

Evaluation of Ublituximab Infusion Tolerability: Analysis of Data Following the ULTIMATE Phase 3 Studies

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CONCLUSIONS

- Ublituximab demonstrates a favorable and consistent infusion tolerability profile across clinical and real-world settings.
- First-infusion IRR rates were substantially lower in ENHANCE (9.1%), ENABLE (18.0%), and ENAMOR (19.2%) compared with 43% in the ULTIMATE Phase 3 studies.
- Premedication practices were consistent across settings, supporting standardized administration approaches.
- Infusion durations were predictable with real-world data aligned closely with clinical study findings, confirming consistency of administration practices.

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}
- Ublituximab is administered in lower doses and with shorter infusion times compared with other currently infused anti-CD20 therapies.^{3,4,5}
- ULTIMATE I (NCT03277261) and ULTIMATE II (NCT03277248) are identical, Phase 3, randomized, multicenter, double-blind, active-control studies evaluating the efficacy and safety of ublituximab versus teriflunomide in participants with relapsing multiple sclerosis (RMS).^{4,5}
- In the ULTIMATE studies, premedications included an antihistamine and corticosteroid; acetaminophen was prohibited at the first infusion to avoid confounding Day 2 labs but was permitted for later infusions.⁶ Infusion-related reactions (IRRs) occurred most frequently with the first infusion (43%) and declined markedly thereafter (10%, 8%, and 7% for infusions two through four). In pooled analyses, 96.6% of participants completed ublituximab infusions without interruption, and 94.6% completed infusions 2-5 within 1 hour±5 minutes.⁷
- The aim of this analysis is to further characterize the tolerability of ublituximab infusions, building on findings from the ULTIMATE studies and leveraging additional data demonstrating a favorable infusion experience, including reduced first-dose IRRs.

RESULTS

Premedications Utilized for the 1st Infusion

ENHANCE

❖ Data from 55 patients receiving their 1st ublituximab infusion

Class / Agent	n (%)
Antipyretic	55 (100)
Paracetamol/Acetaminophen	54 (98.2)
Ibuprofen	1 (1.8)
Corticosteroids	54 (98.2)
Methylprednisolone	54 (98.2)
Antihistamines*	54 (98.2)
Cetirizine	43 (78.2)
Diphenhydramine	8 (14.5)
Loratadine	6 (10.9)
Other Premedications Given	10 (18.2)
Famotidine	9 (16.4)
Ranitidine	1 (1.8)

*Patients may have received more than one antihistamine

ENAMOR

❖ Data from 21 clinics describing standard premedication protocols for the 1st ublituximab infusion in 401 patients

Class / Agent	n (%)
Antipyretic	
Paracetamol/Acetaminophen	19 (90.5)
Ibuprofen	2 (9.5)
Corticosteroid	
Methylprednisolone	21 (100)
Antihistamine	
Diphenhydramine	18 (85.7)
Cetirizine	2 (9.5)
Other	1 (4.8)
Other Premedications Given	
Pepcid (famotidine)	4 (19.0)
Zofran (ondansetron)	2 (9.5)
Other	3 (14.3)

ENABLE

❖ Data from 657 patients receiving their 1st ublituximab infusion

Class / Agent	n (%)
Antipyretic	
Paracetamol/Acetaminophen	544 (82.8)
Ibuprofen	44 (6.7)
Corticosteroids	
Methylprednisolone	578 (88.0)
Dexamethasone	6 (0.9)
Hydrocortisone Sodium Succinate	5 (0.8)
Antihistamine	
Diphenhydramine	499 (76.0)
Cetirizine	99 (15.1)
Loratadine	19 (2.9)
Hydroxyzine	1 (0.2)
Desloratadine	6 (0.9)
Other Premedications Given	
Famotidine	98 (14.9)
Ondansetron	23 (3.5)
Sodium Chloride	14 (2.1)
Ketorolac	1 (0.2)
Ondansetron Hydrochloride	1 (0.2)
Pantoprazole	1 (0.2)

