

# Ublituximab significantly improves patient-reported outcomes: results from the phase 4 observational study ENABLE

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# DISCLOSURES

Carrie M. Hersh has received speaking, consulting, and advisory board fees from Genentech, Genzyme, Biogen, Novartis, EMD-Serono, Bristol Myers Squibb, TG Therapeutics, Horizon Therapeutics, and Alexion. She has received research support paid to her institution by Biogen, Novartis, Bristol-Myers Squibb, National MS Society, and Patient-Centered Outcomes Research Institute (PCORI). Angel R Chinae has received advisory/consulting fees from Biogen, Genentech, Novartis, Sanofi-Genzyme, and Teva Neuroscience; research support from Biogen, Novartis, and Sanofi-Genzyme; speaker fees from Biogen, Genentech, Novartis, Sanofi-Genzyme, and Teva. Emily Riser has received speaker fees from TG Therapeutics and received research support from TG Therapeutics, Alexion, Genentech, Novartis, Sanofi, and Corvitas. Sidarth Dasari is a speaker for TG Therapeutics. Susan Anzalone has done ad boards for TG Therapeutics, Genentech, Biogen, Sanofi and has been a speaker for Teva, Biogen, Genentech, BMS, Sanofi. Jacqueline Rosenthal is a consultant for Speaker's Bureaus, steering committees, and/or advisory boards at TG Therapeutics, Amgen, EMD Serono, and Biogen. Jeanie Cote has received speaking/consulting fees from TG Therapeutics, Biogen, EMD Serono, BMS. Jonathan Calkwood has received honorarium or financial support for promotional speaking, advisory board services and funding for research from TG Therapeutics, AstraZeneca, Biogen, Genentech, Octave Bio, Sanofi and Zenas BioPharma. Michael Hemphill has received honorarium or financial support from TG Therapeutics, Abbvie, Amgen, Alexion, Argenx, Biogen, Bristol Myers Squibb, Eisai, and EMD Serono. Diana Andino has received consulting and/speaking fees from Genentech, Amgen, Merck-EMD Serono, TG Therapeutics, Multiple Sclerosis Association of America, and DKB Med. Matthew C Carraro has received consulting fees and / or Speaking fees on behalf of Biogen, Sanofi, Novartis, TG Therapeutics, EMD Serono, Octave Bioscience. Andrew Bouley has received research funding and/or honoraria for consulting/speaking engagements for the following companies: Biogen, EMD Serono, Genentech, Novartis, Sanofi, TG Therapeutics. Kyle Smoot has received honorarium for consulting or speaking from Biogen, Genentech, Novartis, EMD Serono, and TG Therapeutics. Brendan Lindgren has received honorarium and/or research support from TG Therapeutics and Genentech. Jean-Raphael Schneider is a speaker and consultant for Bristol Myers Squibb and Argenx. Sangin Oh is a consultant for EMD Serono, Vanda, TG, Pfizer, Sanofi, Novartis, Biogen, Allergan, Biohaven, Lily, Teva, Amgen, Genentech, BMS, Avanir, Acorda, and Bayer. Oh is also a Steering Committee Member for Mavenclad / EMD Serono, and participated in advisory board meetings for EMD Serono, Pfizer, Sanofi, Novartis, Biogen, Teva, Amgen, Genentech, BMS, J&J, and TG Therapeutics. Bhupendra Khatri is a consultant and a paid speaker for: Bristol-Meyer Squibb, Sanofi, Genentech, Biogen, Alexion, TG Therapeutics, EMD Serono, UCB, Argenx, Terumo BCT. Jackie Parker, Karthik Bodhinathan, Peter Sportelli, Hari Miskin, and Edward Fox are employees of TG Therapeutics.

# 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</sup>
- The overall safety profile remained consistent over 6 years of continuous treatment.<sup>3,4</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 4-hour infusion).<sup>5</sup>
- 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.
- The study duration is 192 weeks, with a target enrollment of 2,000 participants. Results from patient-reported outcomes of the ongoing 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.
- Patient-reported outcomes (PROs) were collected through an electronic platform.
- A Mixed Model Repeated Measures (MMRM) was used to model the transformed PRO scores. The model included “study visit” as a covariate and an unstructured covariance matrix.\*

\*An unstructured covariance matrix was used to allow for variances and correlations for all pairs of variables to occur over time, without assuming a specific pattern, and applicable to the mixed-effects model for longitudinal data.

