

Real-World Transition to Ublituximab From Prior Anti-CD20 Treatment in the Phase 4 ENABLE Study

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CONCLUSIONS

- Patients switching from prior anti-CD20 therapy to ublituximab demonstrate significant control of disease activity and favorable safety and tolerability.
- Efficacy, convenience, tolerability and safety were reported as the top reasons for switching to ublituximab from prior anti-CD20 therapy.
- ARR during ublituximab treatment in the CD20 switch population was 0.011 (95.2 patient-years), with 99.4% of participants reporting no relapses on ublituximab.
- Infusion durations in the CD20 switch population were consistent with the expected infusion times. Ublituximab was well tolerated in this cohort, and IRRs were significantly lower compared to the overall ENABLE population.
- The overall safety profile in this cohort remained consistent with the overall ENABLE population and pivotal trials.
- Significant and sustained improvements in patient-reported outcomes were observed at Day 15 and week 24.

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}
- The overall safety profile remained consistent over 6 years of continuous treatment.^{3,4}
- 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 4-hour infusion).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.
- Clinical outcomes for patients switching to ublituximab from prior anti-CD20 therapy in the ENABLE study are presented here.

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, 2025 were included in the analysis.
- Annualized relapse rate was calculated as cumulative number of relapses/cumulative treatment time. Duration of infusion (in minutes) was defined as duration between infusion start to stop time.
- A Mixed Model Repeated Measures (MMRM) was used to model the transformed PRO scores for participants who switched from prior anti-CD20 therapy. The model included visit as covariates and an unstructured covariance matrix.

RESULTS

Baseline demographics for ENABLE participants with prior anti-CD20 treatment

Characteristic, Mean ± SD or n (%)	CD20 switch to Ublituximab (N=189)	Non-CD20 switch to Ublituximab (N=469)
Age (years)	44.3 ± 10.96	42.5 ± 11.64
Gender, Female, n (%)	151 (79.9)	350 (74.6)
Race, n (%)		
White	132 (69.8)	336 (71.6)
Black or African American	39 (20.6)	89 (19.0)
Other	15 (8.0)	35 (7.5)
Unknown or Not Reported	3 (1.6)	6 (1.3)
Ethnicity, n (%)		
Hispanic or Latino	22 (11.6)	64 (13.6)
Not Hispanic or Latino	151 (79.9)	349 (74.4)
Unknown or Not Reported	16 (8.5)	56 (11.9)
Weight (kg)	86.4 ± 26.54	85.5 ± 24.38
Height (cm)	167.31 ± 9.02	168.15 ± 10.14
BMI (kg/m ²)	31.09 ± 9.12	30.13 ± 8.20
BMI Category		
<30 kg/m ²	93 (49.2)	252 (53.7)
≥30 kg/m ²	73 (38.6)	179 (38.2)
Unknown or Not Reported	23 (12.2)	38 (8.1)

- The average age of CD20 switch population was 44.3 years, and 79.9% were females.
- 69.8% and 20.6% of participants are White/Caucasian and Black/African-American, respectively.
- The number of participants with body mass index (BMI) ≥30 kg/m² was 38.6%, similar to the overall ENABLE population (38.3%).
- The baseline demographics of non-CD20 switch population was similar to the CD20 switch population.

