Treatment With Sebetralstat Reduces the Cumulative Symptom Severity of Hereditary Angioedema Attacks in a Phase 2 Trial

J. A. Bernstein,* M. A. Riedl,† W. L. Lumley,* P. K. Audhya,* M. D. Smith,* C. M. Year

*University of Cincinnati College of Medicine and Bernstein Clinical Research Center, LLC, Cincinnati, OH; University of California, San Diego, La Jolla, CA, US; **AAARFA Research Center, Dallas, TX, US; ***Takeda Pharmaceuticals, Shikoku, Hyogo, Japan; and ****Takeda Pharmaceuticals, Palo Alto, CA, US

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Introduction

• Hereditary angioedema (HAE) is a rare and potentially life-threatening genetic disease characterized by recurrent episodes of swelling. Attacks are painful and can have a significant adverse impact on patients’ quality of life.
• Treatment guidelines for HAE recommend that all patients have access to medical care on demand. HAE attacks are characterized by swelling of the upper or lower airways, gastrointestinal tract, and extremities, and can be life-threatening.
• There remains an unmet need for a safe and effective on-demand treatment option for HAE attacks to provide fast administration and potentially reduce the treatment burden.

Methods

Phase 2 Study Population and Design

• This 2-phase double-blind, placebo-controlled, crossover trial was conducted at 25 sites in Europe and the United States (ClinicalTrials.gov ID: NCT04208412), and included adults 18 years of age with HAE type I if they had experienced at least 3 or more HAE attacks in the past 30 days and did not have any HAE prophylaxis therapy.
• Following an open-label pharmacodynamic (PD) phase (Part 1), patients were randomized to receive 2 (for eligible HAE attacks) or 3 doses of either the study drug or placebo.
• Overall HAE attack severity was assessed as the Patient Global Impression of Severity (PGI-S) scale ranging from 0 (none) to 100 (very severe) and symptom relief was assessed using Patient Global Impression of Change (PGI-C) scale ranging from 1 (very much worse) to 7 (very much better).

Results

• The mean change in cumulative symptom severity (composite VAS) from baseline through 12 hours after administration of study drug is presented in Figure 1.
• Following sebetralstat administration, PGI-S and PGI-C mean scores showed greater reduction from baseline compared with placebo; larger negative scores indicate greater reduction in attack severity and symptom severity from baseline.
• The mean change in cumulative VAS scores was observed by 9.5 hours after treatment with sebetralstat, but not placebo improvement.
• This analysis demonstrated that treatment with oral sebetralstat significantly decreased cumulative attack and symptom severity and increased cumulative symptom relief of HAE attacks relative to placebo over 12 and 24 hours following administration.

Conclusions

This analysis demonstrated that treatment with oral sebetralstat significantly decreased cumulative attack and symptom severity and increased cumulative symptom relief of HAE attacks relative to placebo over 12 and 24 hours following administration.

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References