

Reductions in Healthcare Resource Utilization Among Patients with Hereditary Angioedema with C1-Inhibitor Deficiency Following the Initiation of Berotralstat

Sandra Christiansen,¹ Tracy Yee,² Sean D. MacKnight,³ François Laliberté,³ Patrick L. Gravelle,³ Sandra Nestler-Parr,² Patrick Gillard,² Bruce Zuraw^{1,4}

¹Department of Medicine, University of California San Diego, La Jolla, CA, USA; ²BioCryst Pharmaceuticals, Inc., Durham, NC, USA; ³Groupe d'analyse SRI, Montreal, QC, Canada; ⁴Veterans Administration Healthcare, San Diego, CA, USA



BACKGROUND

- Hereditary angioedema (HAE) is a rare genetic condition characterized by painful, unpredictable swelling attacks of skin and mucous membranes, which can be life-threatening when affecting the upper airway.¹
- For patients with HAE with C1 esterase inhibitor deficiency (HAE-C1INH; type 1 or 2), low C1INH levels or function lead to increased vascular permeability and subsequent swelling attacks.²
- Berotralstat is the only targeted, once-daily, oral prophylactic therapy for the prevention of HAE attacks in adults and pediatric patients 2 years and older.³
- Significant reductions in healthcare resource utilization (HRU) following berotralstat initiation have been reported in Komodo Healthcare Map claims data.⁴
- This study evaluated HRU following berotralstat initiation among patients 12 years or older with HAE-C1INH stratified by baseline attack rate.

METHODS

Data Source

- Optime Care Specialty Pharmacy data (Dec. 3, 2020 – Jun. 30, 2024) were linked with Komodo Healthcare Map administrative claims data (Oct. 1, 2015 – Jun. 30, 2024) at the patient level using de-identified Datavant tokens.
- Optime Care is the sole dispenser of berotralstat in the United States, and the database includes berotralstat shipment information, self-assessments of HAE attacks, and laboratory results (C1INH levels, C1INH function, and C4 levels) for HAE type identification.
- Komodo Healthcare Map contains pharmacy and medical claims data for more than 320 million patient-lives in the United States.

Study Design and Analysis

- This retrospective pre-post cohort study selected patients with ≥2 berotralstat dispensings based on Optime data (first dispensing = index date), ≥6 months of continuous insurance eligibility prior to the index date based on Komodo data, lab-defined HAE-C1INH, and ≥12 years of age at index.
- The pre-index period spanned from first evidence of HAE to the index date, with a maximum of 6 months. The post-index period spanned the index date to the earliest of the end of continuous eligibility, end of data, or 24 months.
- Patients were stratified by baseline monthly HAE attack rate (≥5, 2–4, 1, and 0; corresponding to categories of ≥4.5, ≥1.5–<4.5, ≥0.5–<1.5, and <0.5, respectively).
- The number of attacks patients reported in the 90 days prior to berotralstat initiation (baseline period) was divided by 3 to obtain a 30-day attack rate. The maximum rate of HAE attacks that patients could experience was assumed to be 1 attack per 2 days.
- Angioedema-related HRU was defined using claims with a primary diagnosis code for HAE or angioedema, on-demand or LTP medications, and diagnostic tests for complement components associated with HAE.
- Rates of visits per patient-year post-index were compared with pre-index using rate ratios, 95% confidence intervals (CIs), and p-values from generalized estimating equation (GEE) Poisson regression models with robust standard errors.