# ENABLE Sites Open to Enrollment



- As of the data cut (01-December-2025), 87 sites were actively enrolling patients across the U.S.
- As of May 2026, over 100 sites were open to enroll in ENABLE with over 1000 patients enrolled.

# Baseline Demographics

<b>Table 1. Baseline Demographics</b>	
<b>Characteristic, Mean ± SD or n(%)</b>	<b>Ublituximab (N=658)</b>
Age (years)	43.0 ± 11.47
Sex, 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)
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)

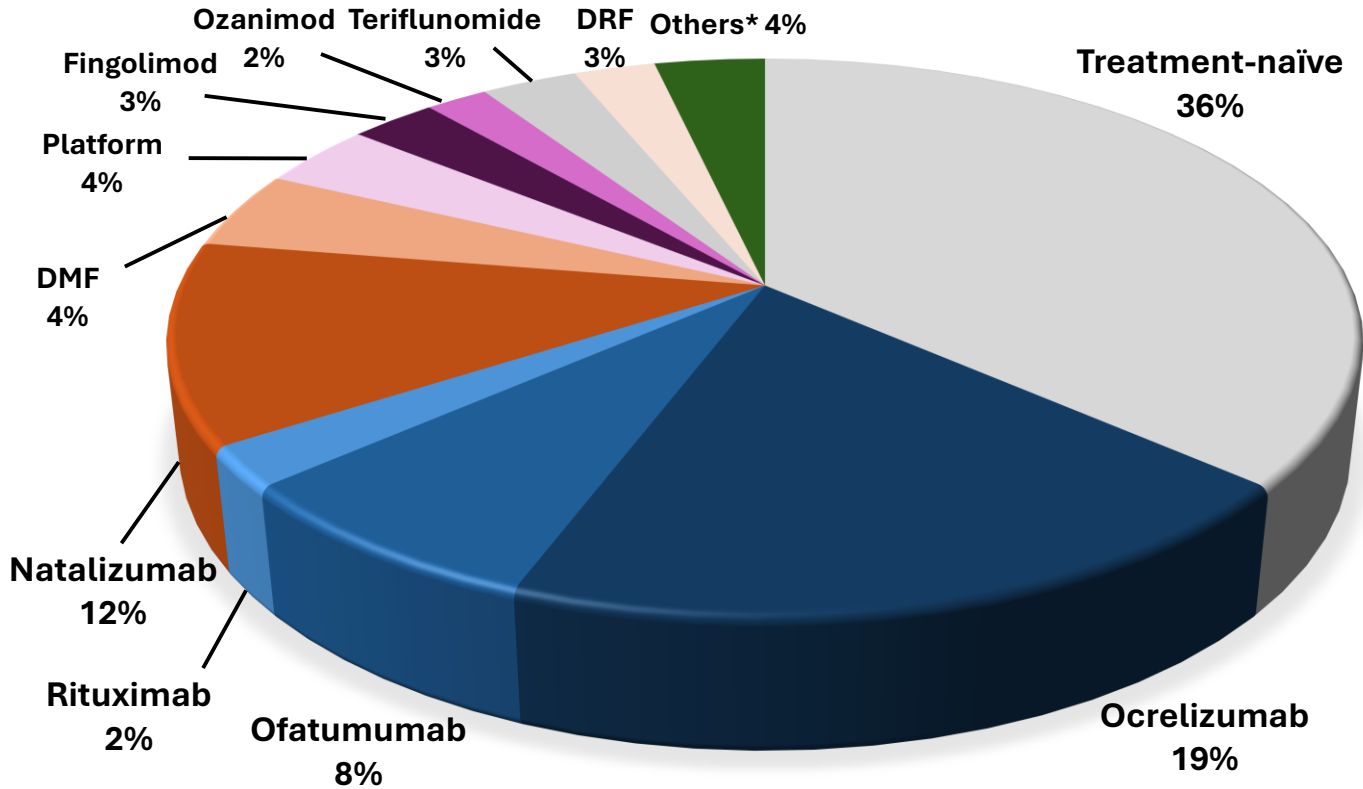
- The average age of ENABLE participants (43.0 years) is higher than that of ULTIMATE I and II participants (35.4 years).
- 76.1% of participants are female, a higher proportion than in ULTIMATE I and II (62.9% female).
- 71.1% and 19.5% of participants are White/Caucasian and Black/African-American, respectively. In ULTIMATE I and II, Black/African American participants were 1.5% of the 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%).