METHODS

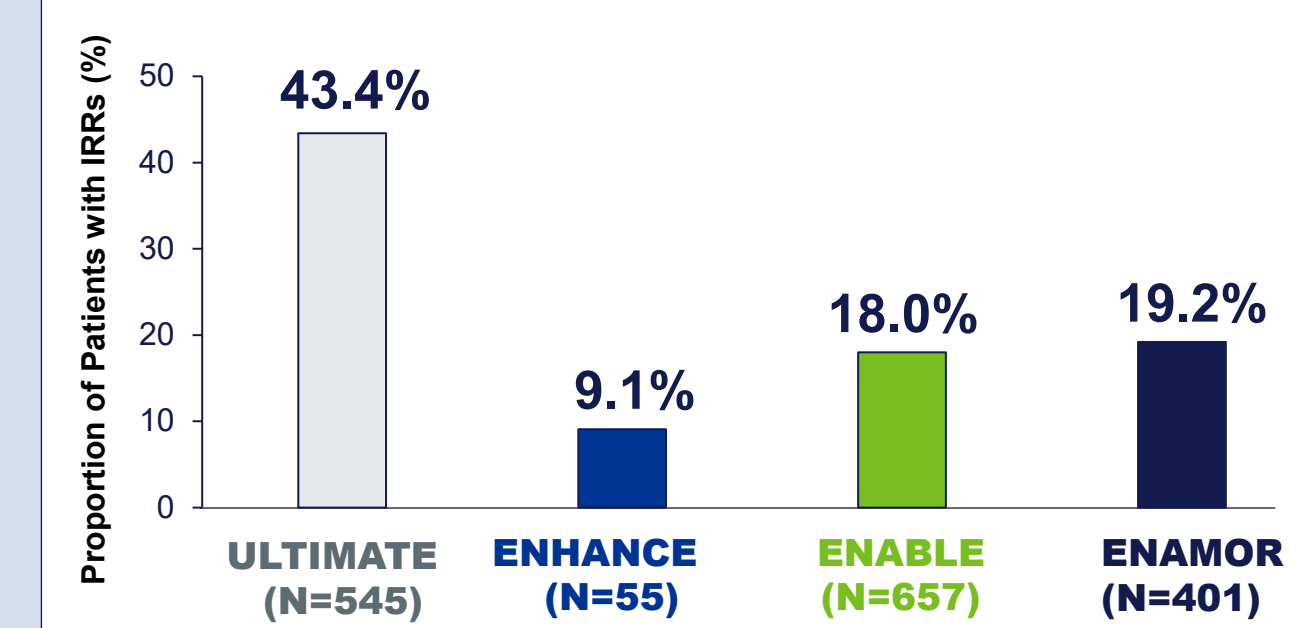
To characterize the tolerability profile of ublituximab infusions, this analysis synthesized data from three independent sources in participants treated with ublituximab according to labeled dosing.

- ENHANCE (Ongoing Clinical Study)**
 - Phase 3b, multicenter, open-label, 48-week study in RMS.
 - The study is actively enrolling participants with RMS who are treatment-naïve or transitioning from other disease-modifying therapies and currently evaluating modified dosing regimens for ublituximab.
 - Analysis was limited to labeled dosing for first two infusions and includes patients with CD19+ B cells ≥10 cells/μL at screening.

- ENABLE (Ongoing Real-World Observational Study)**
 - Phase 4 observational study reflecting routine clinical practice.
 - Inclusion of RMS patients receiving ≥1 dose of ublituximab.
 - Captures real-world effectiveness, safety, and tolerability.
- ENAMOR (Completed Clinic Survey Data)**
 - Retrospective, blinded electronic survey of MS clinics.
 - Captures site-level infusion practices and experiences.
 - Conducted from March–September 2024 and included 10–20 patients per site with relapsing MS treated per USPI.
 - Excluded PPMS, inactive SPMS, and clinical trial participants.

Infusion-Related Reactions

Figure 1. Infusion-Related Reactions with the First Ublituximab Infusion



First Infusion

Across the evaluated datasets (ENHANCE, N=55; ENABLE, N=657; ENAMOR, N=401), first-infusion IRR rates were 9.1%, 18.0%, and 19.2%, respectively (Fig. 1).

Subsequent Infusions

- In ENHANCE, the IRR rate at the second infusion was 9.3% (n=54).
- In ENABLE, IRR rates were 7.4% at the second infusion (n=581), 10.6% at the third infusion (n=236), and 8.3% at the fourth infusion (n=48).
- In ENAMOR, IRR rates were 6.9% at the second infusion (n=394), 7.7% at the third infusion (n=285), and 5.1% at the fourth infusion (n=99).

IRR Severity and Characteristics

ENHANCE: Most IRRs were low grade, with Grade 1 reactions in 4.6% and Grade 2 in 4.6% of infusions.
 ENABLE: None of the IRRs were serious (or ≥Grade 3) in nature. All events were Grade 1 or Grade 2 and resolved completely.