Figure 1. Pre-Post Study Design

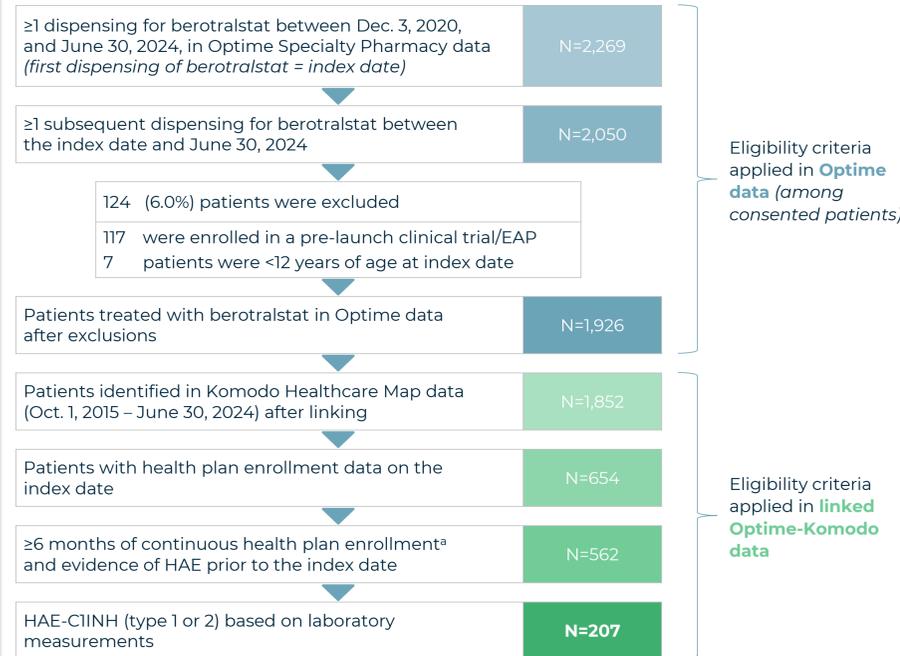


HAE, hereditary angioedema; LTP, long-term prophylaxis. *First evidence of HAE was assessed any time pre-index (during continuous eligibility). Evidence of HAE was defined as a pharmacy or medical claim for an HAE on-demand or LTP medication, an angioedema or HAE diagnosis (in any position), or measurement of complement function. If the first evidence of HAE was ≥6 months pre-index, then the pre-index period was 6 months; if the first evidence of HAE was <6 months pre-index, then the pre-index period spanned from the first evidence of HAE to the index date.

RESULTS

- The study population comprised 207 patients with HAE-C1INH (Figure 2).
- Mean age was 36.9 years, 68.1% were female, and 69.6% had commercial insurance at index (Table 1).
- Among the subset of patients with a self-assessment of HAE attacks at baseline (n=188), 14.4% had ≥5 attacks/month, 27.7% had 2–4 attacks/month, 27.1% had 1 attack/month, and 30.9% had 0 attacks/month at baseline (Figure 3).
- Prior to berotralstat initiation, the mean rates of angioedema-related outpatient/emergency department (OP/ED) visits and hospitalizations were 4.0 and 0.6 per patient-year, respectively.
- Rates of angioedema-related visits significantly decreased by 49% for OP/ED visits and by 61% for hospitalizations after berotralstat initiation (both p<0.05) (Figure 4).
- Significant reductions in OP/ED visits were observed among all baseline attack-rate subgroups (42%–57%; p<0.05), and in hospitalizations among patients with 2–4 and 0 attacks/month at baseline (81% and 63%; p<0.05) (Figure 4).

Figure 2. Berotralstat Patient Disposition



EAP, expanded access program; HAE-C1INH, hereditary angioedema with C1 esterase inhibitor deficiency. *Continuous health plan enrollment was defined as continuous periods with both medical and pharmacy insurance eligibility.

REFERENCES

- Betschel S, et al. *Allergy Asthma Clin Immunol.* 2019;15(1):1-29.
- Gower RG, et al. *World Allergy Organ J.* 2011 Feb 15;4(Suppl 2):S9-S21.
- Berotralstat [package insert]. Durham, NC: November 2023.
- Christiansen S, et al. *J Manag Care Spec Pharm.* 2025;31(6):578-589.

ACKNOWLEDGMENTS

Editorial support was provided by Rukan Saif, BS, of Analysis Group Inc, Boston, MA, USA and Samuel Schwartzbein, MA, of Groupe d'analyse SRI, Montréal, QC, Canada, funded by BioCryst Pharmaceuticals, Inc

Funding

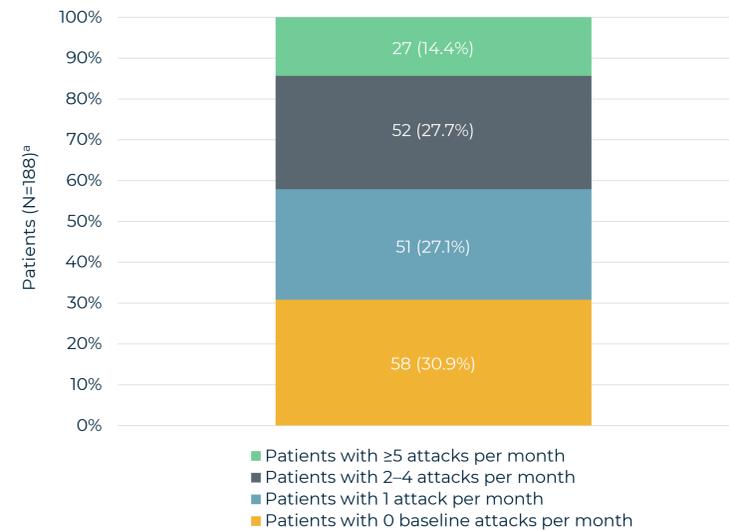
This study was funded by BioCryst Pharmaceuticals, Inc.

