Retrospective Evaluation of Infusion Tolerability: Ublituximab Real-World Observational Survey (ENAMOR)

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American Academy of Neurology (AAN) Annual Meeting, April 5-9, 2025, San Diego, CA

BACKGROUND

- Ublituximab is a novel monoclonal antibody that targets a unique epitope of CD20 and is glycoengineered to exhibit a low fucose content in its fragment crystallizable (Fc) region[1-3]

- Ublituximab is administered in lower doses and with shorter infusion times compared with other currently infused anti-CD20 therapies[4]

- ULTIMATE I (NCT03277261) and ULTIMATE II (NCT03277248) are two identical, Phase 3, randomized, multicenter, double-blind, active-control studies that evaluated the efficacy and safety of ublituximab versus teriflunomide in participants with relapsing multiple sclerosis (RMS)[4]
  - In the ULTIMATE studies, premedications prior to each infusion included an antihistamine and corticosteroid. Acetaminophen was not permitted at the first infusion so as not to confound Day 2 labs but could be utilized for subsequent infusions at the investigator's discretion. The incidence of IRRs was highest with the first infusion (43%) and markedly decreased with subsequent infusions (10% with the second, 8% with the third infusion, and 7% with the fourth infusion)[4]

METHODS

- ENAMOR is a retrospective, blinded electronic survey to assess the tolerability profile in people with multiple sclerosis (MS) who have relapsing disease and treated with ublituximab in the real-world setting.

- During the survey period (March 2024 – September 2024), clinics were sent one survey to collect data for analyses related to the infusion experience, premedications, incidence of infusion-related reactions (IRRs), and infusion time for ublituximab infusions.

- Clinics could only include people with multiple sclerosis who met the following inclusion criteria: >18 years old, confirmed MS diagnosis as deemed by the treating neurologist, and treated with ublituximab per the USPI dosing recommendations. People with MS diagnosed with primary progressive MS or inactive secondary progressive MS were excluded. Additionally, no study or research patients were permitted.

- To ensure a variety of clinical experience, a minimum of 10 and a maximum of 20 people with MS who have relapsing disease per clinic were included in the survey.

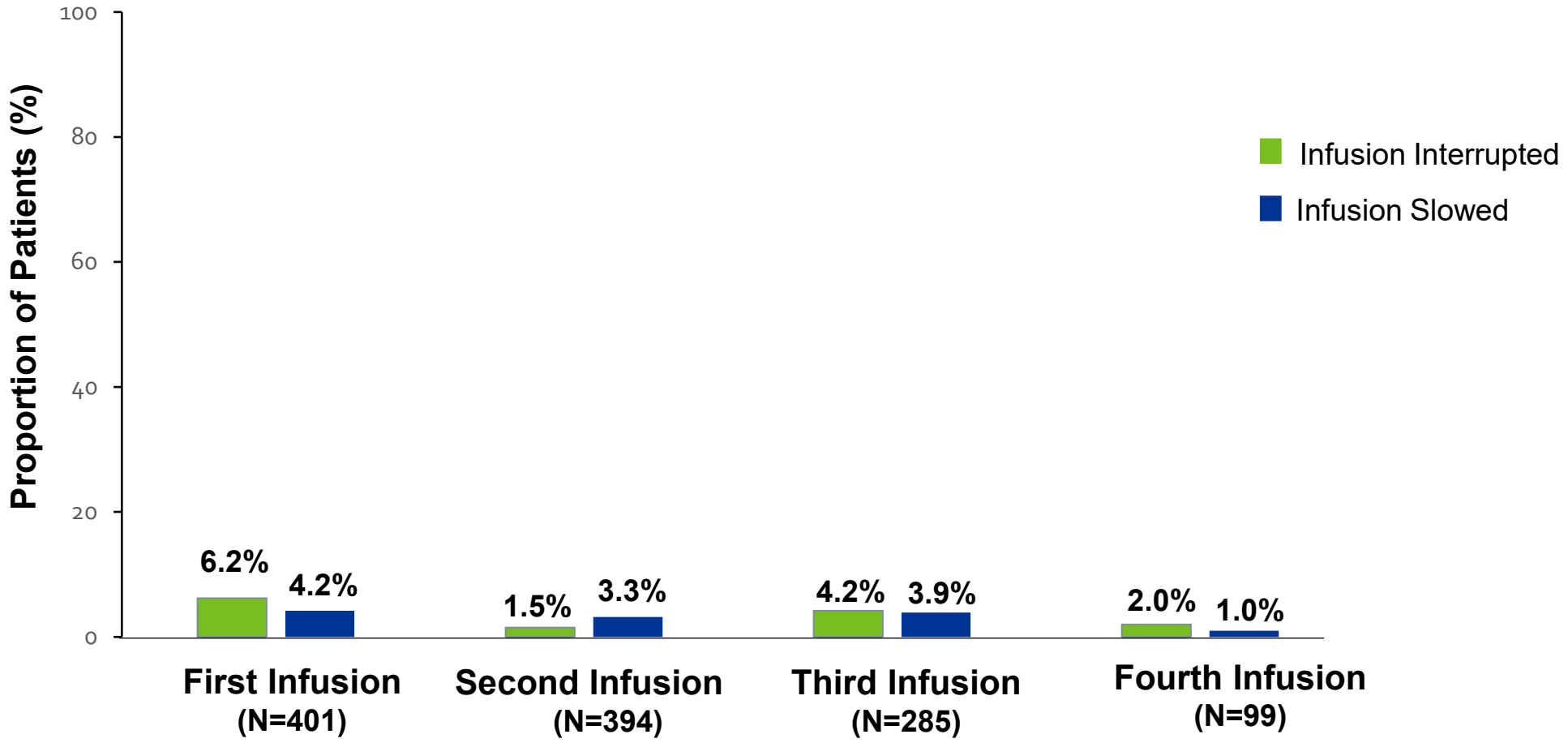
- The primary purpose of the survey was to evaluate ublituximab infusion tolerability by dose. In general, no formal statistical hypotheses were tested, and descriptive methods were used in the analysis of the data.

