

# Real-world Clinical Experience from ENABLE, the First Phase 4 Observational Study for Patients with Relapsing Multiple Sclerosis Initiating Ublituximab

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# Background

- Ublituximab targets a unique epitope of CD20 and is glycoengineered for enhanced antibody-dependent cellular cytotoxicity (ADCC) and enhanced Fcγ-receptor (FcγR) binding.<sup>1,2</sup>
- In 2 identical Phase 3 trials, ULTIMATE I and II, ublituximab demonstrated significant clinical benefit vs teriflunomide, which was sustained for 6 years during the open-label extension (OLE) period.<sup>3,4,5</sup>
- The overall safety profile remained consistent over 6 years of continuous treatment.<sup>4</sup>
- 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 (1-hour infusions after the first infusion).<sup>5</sup>
- ENABLE is an ongoing Phase 4 observational study for patients with RMS treated with ublituximab. The study continues to provide valuable real-world clinical evidence on the effectiveness, safety, and tolerability of ublituximab.
- The study duration is 192 weeks, with a target enrollment of 2,000 participants.
- Results from an interim analysis of the ongoing ENABLE study are presented here.

1. Alvarez E, et al. Presented at the CMSC Annual Meeting; June 1-4, 2022; National Harbor, MD, USA. Oral presentation DMT03.

2. Cree BAC, et al, et al. CNS Drugs. 2025; 545–564.

3. Steinman L, et al. N Engl J Med. 2022;387(8):704-714.

4. Cree BAC, et al, Presented at the ECTRIMS Annual Meeting, September 24-26, 2025, Barcelona, Spain.

5. BRIUMVI® (ublituximab-xiy) Prescribing Information. TG Therapeutics, Inc. 2026.



# Methods

- ENABLE participants who received at least 1 dose of ublituximab and had any baseline assessment for demographics and disease history, as of the data cut-off date of December 1<sup>st</sup>, 2025 were included in the analysis.
- Annualized relapse rate is calculated as cumulative number of relapses divided by the cumulative treatment time. Duration of infusion (in minutes) was defined as duration between infusion start to stop time.
- Premedication use was captured on the day of infusion or the day before infusion.



# Figure 1. ENABLE Sites Open to Enrollment



- As of the data cut (01-December-2025), 87 sites were actively enrolling patients across the U.S.



## Table 1. Baseline Demographics

Characteristic, Mean ± SD or n(%)	Ublituximab (N=658)
Age (years)	43.0 ± 11.47
Gender, Female, n (%)	501 (76.1)
Race, n (%)	
White or Caucasian	468 (71.1)
Black or African American	128 (19.5)
Other	53 (8.0)
Unknown or Not Reported	9 (1.4)
Ethnicity, n (%)	
Hispanic or Latino	86 (13.1)
Not Hispanic or Latino	500 (76.0)
Unknown or Not Reported	72 (10.9)
Weight (kg)	85.7 ± 24.98
Height (cm)	167.91 ± 9.83
BMI (kg/m <sup>2</sup> )	30.40 ± 8.41
BMI Category	
<30 kg/m <sup>2</sup>	345 (52.4)
≥30 kg/m <sup>2</sup>	252 (38.3)
Unknown or Not Reported	61 (9.3)

- The average age of ENABLE participants (43.0 years) is higher than that of ULTIMATE I and II participants (35.4 years).
- 76.1% of participants are female, a higher proportion than in ULTIMATE I and II (62.9% female).
- 71.1% and 19.5% 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<sup>2</sup> is 38.3%, which is relatively higher compared to ULTIMATE I/II participants (11.3%).



