

Ublituximab Mitigates Wearing-Off Effect and Improves B-Cell Depletion Among Participants Transitioning from Ocrelizumab: Updates from the ENHANCE Study



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CONCLUSIONS

- Switching from ocrelizumab to ublituximab with a single 600 mg dose was well tolerated regardless of B-cell depletion status at the time of switch.
- 600 mg infusions resulted in high levels of patient satisfaction on the dimensions of convenience and ease of use among ocrelizumab switches at Week 24 and Week 48.
- Ublituximab demonstrated improved B-cell depletion among participants who transitioned from ocrelizumab in a non-depleted state, with B-cell depletion maintained after a full year.
- Ublituximab reduced the wearing-off effect after a single infusion and maintained reduction in wearing-off after a full year.
- Ublituximab can induce and maintain B-cell depletion among patients who are at a higher risk of B-cell repletion (Black or African American, higher BMI, younger age).

BACKGROUND

- Ublituximab is a novel monoclonal antibody that targets a unique epitope of CD20 and is glycoengineered for enhanced antibody-dependent cellular cytotoxicity (ADCC)¹ and enhanced Fcγ-receptor (FcγR) binding relative to all other currently approved anti-CD20 therapies in multiple sclerosis (MS).^{1,2,3}
- Ublituximab is approved for adults with relapsing forms of multiple sclerosis (RMS) with an administration schedule of a 150 mg dose on Day 1 followed by 450 mg doses on Day 15, Week 24, and subsequently every 24 weeks.⁴
- It has been shown previously that consolidating Day 1 (150 mg) and Day 15 (450 mg) infusions into a single 600 mg dose was well tolerated and resulted in high levels of patient satisfaction on the dimensions of convenience and ease of use.⁵

METHODS

- ENHANCE is a multi center, open-label, 48-week study in participants with RMS evaluating modified dosing regimens for ublituximab.
- Participants received a consolidated 600 mg ublituximab infusion on Day 1, followed by a 450 mg infusion at Week 24.
- Participants who had B-cells counts <10 cells/μL received 600 mg infusions in 1 or 2 hours while participants with B-cells counts ≥10 cells/μL received 600 mg infusions in 2, 3, or 4 hours.
- Recommended premedications included a non-drowsy antihistamine, corticosteroid, and antipyretic at each infusion.
- Wearing-off effect was evaluated at screening, Weeks 24 and 48, while Treatment Satisfaction Questionnaire for Medication (TSQM-9) was administered at Weeks 24 and 48.
- The study is ongoing, now actively enrolling participants with RMS who are transitioning from other anti-CD20 therapies due to a suboptimal experience.
- Data are provided herein on all participants who transitioned from ocrelizumab and received an initial ublituximab infusion of 600 mg (N=106).

RESULTS

Table 1. Participants Who Switched from Ocrelizumab

B-Cell Depletion Status	Non-depleted (≥10 cells/μL) n=28	Depleted (<10 cells/μL) n=78	Overall N=106
B-cell count, median (IQR)	68 (27, 166)	1 (0, 1)	1 (0, 13)
BMI (kg/m ²), median (IQR)	34 (31, 41)	29 (25, 35)	32 (25, 36)
Race, n (%)			
White	18 (64%)	67 (86%)	85 (80%)
Black or African American	8 (29%)	8 (10%)	16 (15%)
Other	1 (3.6%)	2 (2.6%)	3 (2.8%)
American Indian or Alaka Native	1 (3.6%)	1 (1.3%)	2 (1.9%)
Age, years, median (IQR)	43 (33, 53)	47 (40, 55)	45 (39, 55)
Relapses in prior 2 years, median (IQR)	0 (0, 0)	0 (0, 0)	0 (0, 0)
# of prior anti-CD20 infusions, median (IQR)	6 (4, 9)	9 (6, 13)	9 (5, 12)
Years of prior anti-CD20 treatment, median (IQR)	2.0 (1.3, 3.6)	4.5 (2.7, 6.2)	3.8 (2.1, 5.9)
Months since last anti-CD20 dose, median (IQR)	9 (6, 12)	6 (6, 7)	6 (6, 7)
Prior anti-CD20 infusion duration (minutes), median (IQR)	150 (122, 210)	132 (120, 240)	135 (120, 228)
Experienced wearing-off on prior anti-CD20, n (%)	8 (29%)	52 (67%)	60 (57%)