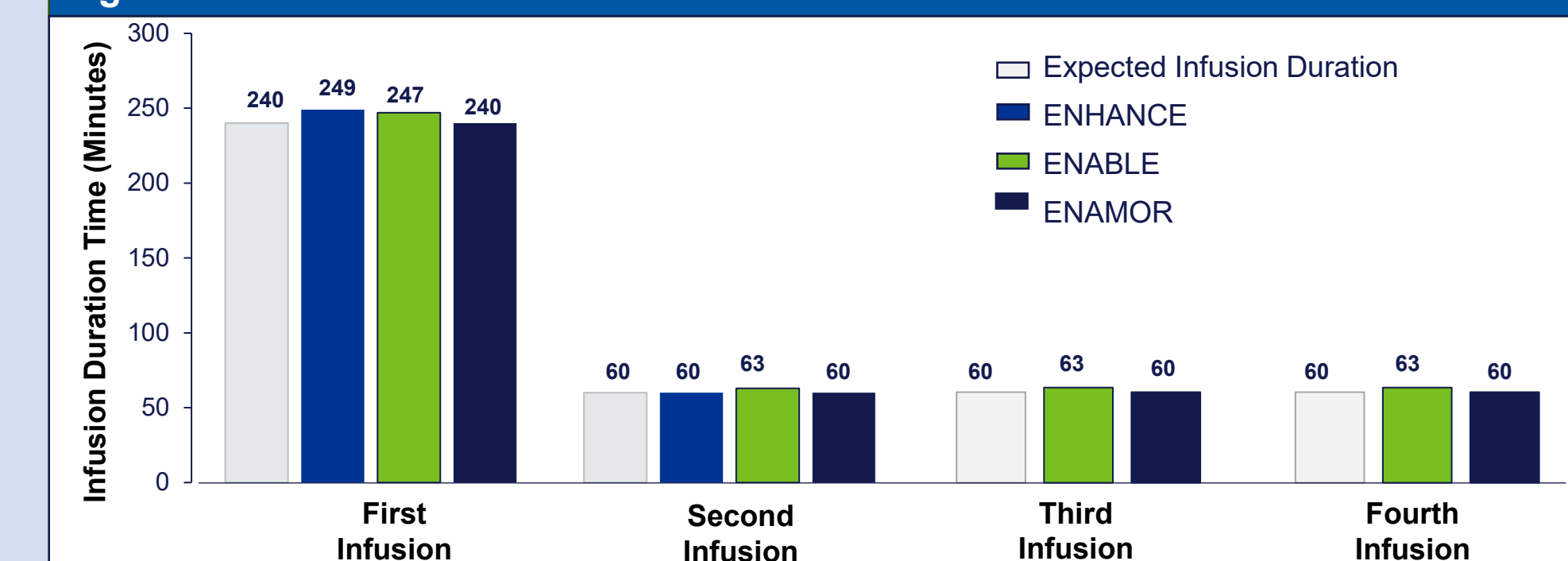
ENAMOR: IRRs reported in ≥4% of patients per infusion:

- 1st infusion: headache (4.5%), nausea (4.0%), other* (10.2%)
- 2nd infusion: other* (4.6%)
- 3rd infusion: none
- 4th infusion: other* (4.0%)

* "other" defined as an IRR not listed in the USPI for ublituximab-xiyi. The types of IRRs listed in the USPI include pyrexia, chills, headache, influenza-like illness, tachycardia, nausea, throat irritation, erythema, and an anaphylactoid reaction

Infusion Duration

Figure 2. Median Infusion Time



- Median infusion durations were consistent with expected timings across all datasets (Fig 2).
- First infusion durations were comparable across ENHANCE, ENABLE, and ENAMOR (240–249 minutes).
- Subsequent infusions demonstrated stable durations, generally ~60–63 minutes.
- Minimal variability was observed across all datasets, supporting reproducibility of infusion timing in both clinical and real-world settings.
- Real-world data (ENAMOR) aligned closely with clinical study findings, confirming consistency of administration practices.

