Oral Berotralstat Reduces Hereditary Angioedema Attack Rates in Pediatric Patients Aged 2 to <12 Years Without Long-Term Prophylaxis During the 12-Week Standard of Care Period: Interim Data from the APeX-P Study

Poster 28

Jolanta Bernatoniene,[1] Mélisande Bourgoin-Heck,[2,3] Mauro Cancian,[4] William H. Yang,[5] Shira Benor,[6] Anne Pagnier,[7] Marcin Stobiecki,[8] Stéphane Gayet,[9] Tamar Kinaciyan,[10] Elsa Phillips-Angles,[11] Noémi-Anna Bara,[12] Michael DeSpirito,[13] Daniel Petroni,[13] Daniel Long,[13] Tam Khuu,[13] Emel Aygören-Pürsün[14]

[1]Paediatric Immunology & Infectious Disease Department, Bristol Royal Hospital for Children, Bristol, United Kingdom; [2]Service d'Allergologie Pédiatrique, Hôpital d'Enfants Armand-Trousseau, AP-HP Sorbonne-University, Paris, France; [3]CRÉAK Hôpital Saint Antoine, AP-HP Sorbonne-University, Paris, France; [4]Department of Systems Medicine, University Hospital of Padua, Padua, Italy; [5]Ottawa Allergy Research Corporation and Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada; [6]Allergy and Clinical Immunology, Tel-Aviv Sourasky Medical Center and Tel-Aviv University, Tel-Aviv, Israel; [7]Department of Pediatrics, Centre Hospitalier Universitaire de Grenoble, Grenoble, France; [8]Department of Clinical and Environmental Allergology, Jagiellonian University Medical College, Kraków, Poland; [9]Internal Medicine Department, La Timone University Hospital, Assistance Publique-Hôpitaux de Marseille, Marseille, France; [10]Department of Dermatology, Medical University of Vienna, Vienna, Austria; [11]Department of Allergy, Hospital Universitario La Paz, IdiPaz, Madrid, Spain; [12]Centrul Clinic Mediquest/Centrul de Expertiza de Angioedem Ereditar, Sângeorgiu de Mureș, Romania; [13]BioCryst Pharmaceuticals, Inc., Durham, NC, USA; [14]Department for Children and Adolescents, Goethe University, Frankfurt, Germany

INTRODUCTION

- Hereditary angioedema (HAE) symptoms typically begin in childhood.[1]
  - Earlier HAE symptom onset in childhood correlates with greater disease severity and negative life impact.[1]
- Most currently approved long-term prophylaxis (LTP) treatments require parenteral administration.[2]
- Berotralstat is an oral, small-molecule, plasma kallikrein inhibitor currently approved in the United States for prophylaxis of HAE attacks in patients aged ≥2 years.[3]
- APeX-P is an ongoing open-label study evaluating the pharmacokinetics, safety, and efficacy of oral berotralstat as LTP in patients with HAE aged 2 to <12 years.[4]
- Here we report safety and efficacy of berotralstat in patients who did not utilize LTP during the 12-week standard of care (SOC) period.

METHODS

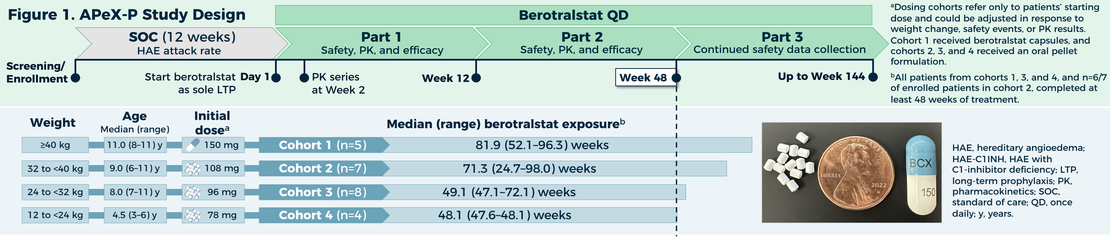
APeX-P Study

- Of the 29 patients in the total population, 24 patients did not receive LTP during the 12-week SOC and were included in this analysis.
- HAE attack rates were assessed over 48 weeks with safety monitoring continuing for up to 144 weeks (**Figure 1**).

Inclusion:
- HAE-C1INH diagnosis
- Age 2 to <12 years; body weight ≥12 kg
- Patient would benefit from oral LTP in the opinion of the investigator

Exclusion:
- Any clinically significant medical condition or medical history that would interfere with patient safety or study participation

Figure 1. APeX-P Study Design



[a]Dosing cohorts refer only to patients' starting dose and could be adjusted in response to weight change, safety events, or PK results. Cohort 1 received berotralstat capsules, and cohorts 2, 3, and 4 received an oral pellet formulation.

[b]All patients from cohorts 1, 3, and 4, and n=6/7 of enrolled patients in cohort 2, completed at least 48 weeks of treatment.

HAE, hereditary angioedema; HAE-C1INH, HAE with C1-inhibitor deficiency; LTP, long-term prophylaxis; PK, pharmacokinetics; SOC, standard of care; QD, once daily; y, years.

