



# Hereditary Angioedema Attack Rates among Patients with Normal C1 Esterase Inhibitor Before and After Switching from Another Long-Term Prophylaxis to Berotralstat

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## BACKGROUND

- Patients with hereditary angioedema (HAE) with normal C1 esterase inhibitor (HAE-nC1INH) face recurrent, potentially life-threatening swelling attacks.<sup>1</sup>
- Berotralstat is the only targeted, once-daily oral long-term prophylactic (LTP) treatment for the prevention of HAE attacks in patients aged 12 years and older, and in pediatric patients aged 2 years and older in the United States (US).<sup>2,3</sup>
- A prior real-world study found reductions in attack rates among patients with HAE-nC1INH after initiating berotralstat.<sup>4</sup> However, there is an evidence gap for patients with HAE-nC1INH who switched LTPs.
- This real-world study compared HAE attack rates before and after initiation of berotralstat among patients with HAE-nC1INH who switched from a prior LTP.

## METHODS

### Data Source and Study Design

- This real-world, retrospective study used Specialty Pharmacy data (December 3, 2020 – September 10, 2025) from Optime Care, Inc., the sole dispenser of berotralstat in the US.
- The follow-up period extended from the index date (first berotralstat dispensing) to the last berotralstat dispensing date; no patient assessment data were collected thereafter.
- Patients with HAE-nC1INH ≥12 years were categorized as switching from a prior non-berotralstat LTP if they self-reported use of ≥1 non-berotralstat LTP prior to index and stopped their last non-berotralstat LTP (defined as the LTP with the latest stop date) within the 60 days before or after the index date.

### Study Outcomes and Statistical Analysis

- Patient self-assessments of HAE attacks were collected from the onboarding assessment at berotralstat initiation 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 the follow-up period (segmented into fixed 90-day intervals) up to 3 years.
  - ◻ The maximum rate of HAE attacks that patients could experience was assumed to be 1 attack per 2 days.
  - ◻ Baseline HAE monthly attack rates were calculated from the onboarding assessment as the 90-day attack rate divided by three. The 30-day baseline attack rate was used if the 90-day baseline attack rate was missing.
  - ◻ To allocate attacks into fixed 90-day follow-up intervals, the recall period for the reported number of HAE attacks was the minimum of (a) the time from the previous self-assessment date, or (b) 30 days. The monthly rate of attacks was calculated as the number of attacks in each 90-day interval divided by three.
- Mean monthly HAE attack rates 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.
- To be included in the analysis of a given 90-day follow-up interval, patients were required to have HAE attack self-assessment data in the interval and a follow-up period extending through the interval. These criteria were further broken down to report reasons for sample size change in the next interval using frequencies and proportions for each 90-day interval.
  - ◻ Reasons for sample size change 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, Sept. 10, 2025, without evidence of discontinuation), no self-assessment of HAE attacks associated with dispensing, and discontinuation then re-initiation.