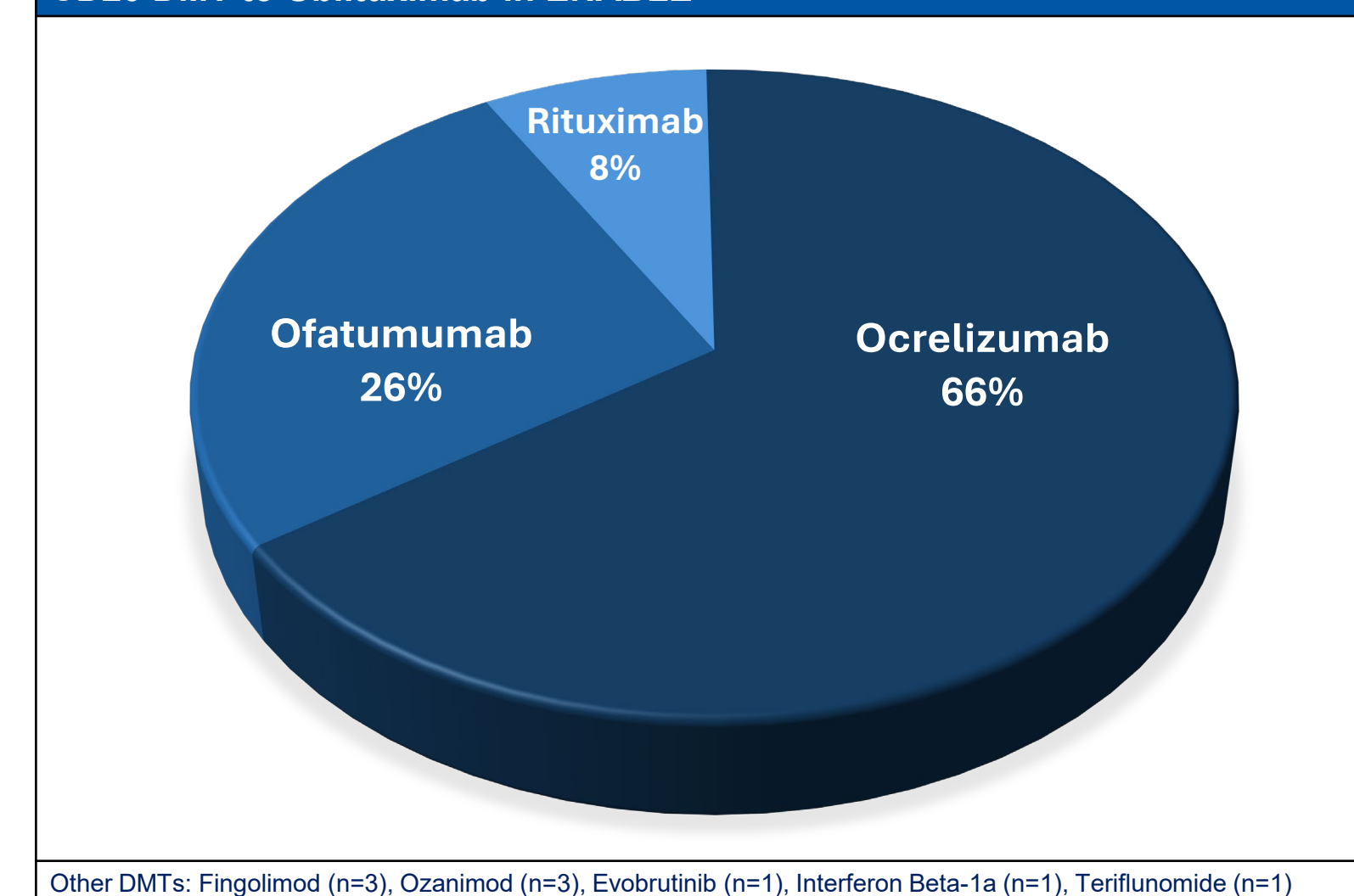
Baseline disease history for ENABLE participants with prior anti-CD20 treatment

