

Oral Berotralstat Reduces the Rate of Moderate and Severe Attacks and Percentage of Days with HAE Symptoms Over 48 Weeks in Children Aged 2 to Less Than 12 Years: Interim Data from APeX-P

Jolanta Bernatoniene,¹ Mélisande Bourgoïn-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 Douglas T. Johnston,¹³ Daniel Long,¹³ Daniel Petroni,¹³ Emel Aygören-Pürsün¹⁴

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

#114



INTRODUCTION

- Symptoms of hereditary angioedema (HAE) often present in childhood, and earlier symptom onset has been associated with negative impacts on daily life and more severe disease course.^{1,2}
- Most currently approved long-term prophylaxis (LTP) treatments require parenteral administration.³
- 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.⁴
- Here, we present interim results from the ongoing open-label APeX-P clinical trial (NCT05453968; EU CTN 2024-511257-22-00), the largest LTP study of pediatric patients with HAE aged 2 to <12 years.

METHODS

- In this interim analysis, HAE attack rates were assessed over 48 weeks, with safety monitoring continuing for up to 144 weeks (**Figure 1**).
- Before berotralstat initiation, patients received standard of care (SOC) for 12 weeks. This could include LTP, on-demand treatment, or both.⁵



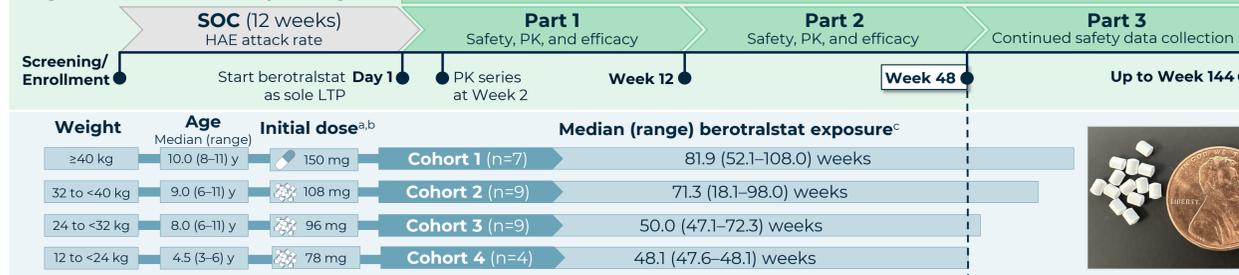
Inclusion:

- 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



^aDosing cohorts refer only to patients' starting dose and could be adjusted in response to weight change, safety events, or PK results. ^bCohort 1 received berotralstat capsules, and Cohorts 2, 3, and 4 received an oral pellet formulation. ^cAll patients from Cohorts 1, 3, and 4, and n=7 of 9 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

- The APeX-P study enrolled 29 patients with a median (range) age of 8.0 (3–11) years (**Table 1**).
 - Over half (51.7%) were male, and 37.9% had a history of prior prophylactic treatment for HAE including lanadelumab, tranexamic acid, and C1-esterase inhibitors.

- Most (93.1%) patients reported ≥1 day of missed education in the year prior to enrollment (**Figure 3**).
 - Patients reported a mean (standard deviation [SD]) of 18.0 (20.5) days of missed education due to angioedema symptoms during this timeframe.

- The mean and median monthly HAE attack rates decreased early and were sustained through 48 weeks of berotralstat treatment (**Figure 5**).

- The most common 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; no patients discontinued due to adverse events.

Table 1. Baseline Characteristics

Characteristic	Total (N=29)
Age at screening, years	
Mean (SD)	8.3 (2.1)
Median (range)	8.0 (3–11)
Race, n (%)	
White	22 (75.9)
Unknown ^a	7 (24.1)
Sex assigned at birth, n (%)	
Male	15 (51.7)
Female	14 (48.3)
Prior LTP exposure, n (%)	11 (37.9%)

LTP, long-term prophylaxis. SD, standard deviation. ^aSites in France reported "Unknown" for race due to local regulations.

Figure 3. Missed Days of Education



- Patients reported a smaller percentage of days with angioedema symptoms during berotralstat treatment (mean: 4%; SD, 3.6%) compared with the SOC period (mean: 11%; SD, 9.4%), which was sustained for 48 weeks (**Figure 4**).

Figure 4. Percentage of Days with Angioedema Symptoms

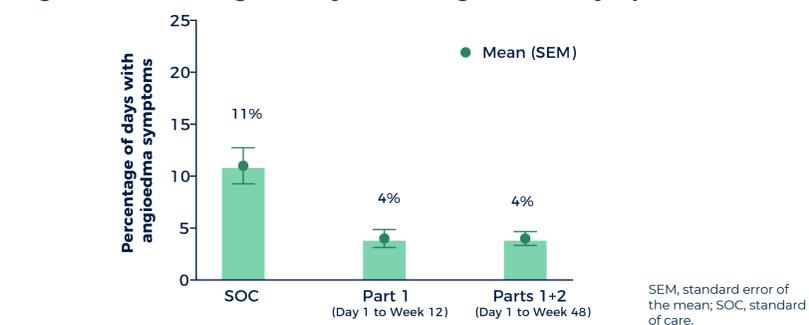
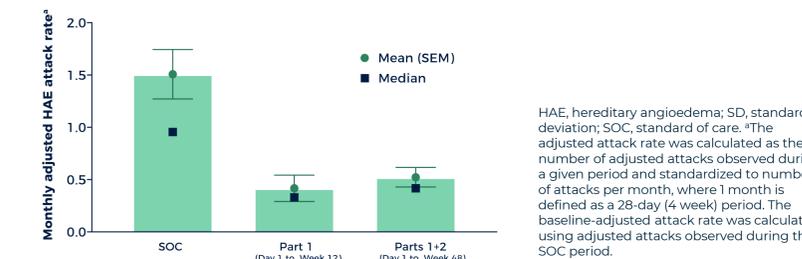