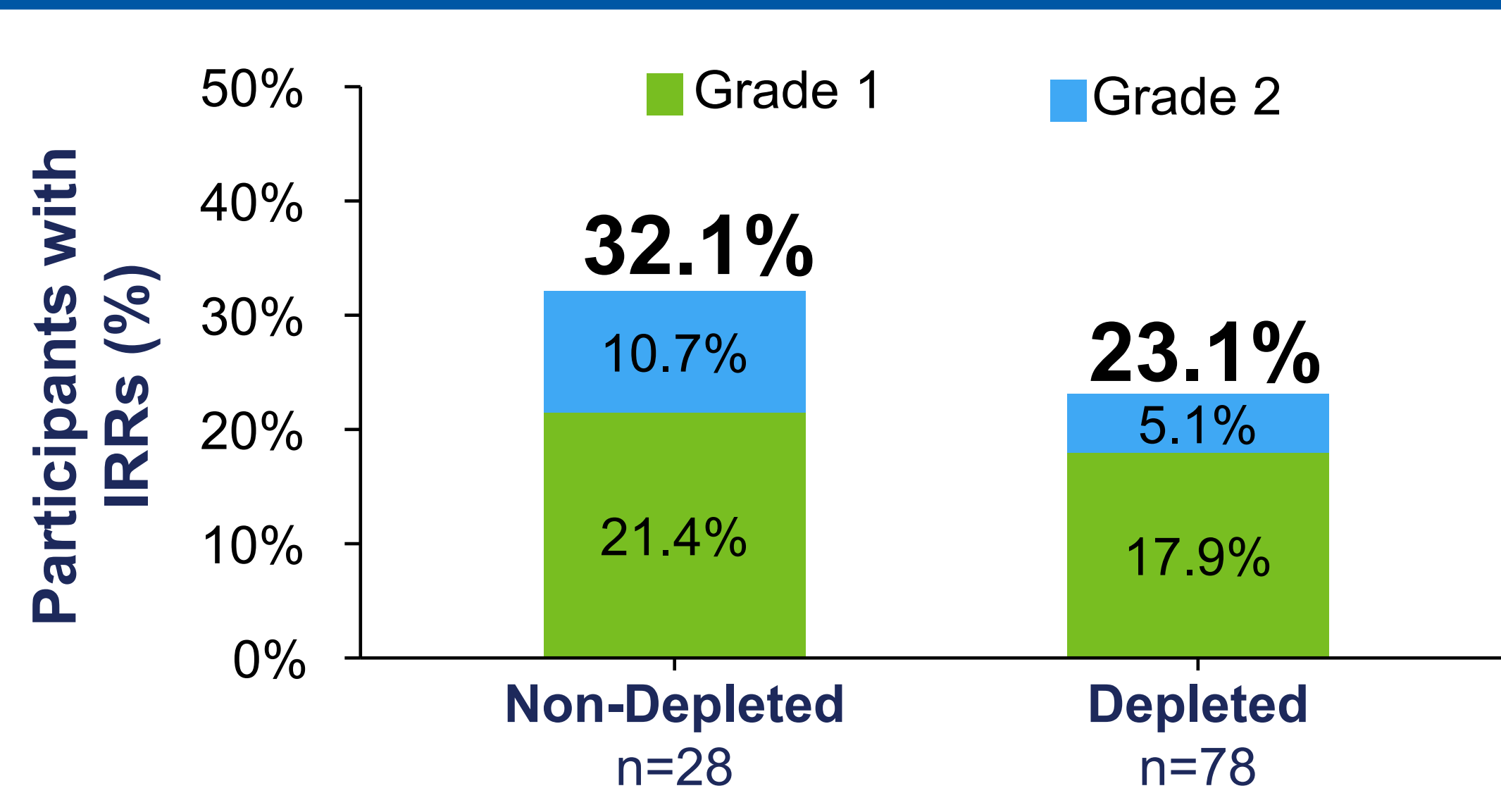
A greater proportion of participants with B-cell counts ≥10 cells/μL at baseline were Black or African American, had a higher body mass index (BMI), and were younger compared to those who were B-cell depleted at baseline.

RESULTS, CONT.

Infusion Tolerability

- The most common infusion-related reaction (IRR) symptoms were throat irritation (8.5%), headache (4.7%), fatigue (3.8%), and nausea (1.9%).
- 92% of infusions were completed without interruption or slowing.
- All IRRs completely resolved and were generally self-limiting with 10% of participants receiving supportive medication for IRRs, primarily diphenhydramine.

