Efficacy and Tolerability of Ublituximab after Transitioning from a Different Disease-Modifying Therapy: Updates from the ENHANCE Study

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OBJECTIVE

- The ENHANCE study evaluates the efficacy, safety, and tolerability of transitioning from a previous disease-modifying therapy (DMT) to ublituximab, exploring the elimination of the initial 150 mg dose in B-cell depleted participants and shorter infusion durations for the full 450 mg doses.

KEY FINDINGS

- Study Objective: First Dose Elimination
  - Duration and dose of the initial infusion did not impact the completion rate or incidence of infusion modification.
  - The incidence of infusion-related reactions (IRRs) remained low among both depleted and non-depleted participants and were primarily Grade 1 (only 1 Grade 2 IRR was observed).
- Study Objective: Faster 450 mg Infusions at Week 24
  - Shorter infusion durations down to 30 minutes were all completed and well tolerated with 82% of participants utilizing a non-drowsy antihistamine.
  - All IRRs were Grade 1 and resolved completely.

CONCLUSIONS

- Data from ENHANCE continues to support that 450 mg may be safely administered in 1 hour as an initial infusion for participants who are B-cell depleted.
- Data supports that ublituximab administered at Week 24 in faster infusions, including 30-minute infusions, is well tolerated with a low incidence of mild IRRs.
- The ENHANCE study is ongoing, and additional efficacy, safety and tolerability will be reported in the future.

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2. BRIUMVI® (ublituximab-xiiy) Prescribing Information. TG Therapeutics, Inc. 2022.

BACKGROUND

- In clinical practice, transition between therapies may occur for a variety of reasons, including suboptimal response, tolerability and participant convenience. Data on switching methodologies, efficacy, safety, and tolerability are therefore necessary to confirm the benefits of the new therapy.
- Additionally, improvements in participant convenience and compliance may be achieved through elimination of infusions and introduction of shorter duration infusions.
- Ublituximab is a novel monoclonal antibody targeting a unique epitope on the CD20 antigen and is glycoengineered for enhanced antibody-dependent cellular cytotoxicity.
  - In the ULTIMATE I and II studies, ublituximab met its primary endpoint of significantly reduced annualized relapse rate, and key secondary endpoints of significantly reduced T1 gadolinium-enhancing [Gd+] lesions and new/enlarging T2 lesions relative to teriflunomide.[1]
  - Ublituximab's labeled dosing is 450 mg intravenous (IV) infusion over 1 hour every 24 weeks after a starting dose of 150 mg IV infusion over 4 hours.[2]
- The ENHANCE study is designed to evaluate the efficacy, safety, and tolerability of transition from a previous DMT with two dose modifications being explored:
  - Elimination of the initial 150 mg dose in B-cell depleted participants transitioning from a prior anti-CD20.
  - Evaluation of shorter infusion durations for full 450 mg doses, less than 1 hour.

