Real-World Infusion Experience with Ublituximab in ENABLE, the Phase 4 Observational Study

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CONCLUSIONS

- In the real-world clinical setting, ublituximab has demonstrated consistent tolerability.
- Most of the patients were treatment naïve, with the second highest category being those transitioning to ublituximab from prior B-cell therapies.
- The infusion durations in this real-world cohort were consistent with the expected infusion times per label.
- Overall infusion-related reactions (IRRs) were low, and first dose IRRs were significantly lower compared to pivotal clinical studies. IRRs showed an overall decrease in frequency during subsequent infusions.
- All IRRs were either Grade 1 or 2 in nature and resolved completely. None were Grade 3 or higher. Most commonly observed IRRs were headache, nausea, and throat irritation.
- Premedication use was consistent with the label and included a mix of corticosteroids, antipyretics, and antihistamines. The use of antipyretics may have contributed to the low first-dose IRR in this cohort compared to the Phase 3 studies where antipyretic use was excluded for the first infusion.

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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.[1,2]
- 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.[3,4]
- Ublituximab is administered at lower doses with shorter infusion times (1-hour infusions after the first infusion) compared to other infused anti-CD20 therapies.[5]
- ENABLE is an ongoing Phase 4 observational study for patients with relapsing multiple sclerosis (RMS) treated with ublituximab. The study continues to provide valuable real-world clinical evidence on the effectiveness, safety, and tolerability of ublituximab.
- Emerging evidence suggests an improved infusion tolerability profile for ublituximab.[6,7]
  - Results from ENABLE on the real-world infusion experience is presented here.

METHODS

- ENABLE participants who received at least 1 dose of ublituximab and any baseline efficacy evaluation as of the data cut-off date of December 1st, 2025 were included in the analysis.
- Duration of infusion in minutes was calculated as time between start and stop of the IV infusion.
- Premedication use was captured on the day of infusion or the day before infusion.

RESULTS

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	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^2)	30.40 ± 8.41
BMI Category	
<30 kg/m^2	345 (52.4)
≥30 kg/m^2	252 (38.3)
Unknown or Not Reported	61 (9.3)

Baseline population included as of data cutoff on 01-December-2025; participants are actively enrolling.

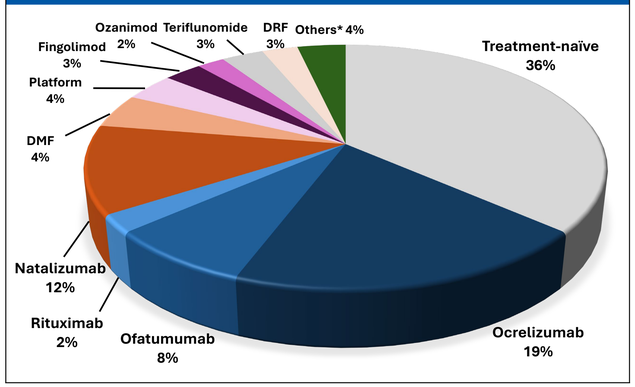
- The average age of ENABLE participants (43.0 years) is higher than that of ULTIMATE I and II participants (35.4 years).
- 76.1% of participants are female, a higher proportion than in ULTIMATE I and II (62.9% female).
- 71.1% and 19.5% of participants are White/Caucasian and Black/African-American, 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^2 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%).

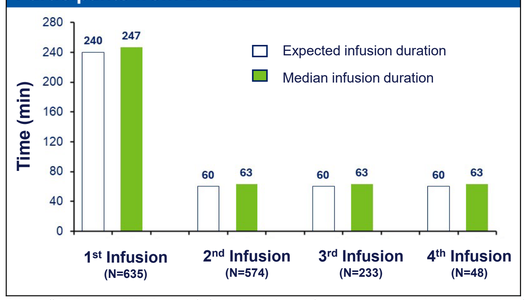
Figure 1. Prior DMT Treatment History for MS Patients Starting Ublituximab on ENABLE



Data cutoff: 01-December-2025. Listed DMTs are immediately prior to start of ublituximab.
*Includes missing input from n=16 (3.8%)

- The majority of patients (36%) were treatment naïve at the start of ENABLE
- A large proportion of patients (29%) transitioned to ublituximab from prior B-cell therapy: ocrelizumab, ofatumumab or rituximab, or natalizumab (12%).

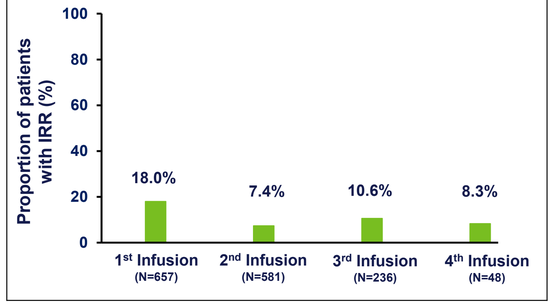
Figure 2. Infusion Times in Ublituximab-treated Participants from ENABLE



Data cutoff: 01-December-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 was 247 minutes for the first infusion and 63 minutes for the second, third and fourth infusions.

Figure 3. Infusion-related Reactions in Ublituximab-treated Participants from ENABLE



Data cutoff: 01-December-2025. IRR= Infusion-related reaction. Events assessed as IRRs by the treating physician

- IRRs were most frequently observed at the 1st infusion (18.0% of participants) and decreased in frequency during subsequent infusions.
- 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, 88.0%), antipyretic (acetaminophen/ paracetamol, 82.8%; ibuprofen, 6.7%), and antihistamines (diphenhydramine, 76.0%; cetirizine, 15.1%; famotidine, 14.9%).

Table 3. Infusion-related Adverse Events with an Incidence of at Least 2%

	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)

Data cutoff: 01-December-2025

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