Evaluating the maintenance of efficacy and tolerability of transitioning from IV anti-CD20 therapy to ublituximab: ENHANCE Study Interim Data

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OBJECTIVES

- To present the ENHANCE study design, baseline demographics and data from cohorts transitioning from IV anti-CD20 therapy to ublituximab

KEY FINDINGS

- In cohort 1, no infusion related reactions (IRRs) were observed for any of the participants transitioning from ocrelizumab directly to 450 mg ublituximab administered over 2 hours
  - No infusion interruptions or infusion rate slowing was observed, resulting in a median infusion time of 120 min
- In cohort 2, which is ongoing, 4 (19%) study participants who transitioned from ocrelizumab directly to 450 mg ublituximab administered over 1 hour experienced mild IRRs (all Grade 1)
  - 86% of participants completed the infusion with no interruption or slowing, resulting in a median infusion time of 60 min

CONCLUSIONS

- Ublituximab administration was well tolerated in all cohorts, with mild IRR observed in a small proportion of participants (none greater than grade 1)
- Consistent with previous reports and post-hoc analysis of ULTIMATE I and II data, participants with low absolute B-cell count at nadir have an excellent infusion tolerability experience
- The ENHANCE study is ongoing, and additional efficacy, safety and tolerability will be reported in the future

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BACKGROUND

- In clinical practice, transition between therapies may occur for a variety of reasons, including suboptimal response, tolerability and patient convenience. Data on switching methodologies, efficacy, safety and tolerability are therefore necessary to confirm the benefits of the new therapy.
- 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 IV infusion over 1 hour every 24 weeks after a starting dose of 150 mg IV infusion over 4 hours.[2]
- Prior exposure to anti-CD20 therapy was excluded from the ULTIMATE I and II trials, therefore, data is needed to inform the efficacy and safety associated with this transition.
- Previously reported anti-CD20 transition studies demonstrated that the presence of CD19+ B-cells (>1%) was associated with increased infusion related reactions.[3] Similarly, post-hoc analysis from ULTIMATE I and II revealed that the presence of B-cells at nadir was significantly associated with infusion related reactions at week 24, 48 and 72.[4]
- Patients transitioning from previous anti-CD20 therapy in a B-cell depleted state were therefore hypothesized to not require a 150 mg starting dose prior to initiating a full 450 mg IV infusion.
- The ENHANCE study is designed to evaluate the efficacy, safety and tolerability of transition from previous IV anti-CD20 therapy to ublituximab, with elimination of the 150 mg starting dose.

STUDY DESIGN

- ENHANCE is a 48-week, Phase 3b, open label, multi-center study designed to assess:
  - the radiologic and clinical outcomes of transition from IV anti-CD20 therapy to ublituximab
  - the tolerability of transition, the incidence of infusion related reactions and infusion times, with elimination of the 150 mg loading dose
  - the impact of ublituximab on patient reported outcome measures
- This study is evaluating two cohorts of participants receiving an initial dose of 450 mg of ublituximab with varying infusion time (1-2 hrs) in an open-label design.

Ublituximab 450 mg		
Cohort	**Week 1 infusion time**	**Week 24 infusion time**
Cohort 1	2 hours	1 hour
Cohort 2	1 hour	

RESULTS

Demographics

- In cohort 1, patients were transitioned from prior IV anti-CD20 therapy to an ublituximab dose of 450 mg over 2 hours
  - 13 participants met the eligibility criteria for inclusion. The median age was 37, most were female (n=10, 77%), white (n=12, 92%), had a median BMI of 29 and a median of 4.3 years since MS diagnosis **(Table 1)**.
  - 8 participants (62%) experienced wearing off with prior ocrelizumab treatment
- In cohort 2, which is ongoing, patients were transitioned from prior IV anti-CD20 therapy to an ublituximab dose of 450 mg over 1 hour
  - 21 participants met the eligibility criteria for inclusion. The median age was 44, most were female (n=13, 62%), white (n=18, 86%), had a median BMI of 28 and a median of 5.0 years since MS diagnosis **(Table 1)**.
  - 12 participants (57%) experienced wearing off with prior ocrelizumab treatment
- Amongst the participants who did not meet eligibility criteria, 5 cases were due to elevated B-cell ≥ 10 cells/μL (211, 103, 60, 93, 210 cells/μL)

