# Multi-protein Biomarker Test Results for Participants Treated with Ublituximab from the Study to Evaluate Safety, Efficacy and Pharmacokinetics (PK) of a Modified Regimen of Ublituximab (ENHANCE)

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P040

## Introduction

Ublituximab is a glycoengineered anti-CD20 monoclonal antibody for adults for relapsing multiple sclerosis (RMS) [1]. The Multiple Sclerosis Disease Activity (MSDA) Test is a validated, multi-protein assay that generates a Disease Activity (DA) score (range 1.0-10.0) from 18 protein biomarkers, sex, and age [2, 3].

## Objectives

This prespecified exploratory analysis evaluates the trajectories of the DA score and its constituent proteins in RMS patients treated with a modified regimen of ublituximab after transition from a prior anti-CD20 agent.

## Methods

- Participants (N=85) were enrolled in the ENHANCE (NCT05877963) trial [1] and met the following criteria: transitioned from a prior anti-CD20 agent and were B-cell depleted (<10 cells/μL), had no relapses in the prior 12 months, and had stable MRI and EDSS in prior 6 months.
- 304 serum samples from 85 participants were assayed by the MSDA Test at baseline, Week 12, Week 24, and Week 48. The MSDA Test returns DA scores (range 1.0-10.0, in half increments) derived from absolute concentrations (pg/mL) of 18 proteins, age, and sex.
- Linear mixed models (LMMs) were used to estimate the average change per week for the DA score (the primary analysis) and log-transformed protein concentrations (18 secondary analyses), adjusted for age at sampling, sex, and a random participant effect.
- Equivalence between baseline and 48-week DA score and log-transformed protein concentration measurements was evaluated using two one-sided paired t-tests (TOST). The equivalence margin was taken to be the minimum detectable change at 95% confidence (MDC95) derived from a cohort of N=34 clinically stable relapsing-remitting multiple sclerosis participants selected from the MOVING MS parent trial [4].
- A Bonferroni correction was separately applied to the LMM and TOST secondary hypotheses (m=18 tests).

## Results

**Table 1:** Characteristics of the 304 samples from the N=85 subset of ENHANCE participants.

| Statistic | Value | Timepoint 0W | Timepoint 12W | Timepoint 24W | Timepoint 48W |
|---|---|---|---|---|---|
| n | | 85 | 85 | 85 | 49 |
| Age at Sampling, mean (SD) | | 44.5 (11.2) | 44.7 (11.2) | 45.0 (11.2) | 45.3 (12.0) |
| Sex, n (%) | Female | 56 (65.9) | 56 (65.9) | 56 (65.9) | 34 (69.4) |
| | Male | 29 (34.1) | 29 (34.1) | 29 (34.1) | 15 (30.6) |
| DA Score, mean (SD) | | 1.5 (0.7) | 1.5 (0.7) | 1.6 (0.8) | 1.6 (0.8) |

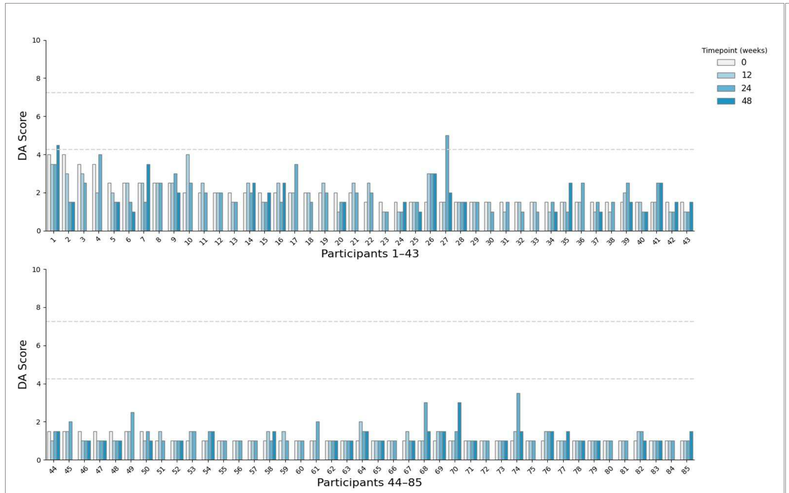


**Figure 1:** Disease Activity (DA) scores for each participant over the study period. Horizontal lines indicate the DA score thresholds distinguishing Low (1.0 - 4.0) from Moderate (4.5 - 7.0) disease activity and Moderate from High (7.5 -10.0) disease activity.

