Study Design of a Phase 2 Ublituximab Dose-Confirmation Study in Children and Adolescents with Relapsing Multiple Sclerosis: ULTIMATE KIDS I

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OBJECTIVE

- The objective of this poster is to present the design of the Phase 2 ULTIMATE KIDS I study, which aims to confirm whether a reduced ublituximab dose in pediatric multiple sclerosis (MS) patients with body weight ≥25 kg to ≤40 kg achieves pharmacokinetic/pharmacodynamic exposure (primary) and safety outcomes (secondary) comparable to adults.

CONCLUSIONS

- The Phase 2 ULTIMATE KIDS I study has been designed to provide data on the pharmacokinetics and pharmacodynamics of ublituximab in pediatric MS participants weighing ≥25 to ≤40 kg.
- ULTIMATE KIDS I is intended to evaluate the bioequivalence of a 300 mg ublituximab maintenance dose based on established adult RMS data.
- Upon confirmation of the dosing regimen, pediatric MS participants weighing ≥25 to ≤40 kg will be enrolled in the Phase 3 ULTIMATE KIDS II study (NCT07220252).
- Patient recruitment will initially commence in the United States and Poland, with planned expansion to additional countries thereafter.
- ULTIMATE KIDS I (NCT07220252) enrollment will begin in Q1 2026.

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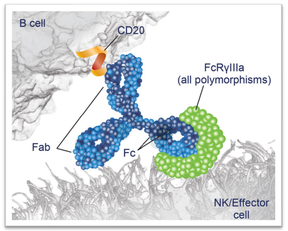
INTRODUCTION

- Ublituximab is approved for the treatment of relapsing forms of multiple sclerosis (RMS) in adults in both the USA and Europe.[2] Compared with other currently approved anti-CD20 therapies used in RMS, ublituximab demonstrates enhanced antibody-dependent cellular cytotoxicity (ADCC) and increased Fcγ-receptor (FcγR) binding (Figure 1).
- Pediatric MS is a highly active disease, characterized by frequent relapses and rapid accrual of MRI lesions occurring early in the disease course.[3]
- Despite numerous treatment options available for adult patients with MS, a high unmet need remains for safe and effective therapies in children and adolescents with MS.
- Modeling and simulation informed a 300 mg ublituximab maintenance dose selection for pediatric MS patients with body weight ≥25 kg to ≤40 kg (Figure 2).
- ULTIMATE KIDS I (NCT07220252) is a 24-week, Phase 2, open-label study designed to confirm a novel dosing regimen for pediatric MS patients with body weight ≥25 kg to ≤40 kg (Figure 3).

Figure 1. Ublituximab is a Novel, Type 1 IgG Chimeric Antibody Optimized for Efficient B-Cell Depletion



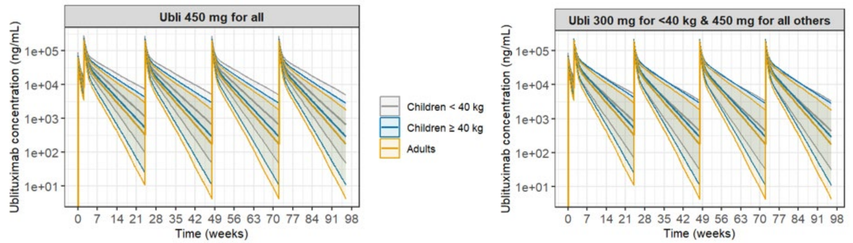
Ublituximab is glycoengineered, resulting in the exclusion of specific oligosaccharides in the Fc region. This allows for:

- Enhanced binding to receptors on NK or effectors cells
- Increased ADCC potential relative to non-glycoengineered antibodies

In vitro data demonstrated better binding to polymorphisms of FcγRIIIa relative to all other anti-CD20 antibodies available in MS.[4-7]

ADCC=antibody-dependent cellular cytolysis. ADCC is one of the presumed mechanisms of B-cell depletion.

Figure 2. Simulated Ublituximab PK Profiles Across Pediatric and Adult Weight Groups



Simulated PK profiles demonstrate overlapping ublituximab concentration ranges between children <40 kg receiving 300 mg and adults receiving 450 mg. Simulations are based on a population PK model derived from adult RMS clinical data (ULTIMATE I & II).

Ubli=ublituximab. Colored lines present the 5th, 50th and 95th percentile with shaded 90% prediction interval for children < 40 kg (grey), children ≥ 40 kg (blue) and adults (yellow).