Results: Characteristics of Clinics/Patients

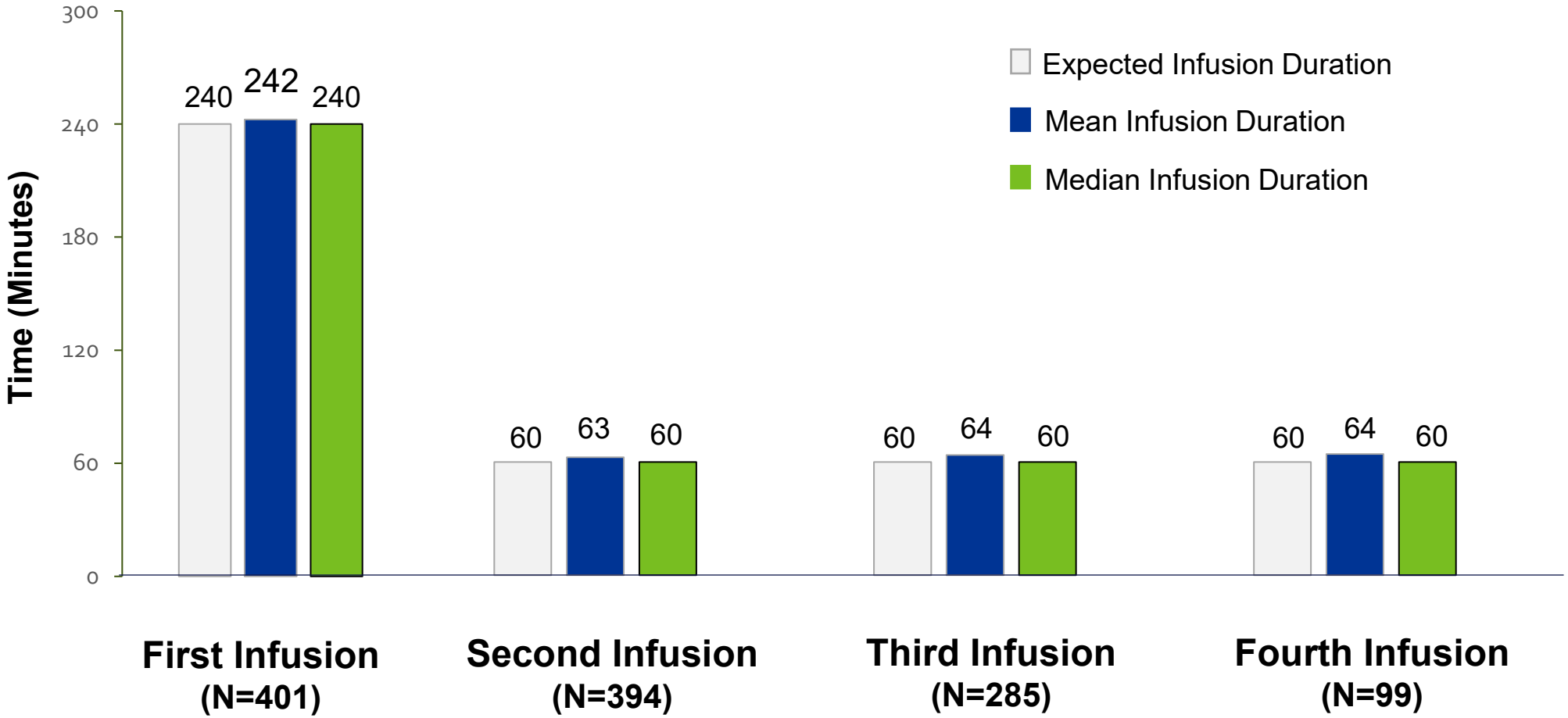
Characteristics of Clinics/Patients	N (%)
Clinic Utilizes a Standardized Protocol for Premedications	
Total Number of Clinics Surveyed	21
Yes	21 (100.0)
No	0
Treatment History	
Total Number of Patients Included in Surveys	401
Treatment Naive	63 (15.7)
Previously Treated with a DMT	338 (84.3)
Previous Infusible Anti-CD20	127 (31.7)