Characteristic, Mean ± SD or n (%)	CD20 switch to Ublituximab (N=189)	Non-CD20 switch to Ublituximab (N=469)
Time Since First MS Symptoms (years)	10.85 ± 8.95	7.80 ± 8.96
Number of Relapses in the 2 Years Prior to Screening	0.3 ± 0.63	0.7 ± 0.87
Number of Relapses in the 2 Years Prior to Screening, n (%)		
0	104 (55.0)	170 (36.2)
1	32 (16.9)	156 (33.3)
2	6 (3.2)	39 (8.3)
≥3	2 (1.1)	13 (2.8)
Unknown or Not Reported	45 (23.8)	91 (19.4)
Number of Baseline Gadolinium-enhancing (Gd+) Lesions	0.5 ± 2.92	1.6 ± 6.26
Number of Baseline Gd+ Lesions, n (%)		
0	104 (55.0)	246 (52.5)
≥1	8 (4.2)	106 (22.6)
Unknown or Not Reported	77 (40.7)	117 (24.9)
Number of New and/or Enlarging T2 Hyperintense Lesions (compared to previous MRI scan)	0.5 ± 2.26	1.8 ± 5.60
Number of New and/or Enlarging T2 Hyperintense Lesions, n (%)		
0	101 (53.4)	227 (48.4)
≥1	16 (8.5)	102 (21.7)
Unknown or Not Reported	72 (38.1)	140 (29.9)

- CD20 switch population in ENABLE had slightly longer duration since onset of MS symptoms (10.85 years) compared to the overall ENABLE population (8.68 years).
- 21.1% of CD20 switch patients had at least one relapse in the 2 years prior to screening.
- Higher proportion of patients were relapse-free in the 2 years prior to screening in the CD20 switch (55%) vs. non-CD20 switch cohort (36.2%).