METHODS

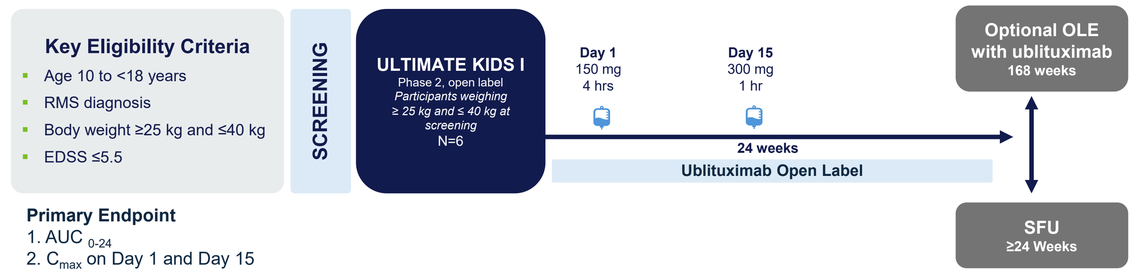
Table 1. Objectives and Endpoints

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To assess the pharmacokinetics of ublituximab in patients ages ≥10 to <18 years and body weight ≥25 kg to ≤40 kg with RMS	• Area under the curve (AUC_{0-24}) • Maximum Concentration (C_{max}) on Day 1 and Day 15
• To assess the pharmacodynamics of ublituximab in patients ages ≥10 to <18 years and body weight ≥25 kg to ≤40 kg with RMS	• Percentage of patients with CD19+ B-cell counts ≤10 cells/μL at Week 24
Secondary Objectives	**Secondary Endpoints**
• To assess the safety, tolerability, and efficacy of ublituximab in patients ages 10 to <18 years and body weight ≥25 kg to ≤40 kg with RMS	• Incidence and severity of adverse events (AEs) • Suicidal Ideation using Columbia-Suicide Severity Rating Scale (C-SSRS) • Percentage of participants with anti-drug antibodies (ADAs) to ublituximab • Number of gadolinium enhancing T1 lesions • Number of new and/or enlarging T2 hyperintense lesions • Annualized relapse rate (ARR)

Study Design

- ULTIMATE KIDS I is a 24-week, Phase 2, open-label study designed to confirm a 300 mg ublituximab dose for pediatric MS patients with body weight ≥25 kg to ≤40 kg.
- Approximately 6-12 participants will be enrolled.
- A total of 2 doses of ublituximab will be administered on Day 1 and Day 15. No dose is administered at Week 24. Participants will receive 150 mg ublituximab in a 4-hour infusion at the initial Week 1 Day 1 visit, followed by a 1-hour infusion of 300 mg ublituximab at Week 3 Day 15.
- Participants will receive premedication prior to each dose of ublituximab with an antihistamine (e.g., diphenhydramine 25-50 mg or equivalent), a corticosteroid (e.g., IV methylprednisolone 1 mg/kg or equivalent), and an antipyretic such as acetaminophen (e.g., 325–650 mg).
- The primary endpoint will evaluate PK and PD parameters (AUC_{0-24}, C_{max}, $CD19^+$ B-cell count).
- Participants completing the 24-week portion will be eligible to enter the 168-week Open-Label Extension (OLE) or will enter the Safety Follow-Up (SFU) study.

Figure 3. ULTIMATE KIDS I Study Schema



Primary Endpoint

1. AUC_{0-24}
2. C_{max} on Day 1 and Day 15
3. Percentage of patients with $CD19^+$ B-cell counts ≤10 cells/μL at Week 24

Study Population

- Enrollment will initially commence in the USA and Poland, expanding to additional countries thereafter.
- Key eligibility criteria are included in Table 2a/2b.

Table 2a. Key Inclusion Criteria

1. Age ≥ 10 years to <18 years (i.e., have not yet had their 18th birthday at randomization)
2. Diagnosis of RMS
3. Body weight ≥ 25 kg to ≤ 40 kg
4. Disease history:
   a. At least 1 relapse experienced in the previous 12 months ***OR***
   b. At least 2 relapses in the previous 24 months and ≥1 Gd+ lesion on T1-weighted brain MRI at any time within the previous 12 months ***OR***
   c. ≥1 new T2 lesions or Gd+ T1 lesions compared to prior MRI conducted within 12 months

Table 2b. Key Exclusion Criteria

1. Known presence or suspicion of other neurologic disorders that may mimic MS (e.g., NMOSD)
2. Treatment with anti-CD20 or other B-cell directed treatment (BTKi, BAFF inhibitors)
3. Chronic or ongoing active infectious disease requiring long-term systemic treatment such as, but not limited to: PML, chronic renal infection, chronic chest infection with bronchiectasis, TB, or active hepatitis B or C
4. Pregnant or nursing

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