Functional Systems Scores and Expanded Disability Status Scale Score Evaluations in the ULTIMATE I and II Studies of Ublituximab Versus Teriflunomide in Participants With Relapsing Multiple Sclerosis

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OBJECTIVE

- To evaluate Functional Systems Scores (FSS) and Expanded Disability Status Scale (EDSS) score with ublituximab versus teriflunomide in pooled post hoc analyses of the ULTIMATE I and II studies

KEY FINDINGS

- Across all visits, significant improvements (odds ratio [95% CI]) with ublituximab versus teriflunomide were seen in EDSS score, 1.7 (1.25-2.37), *P*=0.0010; sensory functions, 1.4 (1.12-1.88), *P*=0.0052; and bowel and bladder functions, 1.4 (1.05-1.81), *P*=0.0222
- By individual visits, significant improvements were seen with ublituximab versus teriflunomide in EDSS score (Weeks 48-96), sensory functions (Weeks 48-96), bowel and bladder functions (Weeks 24-96), cerebellar functions (Weeks 48, 84, 96), cerebral or mental functions (Weeks 48, 72, 84), pyramidal functions (Week 96), and ambulation (Week 96) (all *P*<0.05)

CONCLUSIONS

- Pooled post hoc analyses of ULTIMATE I and II demonstrated significant improvements with ublituximab versus teriflunomide in EDSS score and multiple FSS
- These results further support prior data on improved disability outcomes with ublituximab versus teriflunomide in participants with RMS (relapsing multiple sclerosis)

BACKGROUND

- Ublituximab is a novel monoclonal antibody that targets a unique epitope of CD20 and is glycoengineered for enhanced antibody-dependent cellular cytotoxicity (ADCC)[1,2]
- In vitro studies demonstrate that ublituximab has 25-30× higher ADCC relative to all other currently approved anti-CD20 therapies used in multiple sclerosis[3]
- Ublituximab is administered in lower doses and with shorter infusion times compared with other currently infused anti-CD20 therapies[4]
- ULTIMATE I (NCT03277261) and ULTIMATE II (NCT03277248) are identical, Phase 3, randomised, multicentre, double-blind, active-control studies evaluating the efficacy and safety of ublituximab versus teriflunomide in participants with RMS[5]
- ULTIMATE I and II met their primary endpoint, demonstrating a statistically significant reduction in annualised relapse rate for ublituximab compared with teriflunomide as well as significant improvements in the number of gadolinium-enhancing T1 lesions and the number of new/enlarging T2 lesions[5]
- The EDSS and its component FSS are widely used assessment instruments based on a standard neurological examination[6,7]
- The FSS comprise 8 functional systems (pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral or mental, and "other"), each of which is graded from 0 (normal) to 5 or 6 (maximal impairment)[6]
- EDSS scores are determined by deficits in functional systems and ambulation[6]

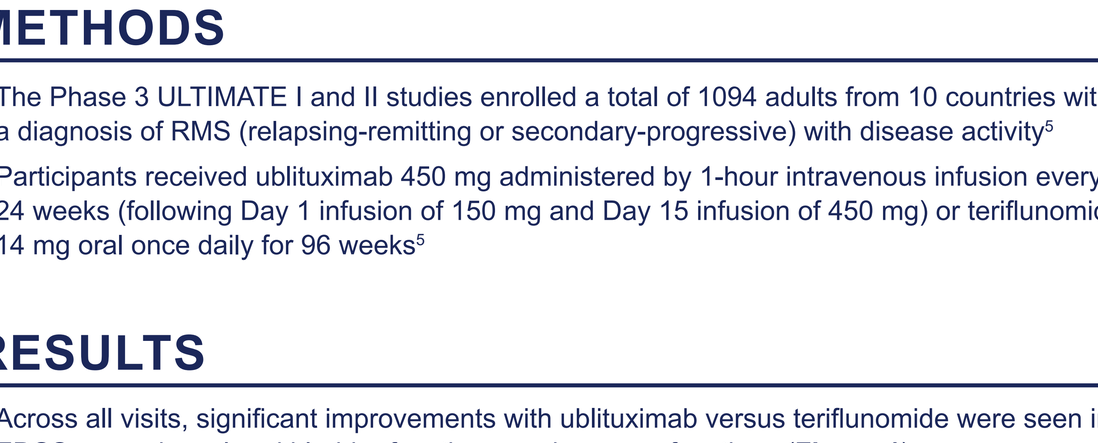
METHODS

- The Phase 3 ULTIMATE I and II studies enrolled a total of 1094 adults from 10 countries with a diagnosis of RMS (relapsing-remitting or secondary-progressive) with disease activity[5]
- 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 oral once daily for 96 weeks[5]
- Clinical evaluations were performed at baseline and every 12 weeks[5]
- Pooled post hoc analyses evaluated the change from baseline in EDSS score and FSS at each visit

