

# Impact of Berotralstat on Hereditary Angioedema Attack Rates in Patients with C1-Inhibitor Deficiency: Real-World Evidence Stratified by Prior Long-Term Prophylaxis

Raffi Tachdjian,<sup>1</sup> Mark Davis-Lorton,<sup>2</sup> Tracy Yee,<sup>3</sup> Sean D. MacKnight,<sup>4</sup> François Laliberté,<sup>4</sup> Robert C. Schell,<sup>5</sup> Sandra Nestler-Parr,<sup>3</sup> Patrick Gillard,<sup>3</sup> William R. Lumry<sup>6</sup>

<sup>1</sup>Department of Pediatrics, University of California Los Angeles, Los Angeles, CA, USA; <sup>2</sup>ENT and Allergy Associates, Tarrytown, NY, USA; <sup>3</sup>BioCryst Pharmaceuticals, Inc., Durham, NC, USA; <sup>4</sup>Groupe d'analyse SRI, Montreal, QC, Canada; <sup>5</sup>Analysis Group, Inc., Menlo Park, CA, USA; <sup>6</sup>Allergy and Asthma Research Associates, Dallas, TX, USA



## BACKGROUND AND OBJECTIVES

- Hereditary angioedema (HAE), a rare genetic disease, is characterized by painful, recurrent, and potentially life-threatening swelling attacks of the skin and mucous membranes.<sup>1</sup>
- Berotralstat is a targeted, once-daily, oral long-term prophylaxis (LTP) medication for the prevention of HAE attacks in adults and pediatric patients 2 years and older.<sup>2,3</sup>
- A prior study among patients with past LTP experience reported sustained low mean HAE attack rates after berotralstat initiation.<sup>4</sup>
- This study compared HAE attack rates before and after berotralstat initiation among patients with C1-inhibitor deficiency (C1-INH), stratified by prior LTP experience (i.e., naïve/experienced).

## METHODS

- This retrospective study used Specialty Pharmacy data (December 15, 2020 – January 8, 2024) from Optime Care, Inc., the sole dispenser of berotralstat in the United States.
- The follow-up period extended from the index date (the first berotralstat dispensing) to the last berotralstat dispensing date during the study period; no patient assessment data were collected after the final berotralstat dispensing.

## Study Outcomes

- Patients aged 12 years and older were categorized as LTP naïve or LTP experienced according to whether they self-reported using another LTP before initiating berotralstat.
- Patient self-assessments of HAE attacks were collected from the onboarding assessment at berotralstat initiation (based on prior 90 days) and from questionnaires administered at each berotralstat refill.
- Mean and median monthly HAE attack rates were evaluated in the 90-day baseline period and in each 90-day follow-up interval.
  - The maximum rate of HAE attacks that patients could experience was assumed to be 1 attack per 2 days.
  - Baseline HAE attack rates were calculated based on the 90-day attack rate (divided by three to yield a 30-day attack rate) from the onboarding assessment. The 30-day baseline attack rate was used if the 90-day baseline attack rate was missing.
  - In follow-up, the number of reported HAE attacks was the numerator, and the denominator was the minimum of (a) the time from the previous berotralstat shipment date, or (b) 30 days.

## Statistical Analysis

- Mean monthly rates of HAE attacks at baseline and in the follow-up period (segmented into fixed 90-day intervals) were compared using mean differences, 95% confidence intervals (CIs), and p-values from generalized estimating equations (GEE) linear regression models with robust standard errors.
- The reasons for sample size decrease from one 90-day follow-up interval to the next were reported using frequencies and proportions.
  - Reasons for sample size decrease included berotralstat discontinuation (i.e., a gap in days' supply of ≥60 days); end of study (i.e., patients reaching the end of the study period, Jan. 8, 2024, without evidence of discontinuation); no HAE attack report associated with dispensing; and discontinuation then re-initiation.