# Baseline Disease History

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 disease 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%).

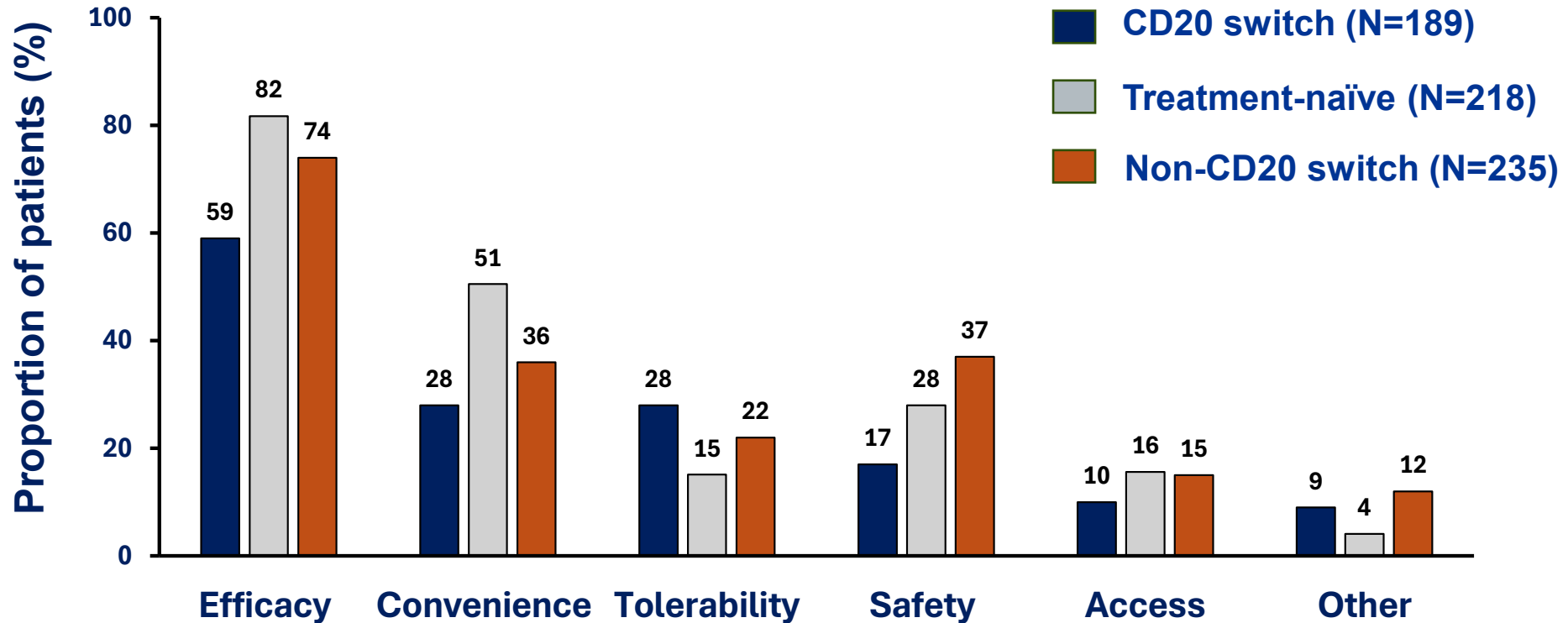
# Prior DMT History for People with MS Starting Ublituximab in ENABLE



- 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%).