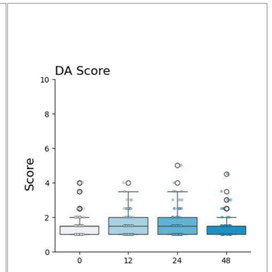


**Figure 2:** Participant DA scores grouped by treatment group and study visit timepoint (in weeks). Circles represent individual data points. The boxplots show the median (center line), interquartile range (IQR; box edges), and whiskers extending to values within ±1.5 × IQR. Outliers beyond this range are shown as open circles.

- Participants were 65.9% female, with a mean (SD) age of 44.5 (11.2) years and a mean DA score of 1.5 (0.7) units at baseline (Table 1).
- The overall DA score remained low and stable over time on ublituximab treatment (Figure 1-2).
- Three proteins exhibited significant adjusted average change per week: TNFSF13B (b=0.0020, 95%CI=[0.0014, 0.0026]), CXCL9 (b=0.0022, 95%CI=[0.0010, 0.0035]), and OPN (b=0.0015, 95%CI=[0.0008, 0.0021]) each increased (all Bonferroni-adj. p≤0.05) (Figure 3).
- The TOST analysis demonstrated that the overall DA score and all proteins at Week 48 were equivalent to baseline except for TNFSF13B (DA score p<0.001; 17 proteins $p_{Bonferroni}$<0.002), also known as B-cell activating factor (BAFF), which increased, indicating potentially deeper B-cell depletion despite all participants having entered the study in a peripherally B-cell depleted state.

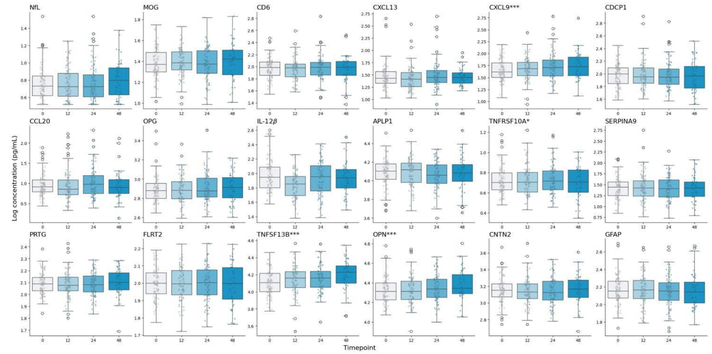


**Figure 3:** Participant log-transformed protein concentration (pg/mL) grouped by treatment group and study visit timepoint (in weeks). Circles represent individual data points. The boxplots show the median (center line), interquartile range (IQR; box edges), and whiskers extending to values within ±1.5 × IQR. Outliers beyond this range are shown as open circles. *Nominally significant ($p < 0.05$); ***Significant after Bonferroni correction. Statistical significance applies to the timepoint coefficients in the LMMs.

## Conclusions

Disease activity remained low and stable in patients transitioning to ublituximab from other anti-CD20 therapies. The 48-week increase in TNFSF13B generates the hypothesis that ublituximab induces more profound B-cell depletion than prior anti-CD20 therapies. These findings highlight the MSDA Test's utility for monitoring disease stability and specific responses to treatment.

**Disclosure:** Shannon McCurdy, Elisa Sheng, Luong Ruiz, Alexander Hari, Srushti Tiwari, Wayne Hu, David Brazel, and Ferhan Qureshi are employees of and have equity interest in Octave Bioscience. Chris Rowland, Christopher Garner, and Hari Miskin are employees of TG Therapeutics. John Foley has received research support from Biogen, Imstem, Octave, Innodem and TG Therapeutics. He received speakers' honoraria and/or acted as a consultant for Biogen, Horizon, and TG Therapeutics. He has equity interest in Octave. He is the founder of InterPro Biosciences.

**References:** [1] TG Therapeutics, Inc. Evaluating Safety, Efficacy and Pharmacokinetics of a Modified Regimen of Ublituximab (ENHANCE). clinicaltrials.gov; 2025 Nov. Report No.: NCT05877963. Available from: https://clinicaltrials.gov/study/NCT05877963. [2] Qureshi F, Hu W, Loh L, et al. Analytical validation of a multi-protein, serum-based assay for disease activity assessments in multiple sclerosis. Proteomics Clinical Applications. Feb 2023. https://doi.org/10.1002/prca.202200018. [3] Chitnis T, Foley J, Ionete C, et al. Clinical Validation of a Multi-protein, Serum-based Assay for Disease Activity Assessments in Multiple Sclerosis. Clinical Immunology. Aug 2023. https://doi.org/10.1016/j.clim.2023.109688. [4] McCurdy S, Sheng E, Jalaleddini K, et al. Longitudinal short-term assessments of single and multi-protein disease activity biomarkers to determine reliability and the minimum detectable change in people with clinically stable RRMS. Submitted Nov 2025.