Study Design and Patient Demographics of the ULTIMATE Phase III Trials Evaluating Ublituximab (UTX), a Novel Glycoengineered Anti-CD20 Monoclonal Antibody (mAb), in Patients with Relapsing Multiple Sclerosis (RMS)

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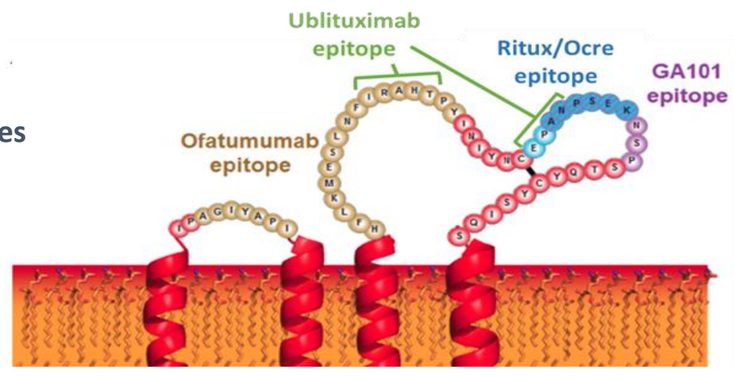
STUDY DESIGN & BACKGROUND

INTRODUCTION

- Ublituximab (UTX; TG-1101) is a novel chimeric monoclonal antibody (mAb) that targets a unique epitope on the CD20 antigen. Ublituximab is glycoengineered to enhance affinity for all variants of FcγRIIIa receptors, thereby demonstrating greater antibody-dependent cellular cytotoxicity (ADCC) activity than rituximab, ofatumumab, or ocrelizumab.
- In *in vitro* studies, ublituximab demonstrated 100 times greater natural killer (NK)-cell-mediated ADCC than rituximab in patient donor chronic lymphocytic leukemia (CLL) cells (Le Garff-Tavernier *et al*, 2011).
- To date, over 1500 patients with various B-cell mediated diseases have been treated with ublituximab, with completed relapsing multiple sclerosis (RMS) studies and oncology studies demonstrating robust activity with favorable safety and tolerability.
- In a Phase 2 study in RMS, ublituximab produced median >99% B-cell depletion by week 4 and complete elimination of gadolinium-enhancing (Gd+) lesions.
- Two parallel Phase 3 trials of identical design, ULTIMATE I (NCT03277261) and ULTIMATE II (NCT03277248), are being conducted to evaluate the efficacy and safety of a rapid one-hour 450mg infusion of ublituximab versus teriflunomide in patients with relapsing multiple sclerosis (RMS).

Binding Epitopes of Anti-CD20 Antibodies



Adapted from Klein et al, 2013

OBJECTIVE

- To present the study design and demographics of patients enrolled in the ULTIMATE I and II Phase 3 trials.

STUDY ENDPOINTS

PRIMARY ENDPOINT:

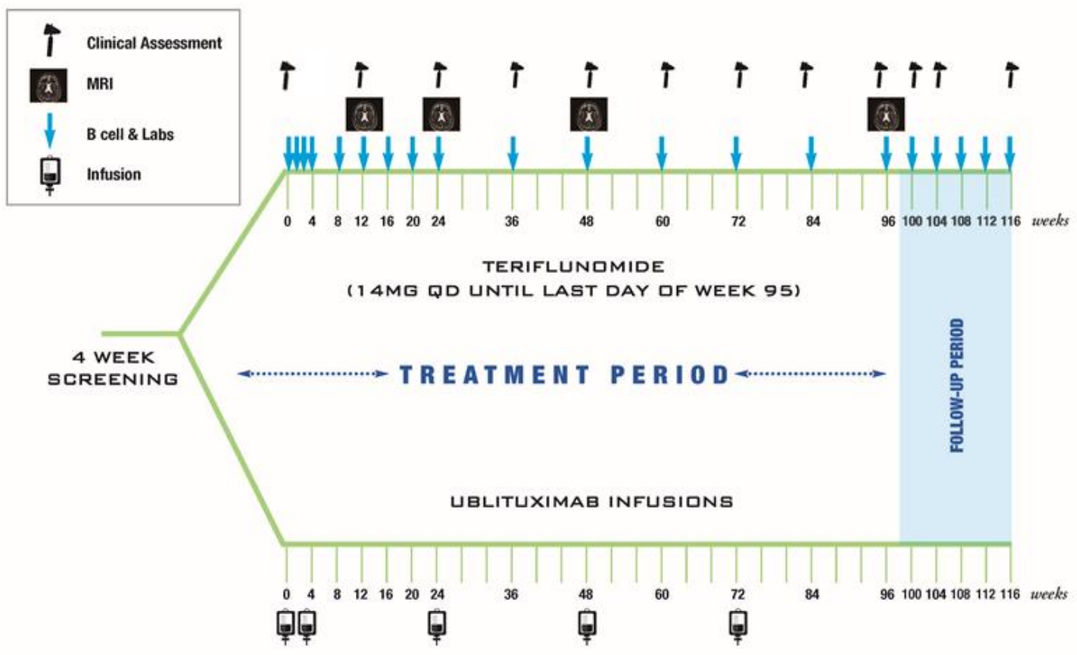
- Annualized Relapse Rate (ARR)