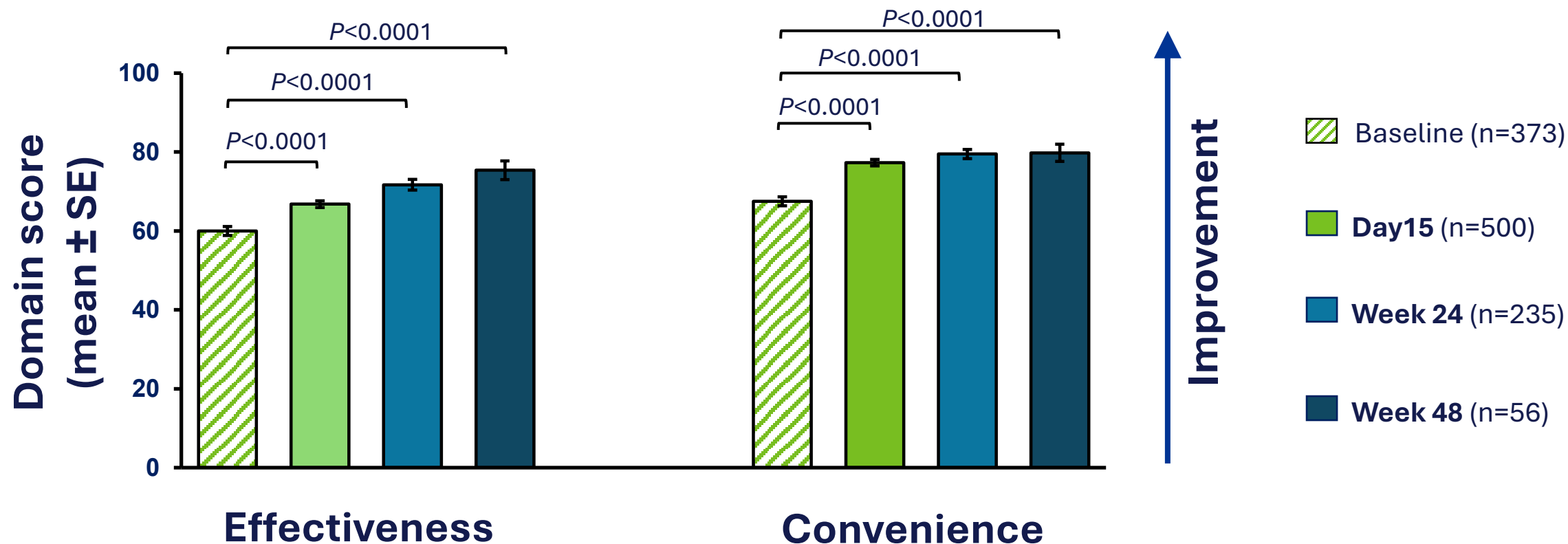
Data cutoff: 01-December-2025. Listed DMTs are immediately prior to start of ublituximab. \*Includes missing input from n=16 (3.8%)

