ENABLE: the first phase 4 observational study for patients with relapsing MS treated with ublituximab in real world clinical settings

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OBJECTIVE

- To evaluate the real-world clinical effectiveness, safety, and tolerability of ublituximab.

BACKGROUND

- Ublituximab, approved for treating relapsing multiple sclerosis (RMS), demonstrated significant clinical benefit vs teriflunomide in two identical phase 3 trials, ULTIMATE I and II. These benefits continued to be observed over 5 years including the open-label extension period.[1,2]
- 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).[3,4,5]
- 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 r**E**al-world experie**N**ce of patients treated with BRIUMVI® (ublituxim**AB**-xiiy) for RMS, in a **L**ongitudinal r**E**gistry (**ENABLE**)” is designed to collect valuable real-world clinical evidence on the effectiveness, safety, and tolerability of ublituximab.
- The study design, preliminary baseline characteristics, and disease history of the currently enrolled participants are presented here.

METHODS

- ENABLE (NCT06433752) is a 96-week, multi center, phase 4 observational study to collect real-world data from ublituximab-treated patients.
- The study aims to enroll at least 500 patients with RMS across 100 centers in the US, capturing a diverse geographic and racial/ethnic population from a wide range of MS centers spanning academic institutions and independent clinics.
- Enrollment is expected to take up to 24 months.
- The primary endpoint is annualized relapse rate at week 96. The secondary endpoint is the proportion of participants experiencing adverse events in addition to documenting the incidence, severity, and type of infusion-related reactions (IRR) at each infusion.
- Exploratory endpoints include PROs (TSQM 1.4 and MSIS-29), infusion time (including premedication and post-infusion observation), and changes in immunoglobulins, B cell counts, MRI activity, Expanded Disability Status Scale, Symbol Digit Modalities Test (SDMT), Timed 25-foot Walk (T25-FW), and Nine-Hole Peg Test (9-HPT).

ENABLE: Phase 4 Study Design Overview

Prospective

Observational, per site's standard of care (SoC)

96-weeks

Enrolling at least 500 patients with RMS

Multicenter US study

The decision to start BRIUMVI® must be independent of the decision to participate in ENABLE

ENABLE: Inclusion and Exclusion criteria

INCLUSION CRITERIA

- ✓ ≥ 18 years old, adult patients with relapsing forms of MS.
- ✓ Confirmed MS diagnosis.
- ✓ Patients who have been prescribed BRIUMVI® (ublituximab-xiiy) but have not yet received their first infusion on Day 1 of 150 mg can be included.

EXCLUSION CRITERIA

- ❖ Have received any live or live-attenuated vaccines (including for varicella-zoster virus or measles) within 4 weeks prior to first BRIUMVI® (ublituximab-xiiy) administration or any non-live vaccines within 2 weeks prior to first BRIUMVI® (ublituximab-xiiy) administration.
- ❖ Any active infection (e.g., active Hepatitis B virus [HBV])
- ❖ Concurrent participation in any interventional MS trials or planned concurrent treatment with other MS DMT during the study period.

ENABLE: Objectives and Endpoints

Objectives	Endpoints (Outcome measures)
Primary	
To collect real world data on effectiveness	• Annualized Relapse Rate (ARR) Week 0-96
Secondary	
To collect real world data on safety and tolerability, including BRIUMVI® (ublituximab-xiiy) infusion experience.	• Proportion of participants experiencing serious adverse events (SAEs) and adverse events (AEs) • Incidence, severity, and type of IRR at each infusion