RESULTS

Baseline Characteristics

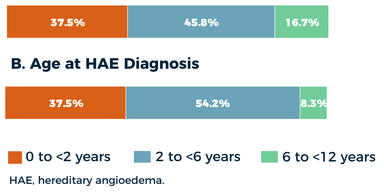
- Patients (n=24) had a median (range) age of 8.5 (3–11) years and 50.0% were female (**Table 1**).
- Most (83.3%) had HAE symptom onset before the age of 6 years (**Figure 2A**).
- Median (range) age at HAE diagnosis was 2.0 (0–10) years, with 91.7% of patients being diagnosed before the age of 6 years (**Figure 2B**).

Table 1. Patient Demographics

	Total (N=24)
Age at consent/assent	
Mean (SD)	8.3 (2.3)
Median (range)	8.5 (3–11)
Race,[a] n (%)	
White	19 (79.2)
Unknown	5 (20.8)
Ethnicity,[a] n (%)	
Hispanic or Latino	0
Not Hispanic or Latino	22 (91.7)
Not reported	2 (8.3)
Sex at birth, n (%)	
Male	12 (50.0)
Female	12 (50.0)

SD, standard deviation.
[a]Sites in France reported "Unknown" for race and "Not reported" for ethnicity because of local regulations.

Figure 2. Disease Onset and Diagnosis

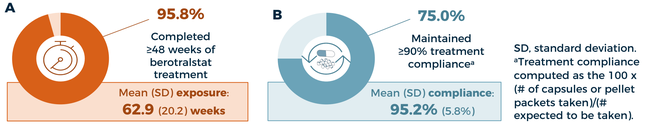


HAE, hereditary angioedema.

Berotralstat Treatment

- This analysis encompasses 24 patients, of whom 23 (95.8%) completed at least 48 weeks of berotralstat treatment (**Figure 3A**).
  - High treatment compliance was maintained across the study to date (**Figure 3B**).

Figure 3. Berotralstat Exposure (A) and Treatment Compliance (B)



SD, standard deviation.
[a]Treatment compliance computed as the 100 x (# of capsules or pellet packets taken)/(# expected to be taken).

Safety

- The most commonly reported treatment-emergent adverse events (TEAEs) were nasopharyngitis, upper respiratory tract infection, and vomiting (**Table 2**).
- No drug-related Grade 3/4 or serious TEAEs, deaths, or discontinuations related to TEAEs occurred.

Table 2. Summary of Safety Data[a]

	Total (N=24)
TEAEs, n (%)[b]	**21 (87.5)**
Nasopharyngitis	9 (37.5)
Upper respiratory tract infection	6 (25.0)
Vomiting	4 (16.7)
Headache	3 (12.5)
Cough	3 (12.5)
Viral upper respiratory tract infection	3 (12.5)
Drug-related TEAEs, n (%)	**4 (16.7)**
TESAEs[c], n (%)	**2 (8.3)**
Drug-related TESAEs, n (%)	**0 (0.0)**

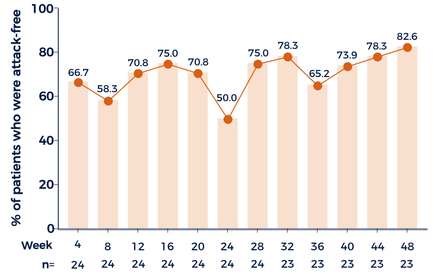
TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event. [a]Safety data include the entire duration of berotralstat exposure as of the data cut on March 24, 2025. [b]TEAEs that occurred in ≥3 patients are listed. [c]TESAEs unrelated to treatment were acute hepatitis, and a skateboarding accident with fractured elbow.

Berotralstat Efficacy

- At least 50% of patients were free from attacks each month through 48 weeks (**Figure 4A**).

Figure 4. HAE Attack Frequency

A. Attack-free Patients



- Median (range) HAE monthly attack rate decreased from 0.93 (0–5.0) during the SOC period to 0.33 (0–2.0) from Week 1 to Week 12 (Part 1) and 0.34 (0–1.8) from Week 1 to Week 48 (Part 1 and Part 2). Adjusted attack rates by month are shown in **Figure 4B**.

B. Monthly Adjusted Attack Rate

HAE, hereditary angioedema; SEM, standard error of the mean; SOC, standard of care. [a]The adjusted attack rate was calculated as the number of adjusted attacks observed during a given period and standardized to number of attacks per month, where 1 month is defined as a 28-day (4 week) period. The baseline-adjusted attack rate was calculated using adjusted attacks during the SOC period.

CONCLUSIONS

1. The ongoing APeX-P study is the largest trial of LTP in patients with HAE aged 2 to <12 years to date.
2. In the subpopulation of patients in APeX-P who did not receive LTP in the SOC period, oral berotralstat was well tolerated and led to early and sustained reductions in monthly attack rates.
3. At least 50% of patients were attack-free each month through 48 weeks and the median monthly attack rate dropped to 0.34 over 48 weeks of treatment.
4. Similar to the overall APeX-P population, results from this subpopulation analysis continue to support a favorable benefit-risk profile for berotralstat LTP of HAE in a pediatric population.

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