Early Initiation of Ublituximab Treatment is Associated with Improved Disability Outcomes Among Treatment-Naïve Participants in ULTIMATE I and II

Derrick Robertson[1], Hans-Peter Hartung[2-5], Peiqing Qian[6], Sibyl Wray[7], Lily Lee[8], Koby Mok[8], Christopher Garner[8], Enrique Alvarez[9]

[1]University of South Florida; [2]Heinrich Heine University Medical Faculty; [3]Brain and Mind Centre, University of Sydney, Sydney, Australia; [4]Medical University of Vienna, Vienna, Austria; [5]Palacký University Olomouc, Olomouc, Czech Republic; [6]Swedish Medical Center; [7]Hope Neurology; [8]TG Therapeutics; [9]University of Colorado

Presented at the 2024 American Academy of Neurology (AAN), April 13-18, Denver, CO. Poster P6:001.

OBJECTIVE

- To evaluate disease progression in treatment-naïve participants enrolled in ULTIMATE I and II who had their MS symptom onset ≤ 3 years prior to study entry.

KEY FINDINGS

- In treatment-naïve participants who had their first MS symptom ≤ 3 years prior to enrollment, improvements in disability outcomes with ublituximab versus teriflunomide were observed at week 96, including:
  - Mean change from baseline in Expanded Disability Status Scale (EDSS) score of -0.16 and 0.02, respectively (P=0.0086)
  - The proportion of participants with Confirmed Disability Improvement (CDI) for at least 12 weeks, 14.4% versus 3.6% (P=0.0015)
  - Improvement in the change from baseline in Multiple Sclerosis Functional Composite (MSFC) score, 0.32 vs 0.09 (3.6x improvement for ublituximab vs teriflunomide).

CONCLUSION

- In post hoc analyses of ULTIMATE studies, early ublituximab treatment was associated with improved disability outcomes versus teriflunomide in treatment-naïve participants who had their first MS symptom ≤ 3 years prior to enrollment.

BACKGROUND

- Ublituximab is a novel monoclonal antibody targeting CD20 and is glycoengineered for enhanced antibody-dependent cellular cytolysis[1-3,a]
  - The exclusion of specific fucose molecules on the Fc region enhances its affinity for all variants of FcγRIIIa receptors, thereby increasing engagement of natural killer (NK) cells and resulting in increased antibody-dependent cellular cytolysis relative to other approved anti-CD20 antibodies[1,4,5]
- Ublituximab is administered in lower doses and with shorter infusion times compared with other currently infused anti-CD20 therapies[6]
- ULTIMATE I (NCT03277261) and ULTIMATE II (NCT03277248) are identical, Phase 3, randomized, multicenter, double-blind, active-control studies evaluating the efficacy and safety of ublituximab versus teriflunomide in participants with relapsing multiple sclerosis (RMS)[6]
- ULTIMATE I and II met their primary endpoint, demonstrating a statistically significant reduction in ARR for ublituximab compared with teriflunomide as well as significant improvements in the number of Gd+ T1 lesions and the number of new/enlarging T2 lesions[6]
- Older age and higher EDSS scores at baseline have shown to be predictors of early disability.[7] Additionally, delay in treatment has shown to increase MS patients' likelihood of future disability progression, and early initiation of treatment can be beneficial in limiting this risk.[7]

[a]Ublituximab was approved by the U.S. Food and Drug Administration for the treatment of relapsing forms of multiple sclerosis in December 2022.

METHODS

- ULTIMATE I and II enrolled a total of 1094 adult participants from 10 countries with a diagnosis of RMS (relapsing-remitting or secondary-progressive) with disease activity[6]

- Participants received ublituximab 450 mg administered by 1-hour intravenous infusion every 24 weeks (following Day 1 infusion of 150 mg and Day 15 infusion of 450 mg) or teriflunomide 14 mg orally once daily for 96 weeks[6]

- Pooled post hoc analyses evaluated disability measures in participants who were treatment-naïve prior to enrollment who had their first MS symptom ≤ 3 years prior to enrollment.