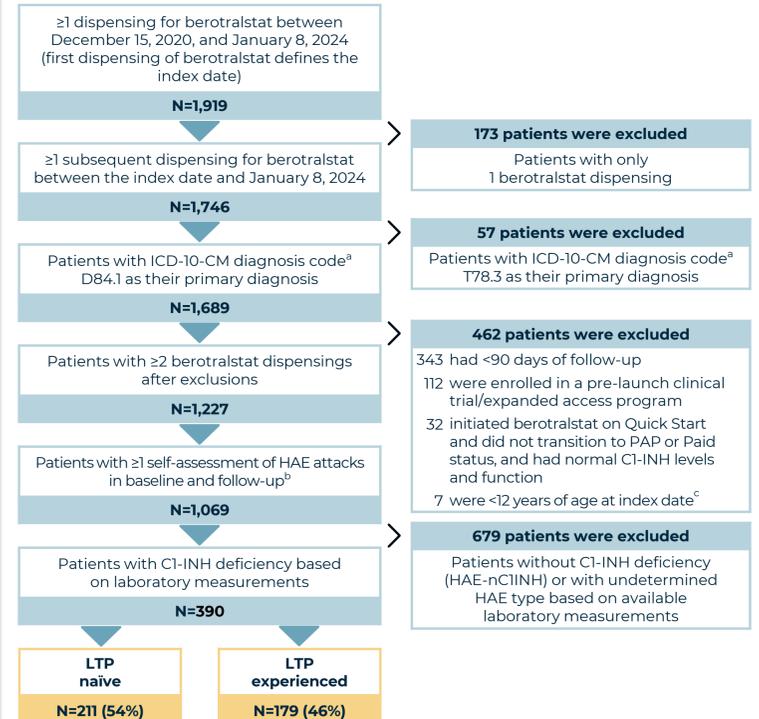
## REFERENCES

1. Betschel S, et al. *Allergy, Asthma, & Clin Immunol.* 2019;15(1):1-29. 2. Berotralstat [package insert]. Durham, NC: December 2025. 3. Powell J, et al. *Ann Pharmacotherapy.* 2022;56(4):488-493. 4. Riedl M, et al. *Ann Allergy, Asthma Immunol.* 2024; 132(4):505-511.e1.

## RESULTS

- The study population consisted of 390 berotralstat initiators with HAE-C1INH, including 211 LTP naïve patients and 179 LTP experienced patients who met the inclusion criteria (Figure 1).
- LTP naïve and experienced patients had a mean age of 36.2 and 43.1 years, respectively, both groups were predominantly female (67.8% and 59.8%), and most patients in each group were treated by an allergist/immunologist (93.8% and 95.0%) (Table 1).
- Among LTP naïve patients, mean HAE attack rates declined from 2.74–2.90 attacks/month during baseline to 0.63–0.82 attacks/month across 90-day follow-up intervals (Figure 2).
- Among LTP experienced patients, mean HAE attack rates declined from 1.71–2.32 attacks/month during baseline to 0.58–0.80 attacks/month across 90-day follow-up intervals (Figure 3).
- HAE attack rate reductions were statistically significant in every 90-day follow-up interval compared to the baseline period for LTP naïve and experienced patients (Figure 4).
- At 12 and 18 months, mean monthly attack rate reductions (95% CI) were 1.97 (1.54, 2.39) and 2.19 (1.67, 2.72), respectively, for LTP naïve patients and 1.32 (0.70, 1.94) and 1.59 (0.85, 2.33) for LTP experienced patients (all p<0.001) (Figure 4).

Figure 1. Eligibility Criteria and Patient Disposition



C1-INH, C1 esterase inhibitor; HAE, hereditary angioedema; ICD-10-CM, *International Classification of Diseases, 10th Revision, Clinical Modification*; LTP, long-term prophylaxis; PAP, patient assistance program. \*All patients in the data had either D84.1 (defects in the complement system) or T78.3 (angioneurotic edema) as their primary diagnosis; however, only patients with D84.1 as their primary diagnosis were included in the sample. †158 patients were excluded with no self assessment of HAE attacks in baseline or follow-up. ‡Berotralstat was only approved for patients aged 12 and older during the study period.

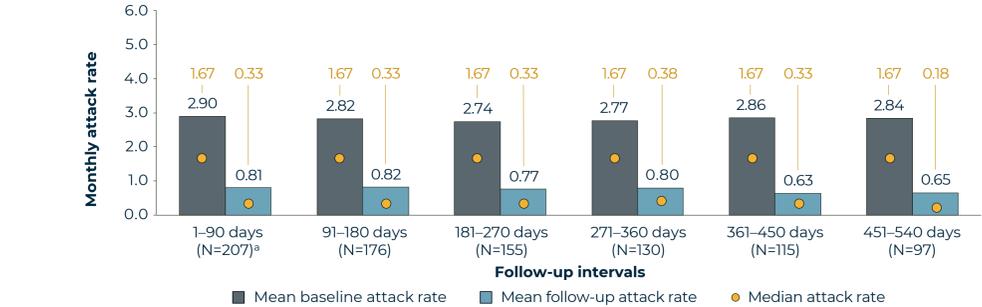
Table 1. Demographics and Clinical Characteristics

Characteristics	LTP Naïve (N=211)	LTP Experienced (N=179)
<b>Follow-up period, mean ± SD [median], days</b>	557 ± 309 [530]	482 ± 327 [376]
<b>Demographics</b>		
Age, mean ± SD [median], years	36.2 ± 18.5 [32]	43.1 ± 19.0 [41]
Female, n (%)	143 (67.8)	107 (59.8)
Patient weight, mean ± SD [median], kg	79 ± 23 [77]	85 ± 23 [82]
<b>Healthcare practitioner specialty, n (%)</b>		
Allergy/Immunology	198 (93.8)	170 (95.0)
Nurse practitioner	5 (2.4)	5 (2.8)
Other	8 (3.8)	4 (2.2)

LTP, long-term prophylaxis; SD, standard deviation.