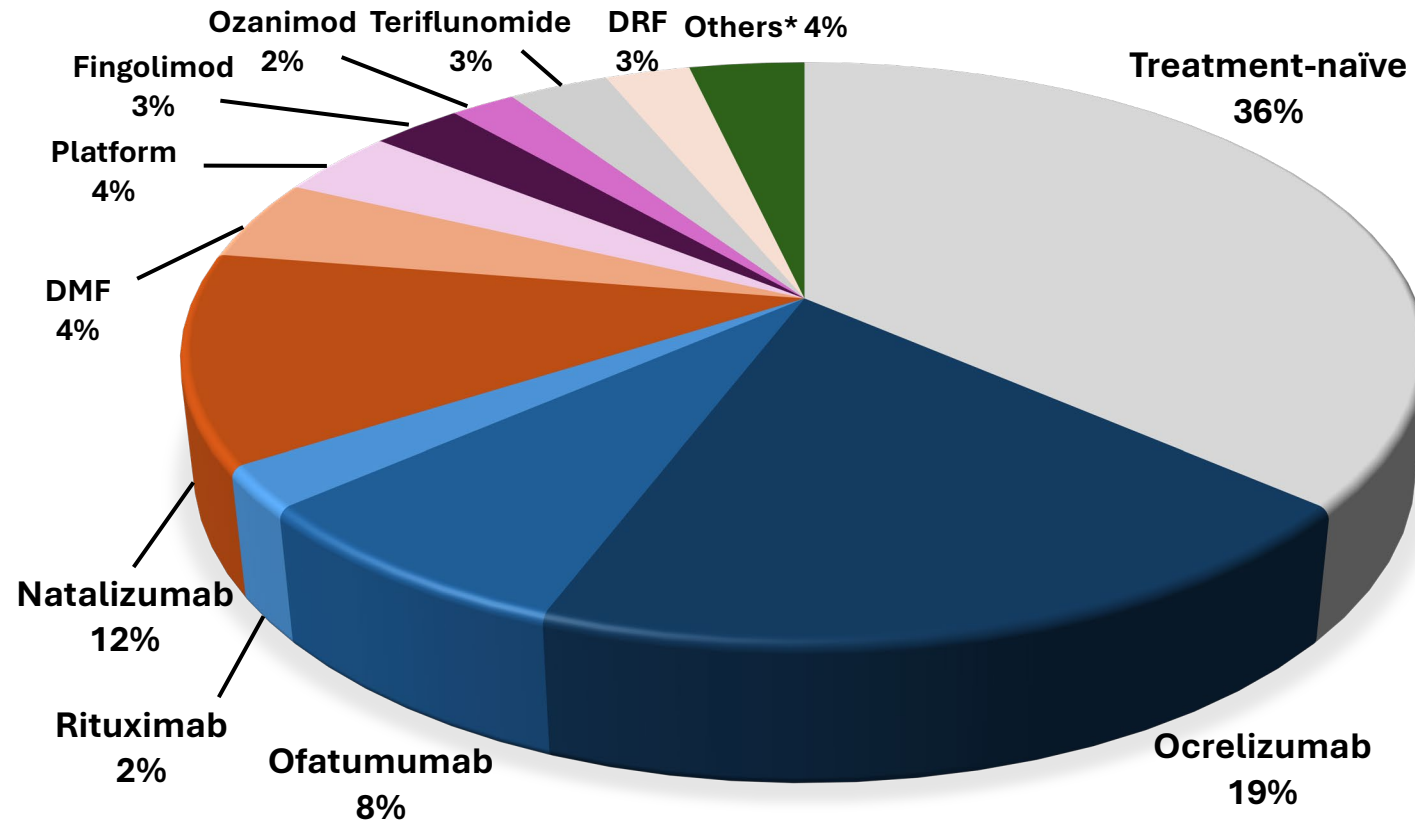
## Table 2. Baseline Disease History

Characteristic, Mean ± SD or n (%)	Ublituximab, (N=658)
Time Since First MS Symptoms (years)	8.68 ± 9.06
Number of Relapses in the 2 Years Prior to Screening	0.6 ± 0.83
Number of Relapses in the 2 Years Prior to Screening, n (%)	
0	274 (41.6)
1	188 (28.6)
2	45 (6.8)
≥3	15 (2.3)
Unknown or Not Reported	136 (20.7)
Number of Baseline Gadolinium-enhancing (Gd+) Lesions	1.3 ± 5.65
Number of Baseline Gd+ Lesions, n (%)	
0	350 (53.2)
≥1	114 (17.3)
Unknown or Not Reported	194 (29.5)
Number of New and/or Enlarging T2 Hyperintense Lesions (compared to previous MRI scan)	1.5 ± 4.98
Number of New and/or Enlarging T2 Hyperintense Lesions, n (%)	
0	328 (49.8)
≥1	118 (17.9)
Unknown or Not Reported	212 (32.2)