DMT, disease modifying therapy

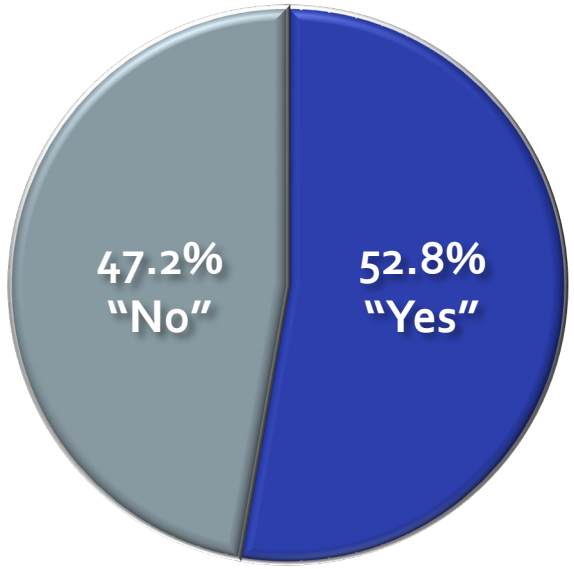
Results (Cont.): Infusions Interrupted or Slowed



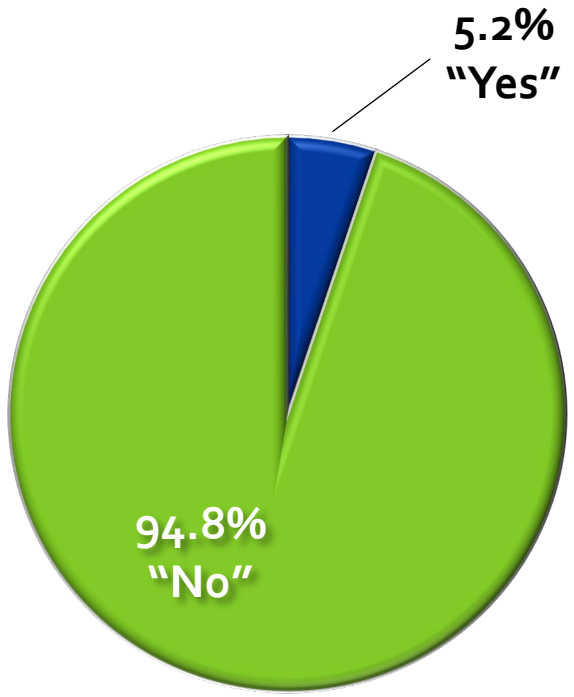
Results (Cont.): Infusion Duration



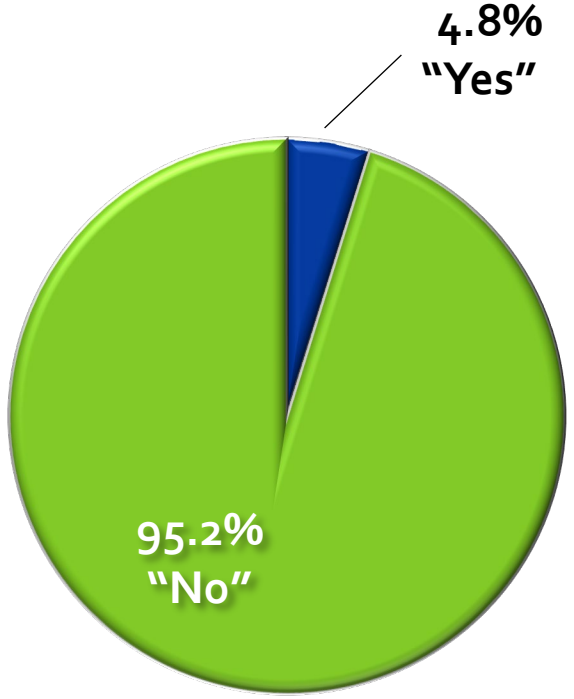
Results (Cont.): Proportion of Patients Experiencing Wearing off*



Reported Wearing Off on Previous Infusible Anti-CD20 (n=127)