# Reasons for Starting Ublituximab Treatment by Prior DMT Use



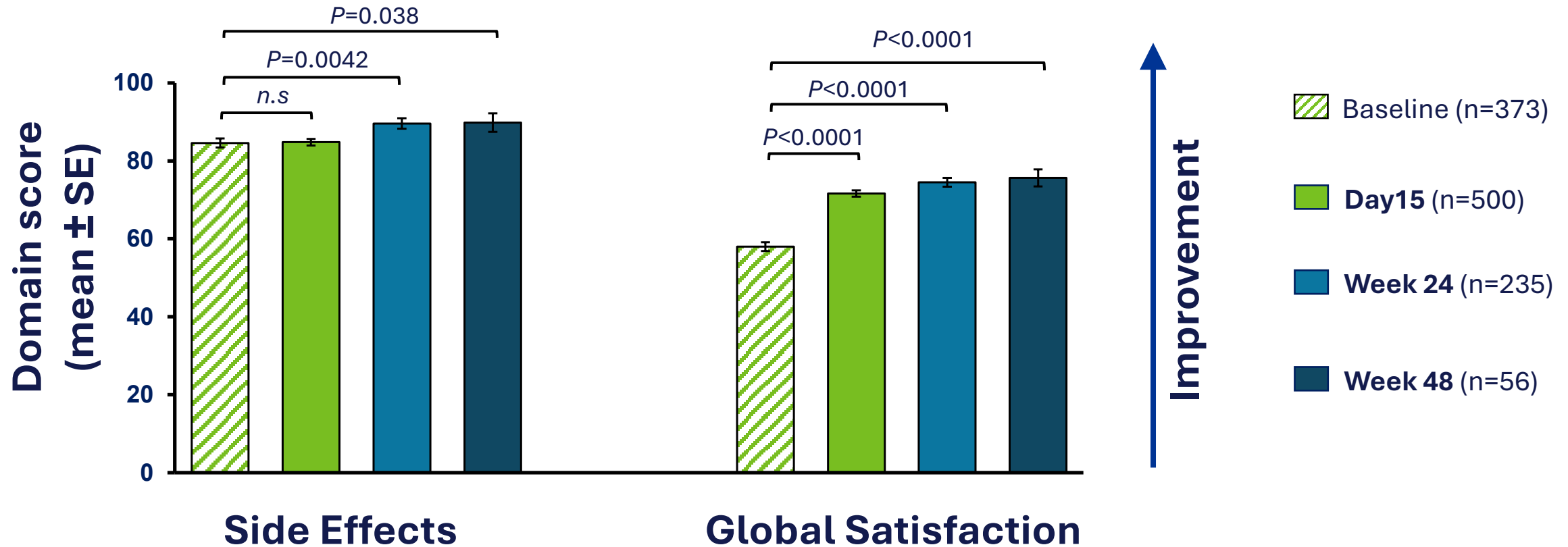
- Efficacy was the top reason for starting ublituximab by treatment-naïve (82%), non-CD20 switch (74%), and CD20 switch (59%) cohorts.
- Convenience was higher in the treatment-naïve cohort (51%), followed by non-CD20 switch (36%), and CD20 switch (28%) participants.
- Tolerability was higher in the CD20 switch cohort (28%) compared to non-CD20 switch (22%) and treatment-naïve cohort (15%).
- Safety was higher in non-CD20 switch cohort (37%), followed by treatment-naïve (28%), and CD20 switch (28%) cohorts.

# TSQM: Effectiveness and Convenience Scores Improved in Ublituximab-Treated Participants in ENABLE



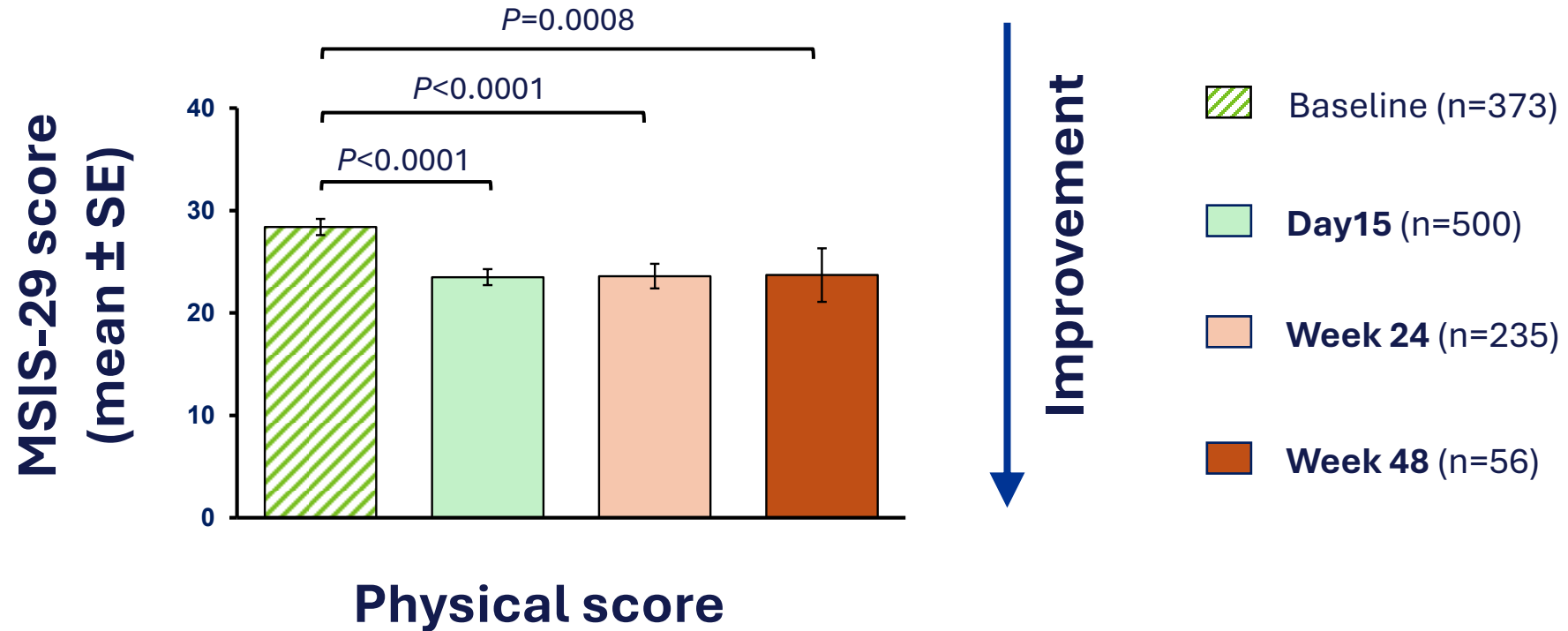
- Significant and durable improvements from baseline were observed for effectiveness and convenience scores as early as **day 15** [LS Mean change: Effectiveness (E), 6.66,  $P < 0.0001$ ; Convenience (C), 9.58,  $P < 0.0001$ ], and sustained at **week 24** [E, 11.05,  $P < 0.0001$ ; C, 12.61,  $P < 0.0001$ ], and **week 48** [E, 15.62,  $P < 0.0001$ ; C, 10.95,  $P < 0.0001$ ]

