Measures) of the transformed score. The model includes visit as covariates and an unstructured covariance matrix.

- Significant improvement in TSQM scores were observed from baseline to Day 15 for effectiveness, convenience, and global satisfaction; the scores for side effects remained stable.
- Improvements in TSQM scores were sustained at week 24 compared to baseline for effectiveness, convenience, and global satisfaction, while scores for side effects remained stable.

Figure 6. Patient-reported MSIS score with ublituximab treatment



Data cutoff: 30-June-2025. MSIS=Multiple Sclerosis Impact Scale
MMRM (Mixed Model Repeated Measures) of the transformed score. The model includes visit as covariates and an unstructured covariance matrix.

- Significant improvements were observed for MSIS-29 as early as Day 15 for physical [LS mean (95% CI): -3.44 (-4.61, -2.28), P<0.0001], and psychological scores [LS mean (95% CI): -5.67 (-7.21, -4.13), P<0.0001].
- Improvements were sustained at week 24 compared to baseline: physical [LS mean (95% CI): -3.38 (-5.92, -0.83), P=0.0094], and psychological scores [LS mean (95% CI): -5.87 (-8.67, -3.06), P <.0001].

CONCLUSIONS

- The real-world observational study with ublituximab, demonstrates consistent clinical outcomes with pivotal clinical studies. The cohort's diversity along racial, ethnic, and geographic sections, provides further understanding of real-world populations on ublituximab.
- On-treatment ARR was 0.015 in RMS patients (132.4 patient-years) transitioning to ublituximab in real-world clinical setting, with 99.5% of participants reporting no relapses on ublituximab.
- Infusion durations in real-world were consistent with the expected infusion times.
- Ublituximab was well tolerated in real-world clinical setting. IRRs were significantly lower compared to pivotal clinical studies.
- The overall safety profile remained consistent in observational study compared to ULTIMATE I and II.
- Significant improvements in patient-reported outcomes were observed at Day 15 (2nd infusion) and week 24 (3rd infusion).

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