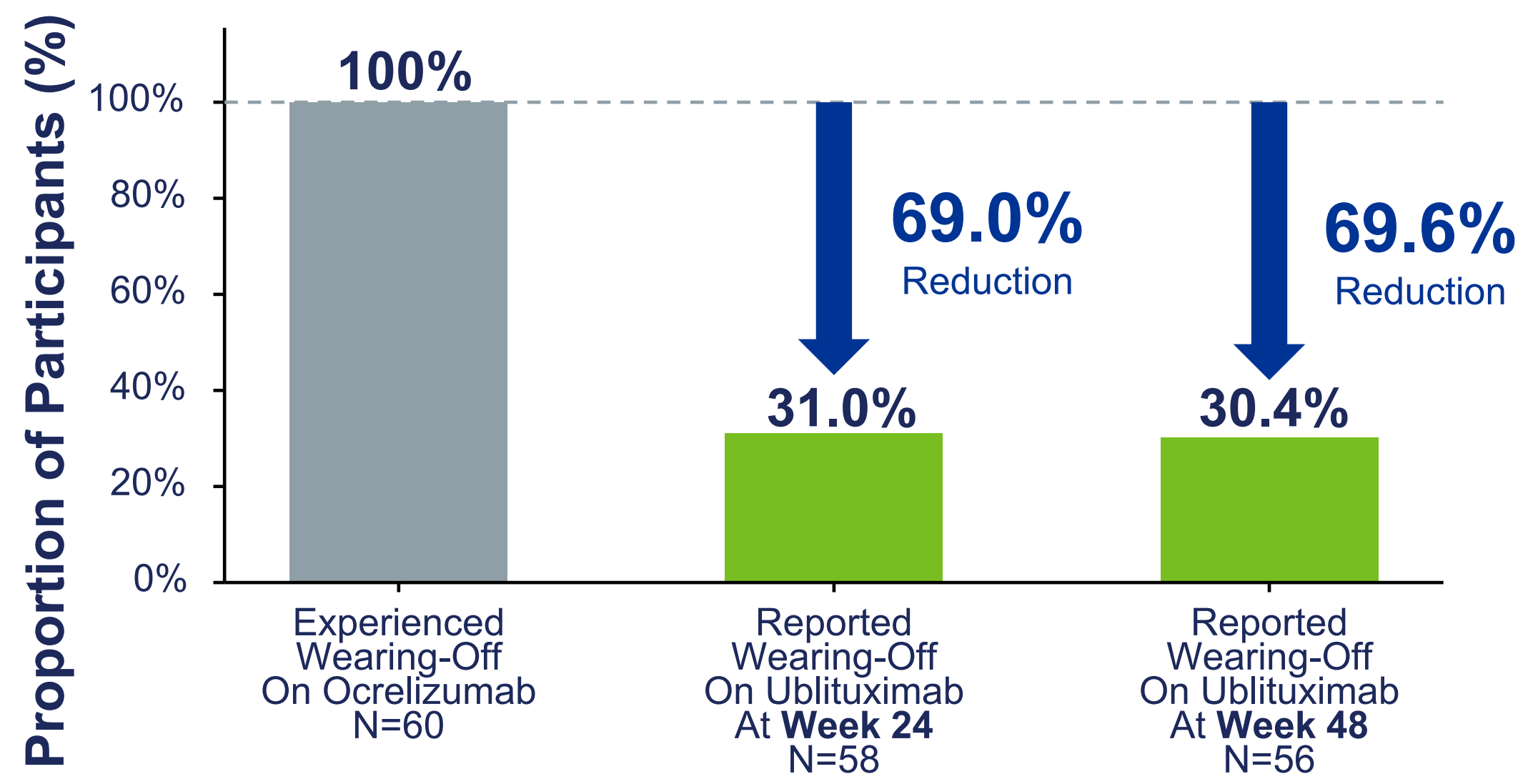
Figure 1. IRRs Associated with Initial 600 mg Ublituximab Dose Among Ocrelizumab Switches



Wearing-Off Effect

- Participants had a median treatment duration of 3.8 years on prior ocrelizumab with 60 participants (57%) reporting a wearing-off effect with ocrelizumab.
- Transitioning to ublituximab yielded a 69% reduction in wearing-off at Week 24, which was sustained at Week 48.