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

Characteristic	Ublituximab Cohort 1 N=13	Ublituximab Cohort 2 N=21
Age, years, median (range)	37 (22, 51)	42 (30, 61)
Sex, female, %	10 (77)	13 (62)
Race, n (%) White Black or African American Asian	 12 (92) 1 (7.7) --	 18 (85.7) 2 (9.5) 1 (4.8)
BMI, median (range)	29 (18, 50)	28 (21, 52)
Years since MS Diagnosis, median (range)	4.3 (2.7, 7.7)	5.1 (1.1, 9.7)
Years since MS Onset, median (range)	6 (2.8, 22.6)	6.5 (1.3, 20.9)
Number of relapses in prior 2 years, median	0	0
Number of prior anti-CD20 therapy, n (%) ocrelizumab	 13 (100)	 21 (100)
Number of prior anti-CD20 infusions, median (range)	9 (5, 12)	7 (3, 14)
Absolute B-cell Count (median, cells/μL)	0 (0, 0)	0 (0, 0)
Immunoglobulins, median (range, mg/dL) IgA IgG IgM	 133 (59, 502) 909 (743, 1153) 59 (17, 120)	 147 (66, 420) 863 (497, 1310) 39 (17, 248)

BMI, body mass index; MS, multiple sclerosis; Immunoglobulin Normal Ranges: IgA: 70-400; IgG: 700-1600; IgM: 40 - 230

Premedications

- All study participants were administered premedications prior to infusion, as indicated in **Table 2**.

Table 2. Premedications Administered - ITT Population

	Route of Delivery	Ublituximab Cohort 1 - Week 1 N=13	Ublituximab Cohort 2 - Week 1 N=21	Ublituximab Week 24 N=7
		N (%)	N (%)	N (%)
Corticosteroid methylprednisolone (100-125 mg)	IV	13 (100)	21 (100)	7 (100)
Antipyretics acetaminophen (500-1000 mg) ibuprofen (800 mg)	Oral	9 (69) 4 (31)	14 (67) 7 (33)	4 (57) 3 (43)
Antihistamines cetirizine (10 mg) loratadine (10 mg) diphenhydramine (25-50 mg)	Oral	9 (69) 4 (31) -	15 (71) 6 (29) 4 (19)	4 (57) 2 (29) 1 (14)

Infusion Tolerability

- In cohort 1, no infusion related reactions were observed in any of the ublituximab doses administered
  - All study participants completed the infusion without interruption or slowing, with a median infusion duration of 120 min
- In cohort 2, 4 (19%) participants experiences infusion related reactions, all of which were Grade 1 (allergic rhinitis, n=1; flushing, n=1; headache, n=2; scratchy throat, n=1)
  - 18 (86%) of participants completed the infusion without interruption or slowing, with a median infusion duration of 60 min
- No infusion related reactions were observed during any of the ublituximab doses administered at week 24 (n=7)
  - All study participants completed the infusion without interruption or slowing, with a median infusion duration of 60 min

Table 3. Infusion Experience for ITT Population

Infusion Experience	Ublituximab Cohort 1 N=13	Ublituximab Cohort 2 N=21	Ublituximab Week 24 dose N=7
Infusions completed, n (%)	13 (100)	21 (100)	7 (100)
Infusions completed without interruption or slowing, n (%)	13 (100)	18 (86)	7 (100)
Infusion duration, minutes, median (IQR)	120 (120-124)	60 (60, 65)	60 (60, 65)

IQR: Interquartile Range

- At baseline, 31 (91%) of participants had undectable B-cells. Following ublituximab treatment, all participants (100%) had undetectable B-cells measured at weeks 12 and 24.

Table 4. Proportion of participants with undetectable B-cell

Timepoint	Proportion of participants with undetectable B-cell, n (%)
Baseline	31 (91)
Week 12	18 (100)
Week 24	11 (100)