Reported Wearing Off Following 2nd Ublituximab Infusion† (n=231)



Reported Wearing Off Following 3rd Ublituximab Infusion‡ (n=83)

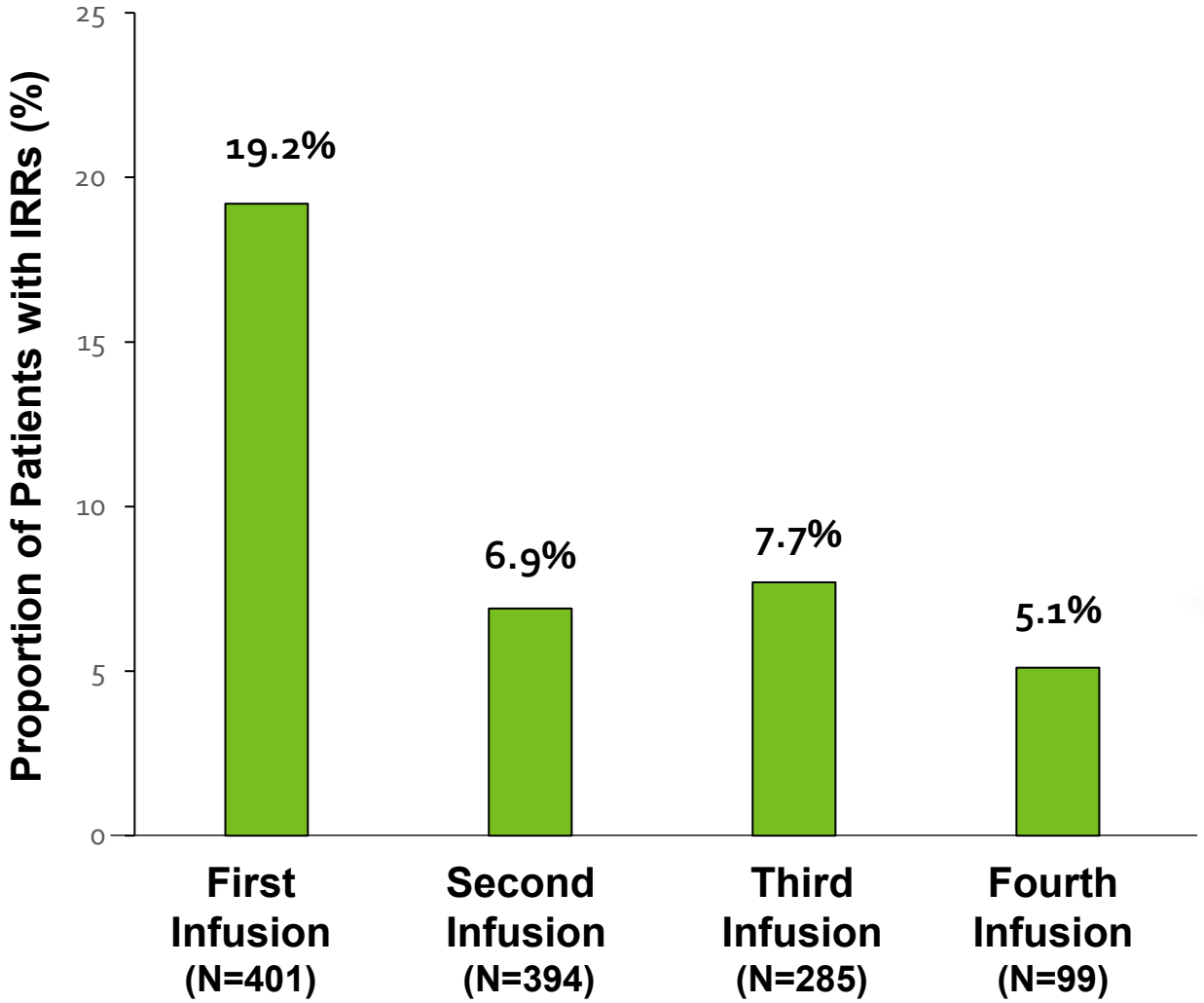
*Calculated from the proportion of patients who had "wearing off" evaluated
†Calculated from the proportion of patients receiving the 3rd infusion
‡Calculated from the proportion of patients receiving the 4th infusion