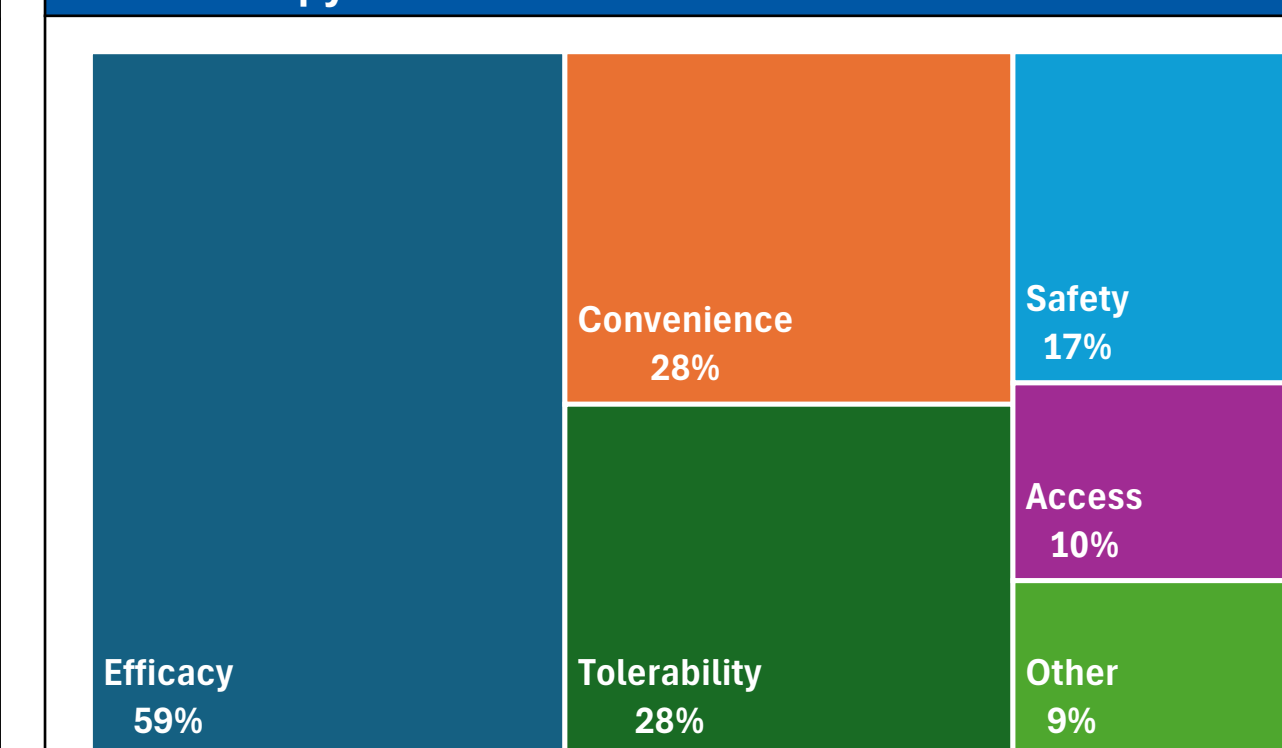
RESULTS, CONT

Figure 1. Prior Treatment History for Participants Switching From Prior Anti-CD20 DMT to Ublituximab in ENABLE



Other DMTs: Fingolimod (n=3), Ozanimod (n=3), Evobrutinib (n=1), Interferon Beta-1a (n=1), Teriflunomide (n=1)

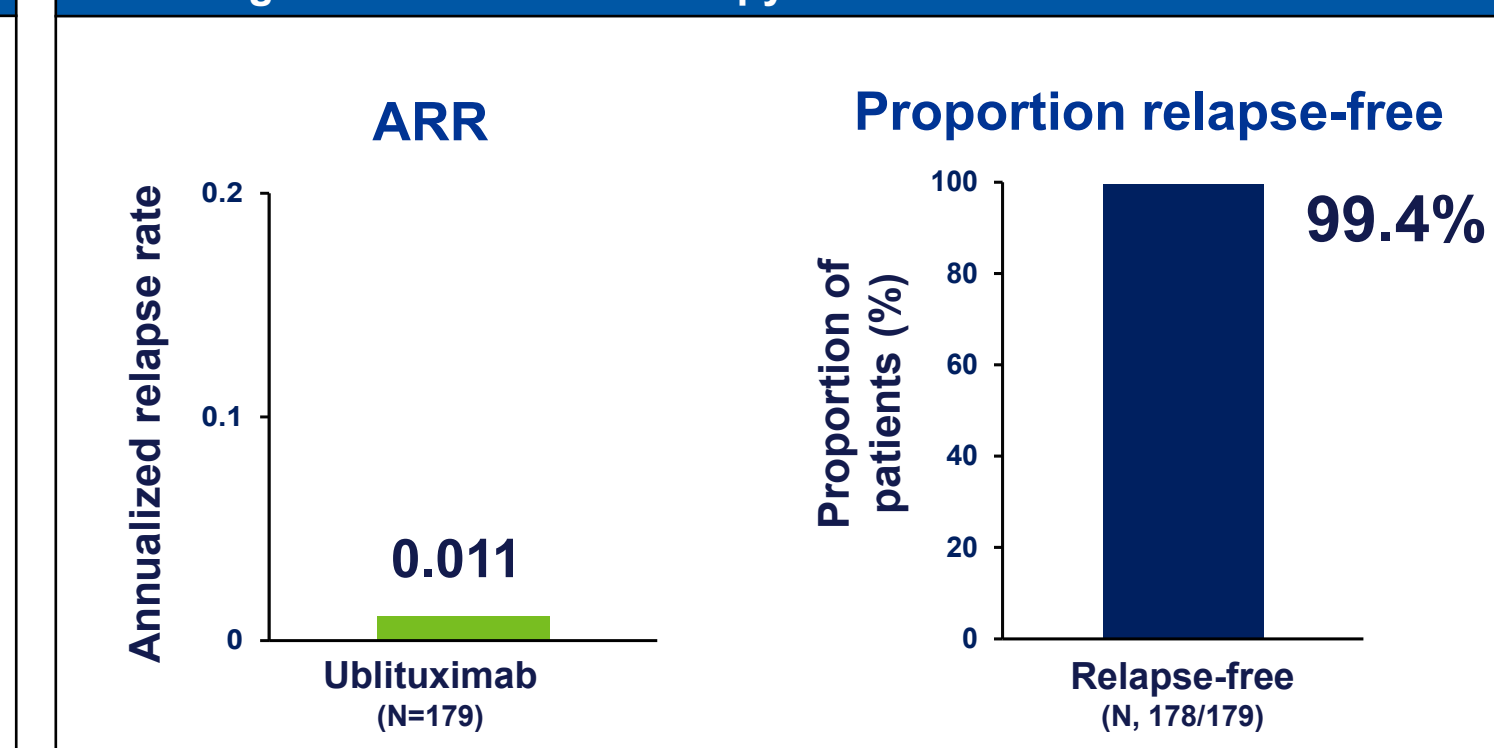
Figure 2. Reasons for Switch to Ublituximab From Prior Anti-CD20 Therapy