## ACKNOWLEDGEMENTS

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## FUNDING

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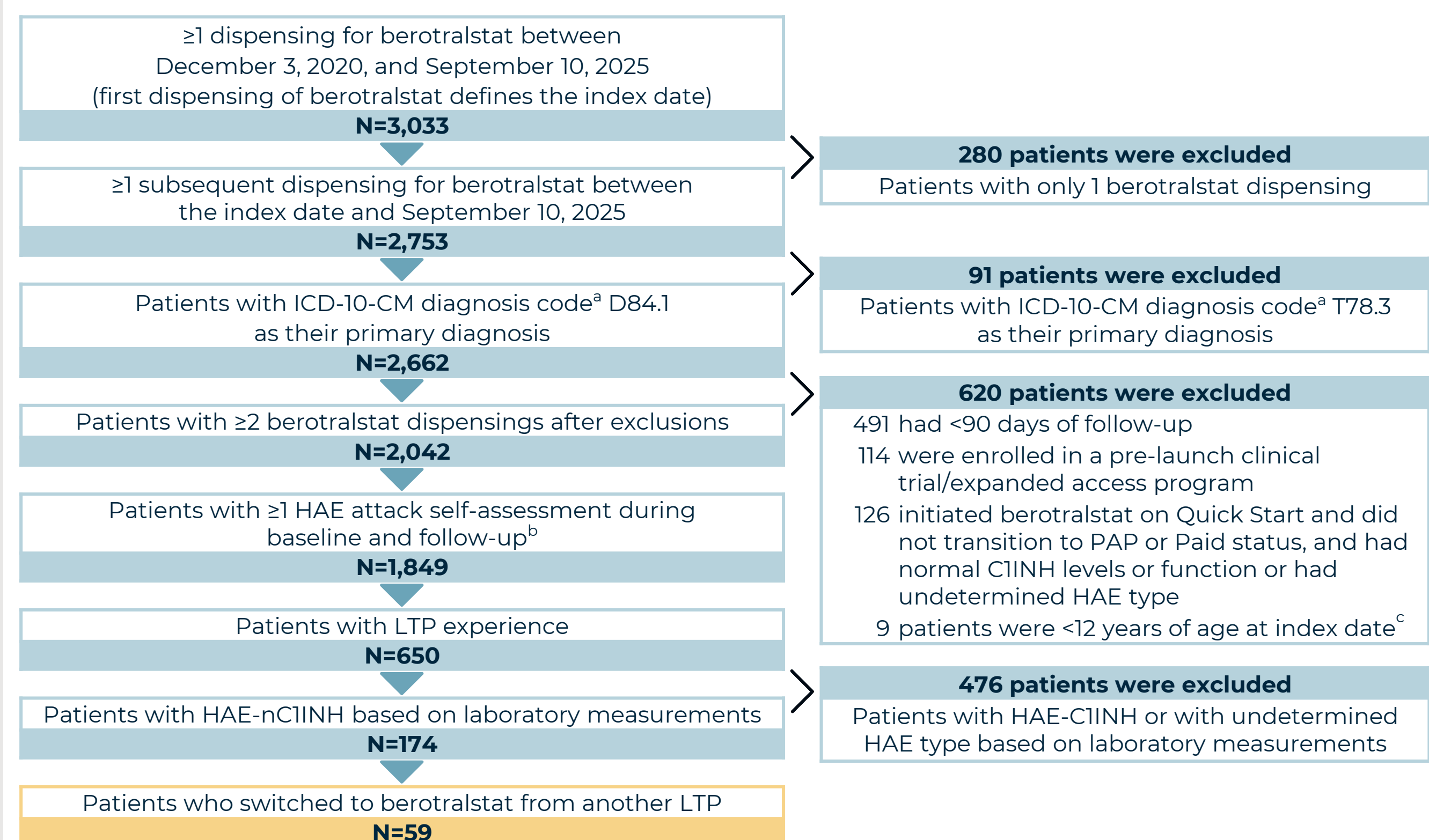
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2. ORLADEYO® (berotralstat) [prescribing information]. BioCryst Pharmaceuticals, Inc. December 2025.
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4. Davis-Lorton M, et al. *Allergy, Asthma, & Clin Immunol.* 2026;22(1):10.

## RESULTS

- The eligible study population consisted of 59 individuals with HAE-nC1INH who switched to berotralstat from another LTP (Figure 1).
- Patients had a mean age of 43.0 years and most (81.4%) were female (Table 1).
- Most patients switched from lanadelumab (54.2%) or SC-pdC1INH (23.7%) (Figure 2).
- Mean baseline attack rates were 4.44, 4.53, and 4.92 attacks/month among patients at 12, 24, and 36 months, respectively (Figure 3).
- HAE attack rate reductions were statistically significant in every 90-day follow-up interval compared to the baseline period (Figure 4).
- At 12, 24, and 36 months, mean monthly attack rate reductions (95% CIs) were 1.93 (0.85, 3.02), 2.57 (1.45, 3.70), and 3.21 (1.78, 4.63) attacks/month, respectively (all p<0.05) (Figure 4).

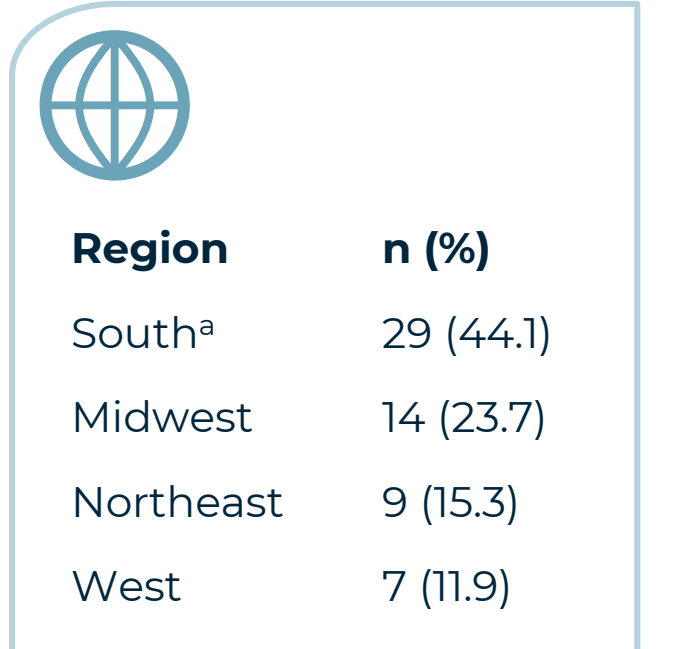
Figure 1. Eligibility Criteria and Patient Disposition