- ENABLE participants had slightly longer duration since onset of MS symptoms (8.68 years) vs ULTIMATE I and II (~7.4 years).
- Most of the participants either had 1 relapse (28.6%) or were relapse-free (41.6%) in the 2 years prior to screening.
- At baseline, 53.2% of participants starting ublituximab had no Gd+ lesions which was similar to ULTIMATE I and II (~53%).



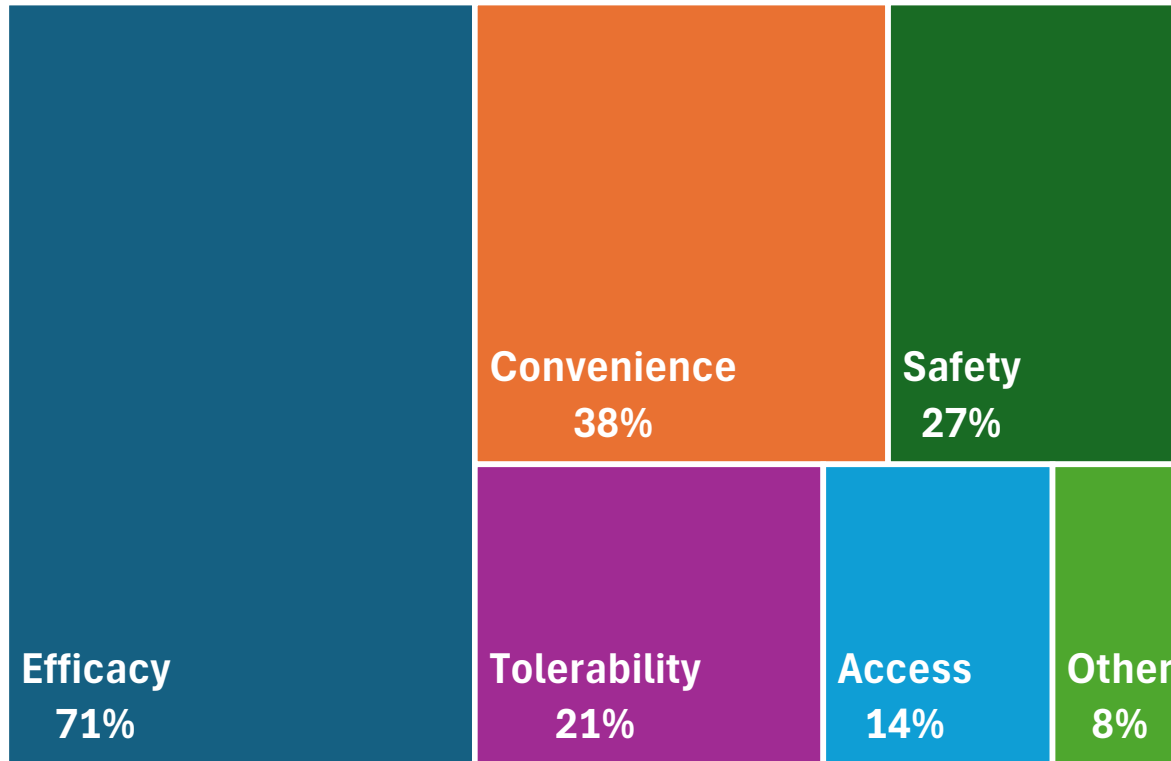
## Figure 2. Prior DMT History for MS Patients Starting Ublituximab in ENABLE



- The largest category of patients starting ublituximab treatment on ENABLE were treatment naïve (36%).
- The second largest proportion of patients (29%) transitioned to ublituximab from prior B-cell therapy (ocrelizumab, ofatumumab or rituximab), followed by natalizumab (12%).