Data cutoff: 01-December-2025, N=189. Each participant could have submitted multiple reasons.

- Perceived efficacy of the prior anti-CD20 therapy versus ublituximab was the leading reason for switching to ublituximab, by 59% of patients.
- Other factors influencing patients' decisions to start ublituximab included convenience (28%), tolerability (23%), safety (17%), and access (10%).

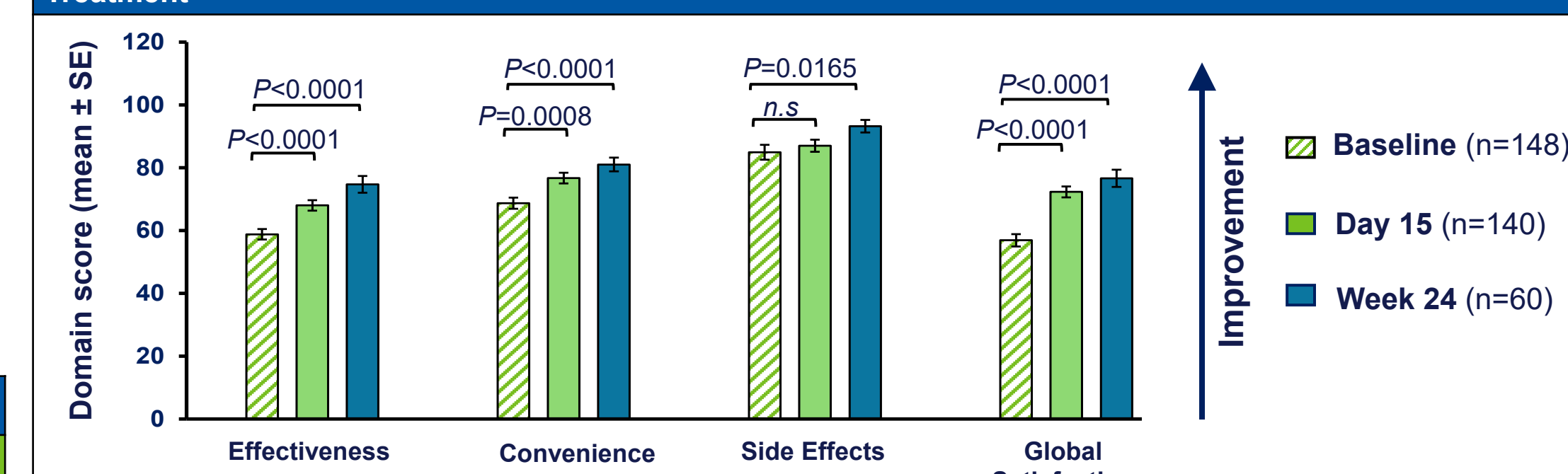
Figure 3. Summary of On-treatment ARR and Relapses for Participants Switching From Anti-CD20 Therapy to Ublituximab



Data cutoff: 01-December-2025. The relapse analysis is based on participants with at least one dose of ublituximab and any post-baseline efficacy evaluation.