Infusion Interruption or Slowing

Figure 3. ENHANCE Infusions Completed without Interruption or Slowing

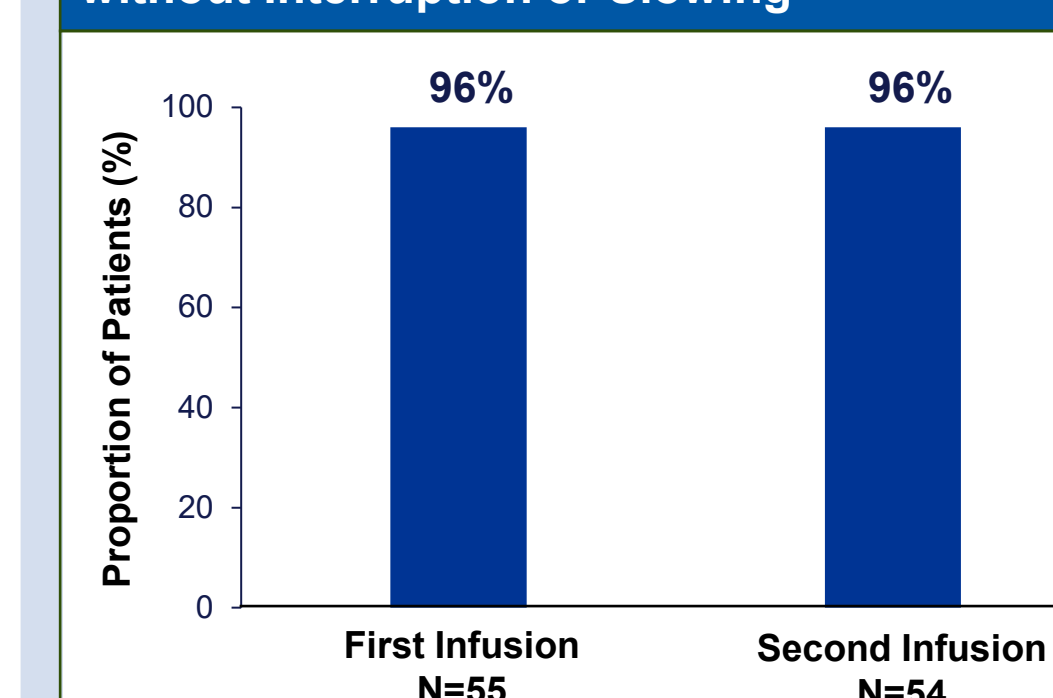
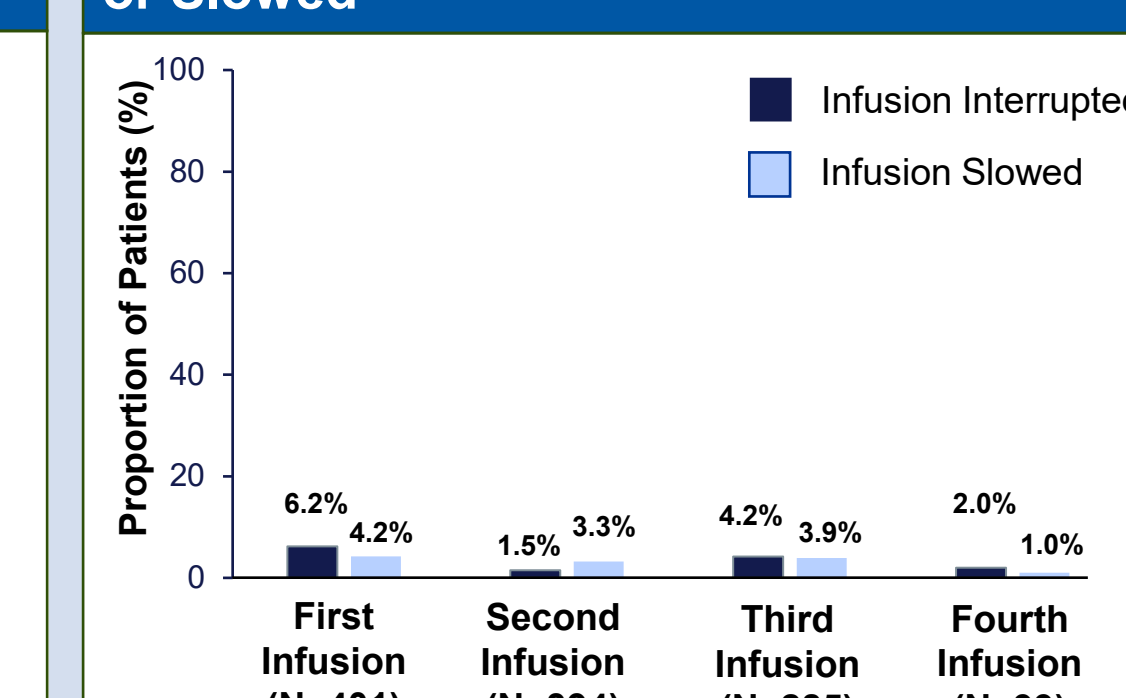


Figure 4. ENAMOR Infusions Interrupted or Slowed



- The majority of patients in ENHANCE completed infusions without interruption or slowing (96%) for both the first and second infusions (Fig. 3).
- Infusion interruptions and slowing were infrequent in ENAMOR, occurring in ≤6.2% and ≤4.2% of patients, respectively, across infusions (Fig. 4).
- Findings demonstrate a high level of infusion tolerability and minimal need for rate modification across clinical and real-world settings.
- Infusion interruptions and rate reductions were not captured in the ENABLE study.

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