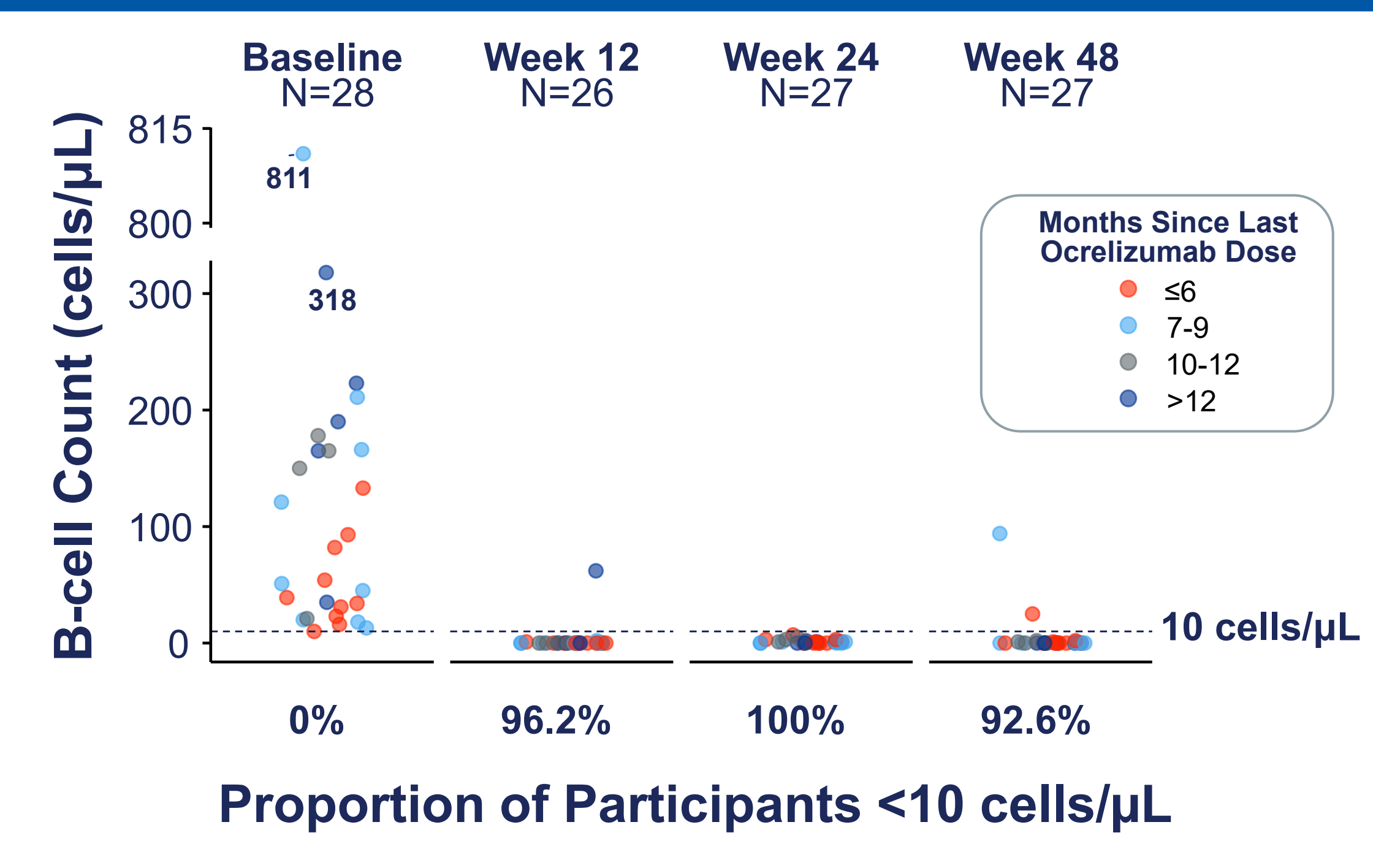
Figure 3. Ublituximab Reduces Wearing-off Effect Among Participants Who Previously Complained of Wearing-off



B-cell Depletion

- Among participants who were non-depleted (cell counts ≥10 cells/μL) at baseline, 10 repleted within 6 months of their last ocrelizumab dose.
- Ublituximab induced rapid and sustained B-cell depletion in this “early repleter” population with 100% (10/10) and 90% (9/10) having <10 cells/μL at Week 24 and Week 48, respectively.

Figure 2. B-Cell Distribution in Ocrelizumab Participants Who Were Not Depleted Upon Initiating Ublituximab



Treatment Satisfaction

- Ublituximab was associated with ≥98% treatment satisfaction on the dimensions of convenience and ease of use at both Week 24 and Week 48.

Figure 4. TSQM-9 Evaluation of Convenience Among Ocrelizumab Switches

