Safety and Tolerability of a Modified Dosing Regimen of Ublituximab: Updates from the ENHANCE Study

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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 150 mg dose on Day 1 followed by 450 mg doses on Day 15, Week 24, and subsequently every 24 weeks.

METHODS

- ENHANCE is a multi-center, open-label, 48-week study in participants with RMS designed to evaluate optimized dosing regimens for ublituximab.
- The study is actively enrolling participants with RMS who are treatment-naïve or transitioning from other disease-modifying therapies.
- Herein we report on participants who transitioned from prior anti-CD20 therapy in a B-cell depleted state (<10 cells/μL) and received a 600 mg ublituximab infusion in 1 hour on Day 1. Non-depleted participants (B-cells ≥10 cells/μL) received 600 mg of ublituximab at an assigned duration on Day 1.
- At Week 24, all participants received a 30-minute, 450 mg ublituximab infusion.
- Recommended premedications included a non-drowsy antihistamine, corticosteroid, and antipyretic at each infusion.

STUDY SCHEMA

Figure 1. Study Schema

Key Eligibility Criteria

- 18 – 65 years
- RMS diagnosis[1]
- EDSS ≤ 5.5
- Treatment-Naïve or Previously treated

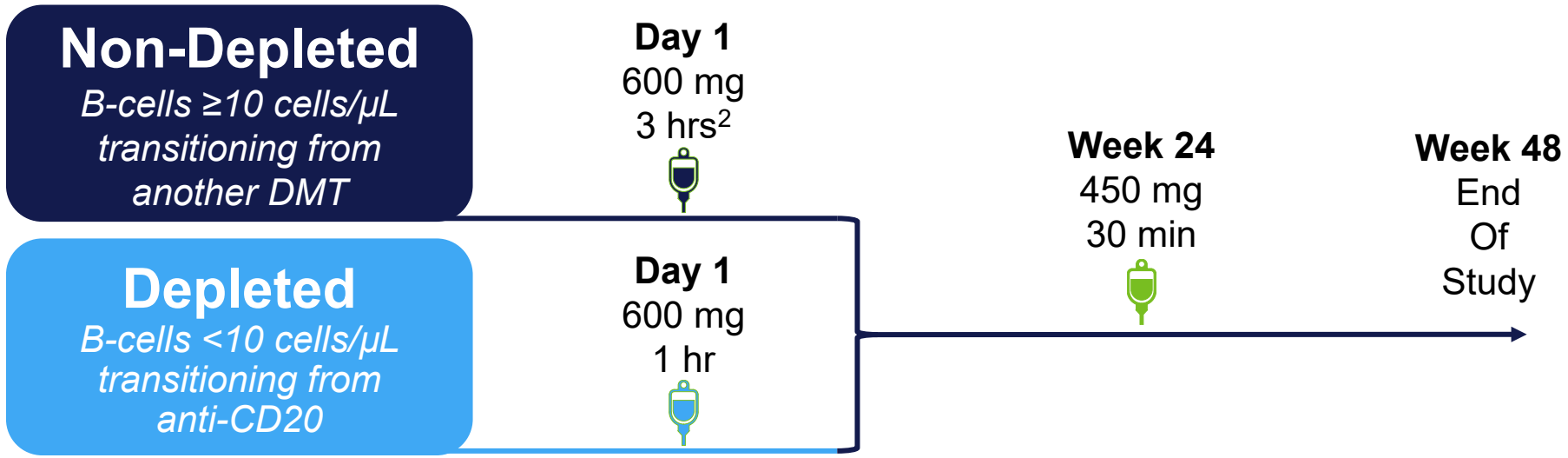


Table 1. Flow Rates for 600 mg doses

Time Interval (min)	4 Hour	3 Hour	2 hour	1 hour
0 – 30	10 mL/H	10 mL/H	10 mL/H	100 mL/H
30 – 60	20 mL/H	20 mL/H	40 mL/H	450 mL/H
60 – 120	35 mL/H	35 mL/H	250 mL/H	
120 – End	110 mL/H	225 mL/H		

1) 2017 Revised McDonald criteria
2) Non-Depleted population (N=70) includes a safety run-in cohort of 13 participants who received 4 hr infusions of 600 mg

RESULTS

Table 2. Baseline Characteristics by Population

B-cell Depletion Status	Depleted N=33	Non-depleted N=70	Overall N=103
B-cell count at screening, median (IQR)	1 (0, 1)	179 (101, 291)	106 (1, 215)
Treatment Naïve, n (%)	0 (0%)	19 (27%)	19 (18%)
Transitioned from anti-CD20, n (%)	33 (100%)	19 (27%)	52 (50%)
Transitioned from other DMT, n (%)	0 (0%)	32 (46%)	32 (31%)
Age, years, median (range)	45 (18, 62)	46 (25, 63)	45 (18, 63)
Female, n (%)	25 (76%)	46 (66%)	71 (69%)
Race, n (%)			
White	29 (88%)	54 (77%)	83 (81%)
Black or African American	3 (9.1%)	12 (17%)	15 (15%)
Asian	0 (0%)	3 (4.3%)	3 (2.9%)
Other	1 (3.0%)	1 (1.4%)	2 (1.9%)
Years since MS diagnosis, median (range)	13 (1, 28)	6 (0, 27)	8 (0, 28)
Relapses in prior 2 years, median (range)	0 (0, 4)	0 (0, 3)	0 (0, 4)