RESULTS

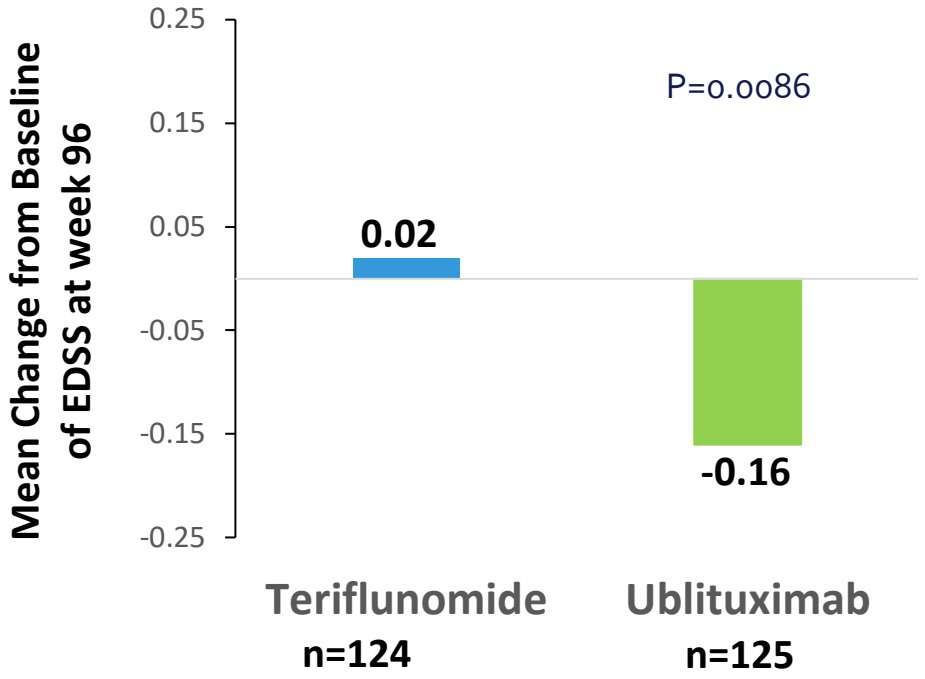
- Demographic and baseline characteristics for treatment-naïve participants. **Table 1**

Characteristic *Mean ± standard deviation or %*	**Treatment-naïve participants who had their first MS symptom ≤ 3 years prior to enrollment**	
	Teriflunomide (n=140)	**Ublituximab (n=139)**
Age, years	32.5±8.7	32.6±8.5
Sex, female, %	64.3	64.0
Time since first MS symptoms, years	1.4±0.8	1.5±0.8
Time since diagnosis, years	0.7±0.7	0.8±0.7
Time since most recent relapse, months	5.0±2.9	5.6±3.2
Number of relapses in the year prior to screening	1.4±0.7	1.5±0.6
Number of relapses in the 2 years prior to screening	2.0±0.9	1.8±0.8
Baseline EDSS score	2.3±1.0	2.2±1.2
Number of baseline Gd+ T1 lesions	2.8±5.5	2.4±5.3
Baseline T2 lesions count	52.7±35.5	56.3±40.0
BaselineT2 lesion volume, mL	9.4±10.4	10.3±10.5

RESULTS (continued)

- Estimated 12-week confirmed disability progression was low in both groups of the treatment-naive participants who had their first MS symptom ≤ 3 years prior to enrollment, hazard ratio (95% CI), 0.514 (0.184-1.433; P=0.1956)
- In treatment-naïve participants who had their first MS symptom ≤ 3 years prior to enrollment, significant improvement at week 96 in EDSS score was observed for ublituximab vs teriflunomide [-0.16 and 0.02, respectively (P=0.0086)] **Figure 1**

Figure 1. Change from Baseline of EDSS at Week 96 For Treatment-Naïve Participants Who Had Their First MS Symptom ≤ 3 Years Prior to Enrollment