# TSQM: Side Effects and Global Satisfaction Scores Improved in Ublituximab-Treated Participants in ENABLE



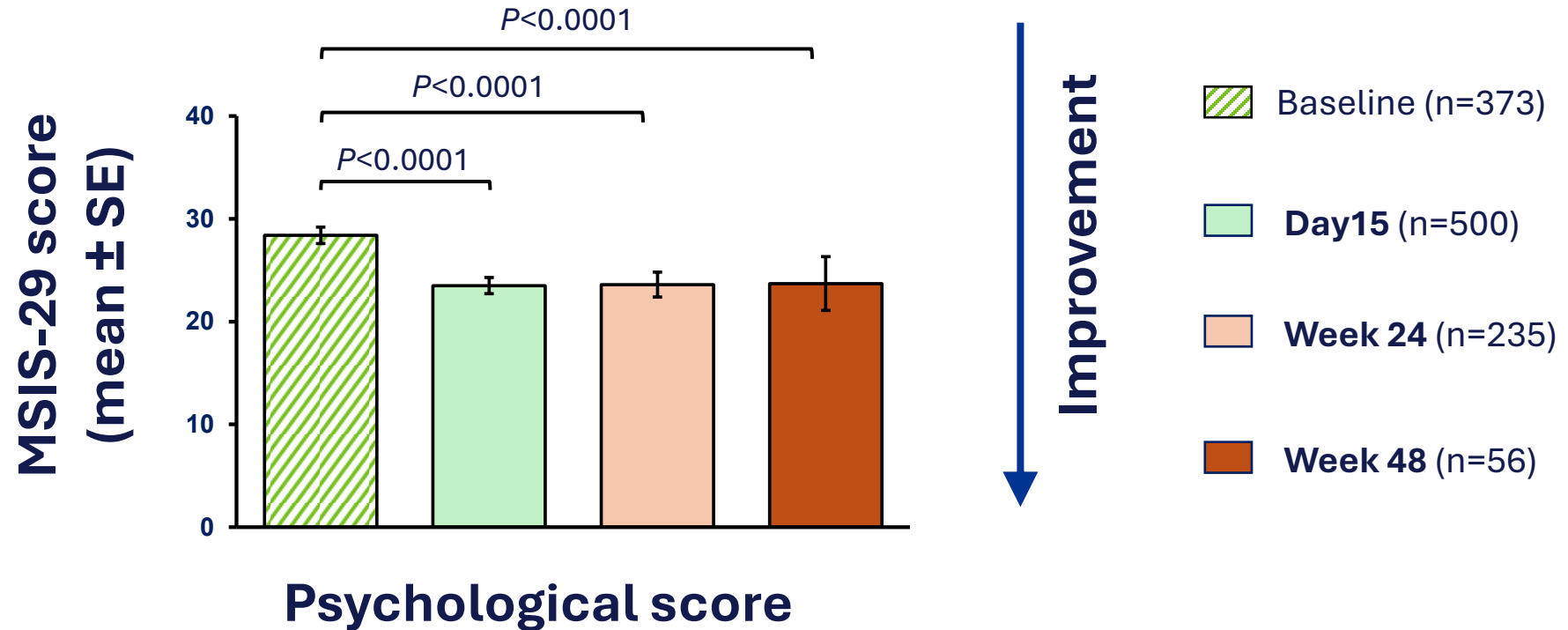
- Significant and durable improvement in global satisfaction scores were observed as early as day 15 [LS Mean change: Global Satisfaction, 13.21, P<0.0001], and sustained at week 24 [15.62, P<0.0001] and week 48 [17.46, P<0.0001].
- Side effects score showed significant improvements at week 24 and week 48 [LS Mean change for Side effects, day 15: 0.26, P= 0.8676; week 24, 5.08, P=0.0042; and week 48, 5.27, P=0.0380]