Region, n(%)	LTP naïve	LTP experienced
South	100 (47.4)	82 (45.8)
Midwest	50 (23.7)	41 (22.9)
West	28 (13.3)	37 (20.7)
Northeast	32 (15.2)	18 (10.1)
Unknown	1 (0.5)	1 (0.6)

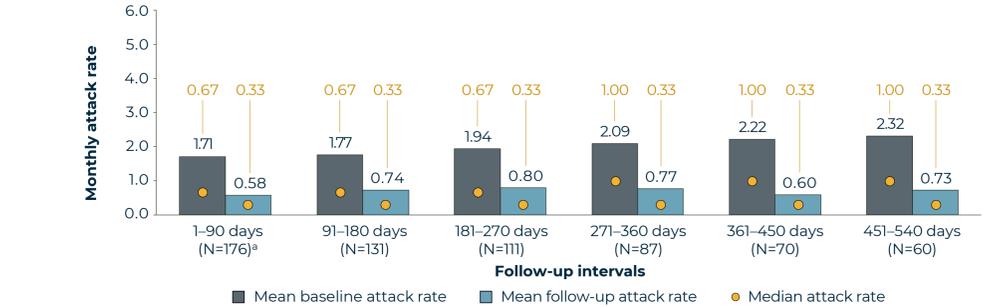
Figure 2. Monthly HAE Attack Rates (Mean and Median) Before and After Berotralstat Initiation Among Patients who were LTP Naïve



Reasons for sample size decrease in the next interval, n (%) <sup>a,b</sup>	1-90 days (N=207)	91-180 days (N=176)	181-270 days (N=155)	271-360 days (N=130)	361-450 days (N=115)	451-540 days (N=97)
Discontinuation	10 (4.8)	4 (2.3)	6 (3.9)	4 (3.1)	6 (5.2)	—
End of study	20 (9.7)	14 (8.0)	19 (12.3)	11 (8.5)	8 (7.0)	—

HAE, hereditary angioedema; LTP, long-term prophylaxis. \*The sample size for the 1-90 day interval (N=207) was smaller than the eligible study population (N=211) as 4 patients had ≥1 self-assessment of HAE attacks during follow-up but none during the first interval. †Other reasons for sample size decrease were no HAE attack report associated with dispensing in interval (0.0%–2.6%) and discontinuation and later re-initiation (0.0%–1.1%).

Figure 3. Monthly HAE Attack Rates (Mean and Median) Before and After Berotralstat Initiation Among Patients who were LTP Experienced



Reasons for sample size decrease in the next interval, n (%) <sup>a,b</sup>	1-90 days (N=176)	91-180 days (N=131)	181-270 days (N=111)	271-360 days (N=87)	361-450 days (N=70)	451-540 days (N=60)
Discontinuation	16 (9.1)	8 (6.1)	6 (5.4)	6 (6.9)	2 (2.9)	—
End of study	26 (14.8)	13 (9.9)	14 (12.6)	10 (11.5)	6 (8.6)	—

HAE, hereditary angioedema; LTP, long-term prophylaxis. \*The sample size for the 1-90 day interval (N=176) was smaller than the eligible study population (N=179) as 3 patients had ≥1 self-assessment of HAE attacks during follow-up but none during the first interval. †Other reasons for sample size decrease were no HAE attack report associated with dispensing in interval (0.8%–4.3%) and discontinuation and later re-initiation (0.0%–3.6%).

Figure 4. Reductions in HAE Attack Rates After Berotralstat Initiation for LTP Naïve and Experienced Subgroups



CI, confidence interval; HAE, hereditary angioedema; LTP, long-term prophylaxis. \* Indicates p<0.05.

## Limitations

- The presence of a berotralstat dispensing in the data does not indicate that the medication was consumed or taken as prescribed.
- Prior experience with LTPs other than berotralstat was defined based on self-reported medication use, which could be subject to recall bias or incomplete reporting.

## CONCLUSION

This real-world study among patients with HAE-C1INH observed significant, sustained reductions in HAE attack rates after berotralstat initiation regardless of prior LTP treatment history.

## FUNDING

This study was funded by BioCryst Pharmaceuticals, Inc.