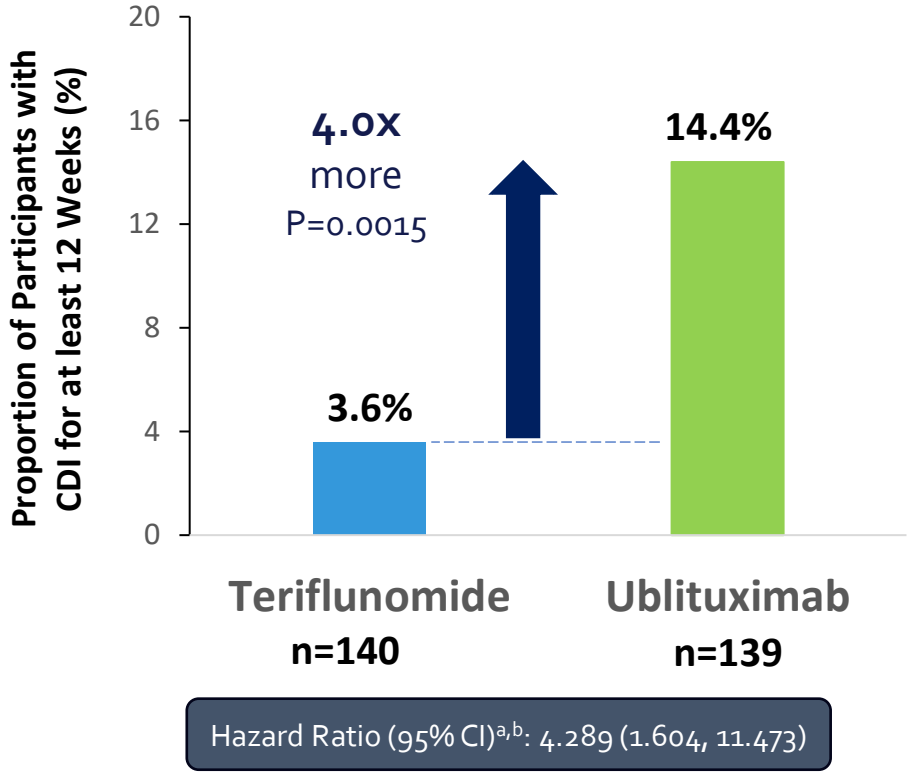


Pooled post hoc analysis. Modified intention-to-treat population.
P value based on t test.
EDSS, Expanded Disability Status Scale

RESULTS (continued)

- In treatment-naïve participants who had their first MS symptom ≤ 3 years prior to enrollment, significant improvement in the proportion of participants with CDI for at least 12 weeks for ublituximab vs teriflunomide [14.4% and 3.6%, respectively (P=0.0015)] **Figure 2**

Figure 2. CDI For Treatment-Naïve Participants Who Had Their First MS Symptom ≤ 3 Years Prior to Enrollment

