Hospitalization and Emergency Department Reductions After Initiating Berotralstat, Lanadelumab, or Subcutaneous Plasma-Derived-C1-Inhibitor for Hereditary Angioedema

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INTRODUCTION

- Hereditary angioedema (HAE) is a rare genetic disorder in which patients experience recurrent, potentially life-threatening episodes of swelling affecting the extremities, face, abdomen, and larynx.[1]
- Guidance from the European Academy of Allergy and Clinical Immunology, the World Allergy Organization, and the United States Hereditary Angioedema Association Medical Advisory Board supports targeted long-term prophylaxis (LTP) in the management of HAE.[2,3]
- Guideline-recommended first-line LTPs include berotralstat, lanadelumab, and subcutaneous (SC) plasma-derived C1-inhibitor (pdC1-INH).
- This study assessed changes in hospitalizations and emergency department (ED) visits following initiation of berotralstat, lanadelumab, or SC-pdC1-INH among LTP treatment naïve patients with HAE.

METHODS

Data Source

- Veradigm Network EHR linked to closed claims from Komodo's Healthcare Map.

Study Design and Patient Selection

- Retrospective observational pre-post cohort study among LTP treatment naïve patients aged ≥12 years who initiated treatment with berotralstat, lanadelumab, or SC-pdC1-INH between 06/22/2017 and 10/10/2024 (mutually exclusive cohorts) with ≥6 months of continuous insurance enrollment (medical and pharmacy benefits) and evidence of HAE prior to LTP treatment initiation (index date).

Figure 1 Patient Selection

Patients with ≥1 pharmacy claim for berotralstat or ≥1 pharmacy or medical claim for lanadelumab or SC-pdC1-INHs on or after their respective FDA approval dates[a] (index date = date of 1st LTP claim)
Berotralstat (N=621) | Lanadelumab (N=1,259) | SC-pdC1-INH (N=466)

↓

≥6 months of continuous insurance enrollment prior to the index date
Berotralstat (n=306) | Lanadelumab (n=573) | SC-pdC1-INH (n=224)

↓

Age ≥12 years at index date
Berotralstat (n=306) | Lanadelumab (n=560) | SC-pdC1-INH (n=214)

↓

Evidence of HAE prior to the index date[b]
Berotralstat (n=234) | Lanadelumab (n=453) | SC-pdC1-INH (n=160)

↓

No evidence of LTP treatment prior to the index date
Berotralstat (n=128) | Lanadelumab (n=236) | SC-pdC1-INH (n=95)

pdC1-INH, plasma-derived C1-inhibitor; SC, subcutaneous.
a) 12/3/2020: berotralstat, 8/23/2018: lanadelumab, 6/22/2017: SC-pdC1-INH
b) A pharmacy or medical claim for an HAE on-demand or LTP medication, a diagnosis of International Classification of Diseases, Tenth Revision, Clinical Modification codes D84.1, D68.2, or T78.3, or measurement of complement function

Inverse Probability of Treatment Weighting (IPTW)

- Differences among treatment cohorts were balanced with IPTW using a multinomial propensity score model and stabilized weights. [4]
- Covariates included age, sex, race, ethnicity, geographic region, and payer type at index.

Time Periods

- Fixed baseline period: 6 months preceding the index date.
- Variable-length baseline period: began on the later of 6 months pre-index or the first HAE evidence and ended the day before the index date.
- Variable length follow-up period: from the index date until the earliest of the end of continuous enrollment or end of data availability (10/10/2024).

FUNDING

This study was funded by BioCryst Pharmaceuticals, Inc.

METHODS (cont'd)

Study Outcomes

- All-cause and angioedema-related hospitalization and ED visits were assessed in the baseline and follow-up periods.
  - The all-cause analysis used the fixed baseline and variable follow-up periods.
  - The angioedema-related analysis used the variable baseline (the period when angioedema-related care was being captured) and variable follow-up periods.
  - Angioedema-related care included medical claims with International Classification of Diseases, Tenth Revision, Clinical Modification codes D84.1, D68.2, or T78.3, or a sign or symptom of HAE as defined by Zuraw et al.[5]
- Utilization rates were normalized as per-patient per-year.