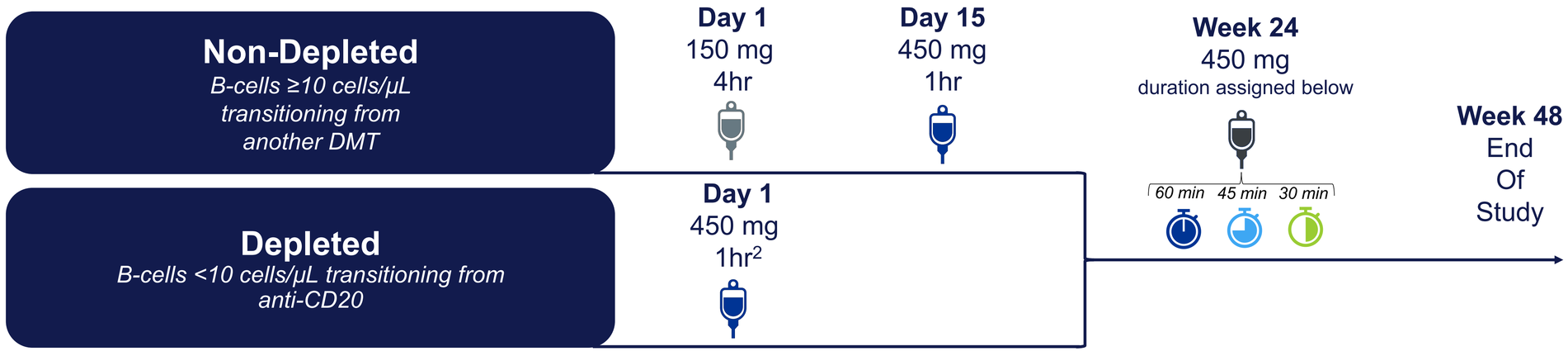
METHODS

- ENHANCE is a multi-center, open-label, 48-week study in participants with relapsing forms of multiple sclerosis (RMS) designed to evaluate optimized dosing regimens for ublituximab.
- ENHANCE was initially restricted to B-cell depleted participants switching from a prior IV anti-CD20 (ocrelizumab or rituximab), with a later amendment allowing prior subcutaneous anti-CD20 (ofatumumab) as well as switches from other DMTs, and no longer requiring all participants to be B-cell depleted.
- B-cell depleted is defined as <10 cells/μL.
- Standard protocol recommended pre-medications included a non-drowsy antihistamine, corticosteroid, and antipyretic at each infusion.

STUDY SCHEMA

Primary Endpoint: Change in T1 Gd+ lesions from baseline to Week 48
Secondary Endpoints: T1 Gd+ lesions at Week 48, IRRs, TSQM-9

Key Eligibility Criteria
- 18 – 65 years
- RMS diagnosis[1]
- EDSS ≤5.5
- Previously treated



1) 2017 Revised McDonald criteria; 2) Safety run-in of 13 participants received initial infusion of 450 mg in two hours

RESULTS

Demographics and Baseline Characteristics

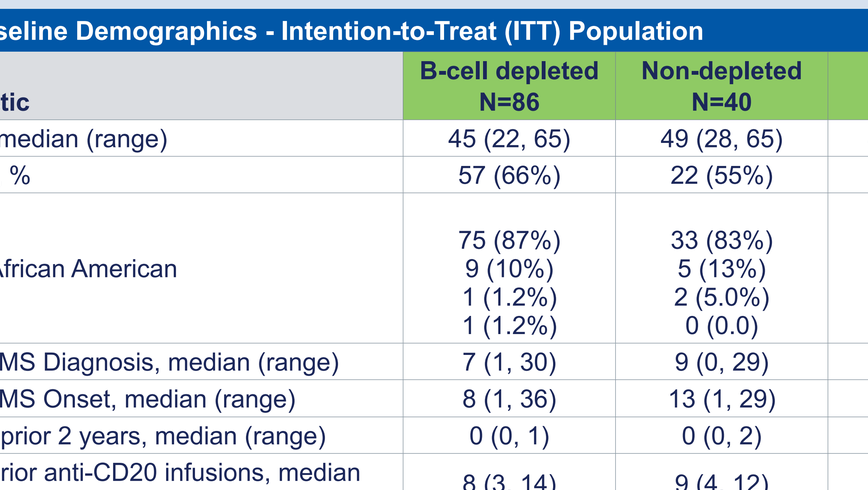
Table 1. Baseline Demographics - Intention-to-Treat (ITT) Population

Characteristic	B-cell depleted N=86	Non-depleted N=40	Overall N=126
Age, years, median (range)	45 (22, 65)	49 (28, 65)	45 (22, 65)
Sex, female, %	57 (66%)	22 (55%)	79 (63%)
Race, n (%)			
White	75 (87%)	33 (83%)	108 (86%)
Black or African American	9 (10%)	5 (13%)	14 (11%)
Asian	1 (1.2%)	2 (5.0%)	3 (2.4%)
Other	1 (1.2%)	0 (0.0)	1 (0.8%)
Years since MS Diagnosis, median (range)	7 (1, 30)	9 (0, 29)	7 (0, 30)
Years since MS Onset, median (range)	8 (1, 36)	13 (1, 29)	9 (1, 36)
Relapses in prior 2 years, median (range)	0 (0, 1)	0 (0, 2)	0 (0, 2)
Number of prior anti-CD20 infusions, median (range)[a]	8 (3, 14)	9 (4, 12)	8 (3, 14)
Duration of last anti-CD20 infusion, median (range)[a]	154 (119, 300)	127 (120, 140)	153 (119, 300)
Reported wearing off effect on prior ocrelizumab, % (n/N)[b]	58% (47/81)	60% (3/5)	58% (50/86)

