Study Design of a Phase 3 Trial Evaluating Teriflunomide in Children and Adolescents With Relapsing Multiple Sclerosis

Tanuja Chitnis¹, Brenda L Banwell², Douglas L Arnold³, Philippe Truffinet⁴, Deborah A Dukovic⁵, Michael A Panza⁶, Ludwig Kappos⁷

¹Massachusetts General Hospital for Children, Boston, MA, USA; ²Children’s Hospital of Philadelphia, Philadelphia, PA, USA; ³McGill University, Montreal Neurological Institute, Montreal, QC, Canada; ⁴Genzyme, a Sanofi company, Chilly-Mazarin, France; ⁵Sanofi, Bridgewater, NJ, USA; ⁶Genzyme, a Sanofi company, Cambridge, MA, USA; ⁷University Hospital Basel, Basel, Switzerland

INTRODUCTION

Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting MS.

In phase 3 clinical studies in adult patients, teriflunomide 14 mg showed consistent and significant clinical benefits compared with placebo. TEMSC (Teriflunomide Multiple Sclerosis Oral, NCT0134563): 31.5% reduction in annualized relapse rate (ARR; P<0.001) and 29.8% decrease in sustained disability progression (confirmed for 12 weeks; P<0.028).

TOWER (Teriflunomide Oral in people With relapsing multiple sclerosis, NCT00751881): 36.3% reduction in ARR (P<0.001) and 31.5% decrease in relapse rate (P<0.004).

Teriflunomide 7 mg also showed significant benefits on ARR, and although not significant, showed a reduction in risk of disability progression.

Both teriflunomide doses showed similar and manageable safety and tolerability profiles across the two studies.

Pediatric patients represent approximately 5% of MS cases, and many children with MS experience substantial cognitive impairment.

However, none of the currently approved treatments for adult relapsing MS have been formally evaluated in pediatric clinical trials and none are approved for pediatric use by the US Food and Drug Administration.

Teriflunomide is the active metabolite of leflunomide, approved for the treatment of rheumatoid arthritis since 1998.

Leflunomide has been evaluated in children with juvenile arthritis, and the safety profile was similar to that observed in adults.

Here we report the design of the TERIKIDS study, which will evaluate teriflunomide treatment in pediatric patients with relapsing MS.

OBJECTIVES

Primary Objective

To assess the effect of teriflunomide compared with placebo on time to first clinical relapse after randomization.

Key Secondary Objectives

To assess the effects of teriflunomide compared with placebo on brain magnetic resonance imaging (MRI) parameters and cognitive function.

To evaluate the safety and tolerability of teriflunomide compared with placebo.

To measure the pharmacokinetics (PK) of teriflunomide.

METHODS

Study Design

TERIKIDS is a 2-year, multicenter, multinational, randomized, double-blind, placebo-controlled, parallel-group, phase 3 study (Figure 1).

RESULTS

A total of 165 pediatric patients will be randomized (2:1) to once-daily oral teriflunomide or placebo for 96 weeks.

After an 8-week titration and adaptation process, the pediatric teriflunomide dose will correspond to the adult 14-mg dose.

Open-label period:

Patients will switch to open-label teriflunomide treatment in the event of a confirmed relapse following the 8-week titration phase, with high MRI activity or high ARR (19 new/enlarged T2 lesions at Week 36 or 35 new/enlarged T2 lesions at both Week 36 and Week 48).

Entry Criteria

Key study eligibility criteria are shown in Table 1. Assumptions

The primary and secondary efficacy endpoints are presented in Table 2.

Efficacy measures and PK parameters will be assessed during the double-blind treatment phase, as shown in Table 3.

PK parameters will also be assessed at the same time points in patients entering the open-label period.

Conclusions

The TERIKIDS study will provide data on the use of teriflunomide in children and adolescent patients with relapsing forms of MS.

CONCLUSIONS

REFERENCES


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