Statistical Analyses

- Mean and standard deviation (SD) are reported for continuous variables and number and percent for categorical variables.
- Within cohort comparisons of baseline and follow-up rates were estimated using generalized estimating equations with a negative binomial distribution with robust standard errors.
- Results are reported as rate ratios with 95% confidence intervals (95% CI) and p-values.
- Comparisons between berotralstat and other LTPs were made with difference-in-difference models using the same distributions as used to derive the rate ratios.

RESULTS

Study Population

- This study included 3 LTP treatment-naïve cohorts: 128 initiating berotralstat, 236 initiating lanadelumab, and 95 initiating SC-pdC1-INH **(Figure 1)**.
- Prior to IPTW, patients were on average 39–40 years of age and a majority were female (73%–81%) **(Table 1)**.
- Effective sample sizes following IPTW were 128.3 (berotralstat), 236.1 (lanadelumab), and 94.6 (SC-pdC1-INH).
- A majority of patients in all cohorts had commercial insurance (52.6%–75.0%), and Medicaid insurance was the second most common (14.8%–30.5%); however, payer type differed substantially across cohorts.
- Baseline characteristics were well balanced (SMD <0.1) after IPTW **(Figure 2)**.
- The mean follow-up time was over 1.5 years in all cohorts (20.9–31.4 months).

Healthcare Resource Utilization

- All cohorts experienced reductions in hospitalizations and ED visits after LTP initiation, with significant reductions in all-cause and angioedema-related ED visits **(Figure 3)**.
  - Reductions in all-cause hospitalization ranged from -26% (SC-pdC1-INH cohort) to -53% (berotralstat cohort).
  - Reductions in all-cause ED visits ranged from -34% (SC-pdC1-INH cohort) to -48% (lanadelumab cohort).
  - Reductions in angioedema-related hospitalization ranged from -46% (SC-pdC1-INH cohort) to -59% (lanadelumab cohort).
  - Reductions in angioedema-related ED visits ranged from -43% (SC-pdC1-INH cohort) to -61% (berotralstat cohort).
- No statistically significant differences in magnitude of reductions were observed between berotralstat and lanadelumab or SC-pdC1-INH **(Table 2)**.

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RESULTS (cont'd)

Table 1 Unweighted Baseline Patient Demographics

	Berotralstat n=128	Lanadelumab n=236	SC-pdC1-INH n=95
Age, mean (SD), years	39.9 (15.6)	39.9 (16.3)	38.9 (14.6)
Female, n (%)	104 (81.3)	179 (75.8)	69 (72.6)
Race, n (%)			
White	80 (62.5)	134 (56.8)	59 (62.1)
Black	11 (8.6)	23 (9.7)	10 (10.5)
Other	20 (15.6)	29 (12.3)	11 (11.6)
Unknown/Not Reported	17 (13.3)	50 (21.2)	15 (15.8)
Ethnicity, n (%)			
Hispanic	7 (5.5)	9 (3.8)	5 (5.3)
Non-Hispanic	88 (68.8)	158 (66.9)	58 (61.1)
Unknown/Not Reported	33 (25.8)	69 (29.2)	32 (33.7)
Geographic region, n (%)			
Northeast	24 (18.8)	53 (22.5)	19 (20.0)
South	60 (46.9)	98 (41.5)	40 (42.1)
West	24 (18.8)	51 (21.6)	18 (18.9)
Midwest	20 (15.6)	33 (14.0)	18 (18.9)
Other/Unknown	0 (0.0)	1 (0.4)	0 (0.0)
Payer type, n (%)			
Commercial	96 (75.0)	152 (64.4)	50 (52.6)
Medicaid	19 (14.8)	46 (19.5)	29 (30.5)
Medicare Advantage	7 (5.5)	26 (11.0)	10 (10.5)
Medicare Fee-for-Service	6 (4.7)	12 (5.1)	6 (6.3)
Variable-length baseline period, months, mean (SD)	4.2 (2.0)	5.0 (1.7)	5.2 (1.3)
Variable-length follow-up period, months, mean (SD)	20.9 (9.3)	31.4 (18.7)	31.0 (18.4)