RESULTS

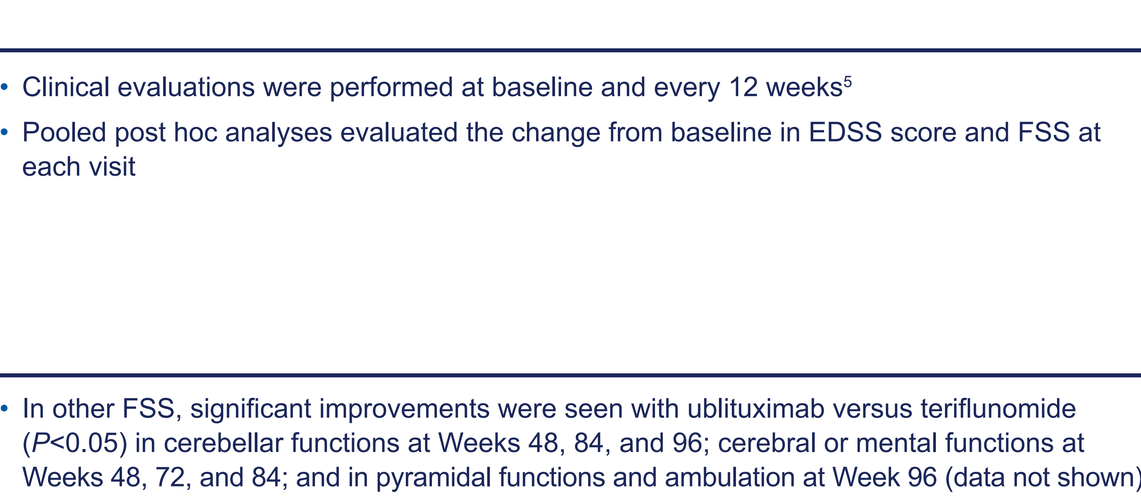
- Across all visits, significant improvements with ublituximab versus teriflunomide were seen in EDSS score, bowel and bladder functions, and sensory functions (**Figure 1**)
- By individual visits, significant improvements were seen with ublituximab versus teriflunomide (*P*<0.05) after 48 weeks of treatment in EDSS score (**Figure 2**) and sensory functions (**Figure 3**), and after 24 weeks of treatment in bowel and bladder functions (**Figure 4**)
- In other FSS, significant improvements were seen with ublituximab versus teriflunomide (*P*<0.05) in cerebellar functions at Weeks 48, 84, and 96; cerebral or mental functions at Weeks 48, 72, and 84; and in pyramidal functions and ambulation at Week 96 (data not shown)
- No significant differences were observed between treatment arms for brainstem functions and visual or optic functions

Figure 1. Proportional Odds for EDSS and FSS



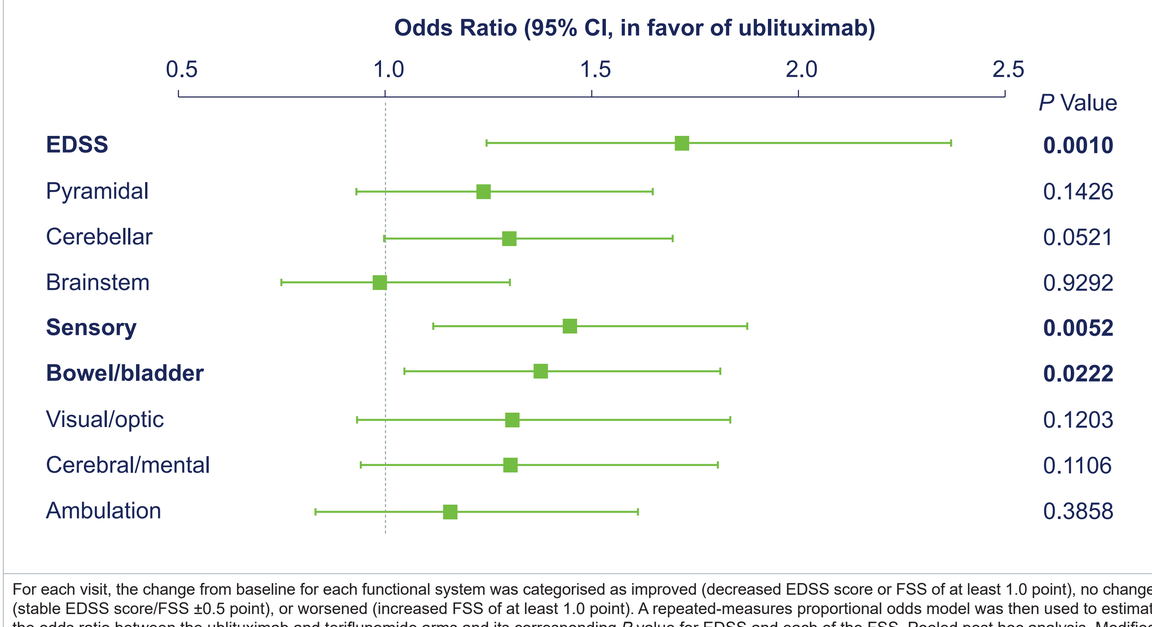
For each visit, the change from baseline for each functional system was categorised as improved (decreased EDSS score or FSS of at least 1.0 point), no change (stable EDSS score/FSS ±0.5 point), or worsened (increased FSS of at least 1.0 point). A repeated-measures proportional odds model was then used to estimate the odds ratio between the ublituximab and teriflunomide arms and its corresponding *P* value for EDSS and each of the FSS. Pooled post hoc analysis. Modified intention-to-treat population.
EDSS, Expanded Disability Status Scale; FSS, Functional Systems Scores.