- On-treatment annualized relapse rate for CD20 switch population was 0.011, with cumulative treatment time of 95.2 patient-years.
- On-treatment relapses were rare in the CD20 switch population, and 99.4% of participants reported no relapses during treatment with ublituximab.

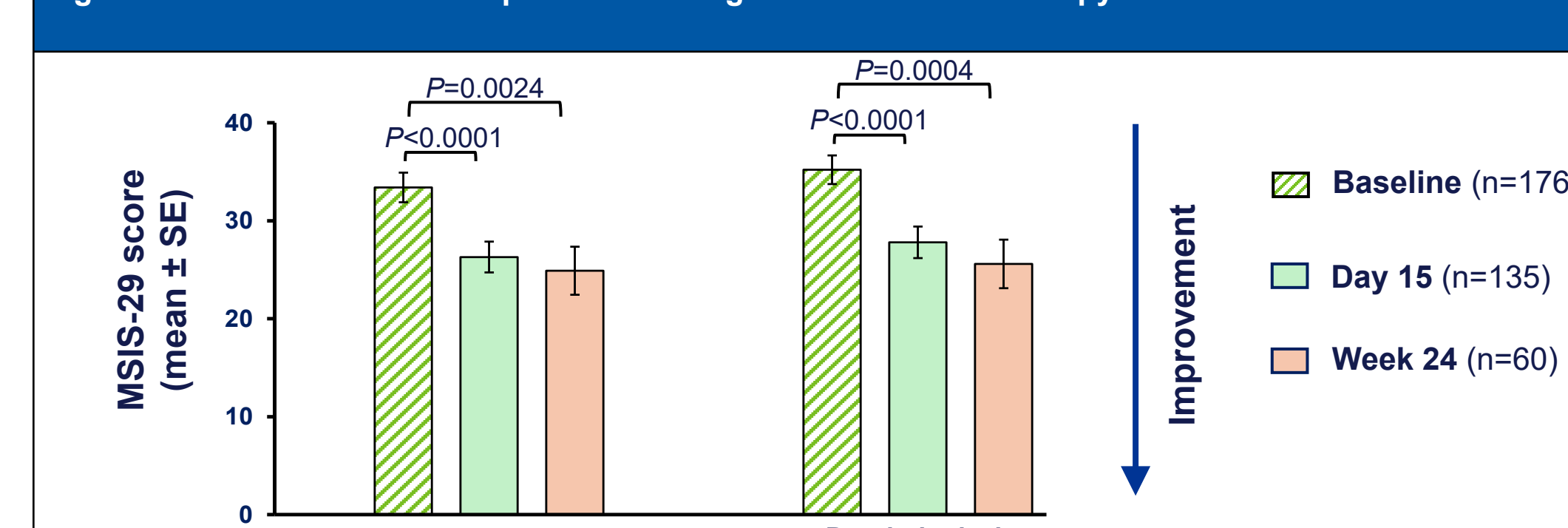
Figure 4. Treatment Satisfaction (TSQM) in Participants Switching From Anti-CD20 Therapy to Ublituximab Treatment



Data cutoff: 01-December-2025. TSQM=Treatment Satisfaction Questionnaire for Medication; n.s.=not significant MMRM (Mixed Model Repeated Measures) of the transformed score. The model includes visit as covariates and an unstructured covariance matrix.

- Significant improvement in TSQM scores were observed from baseline to Day 15 for effectiveness, convenience, and global satisfaction; the scores for side effects remained stable.
- TSQM scores showed significant improvement at week 24 compared to baseline for effectiveness, convenience, side effects and global satisfaction.