# MSIS-29 Physical Scores Improved in Ublituximab-Treated Participants in ENABLE



- Significant and durable improvements were observed in MSIS-29 Physical scores in ublituximab-treated patients.
- Improvements were observed as early as **day 15** [LS Mean change: Physical, -3.91,  $P < 0.0001$ ] and sustained at **week 24** [-3.46,  $P < 0.0001$ ], and **week 48** [-4.25,  $P = 0.0008$ ]

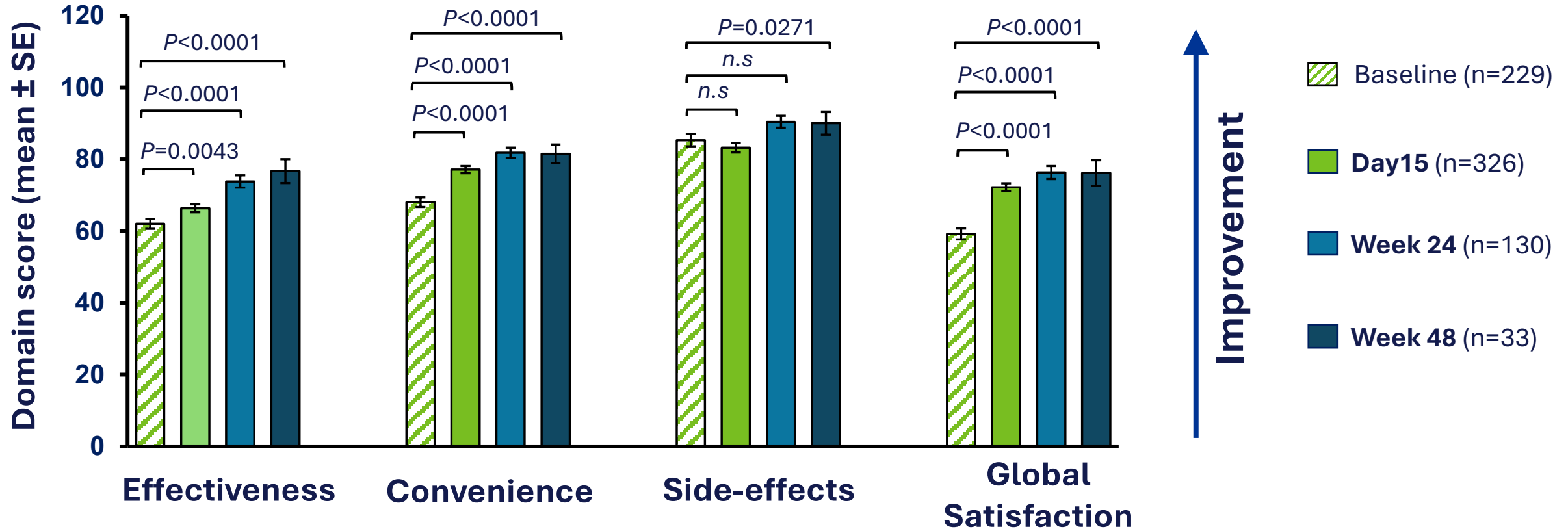
# MSIS-29 Psychological Scores Improved in Ublituximab-Treated Participants in ENABLE