MS, multiple sclerosis
[a]Calculated out of participants who transitioned from ocrelizumab
[b]n: participants who reported experiencing a wearing-off effect on ocrelizumab; N: total number of participants who transitioned from ocrelizumab in this cohort

Participants Transitioning from Respective DMTs

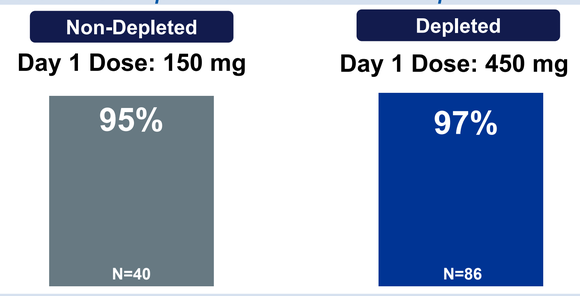
Figure 1. Participants Transitioning from Respective DMTs



- 5 participants transitioned from prior ocrelizumab in a non-depleted state.
  - Median prior ocrelizumab infusions: 9 (range, 4-12).
  - Median time since last ocrelizumab infusion: 7 months.

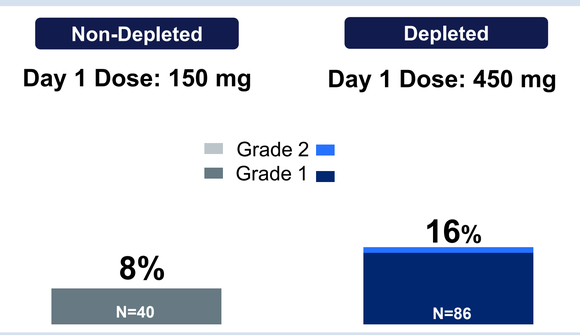
Study Objective: First Dose Elimination

Infusions Completed without Interruption or Slowing



- 100% of initial ublituximab infusions were completed.
- Neither duration nor dose impacted the completion rate or incidence of infusion modification.
- Data continue to support that 450 mg may be safely administered in 1 hour as an initial infusion for participants who are B-cell depleted.

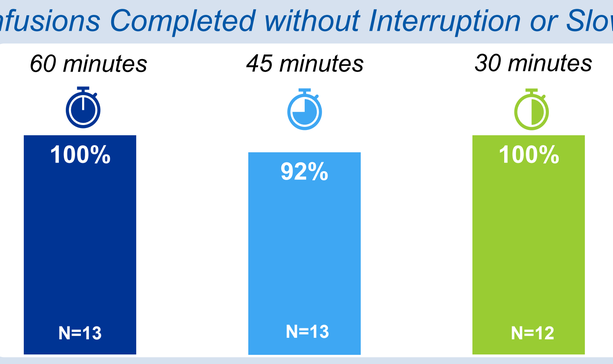
Proportion of Participants who experienced IRRs



- The incidence of IRRs remained low among both depleted and non-depleted participants.
- All participants had an antipyretic at each infusion.
- IRRs were primarily Grade 1 with the most frequent symptoms being throat irritation (n=7) and headache (n=5).
- One Grade 2 IRR was observed (minor throat itchiness), which completely resolved without infusion modification.

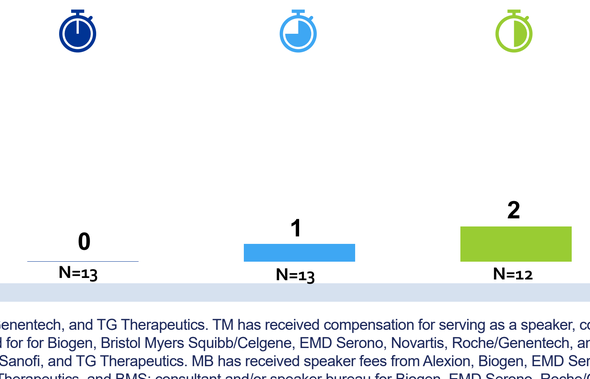
Study Objective: Faster 450 mg Infusions at Week 24

Infusions Completed without Interruption or Slowing



- 450 mg ublituximab infusions were well tolerated at shorter infusion durations down to 30 minutes.
- All Week 24 infusions were completed.
- 82% of participants received non-drowsy antihistamines for their Week 24 infusion.

Number of Participants with IRRs



- There were 3 participants with Grade 1 IRRs reported (itching, throat irritation and headache).
- All IRRs were Grade 1 and resolved completely.

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