IQR: Interquartile range, DMT: disease-modifying treatment

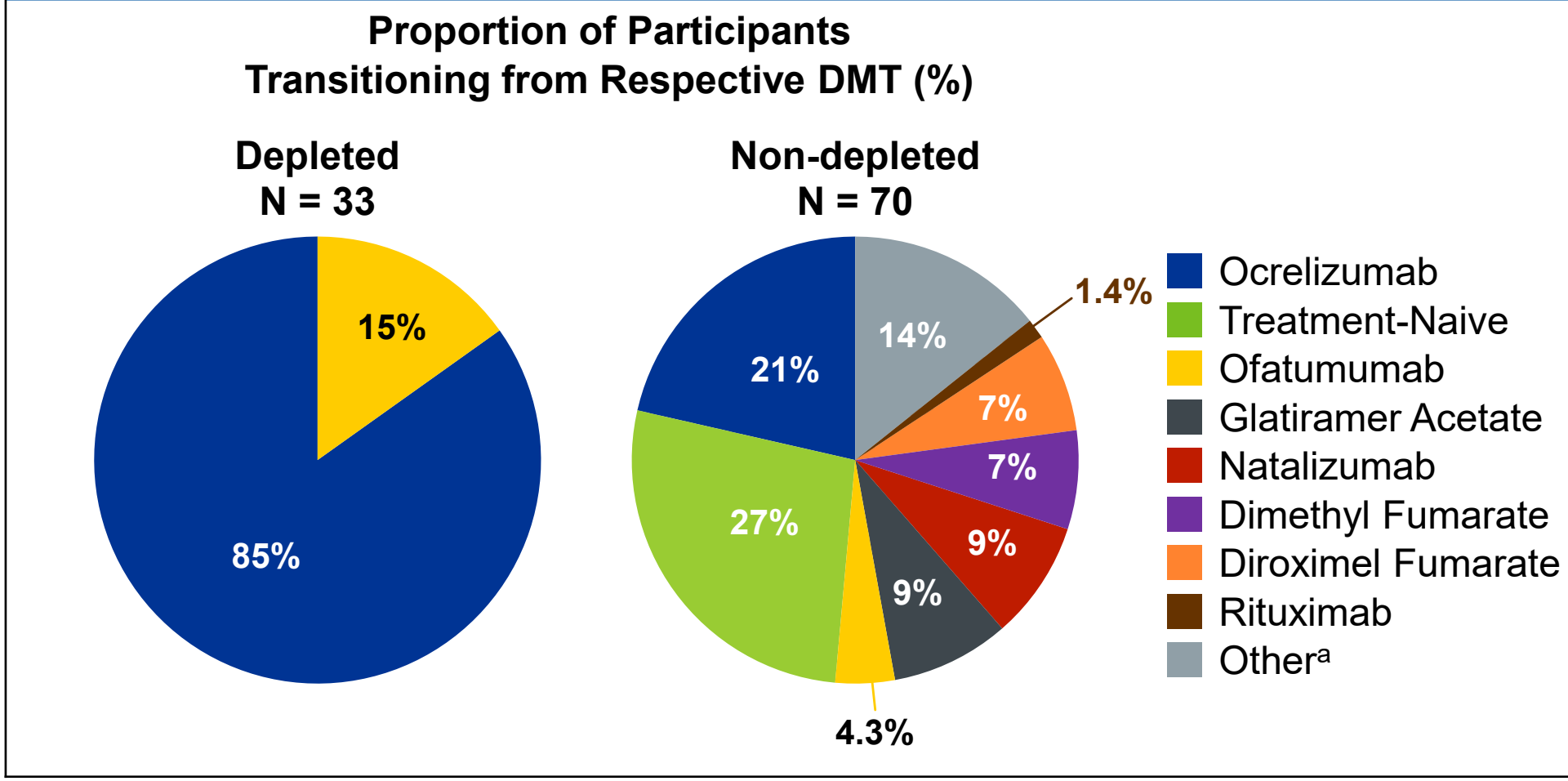
RESULTS

Table 3. Participants Who Switched from Ocrelizumab			
B-cell Depletion Status	**Depleted N=28**	**Non-depleted N=15**	**Overall N=43**
B-cell Count at Screening, median (IQR)	1 (0, 1)	82 (18, 188)	1 (0, 20)
# of Prior Anti-CD20 Infusions, median (range)	11 (3, 16)	5 (1, 11)	8 (1, 16)
Duration of Last Anti-CD20 Infusion (minutes), median (IQR)	136 (120, 236)	147 (123, 196)	136 (122, 217)
Experienced Wearing-Off Effect on Prior Anti-CD20, %	64%	33%	53%