Table 1. Demographics and Clinical Characteristics

Characteristics	Patients (N=207)
Demographics^a	
Age, years, mean ± SD [median]	36.9 ± 17.2 [34.7]
Female, n (%)	141 (68.1)
Region of residence, n (%)	
South	90 (43.4)
Midwest	48 (23.2)
Northeast	35 (16.9)
West	34 (16.4)
Insurance plan type, n (%)^a	
Commercial	144 (69.6)
Medicaid	50 (24.2)
Medicare	12 (5.8)
Unknown	1 (0.5)
Healthcare practitioner specialty, n (%)^a	
Allergist/Immunologist	195 (94.2)
Nurse practitioner	6 (2.9)
Other	6 (2.9)
Quan-CCI score, mean ± SD [median] ^b	0.48 ± 1.13 [0]
Patients with ≥1 claim for an LTP any time pre-index, n (%) ^c	65 (31.4)
Patients with ≥1 claim for an ODT any time pre-index, n (%) ^c	83 (40.1)

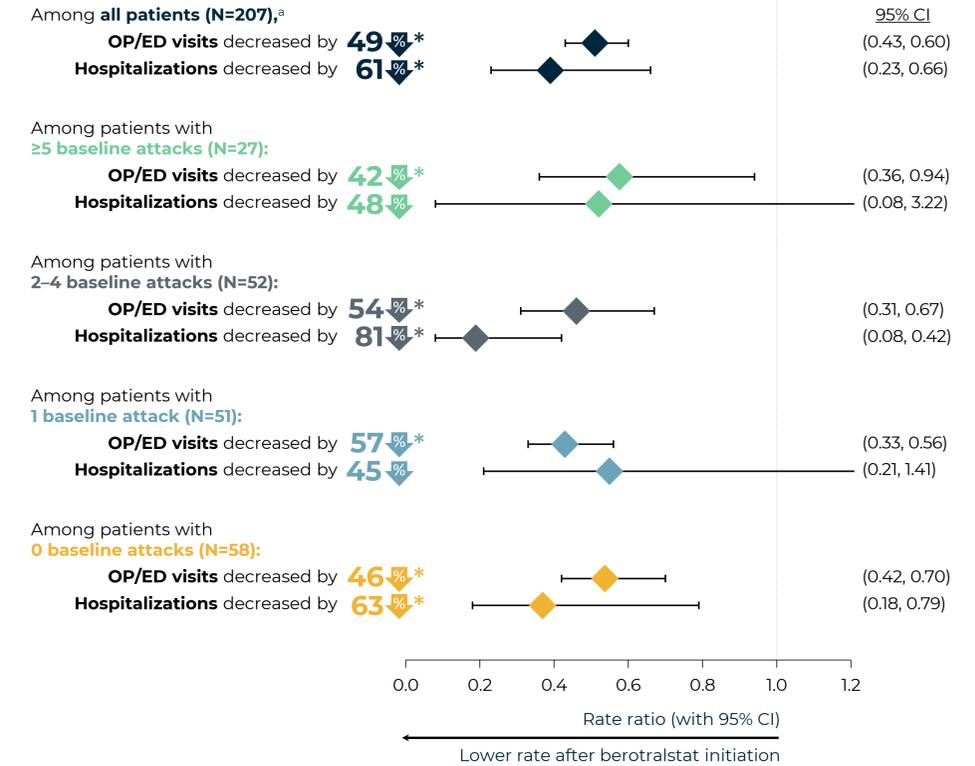
CCI, Charlson comorbidity index; LTP, long-term prophylaxis; ODT, on-demand therapy; SD, standard deviation. *Identified from Optime Care Specialty Pharmacy data. †Identified from Komodo Healthcare Map data. ^aAssessed on the index date. ^bAssessed during the 6 months pre-index. ^cAssessed any time pre-index, from the start of continuous eligibility to the index date.

Figure 3. Monthly Baseline Attack Frequency



^aAmong patients with a baseline self-assessment of attacks

Figure 4. Angioedema-Related Healthcare Resource Utilization



CI, confidence interval; ED, emergency department; OP, outpatient. *P<0.05. ^aIncluding patients with unknown baseline attacks.

Limitations

- Dispensed medications do not indicate that the medication was ingested.
- While matching data sources via tokenization achieves high precision, it does not ensure perfect accuracy in matching patients between different sources within the Komodo database or between Optime and Komodo data.

CONCLUSIONS

Individuals with HAE-C1INH experienced significant reductions in angioedema-related medical visits after the initiation of berotralstat.

- Rates of angioedema-related OP/ED visits were significantly lower after berotralstat initiation overall and regardless of baseline attack rate.
- Rates of angioedema-related hospitalizations were significantly lower overall and in patients with a baseline attack rate of 2-4 and 0.