Results (Cont.): Premedications by Clinic

	First Infusion (N=21)	Second Infusion (N=21)	Third Infusion (N=21)	Fourth Infusion (N=18)
Corticosteroid				
Methylprednisolone	21 (100%)	21 (100%)	21 (100%)	18 (100%)
Corticosteroid Route of Administration				
IV	21 (100%)	21 (100%)	21 (100%)	18 (100%)
Timing of Corticosteroid				
30 min prior to infusion	19 (90.5%)	19 (90.5%)	20 (95.2%)	17 (94.4%)
60 min prior to infusion	2 (9.5%)	2 (9.5%)	1 (4.8%)	1 (5.6%)
Antihistamine				
Cetirizine	2 (9.5%)	3 (14.3%)	4 (19.0%)	4 (22.2%)
Diphenhydramine	18 (85.7%)	16 (76.2%)	14 (66.7%)	12 (66.7%)
Other	1 (4.8%)	2 (9.5%)	3 (14.3%)	2 (11.1%)
Antihistamine Route of Administration				
IV	7 (33.3%)	6 (28.6%)	4 (19.0%)	3 (16.7%)
Oral	14 (66.7%)	15 (71.4%)	17 (81.0%)	15 (83.3%)
Timing of Antihistamine				
30 min prior to infusion	17 (81.0%)	17 (81.0%)	17 (81.0%)	15 (83.3%)
60 min prior to infusion	3 (14.3%)	2 (9.5%)	1 (4.8%)	1 (5.6%)
>60 min prior to infusion	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (5.6%)
Other		1 (4.8%)	2 (9.5%)	1 (5.6%)
Antipyretic				
Acetaminophen	19 (90.5%)	19 (90.5%)	19 (90.5%)	16 (88.9%)
Ibuprofen	2 (9.5%)	2 (9.5%)	2 (9.5%)	2 (11.1%)
Other Premedications Given				
Pepcid (famotidine)	4 (19.0%)	3 (14.3%)	4 (19.0%)	3 (16.7%)
Zofran (ondansetron)	2 (9.5%)	3 (14.3%)	2 (9.5%)	--
Other	3 (14.3%)	3 (14.3%)	2 (9.5%)	2 (11.1%)

IV, intravenous

Results (Cont.): Infusion-Related Reactions



IRR, infusion-related reaction

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-xiiy. The types of IRRs listed in the USPI include pyrexia, chills, headache, influenza-like illness, tachycardia, nausea, throat irritation, erythema, and an anaphylactic reaction

Key Findings

- The ENAMOR survey demonstrated a favorable tolerability profile for Ublituximab in the real-world clinical practice setting, including:
  - Clinics reported that all infusions were completed in the specified time (median time for the first infusion was 240 minutes, and 60 minutes for infusions 2-4).
  - A lower proportion of patients experienced wearing off after the 2nd and 3rd ublituximab infusions than was reported for previous infusible anti-CD20 therapy (5.2%, 4.8%, and 52.8%, respectively).
  - Most clinics utilized an oral antihistamine as premedication, indicating a clinical preference for oral administration over intravenous (IV). Notably, all clinics utilized an antipyretic with the first infusion.
  - A lower incidence of IRRs with the 1st infusion was reported in the real-world setting compared to the rate observed in the ULTIMATE I and II[4] studies (19.2% and 43.0%, respectively).

Conclusions

- Data from the ENAMOR survey supports that ublituximab infusions are well tolerated in the real-world clinical practice setting.

References

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3. Babiker HM, et al. *Expert Opin Investig Drugs*. 2018;27(4):407-412.
4. Steinman L, et al. *N Engl J Med*. 2022;387(8):704-714.

Disclosures

- EF, PS, HM, and CG are employed by TG Therapeutics.