IQR: Interquartile range

RESULTS

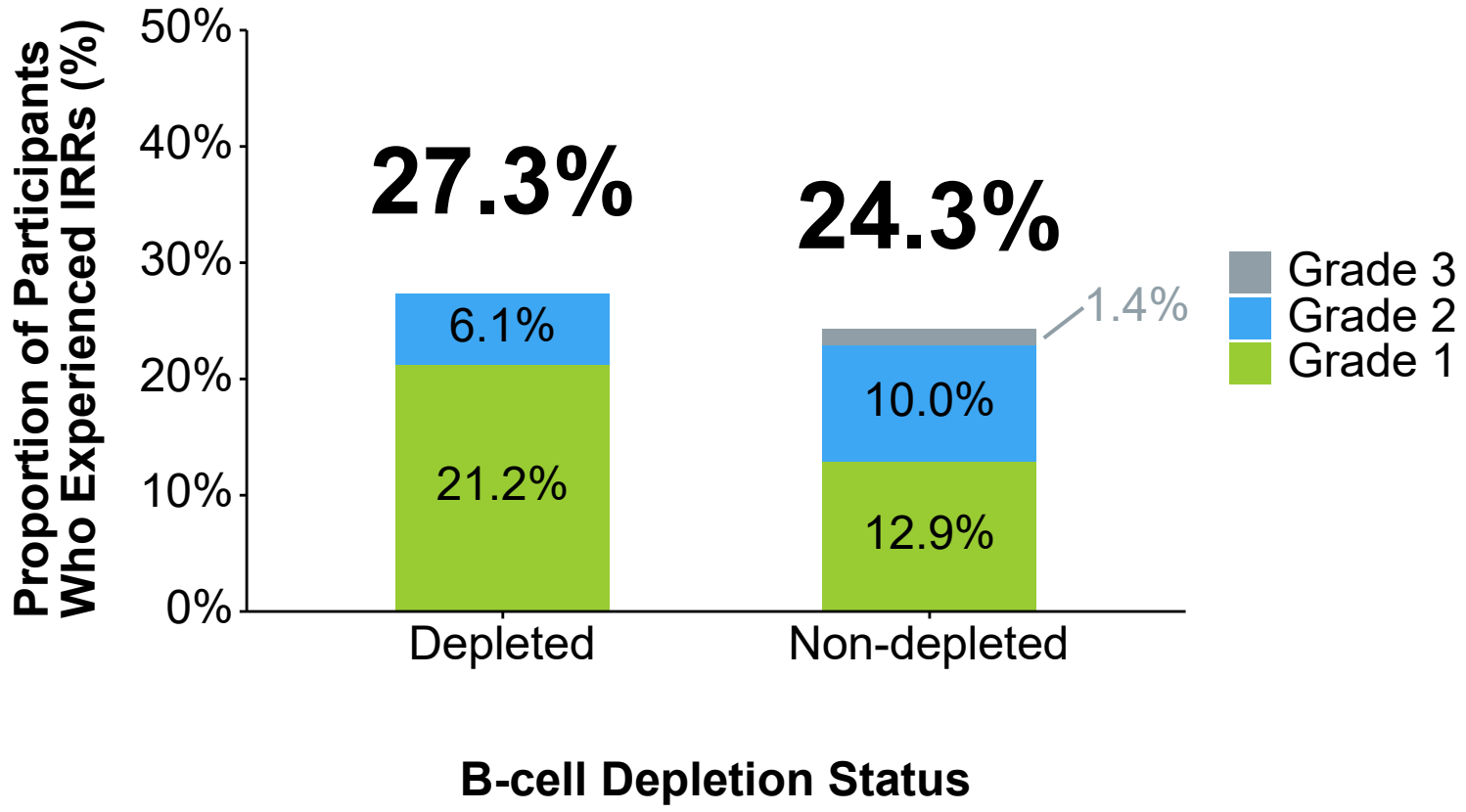
Figure 2. Most Recent DMTs by B-cell Depletion Status



[a] Other DMTs: Fingolimod (N=3), Teriflunomide (N=3), Mycophenolate Mofetil (N=1), Orelabrutinib (N=1), Ozanimod (N=1), Siponimod (N=1)

RESULTS

Figure 3. Incidence and severity of IRRs during 600 mg initial infusions



IRRs, Infusion Related Reactions

600 mg Infusion Experience:

- 88% of infusions were completed without interruption or slowing
- IRR Symptoms Reported in >2 Participants
  - Headache 5.8%
  - Dyspnea 3.9%
  - Nausea 3.9%
  - Throat irritation 3.9%
  - Chills 2.9%
  - Myalgia 2.9%
  - Pruritus 2.9%
- All IRRs resolved completely

CONCLUSIONS

- Data from ENHANCE supports that combining the initial Day 1 (150 mg) and Day 15 (450 mg) infusions into a single 600 mg dose is well-tolerated in all participants regardless of B-cell depletion status.
- The ENHANCE study is ongoing with initial 600 mg infusions being evaluated at a duration of 2 hours.
- A randomized trial to evaluate a modified ublituximab regimen will commence later this year.

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DISCLOSURES

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