Study Design of a Phase 3, Randomized, Double-Blind Study of Ublituximab Versus Fingolimod in Children and Adolescents with Relapsing Multiple Sclerosis: ULTIMATE KIDS II

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OBJECTIVE

- The objective of this poster is to present the design of the Phase 3 ULTIMATE KIDS II study, which aims to assess the efficacy and safety of ublituximab versus fingolimod in patients with pediatric MS (multiple sclerosis) aged 10 to <18 years.

CONCLUSIONS

- ULTIMATE KIDS II is a 96-week, Phase 3, randomized, double-blind, double-dummy study that will evaluate the safety and efficacy of ublituximab compared to fingolimod in pediatric MS.
- Patient recruitment will initially commence in the USA and Poland, expanding to additional countries thereafter.
- ULTIMATE KIDS II will initially include participants >40 kg, with participants weighing ≥25 kg and ≤40 kg to be added following confirmation of dosing from a parallel Phase 2 study (ULTIMATE KIDS I).
- The staged enrollment approach is designed to support safe and appropriate pediatric dose evaluation.
- Enrollment of ULTIMATE KIDS II (NCT07220252) will begin in Q1 2026.

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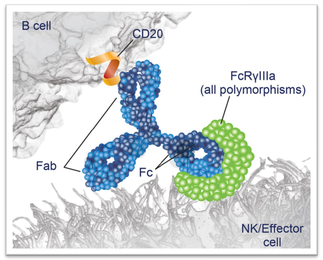
INTRODUCTION

- Ublituximab is approved for the treatment of relapsing forms of multiple sclerosis (RMS) in adults in both the United States[1] 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.
- Based on its demonstrated efficacy and safety in adult RMS, ublituximab has the potential to improve outcomes and may address an unmet need in pediatric MS patients. ULTIMATE KIDS II is a 96-week, Phase 3, double-blind, double-dummy study comparing ublituximab to fingolimod in pediatric MS (NCT07220252).

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]

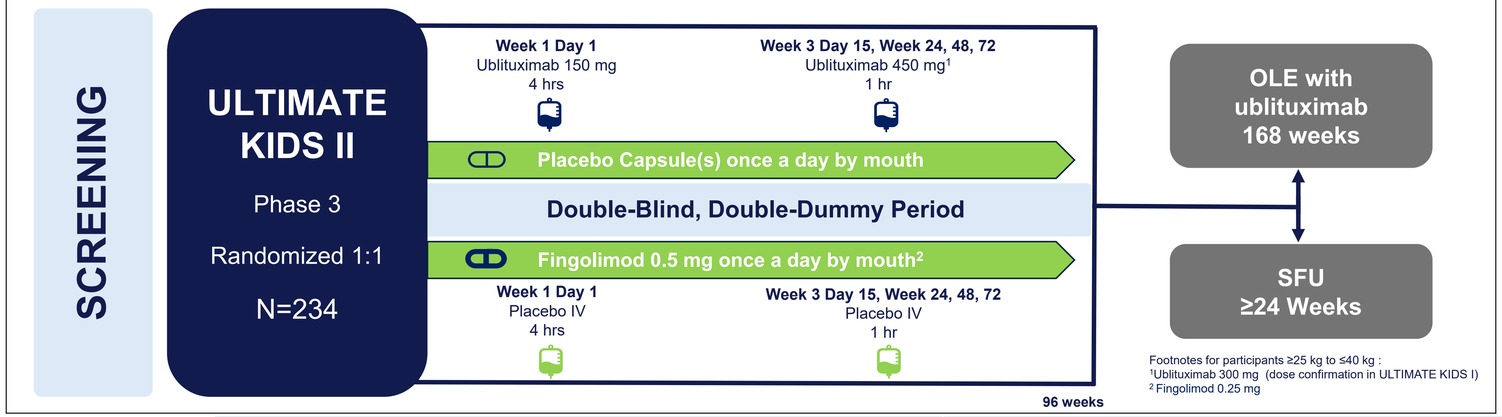
ADCC=antibody-dependent cellular cytolysis. ADCC is one of the presumed mechanisms of B-cell depletion.

METHODS

Study Design

- ULTIMATE KIDS II is a 96-week, Phase 3, randomized, double-blind, double-dummy study comparing ublituximab to fingolimod in pediatric MS.
- Approximately 240 participants will be enrolled to establish non-inferiority of annualized relapse rate (ARR) between the ublituximab and the fingolimod treatment group.
- Initial enrollment will only include participants weighing >40 kg. Participants weighing ≥25 kg to ≤40 kg will be added following confirmation of the dosing regimen from a parallel Phase 2 study (ULTIMATE KIDS I).
- Participants are randomized 1:1, stratified by region and body weight, to receive either:
  1. intravenous ublituximab plus oral placebo or
  2. oral fingolimod plus intravenous placebo
- Blinding procedures include dual assessors for relapse evaluation (treating and examining neurologist), independent first-dose monitor (supervision of first-dose administration), and an independent ophthalmologist.
- Participants who complete the 96-week double-blind portion may be eligible to enter the 168-week Open Label Extension (OLE) or will enter the Safety Follow-Up (SFU).

Figure 2. ULTIMATE KIDS II Study Schema



Study Population

- Enrollment will initially commence in the USA and Poland, expanding to additional countries thereafter.
- Key eligibility criteria are included in Table 1a/1b.

Table 1a. 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; Note: Participants weighing ≥25 kg and ≤40 kg at screening will initially be eligible for the Phase 2 ULTIMATE KIDS I study only. Once a dose is confirmed, new participants within this weight category will enroll into the Phase 3 ULTIMATE KIDS II study
4. Disease history:
   a) At least one relapse experienced in the 12 months or
   b) At least two 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-enhancing T1 lesions compared to prior MRI conducted within 12 months

Table 1b. Key Exclusion Criteria

1. Known presence or suspicion of other neurologic disorders that may mimic MS (e.g., NMOSD)
2. Prior treatments:
   - Treatment with anti-CD20 or other B-cell directed treatment (BTKi, BAFF inhibitors)
   - Treatment with fingolimod or other S1P1 modulators (siponimod, ozanimod, ponesimod)
3. Medication that may prolong QTc interval and who have relevant risk factors such as hypokalemia or congenital QT prolongation
4. Diagnosis of macular edema
5. Severe cardiac disease or significant findings on the screening ECG
6. 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
7. Pregnant or nursing

Table 2. Objectives and Endpoints

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To establish non-inferiority of ublituximab compared to fingolimod based on protocol-defined ARR in children with RMS between 10 and < 18 years old and body weight ≥ 25 kg	• ARR defined as the number of Independent Relapse Adjudication Panel (IRAP)-confirmed relapses per participant year (non-inferiority)
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 with RMS	• Incidence and severity of adverse events • CD19+ B-cell counts • Number of gadolinium-enhancing T1 lesions • Number of new and/or enlarging T2 hyperintense lesions • Time to Confirmed Disability Progression for at least 24 weeks • Time to Confirmed Disability Improvement for at least 24 weeks • Single Digit Modalities Test • Timed 25-Foot Walk • 9-Hole-Peg-Test • Pediatric Quality of Life Inventory

Independent Study Committees:

IRAP

- All protocol-defined relapses in the study will be adjudicated by the IRAP for the purpose of calculating the ARR

Data Safety Monitoring Board (DSMB)

- An independent DSMB will review data and advise the Sponsor throughout the study.

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