# Figure 3. Reasons for Starting Ublituximab and Patient-reported Outcomes



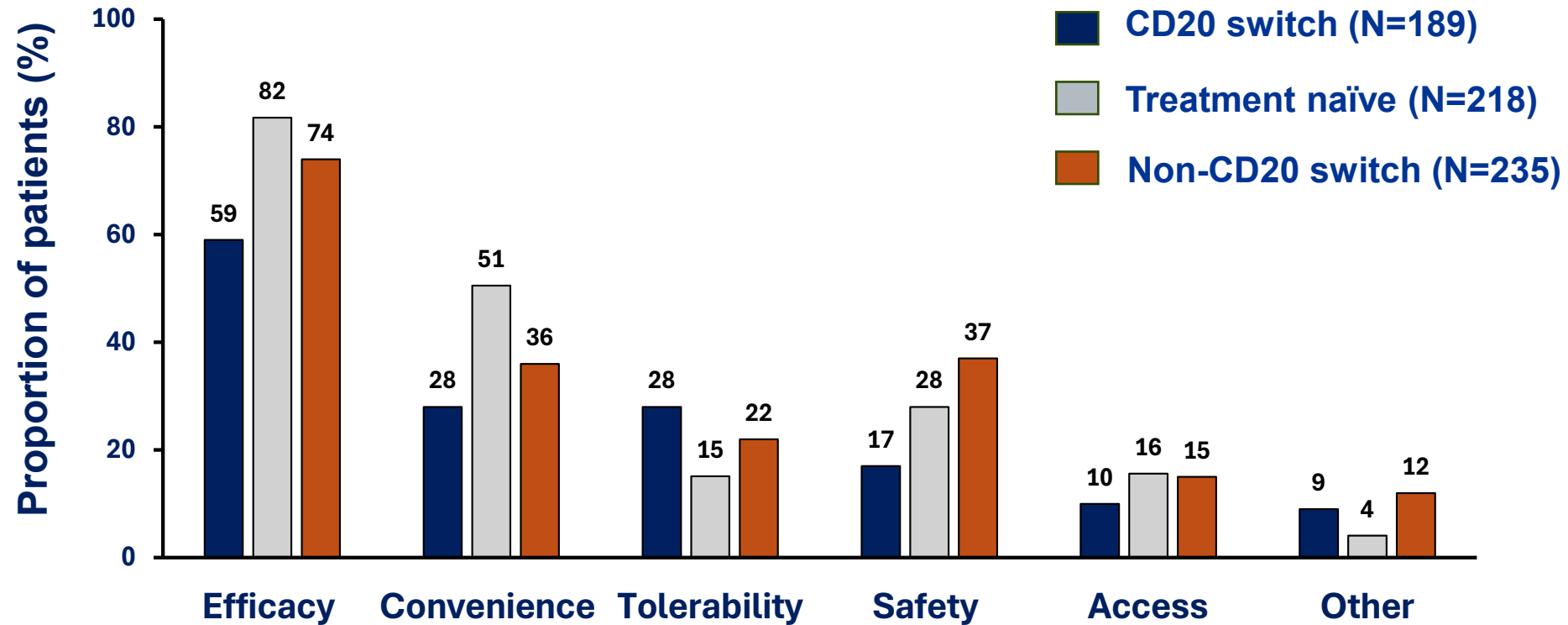
- Perceived efficacy of the prior DMT was the leading reason for initiating ublituximab treatment, reported by 71% of patients.
- Other factors influencing patients' decisions to start ublituximab included convenience (38%), safety (27%), and tolerability (21%) of the prior DMT.

