Impact of Berotralstat on Healthcare Resource Utilization in Patients with Hereditary Angioedema with Normal C1-Inhibitor

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BACKGROUND

- Hereditary angioedema (HAE) is a rare inherited condition marked by recurrent attacks of painful and unpredictable swelling of the skin and mucous membranes, which can be life-threatening when affecting the upper airway.[1]
- Some individuals with HAE experience bradykinin-driven angioedema attacks despite having normal C1 esterase inhibitor levels and function (HAE-nC1INH).[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 and older with HAE-nC1INH stratified by baseline attack rate.

METHODS

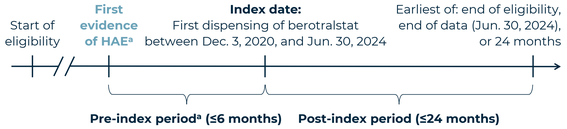
Data Source

- 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), ≥6 months of continuous insurance eligibility prior to the index date based on Komodo data, HAE-nC1INH based on normal C1INH levels/function, 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 experiencing 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

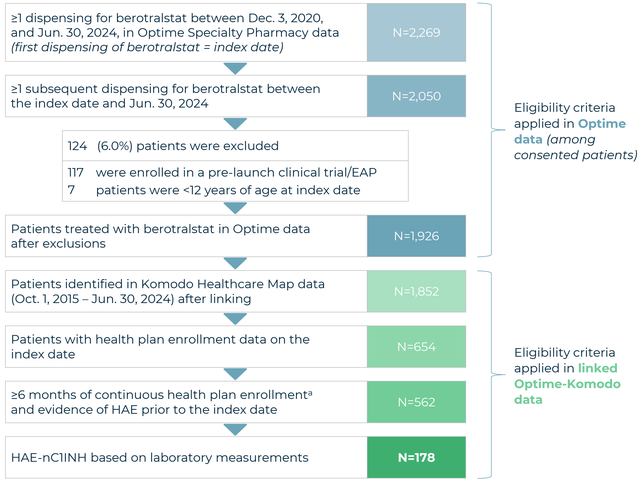


HAE, hereditary angioedema; LTP, long-term prophylaxis. [a]First evidence of HAE was assessed any time pre-index (during continuous eligibility). Evidence of HAE was defined as a pharmacy or medical claim for an HAE on-demand or LTP medication, an angioedema or HAE diagnosis (in any position), or measurement 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 178 patients with HAE-nC1INH (**Figure 2**).
- Mean age was 47.1 years, 79.2% were female, and 70.8% had commercial insurance at index (**Table 1**).
- Among the subset of patients with a self-assessment of HAE attacks at baseline (n=148), 35.1% had ≥5 attacks/month, 27.0% had 2–4 attacks/month, 24.3% had 1 attack/month, and 13.5% 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 6.6 and 1.1 per patient-year, respectively.
- Rates of angioedema-related visits significantly decreased by 49% for OP/ED visits and by 36% 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 (44%–64%; p<0.05) (**Figure 4**).

Figure 2. Berotralstat Patient Disposition



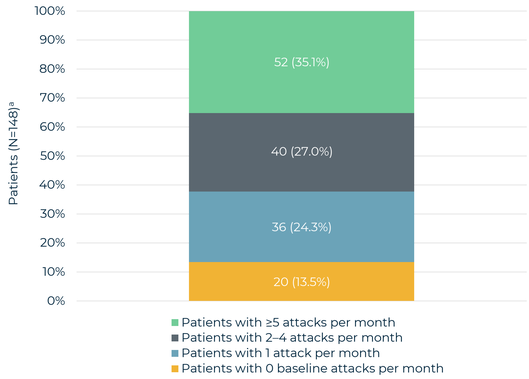
EAP, expanded access program; HAE-C1INH, hereditary angioedema with C1 esterase inhibitor deficiency.
[a]Continuous health plan enrollment was defined as continuous periods with both medical and pharmacy insurance eligibility.

Table 1. Demographics and Clinical Characteristics

Characteristics	Patients (N=178)
Demographics[*,a]	
Age, years, mean ± SD [median]	47.1 ± 15.1 [48]
Female, n (%)	141 (79.2)
Region of residence, n (%)	
South	75 (42.1)
Midwest	36 (20.2)
West	34 (19.1)
Northeast	33 (18.5)
Insurance plan type, n (%)[†,a]	
Commercial	126 (70.8)
Medicaid	28 (15.7)
Medicare	24 (13.5)
Healthcare practitioner specialty, n (%)*[,a]	
Allergist/Immunologist	161 (90.4)
Nurse practitioner	10 (5.6)
Other	7 (4.0)
Quan-CCI score, mean ± SD [median][‡,b]	0.73 ± 1.22 [0]
Patients with ≥1 claim for an LTP any time pre-index, n (%)[†,c]	37 (20.8)
Patients with ≥1 claim for an ODT any time pre-index, n (%)[†,c]	56 (31.5)

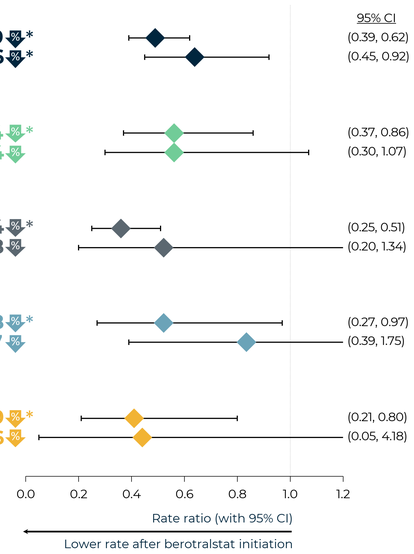
CCI, Charlson comorbidity index; LTP, long-term prophylaxis; ODT, on-demand therapy; SD, standard deviation. *Identified from Optime Care Specialty Pharmacy data. †Identified from Komodo Healthcare Map data. [a]Assessed on the index date. [b]Assessed during the 6 months pre-index. [c]Assessed any time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

Figure 3. Monthly Baseline Attack Frequency



[a]Among 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.
[a]Including 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-nC1INH 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.

REFERENCES

1. Betschel S, et al. *Allergy Asthma Clin Immunol.* 2019;15(1):1-29. **2.** Busse P, et al. *N Engl J Med.* 2020;382(12):1136-1148. **3.** Berotralstat [package insert]. Durham, NC: November 2023. **4.** Christiansen S, et al. *J Manag Care Spec Pharm.* 2025;31(6):578-589.

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