Figure 2. Change From Baseline in EDSS Score



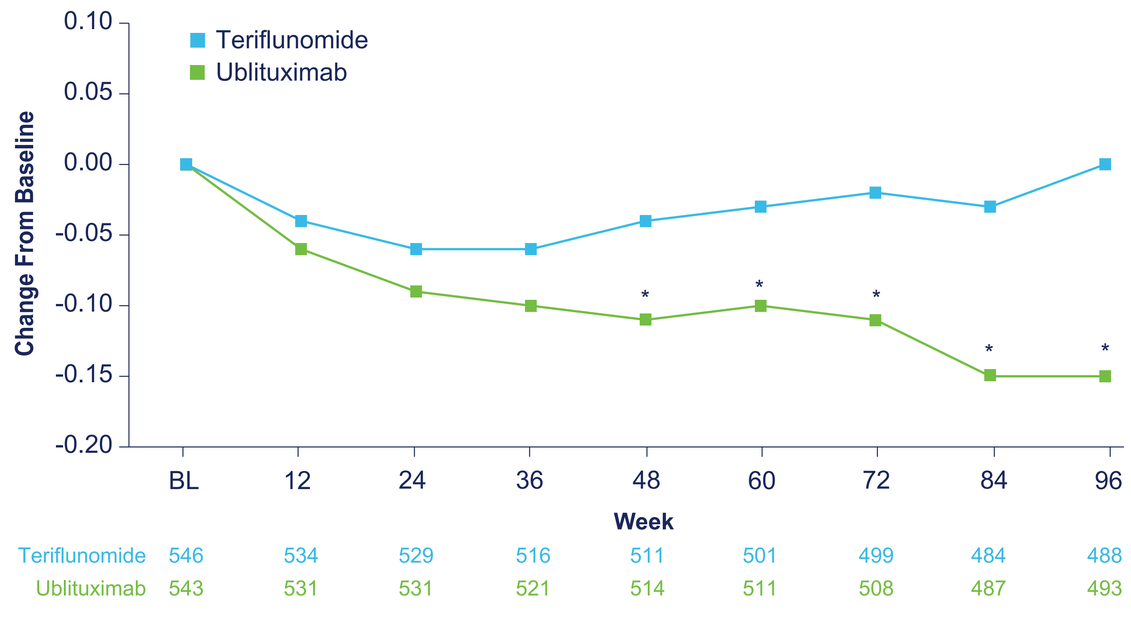
*P<0.05. Pooled post hoc analysis. Modified intention-to-treat population. *P* value based on *t* test.
BL, baseline; EDSS, Expanded Disability Status Scale.

Figure 3. Change From Baseline in FSS: Sensory Functions



*P<0.05. Pooled post hoc analysis. Modified intention-to-treat population. *P* value based on *t* test.
BL, baseline; FSS, Functional Systems Scores.

Figure 4. Change From Baseline in FSS: Bowel and Bladder Functions



*P<0.05. Pooled post hoc analysis. Modified intention-to-treat population. *P* value based on *t* test.
BL, baseline; FSS, Functional Systems Scores.

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