# Evaluating the maintenance of efficacy and tolerability of transitioning from IV anti-CD20 therapy to ublituximab: ENHANCE Study Design, Patient Demographics and Preliminary Data

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## OBJECTIVE

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

## KEY FINDINGS

- In Cohort 1, no infusion related reactions (IRR) and no adverse events (AEs) 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
- Similarly, in Cohort 2, which is ongoing, no IRRs or AEs were observed for study participants transitioning from ocrelizumab to ublituximab
  - No infusion interruptions or infusion rate slowing occurred, and all participants completed the infusion in a median time of 60 min

## CONCLUSIONS

- Ublituximab administration was well tolerated in all cohorts, with no infusion related reactions or adverse events observed
- 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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**REFERENCES**
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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 cytolysis
  - 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
  - Ublituximab's labelled dosing is 450 mg IV infusion over 1 hour every 24 weeks, after a starting dose of 150 mg IV infusion over 4 hours
- 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[1]
- 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[2]
- 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. Cohorts will be expanded as further results are collected

| Ublituximab 450 mg | |
|---|---|
| **Cohort** | **Week 1 - Infusion Time** |
| Cohort 1 | 2 hours |
| Cohort 2 | 1 hour |

## KEY ENDPOINTS

### PRIMARY

- The proportion of participants with no change or reduction in number of T1 $Gd^+$ lesions from baseline to Week 48

### SECONDARY

- The proportion of participants free of T1 $Gd^+$ lesions at Week 48
- The proportion of participants experiencing IRRs as reported by the Investigator
- Treatment Satisfaction Questionnaire for Medication (TSQM-9) scores at Week 24 and Week 48

## KEY INCLUSION CRITERIA

- Diagnosis of RMS (2017 Revised McDonald criteria) within prior 10 years
- Participants currently treated with ocrelizumab must have received 2 fully infused initial 300 mg ocrelizumab IV infusions and at least 1 fully infused 600 mg ocrelizumab IV infusion 6 months later (+/- one month)
- Participants currently being treated with rituximab must have received at least 2 full infusions of rituximab 500 mg - 1000 mg IV every 6 months (+/- one month) or initial loading regimens of rituximab (i.e., 500 mg - 1000 mg on Day 1 and on Day 15), and at least 1 fully infused rituximab dose (i.e., 500 mg - 1000 mg) 6 months later (+/- one month)
- Expanded Disability Status Scale (EDSS) score ≤ 5.5
- Neurologically stable for > 30 days prior to first dose of ublituximab
- $CD19^+$ B cells < 10 cells/μL at screening

## RESULTS

*Demographics*

- In Cohort 1, patients were transitioned from prior IV anti-CD20 therapy to an ublituximab dose of 450 mg over 2 hours
  - 16 patients were screened and 13 met the eligibility criteria for inclusion
    - 3 patients who did not meet eligibility criteria had elevated $CD19^+$ B-cell (n=2; 93 and 210 cells/μL at screening), and active prostate cancer (n=1)
  - Most study participants were female (n=10, 77%), white (n=12, 92%), had an average BMI of 30, mean 4.7 years since MS diagnosis and all had undetectable absolute B-cell counts at baseline (Table 1)
  - All were stable at entry and had no relapses in the 2 years prior to study enrolment. Eight of the 13 participants (62%) transitioned therapy due to wearing off experienced with ocrelizumab
- In Cohort 2, the participants had a median age of 49, are white (n=2, 100%), had a median BMI of 23.4 and median 2.3 years since MS diagnosis. One participant had 1 relapse in the 2 years prior to enrolment (Table 1).

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

| Characteristic | Ublituximab Cohort 1 Enrolment Complete (n=13) | Ublituximab Cohort 2 Enrolment Ongoing (n=2) |
|---|---|---|
| Age, years, median (range) | 37 (22, 51) | 49 (37, 60) |
| Sex, female, % | 10 (77%) | 1 (50%) |
| Race, n (%)<br>White<br>Black or African American | <br>12 (92%)<br>1 (7.7) | <br>2 (100%) |
| BMI, median (range) | 29 (18, 50) | 23.4 (22.8, 24.1) |
| Years since MS Diagnosis, median (range) | 4.4 (2.7, 7.7) | 2.3 (2.2, 2.4) |
| Years since MS Onset, median (range) | 6 (2.8, 22.6) | 2.3 (2.2, 2.4) |
| Number of relapses in prior 2 years, median | 0 | 1 |
| Prior anti-CD20 therapy, n (%)<br>ocrelizumab | <br>13 (100%) | <br>2 (100%) |
| Number of prior anti-CD20 infusions, median (range) | 9 (5, 12) | 4 (3, 5) |
| Absolute B-cell Count (median, cells/μL) | 0 (0, 0) | 0 (0, 0) |
| Immunoglobulins, median (range) mg/dL<br>IgA<br>IgG<br>IgM | <br>133 (59, 502)<br>909 (743, 1153)<br>59 (17, 120) | <br>264 (107, 420)<br>751 (497, 1005)<br>33 (25, 40) |

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
  - In Cohort 1, participants received IV methylprednisolone (n=13, 100%), an antipyretic (paracetamol, n=8, 62%; ibuprofen, n=5, 38%) and an antihistamine (cetirizine, n=9, 69%; loratadine, n=4, 31%)
  - In Cohort 2, participants received IV methylprednisolone and paracetamol (n=2, 100%); one participant received cetirizine and the other received loratadine

**Table 2. Premedications Administered - ITT Population**

| | Ublituximab Cohort 1 Enrolment Complete (n=13) | | Ublituximab Cohort 2 Enrolment Ongoing (n=2) | |
|---|---|---|---|---|
| | Route of Delivery | n (%) | Route of Delivery | n (%) |
| **Corticosteroid**<br>methylprednisolone (100-125 mg) | IV | 13 (100) | IV | 2 (100%) |
| **Antipyretics**<br>paracetamol (500-1000 mg)<br>ibuprofen (800 mg) | Oral | 8 (62)<br>5 (38) | Oral | 2 (100%) |
| **Antihistamines**<br>cetirizine (10 mg)<br>loratadine (10 mg) | Oral | 9 (69)<br>4 (31) | Oral | 1 (50%)<br>1 (50%) |

*Infusion Tolerability*

- No infusion related reactions were observed in any of the ublituximab doses administered in Cohort 1
  - All study participants in Cohort 1 completed the infusion without interruption or slowing. The median infusion duration was 120 min
- In Cohort 2, for the initial 2 participants, no infusion related reactions were observed
  - Each participant 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 Enrolment Complete (n=13) | Ublituximab Cohort 2 Enrolment Ongoing (n=2) |
|---|---|---|
| Infusions completed, n (%) | 13 (100%) | 2 (100%) |
| Infusions completed without interruption or slowing, n (%) | 13 (100%) | 2 (100%) |
| Infusion duration, minutes, median (IQR) | 120 (120-124) | 60 (60, 60) |

IQR: Interquartile Range

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