- Significant and durable improvements were observed in MSIS-29 Psychological scores in ublituximab-treated patients.
- Improvements were observed as early as **day 15** [LS Mean change: Psychological, -5.54,  $P<0.0001$ ], and sustained at **week 24** [-5.29,  $P<0.0001$ ], and **week 48** [-5.57,  $P<0.0001$ ]

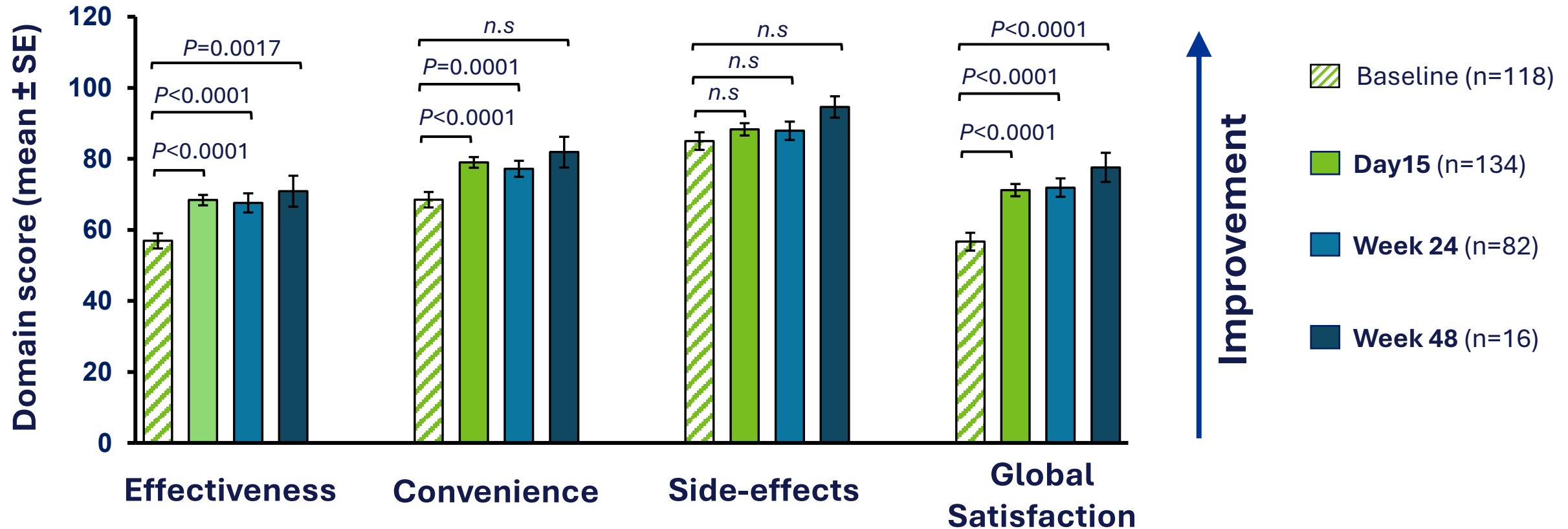
# **Patient-Reported Outcomes for Ublituximab-Treated People with MS in ENABLE by Race and Ethnicity**

# TSQM Scores Improved in White/Caucasian Patients Treated with Ublituximab in ENABLE



- Significant and durable improvements from baseline were observed for most domains of TSQM in the White/Caucasian cohort, as early as day 15 and sustained at week 24, and week 48.

# TSQM Scores Improved in African American and Hispanic Patients Treated with Ublituximab in ENABLE



- Significant and durable improvements from baseline were observed for most domains of TSQM in the African American/Hispanic cohort, as early as day 15 and sustained at week 24, and week 48.





# CONCLUSIONS

- Real-world evidence from the phase 4 study ENABLE reinforces the clinical profile observed in the pivotal clinical trials.
- Patient-reported outcomes were significantly improved in ublituximab-treated patients.
- Patients reported significant and durable improvements in all sub-domains of treatment satisfaction, measured by TSQM, across racial and ethnic cohorts.
  - Improvements were observed as early as day 15 and sustained at week 24 and week 48.
- Significant and durable improvements were also observed in MSIS-29 scores in ublituximab-treated patients, across racial and ethnic cohorts.
  - Improvements were observed as early as day 15 and sustained at week 24 and week 48.
- 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

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