## Patient-reported outcomes:

- Ublituximab-treated patients reported significant and durable improvements in all sub-domains of **TSQM** (1.4), compared to baseline.
  - Improvements were observed at day 15 [LS Mean change: Effectiveness (E), 6.66,  $P < 0.0001$ ; Convenience (C), 9.58,  $P < 0.0001$ ; Side effects (S), 0.26,  $P = 0.8676$ ; Global Satisfaction (G), 13.21,  $P < 0.0001$ ], and sustained at week 24 [E, 11.05,  $P < 0.0001$ ; C, 12.61,  $P < 0.0001$ ; S, 5.08,  $P = 0.0042$ ; G, 15.62,  $P < 0.0001$ ], and week 48 [E, 15.62,  $P < 0.0001$ ; C, 10.95,  $P < 0.0001$ ; S, 5.27,  $P = 0.0380$ ; G, 17.46,  $P < 0.0001$ ]
- Significant and durable improvements were also observed in **MSIS-29** scores in ublituximab-treated patients.
  - Improvements were observed as early as day 15 [LS Mean change: Physical, -3.91,  $P < 0.0001$ ; Psychological, -5.54,  $P < 0.0001$ ], and sustained at week 24 [Physical, -3.46,  $P < 0.0001$ ; Psychological, -5.29,  $P < 0.0001$ ], and week 48 [Physical, -4.25,  $P = 0.0008$ ; Psychological, -5.57,  $P < 0.0001$ ]



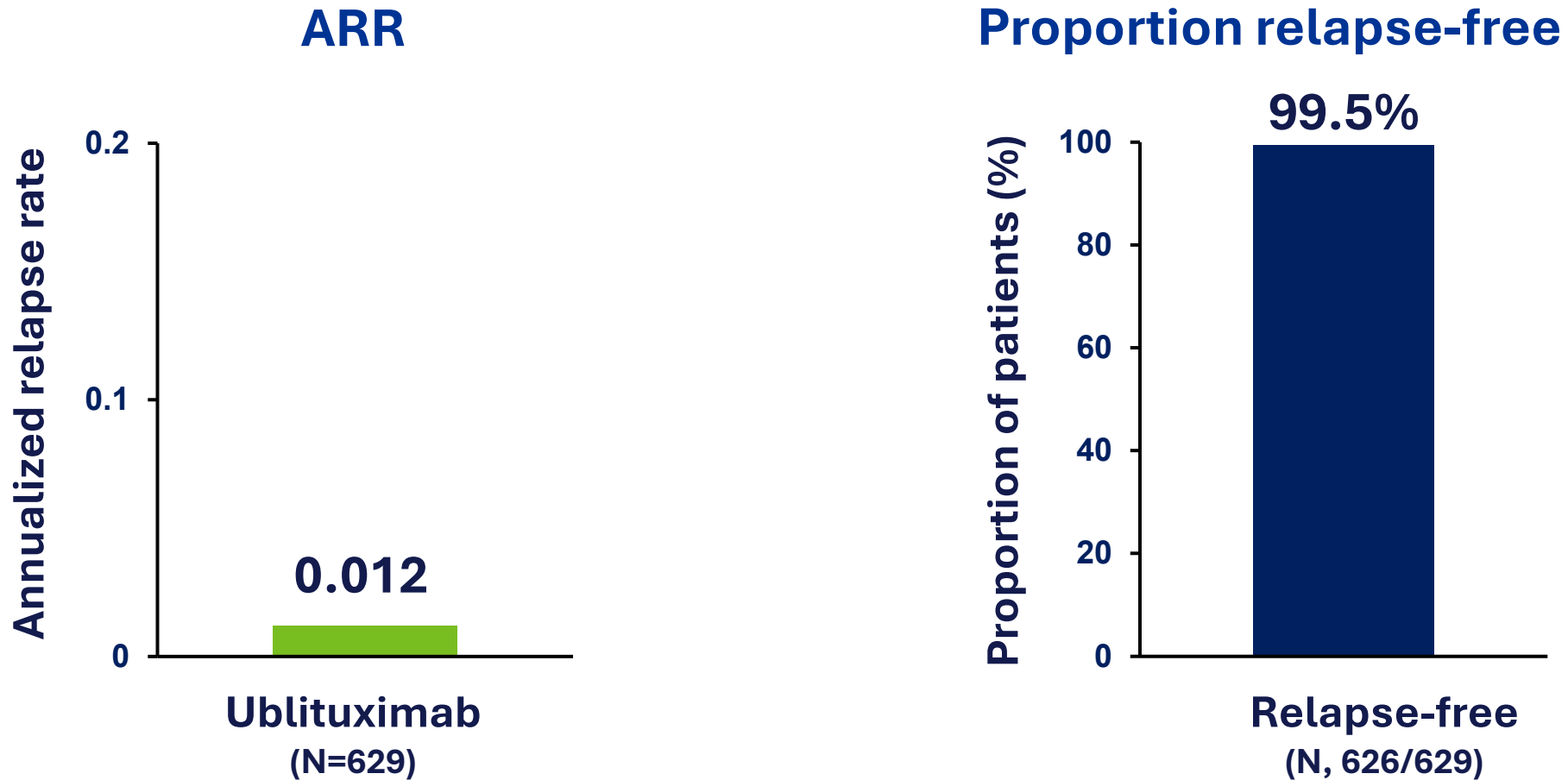
# Figure 4. Reasons for Starting Ublituximab Treatment by Prior DMT History