ENABLE: Objectives and Endpoints

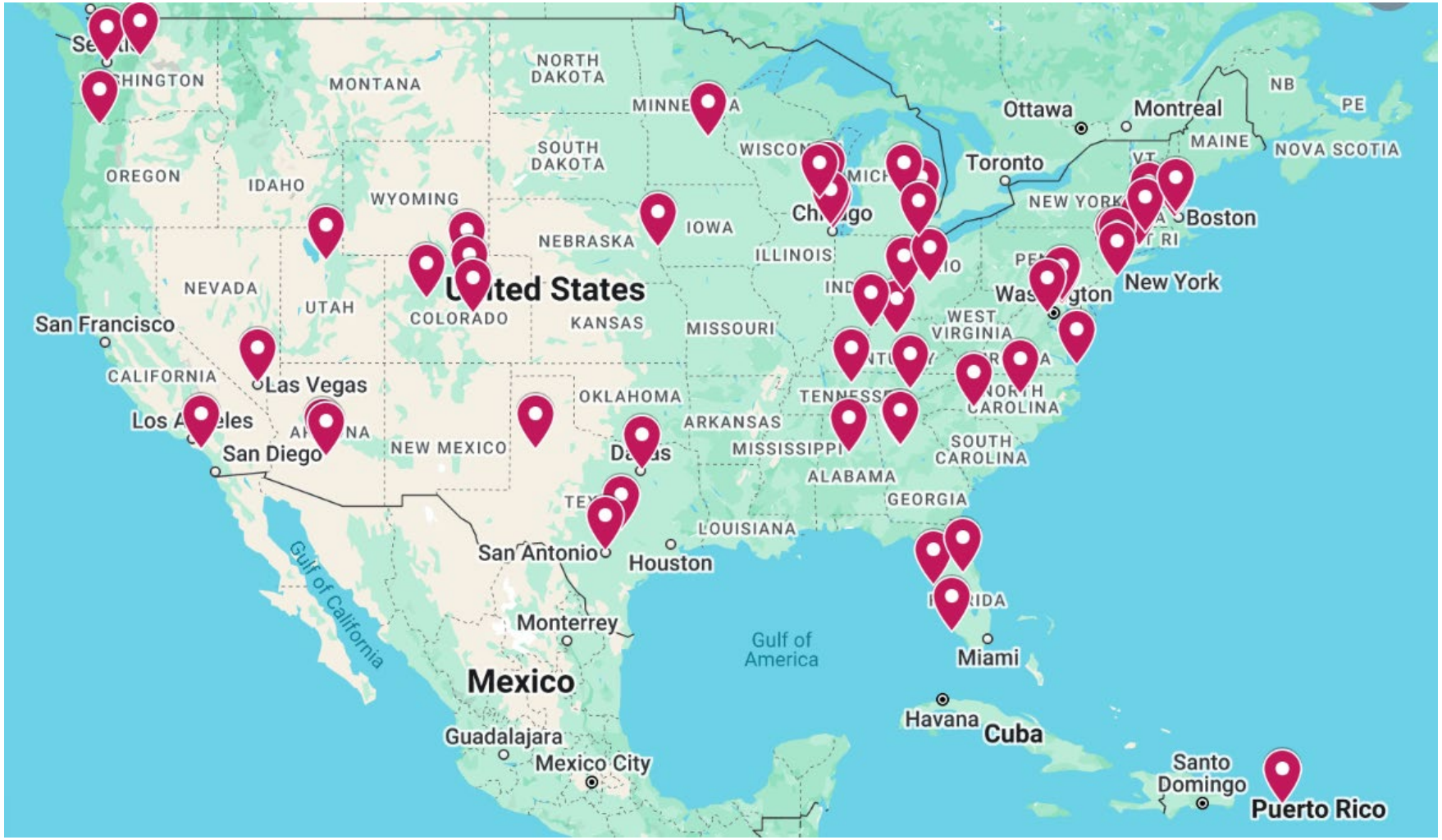
Objectives	Endpoints (Outcome measures)
Exploratory	
To collect demographics and medical history for patients initiating BRIUMVI® (ublituximab-xiiy) To understand rationale for transitioning therapies, if on a prior disease modifying therapy (DMT) To collect real world data on: • Effectiveness outcomes, including the incidence of relapses. • Safety and tolerability, including BRIUMVI® (ublituximab-xiiy) infusion experience. • Laboratory values assessed during routine clinical care.	• Baseline characteristics and previous treatments of patients receiving BRIUMVI® (ublituximab-xiiy) • Proportion of participants relapse-free • Total score on Treatment Satisfaction Questionnaire for Medication (TSQM Version 1.4) • Total score on Multiple Sclerosis Impact Scale-29 (MSIS-29) • Total time for BRIUMVI® (ublituximab-xiiy) infusion per dose • Total time in infusion chair (including premedication and post-infusion observation, if applicable)

ENABLE: Objectives and Endpoints

Objectives	Endpoints (Outcome measures)
Exploratory (contd.)	