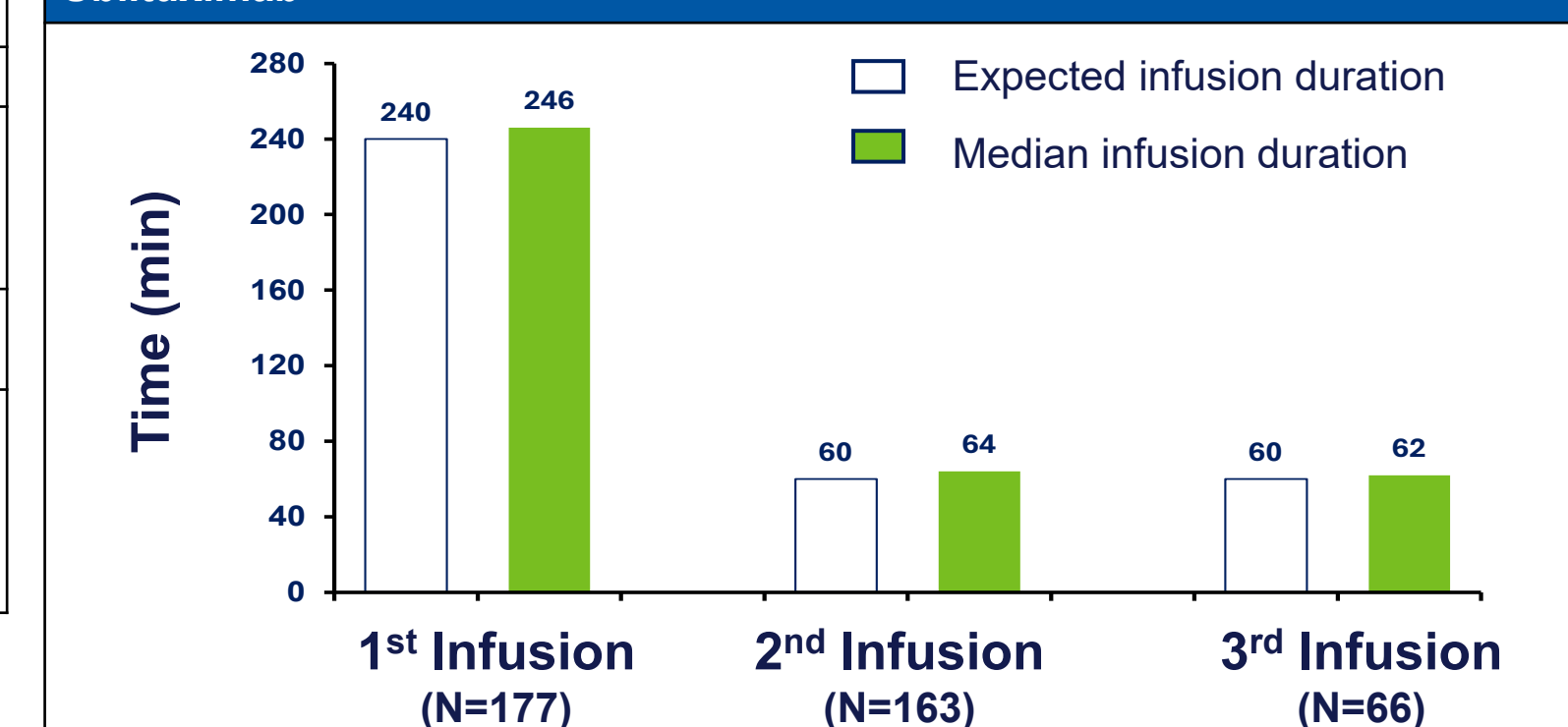
Figure 5. MSIS-29 Score in Participants Switching from Anti-CD20 Therapy to Ublituximab



Data cutoff: 01-December-2025. MSIS-29=Multiple Sclerosis Impact Scale MMRM (Mixed Model Repeated Measures) of the transformed score. The model includes visit as covariates and an unstructured covariance matrix.