Figure 5. Monthly Adjusted HAE Attack Rate by Part



- Of the HAE attack rates reported during the SOC period, a median of 0.33 attacks per month were moderate and 0.31 attacks per month were severe (**Figure 6**).
- Over 48 weeks of berotralstat treatment, the median HAE attack rates for moderate and severe attacks decreased to 0.16 attacks per month and 0.0 attacks per month, respectively (**Figure 6**).

Figure 6. Adjusted HAE Attack Rate by Symptom Severity^a

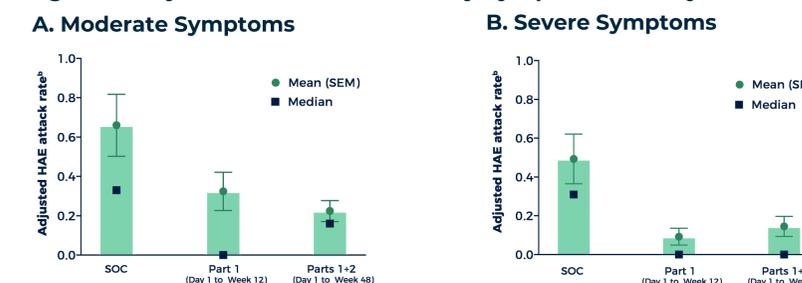


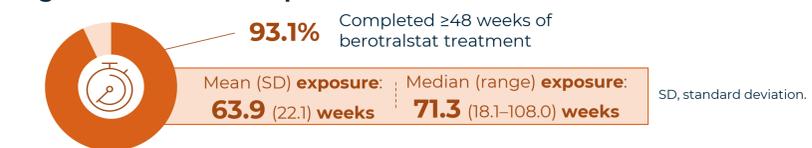
Table 2. Summary of Safety Data^a

TEAEs, n (%) ^b	Total (N=29)
Nasopharyngitis	10 (34.5)
Upper respiratory tract infection	8 (27.6)
Vomiting	5 (17.2)
Headache	4 (13.8)
Cough	3 (10.3)
Gastroenteritis	3 (10.3)
Viral upper respiratory tract infection	3 (10.3)
Drug-related TEAEs, n (%)	4 (13.8)
TESAEs^c, n (%)	3 (10.3)
Drug-related TESAEs, n (%)	0 (0.0)

TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event. ^aSafety data include the entire duration of berotralstat exposure as of the data cut on March 24, 2025. ^bTEAEs that occurred in ≥3 patients are listed. ^cTESAEs unrelated to treatment were acute hepatitis, skateboarding accident with fractured elbow, and worsening hemiparesis.

- Median (range) age at angioedema symptom onset was 2.0 (0.3–8.0) years.
 - Most (82.8%) had onset of angioedema symptoms before the age of 6 years.
- This updated analysis encompasses all 29 enrolled patients, of whom 27 (93.1%) completed at least 48 weeks of berotralstat treatment (**Figure 2**).

Figure 2. Treatment Exposure



ACKNOWLEDGMENTS & FUNDING

The authors would like to extend gratitude to the patients and site staff who were involved in the APeX-P study. Special thanks to Maria Pedrosa MD, PhD, Aimee Liu, MD, PhD, and Heather Iocca, PhD (BioCryst Pharmaceuticals, Inc.). Medical writing and editorial support were provided by Candice Dcosta, MSc, of Porterhouse Medical US. This study and medical writing support was funded by BioCryst Pharmaceuticals, Inc.

REFERENCES

1. Pagnier et al. *Pediatr Allergy Immunol*. 2024;35(12):e14268. 2. Christiansen et al. *Clin Pediatr (Phila)*. 2016;55(10):935–942. 3. Maurer et al. *Allergy*. 2022;77(7):1961–1990. 4. BioCryst Pharmaceuticals, Inc. ORLADEYO (berotralstat) capsules, for oral use – prescribing information; 2025. 5. Bernatoniene et al. *Ann Allergy Asthma Immunol*. 2025;135(6):681–688.e3.

CONCLUSIONS

- Berotralstat was well tolerated and demonstrated early and sustained reductions in overall monthly HAE attack rates regardless of attack severity.
- Berotralstat treatment reduced the percentage of days with angioedema symptoms, reflecting sustained symptom control over 48 weeks.
- These findings suggest that berotralstat may help the management of HAE in children, regardless of symptom severity.
- The updated data from APeX-P continue to support a favorable benefit-risk profile for berotralstat LTP of HAE in a pediatric population.