KEY SECONDARY ENDPOINTS:

- MRI parameters including number of Gd+ T1 lesions
- Percentage of subjects with no evidence of disease activity (NEDA)
- Percentage of subjects with three month confirmed disability worsening
- Percentage of subjects with a relapse
- Time to first confirmed relapse

METHODS

- ULTIMATE I & II are two identical Phase 3 randomized, multi-center, double-blinded, double dummy, active controlled trials, evaluating a one-hour 450mg infusion of ublituximab in RMS.



KEY ELIGIBILITY CRITERIA

KEY INCLUSION CRITERIA:

- Male or female patients aged 18–55 years (inclusive) at screening
- Diagnosis of MS according to the 2010 Revised McDonald criteria
- Relapsing MS: relapsing-remitting course, or secondary progressive course with disease activity
- Disability status at screening with an EDSS score of 0–5.5 (inclusive)
- Documentation of at least one relapse during the 1 year prior to screening or two relapses during the 2 years prior to screening or a positive Gd+ MRI scan during the year prior to randomization
- Neurologically stable within 1 month prior to randomization

KEY EXCLUSION CRITERIA:

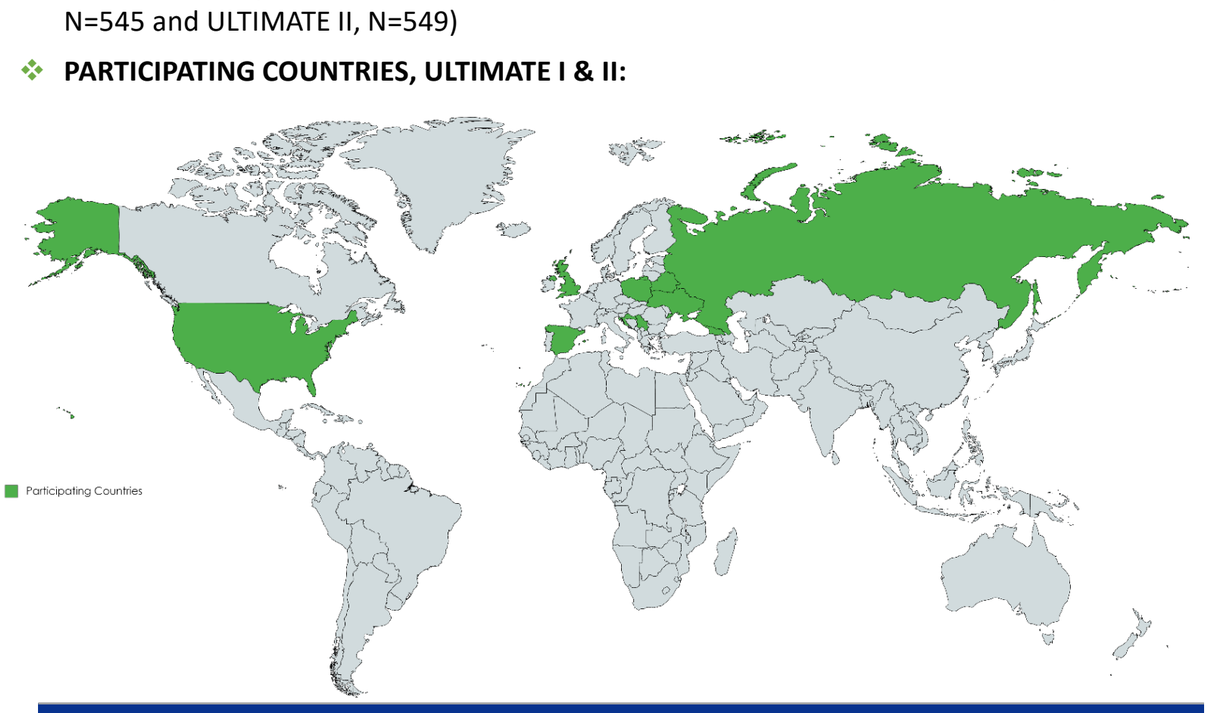
- Patients with primary progressive MS or SPMS without disease activity
- Patients with previous Anti-CD20 or other B cell directed treatment
- Patients with disease duration >10 years with an EDSS score of ≤2.0
- Patients with active chronic disease of the immune system other than MS or immunodeficiency syndrome
- Patients with neurological findings consistent or confirmed with progressive multifocal leukoencephalopathy

EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; MRI, magnetic resonance imaging; MS, multiple sclerosis; SPMS, secondary progressive MS

RESULTS

PATIENT DEMOGRAPHICS

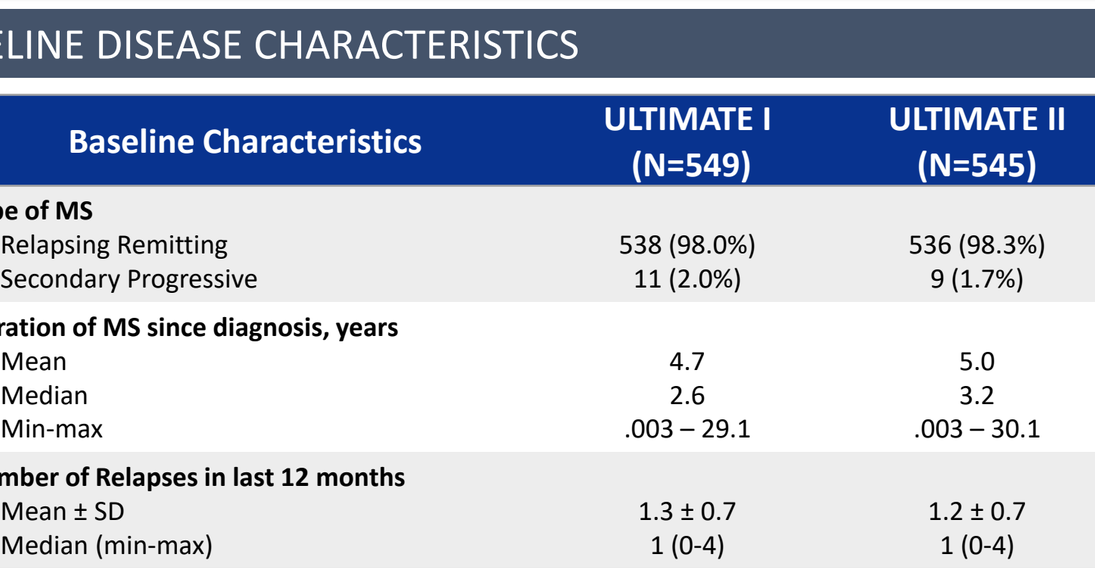
- A total of 1094 patients have been randomized across 106 sites in 10 countries (ULTIMATE I, N=545 and ULTIMATE II, N=549)
- **PARTICIPATING COUNTRIES, ULTIMATE I & II:**



Patient Characteristics	ULTIMATE I (N=549)	ULTIMATE II (N=545)
Age		
Median	36	35
Mean ± SD	36.7 ± 9.07	35.3 ± 8.9
Min/Max	18/55	18/55
Gender, %		
Female	63.3%	65.0%
Male	36.7%	35.0%
Race, %		
Caucasian	97.3%	98.7%
African American	2.2%	0.9%
Other	0.5%	0.4%

BASELINE DISEASE CHARACTERISTICS

Baseline Characteristics	ULTIMATE I (N=549)	ULTIMATE II (N=545)
Type of MS		
Relapsing Remitting	538 (98.0%)	536 (98.3%)
Secondary Progressive	11 (2.0%)	9 (1.7%)
Duration of MS since diagnosis, years		
Mean	4.7	5.0
Median	2.6	3.2
Min-max	.003 – 29.1	.003 – 30.1
Number of Relapses in last 12 months		
Mean ± SD	1.3 ± 0.7	1.2 ± 0.7
Median (min-max)	1 (0-4)	1 (0-4)
Number of Relapses in last 24 months		
Mean ± SD	1.9 ± 1.0	1.8 ± 0.9
Median (min-max)	2 (0-11)	2 (0-7)
Treatment naïve, %	59.2%	53.2%
EDSS at screening		
Mean ± SD	2.9 ± 1.2	2.9 ± 1.3
Median (min-max)	3 (0-5.5)	3 (0-5.5)



CONCLUSIONS

- **Patient recruitment for ULTIMATE I & ULTIMATE II was successfully completed in the second half 2018.**
- **Baseline characteristics of patients enrolled in ULTIMATE I & II are consistent with a typical RMS population.**
- **The ULTIMATE I & II trials are expected to elucidate the therapeutic potential of a one hour, 450mg infusion of ublituximab in patients with RMS. Topline results are expected in the second half of 2020.**

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