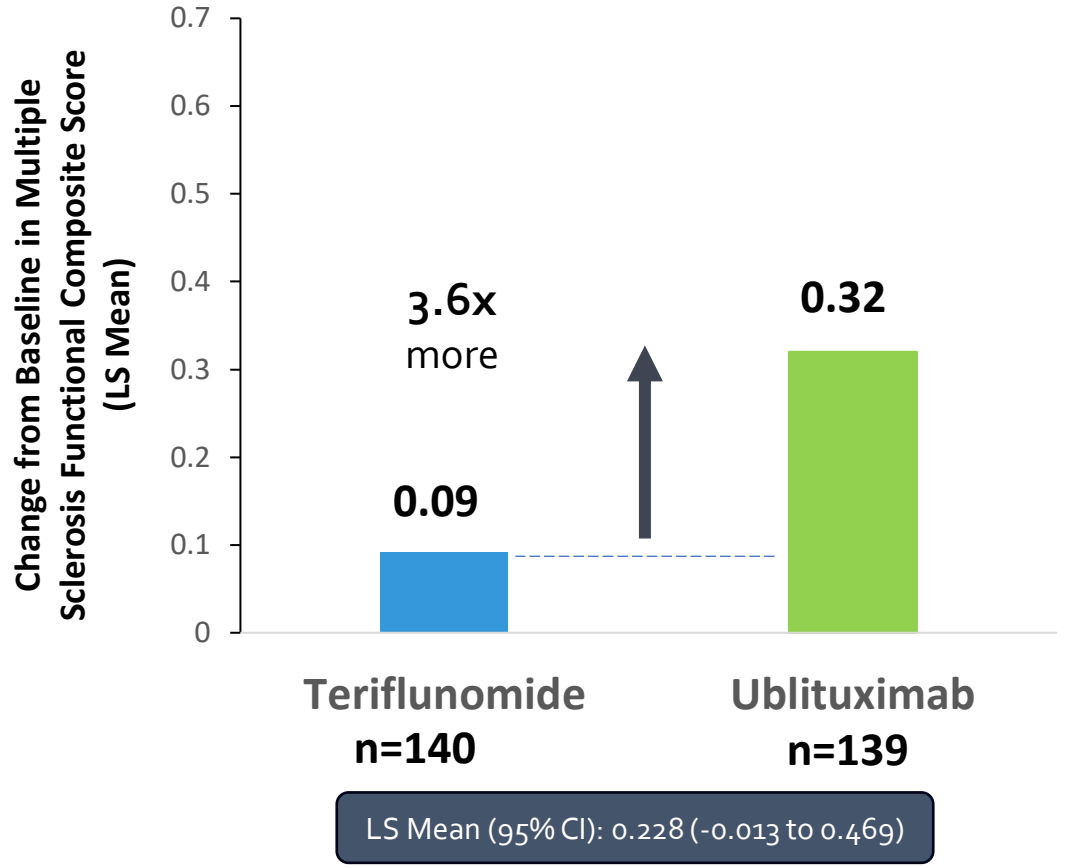


Pooled post hoc analysis. Modified intention-to-treat population. Estimated by Kaplan-Meier method.
[a] Hazard ratio is estimated using Cox regression model with treatment group as covariate.
[b] The stratification factors include region, baseline EDSS and study.
CDI, confirmed disability improvement; CI, confidence interval

RESULTS (continued)

- Among treatment-naive participants who had their first MS symptom ≤ 3 years prior to enrollment, there was improvement in change from baseline in MSFC score with ublituximab versus teriflunomide (LS mean: 0.32 versus 0.09) **Figure 3**

Figure 3. Change from Baseline in MSFC Score In Treatment-Naïve Participants Who Had Their First MS Symptom ≤ 3 Years Prior to Enrollment



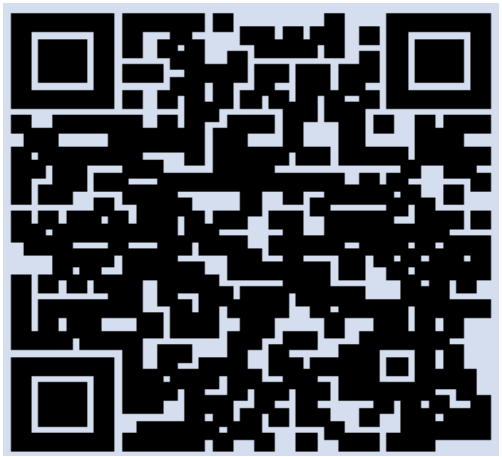
Pooled post hoc analysis. Modified intention-to-treat population. MMRM (Mixed Model Repeated Measures) of the change from baseline at all post-baseline time points. The model includes treatment, study, region, baseline EDSS strata, visit, treatment-by-visit interaction, and baseline value as covariates and uses an unstructured covariance matrix, restricted maximum likelihood estimation and the Satterthwaite method for degrees of freedom.
MSFC, Multiple Sclerosis Functional Composite

REFERENCES

1. de Romeuf C, et al. *Br J Haematol*. 2008;140(6):635-643.
2. Le Garff-Tavernier M, et al. *Leukemia*. 2014;28(1):230-233.
3. Babiker HM, et al. *Expert Opin Investig Drugs*. 2018;27(4):407-412.
4. Konno Y, et al. *Cytotechnology*. 2012;64(3):249-265.
5. Steinman L, et al. Presented at: AAN; April 2-7, 2022; Seattle, WA; April 24-26, 2022; Virtual. Oral presentation (Abstract 1011).
6. Steinman L, et al. *N Engl J Med*. 2022;387(8):704-714.
7. Kavaliunas A,et al. *Mult Scler*. 2017 Aug;23(9):1233-1240.

ACKNOWLEDGMENTS

- The authors thank the participants and their families for participating in the ULTIMATE I and II studies. The ULTIMATE I and II studies were sponsored by TG Therapeutics.



Copies of this poster obtained by QR code are for reference only and may not be reused as a whole or in part without the permission of the authors and study sponsor.