- Efficacy was the top reason for starting ublituximab by treatment-naïve (82%), non-CD20 switch (74%), and CD20 switch (59%) cohorts.
- Convenience was higher in the treatment-naïve cohort (51%), followed by non-CD20 switch (36%), and CD20 switch (28%) participants.
- Tolerability was higher in the CD20 switch cohort (28%) compared to non-CD20 switch (22%), and treatment-naïve cohort (15%).



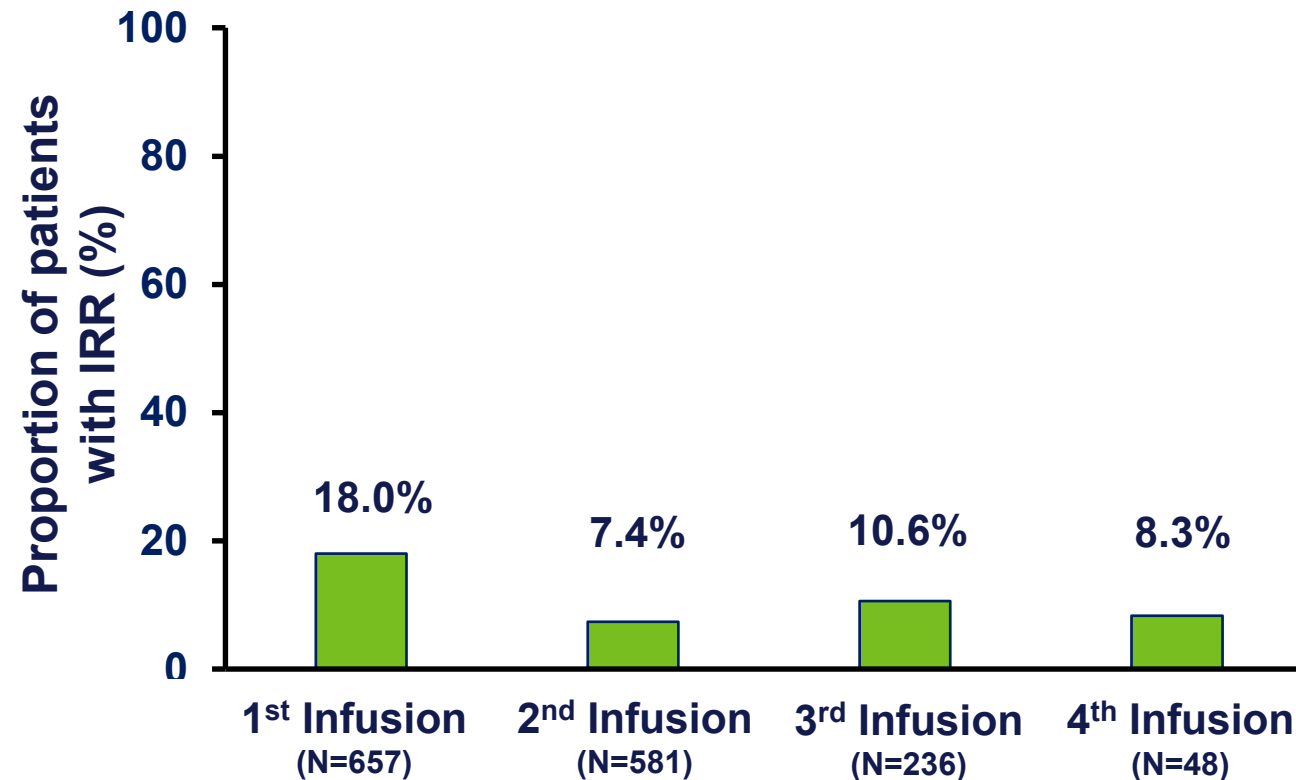
## Figure 5. Summary of On-treatment ARR and Relapses