	• Proportion of patients experiencing relapse-related hospitalization
	• Changes in the following from Baseline to 96 weeks:
	  ○ Immunoglobulins (IgG, and IgM)
	  ○ B cell counts
	  ○ Magnetic resonance imaging (MRI) disease activity, such as number of T1 Gd+ lesions or number of new/enlarging T2 lesions
	  ○ Expanded Disability Status Scale (EDSS)
	  ○ Symbol Digit Modalities Test (SDMT)
	  ○ Timed 25-foot Walk (T25-FW)
	  ○ Nine-hole peg test (9-HPT)

ENABLE Sites Open to Enrollment



Open to enroll as of Feb 2025

Table 1. ENABLE Participant Baseline Demographics

- The average age of ENABLE participants (42.8 years) is higher than that of UILTIMATE I and II participants (35.4 years)
- 72.9% of participants are female, a higher proportion than in ULTIMATE I and II (62.9% female) .
- 70.1% and 19.8% 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.
- Baseline population included as of data cutoff on 28-Feb-2025; patients are actively enrolling.

Characteristic Mean ± SD or %	Ublituximab (N=177)
Age (years)	42.8 ± 11.67
Gender, Female, n (%)	129 (72.9%)
Race, n (%)	
White	124 (70.1%)
Black or African-American	35 (19.8%)
Other	15 (8.5%)
Unknown or Not Reported	3 (1.7%)
Ethnicity	
Hispanic or Latino	30 (16.9%)
Not Hispanic or Latino	127 (71.8%)
Unknown or Not Reported	20 (11.3%)
Weight (kg)	84.60 ± 27.76
Height (cm)	169.55 ± 33.19
BMI (kg/m^2)	29.77 ± 9.05
BMI category	
<30 kg/m^2	95 (53.7%)
≥30 kg/m^2	61 (34.5%)
Unknown or Not Reported	21 (11.9%)

Table 2. ENABLE Participant Baseline Disease History

- ENABLE participants had slightly longer duration since onset of MS symptoms (8.8 years) vs ULTIMATE I and II (~7.4 years)
- Most of the participants either had one relapse (28.8%) or were relapse-free (44.1%) in the 2 years prior to screening.
- Most participants did not have Gadolinium (Gd)-enhancing lesions (57.1%) or new/enlarging T2 hyperintense Lesions compared to previous scan (45.2%).
- Baseline population included as of data cutoff on 28-Feb-2025; patients are actively enrolling.

Characteristic, Mean ± SD or %	Ublituximab, (N=177)
Time since first MS Symptoms (years)	8.8 ± 9.4
Number of relapses in the 2 years prior to screening	0.6 ± 0.77
Number of relapses in the 2 years prior to screening, n(%)	
0	78 (44.1%)
1	51 (28.8%)
2	13 (7.3%)
≥3	3 (1.7%)
Unknown or Not Reported	32 (18.1%)
Number of baseline Gadolinium (Gd)-enhancing lesions	1.0 ± 3.81
Number of baseline Gadolinium (Gd+) lesions, n (%)	
0	101 (57.1%)
≥1	24 (13.6%)
Unknown or Not Reported	52 (29.4%)
Number of New or Enlarging T2 hyperintense Lesions (compared to previous MRI scan)	2.4 ± 7.33
Number of New or Enlarging T2 Hyperintense Lesions	
0	80 (45.2%)
≥1	37 (20.9%)
Unknown or Not Reported	60 (33.9%)

Conclusions

- ENABLE is the first Phase 4 observational study that will provide valuable real-world clinical evidence on the effectiveness, safety, and tolerability of ublituximab from MS centers across the US.

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Dr. Fox, Jackie Parker, Karthik Bodhinathan, Peter Sportelli, and Hari P. Miskin are all employees of TG Therapeutics, Inc.