- Significant improvements were observed for MSIS-29 as early as **Day 15** for physical [LS mean (95% CI): -5.86 (-7.72, -4.00), P<0.0001], and psychological scores [LS mean (95% CI): -6.97 (-9.31, -4.62), P<0.0001].
- Improvements were sustained at **Week 24** compared to baseline: physical [LS mean (95% CI): -3.86 (-6.33, -1.39), P=0.0024], and psychological scores [LS mean (95% CI): -4.75 (-7.32, -2.18), P=0.0004].

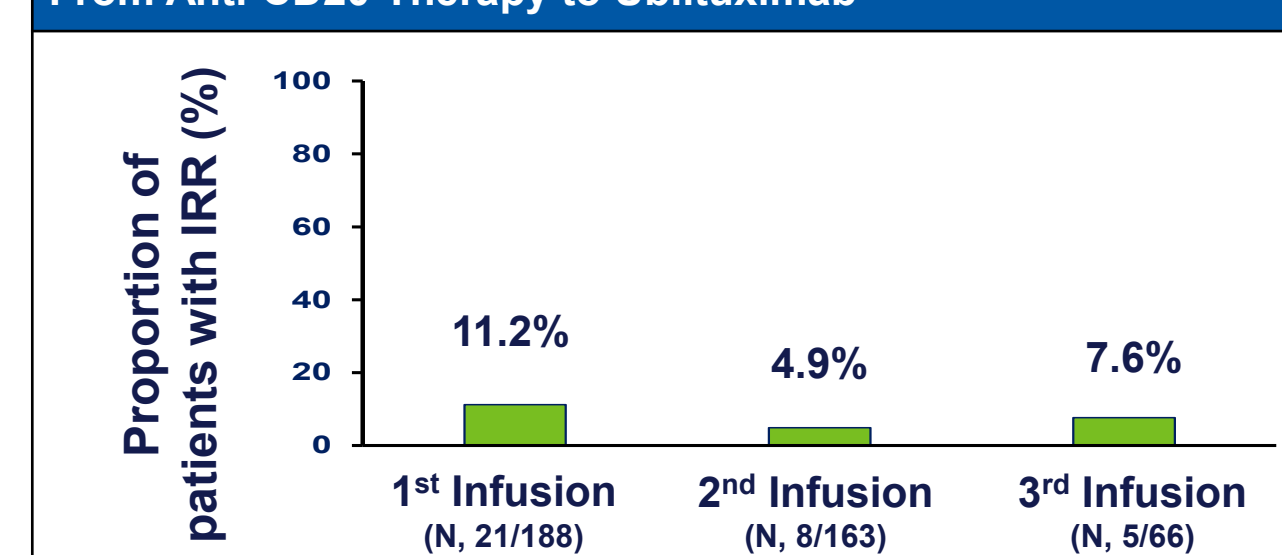
Figure 6. Infusion times in participants switching from anti-CD20 therapy to Ublituximab



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 (in mins) was 246, 64, and 62 for the first, second and third infusions.

Figure 7. Infusion-Related Reactions in Participants Switching From Anti-CD20 Therapy to Ublituximab



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 (11.2% of participants) and decreased during subsequent infusions.
- None of the IRRs were serious in nature (≥Grade 3). All IRRs were Grade 1 or Grade 2 and resolved completely.
- Most commonly reported IRRs were Throat irritation (n=7, 3.7%), Pruritus (n=6, 3.2%), Fatigue (n=5, 2.6%), Headache (n=5, 2.6%), Nausea (n=4, 2.1%).

Table 3. Adverse Events with an Incidence Rate of at Least 2% in Participants Switching From Anti-CD20 Therapy to Ublituximab

Adverse event	Ublituximab, n=189, n (%)
Any treatment emergent adverse event (TEAE)	47 (24.9)
Infusion-related reaction	27 (14.3)
Urinary tract infection	6 (3.2)
Fatigue	4 (2.1)
Headache	4 (2.1)
Nausea	4 (2.1)

Data cutoff: 01-December-2025. TEAE=Treatment emergent adverse event, IRR=Infusion-related reaction.

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