- On-treatment annualized relapse rate was 0.012, with cumulative treatment time of 342.9 patient-years.
- On-treatment relapses were rare, and 99.5% of participants reported no relapses during treatment with ublituximab.



## Figure 6. Infusion-related Reactions in Ublituximab-treated Participants from ENABLE



- IRRs were most frequently observed at the 1<sup>st</sup> infusion (18.0% of participants) and decreased in frequency during subsequent infusions.
- None of the IRRs were serious (or  $\geq$  Grade 3) in nature. All IRRs were Grade 1 or Grade 2 and resolved completely.
- Most infusions were completed within the specified time. The median infusion duration was 247 minutes for first infusion and 63 minutes for the second, third and fourth infusions.



**Table 3. Infusion-related Reactions with an Incidence Rate of at Least 2%**

IRR symptom	Ublituximab, (N=658) n (%)
Headache	39 (5.9)
Nausea	26 (4.0)
Throat irritation	25 (3.8)
Pruritus	24 (3.6)
Flushing	18 (2.7)
Fatigue	14 (2.1)

**Table 4. Adverse Events with an Incidence Rate of at Least 1%**

Adverse event	Ublituximab, (n=658) n (%)
Any treatment emergent adverse event (TEAE)	208 (31.6)
Infusion-related reaction (IRR)	139 (21.1)
Headache	24 (3.6)
Fatigue	11 (1.7)
Urinary tract infection	10 (1.5)
Insomnia	8 (1.2)
Nausea	7 (1.1)
Pain	7 (1.1)
Arthralgia	7 (1.1)



# Conclusions

- The real-world evidence from ENABLE reinforces the clinical outcomes observed in the pivotal clinical trials.
- The largest category of patients starting ublituximab treatment on ENABLE were treatment naïve followed by transitions from prior B-cell therapies.
- On-treatment ARR was 0.012 in RMS patients starting ublituximab in real-world clinical setting, with 99.5% of participants reporting no relapses on ublituximab. Although most participants did not report MRI data, the growing patient enrollment is anticipated to enrich the MRI dataset.
- Improved tolerability was observed in real-world clinical setting compared to pivotal trials. Overall IRRs, and first dose IRRs were significantly lower compared to pivotal clinical studies.
- All IRRs were either Grade 1 or 2 in nature and resolved completely. IRRs showed an overall decrease in frequency during subsequent infusions.
- The overall safety profile remained consistent in the observational study compared to the pivotal trials.
- As an observational study, an inherent limitation is that participants are treated per standard of care at sites that have heterogenous data collection, thus leading to missing inputs for some categories (e.g., MRI).



# REFERENCES

1. Alvarez E, et al. Presented at the CMSC Annual Meeting; June 1-4, 2022; National Harbor, MD, USA. Oral presentation DMT03
2. Cree BAC, et al, et al. CNS Drugs. 2025; 545–564
3. Steinman L, et al. N Engl J Med. 2022;387(8):704-714
4. Cree BAC, et al, Presented at the ECTRIMS Annual Meeting, September 24-26, 2025, Barcelona, Spain
5. BRIUMVI® (ublituximab-xiiy) Prescribing Information. TG Therapeutics, Inc. 2026

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