pdC1-INH, plasma-derived C1-inhibitor; SC, subcutaneous; SD, standard deviation

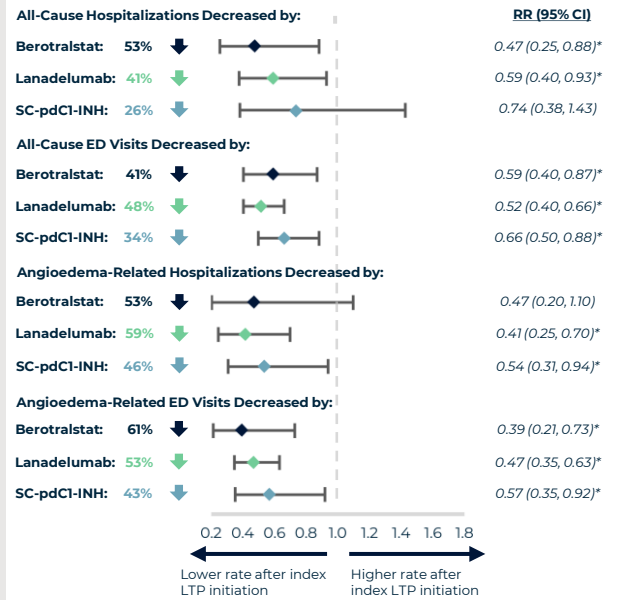
Figure 2 Standardized mean difference after inverse probability of treatment weighting (IPTW)



Limitations

- This study is subject to limitations common to all retrospective database studies, including data entry errors, missing data, and coding limitations.
- This analysis is restricted to insured individuals, and the results may not be representative of patients without insurance.
- Cohort selection was not randomized, and residual confounding may persist after IPTW due to unavailable variables, such as disease severity and HAE subtype

Figure 3. Rate Ratios of Healthcare Visits Before and After LTP Initiation



* p-values are <0.05
CI, confidence interval; ED, emergency department; LTP, long-term prophylaxis; pdC1-INH, plasma-derived C1-inhibitor; RR, rate ratio; SC, subcutaneous

Table 2 Results of Difference-in-Difference Models

	Berotralstat vs Lanadelumab		Berotralstat vs SC-pdC1-INH	
	exp(treatment* period; 95% CI)	p-value	exp(treatment* period; 95% CI)	p-value
All-cause				
Hospitalization	0.79 (0.37–1.68)	0.545	0.64 (0.26–1.56)	0.324
ED Visit	1.14 (0.74–1.77)	0.551	0.89 (0.55–1.44)	0.642
Angioedema-related				
Hospitalization	0.95 (0.42–2.12)	0.897	0.78 (0.32–1.91)	0.582
ED Visit	0.87 (0.49–1.56)	0.646	0.72 (0.36–1.43)	0.347

CI, Confidence Interval; pdC1-INH, plasma-derived C1-inhibitor; SC, subcutaneous;

CONCLUSIONS

1. The study showed that berotralstat, lanadelumab, and SC-pdC1-INH decreased hospitalizations and ED visits in patients with HAE.
2. No significant differences were observed between berotralstat and either lanadelumab or SC-pdC1-INH in the magnitude of these reductions.

DISCLOSURES

BLZ: Consultant for BioCryst and CSL Behring, Laboratory service agreement with Ionis; **SCC**: Consultant for BioCryst, Medical Advisory Board Member of US HAEA, Advisory Board Member for CSL Behring and KalVista; **IW, AD, JM, and AT** are employees of Veradigm and consultants for BioCryst; **TY, SNP, and PG** are employees of BioCryst.

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