C1INH, C1 esterase inhibitor; HAE, hereditary angioedema; ICD-10-CM, *International Classification of Diseases, 10th Revision, Clinical Modification*; LTP, long-term prophylaxis; nC1INH, normal C1 esterase inhibitor; PAP, patient assistance program. \*All patients had either D84.1 (defects in the complement system) or T78.3 (angioneurotic edema) as their primary diagnosis. †93 patients were excluded without a self-assessment of HAE attacks in baseline or follow-up. ‡Berotralstat was only approved for patients aged ≥12 years during the study period.

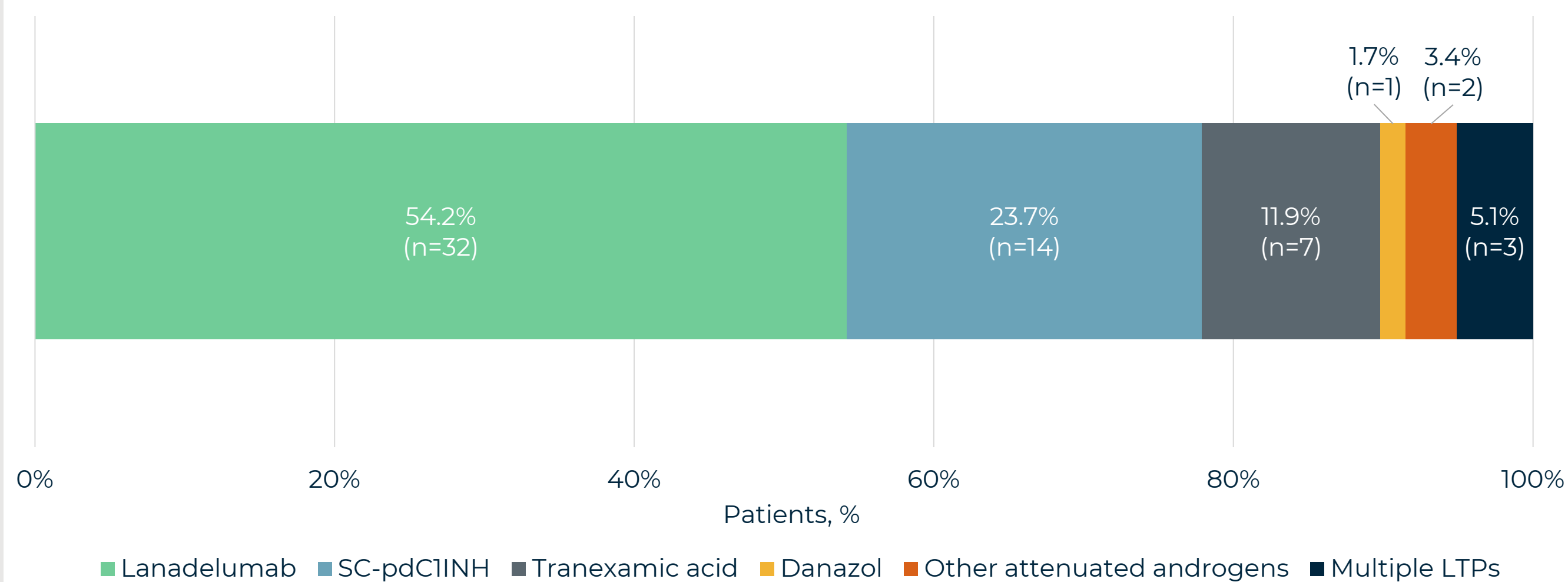
Table 1. Demographics and Clinical Characteristics

Characteristics	Patients (N=59)
Follow-up period, mean ± SD [median], days	753 ± 501 [683]
<b>Demographics</b>	
Age, mean ± SD [median], years	43.0 ± 15.9 [42]
Female, n (%)	48 (81.4)
Patient weight, mean ± SD [median], kg	83 ± 25 [77]
<b>Healthcare practitioner specialty, n (%)</b>	
Allergy/immunology	56 (94.9)
Other	3 (5.1)



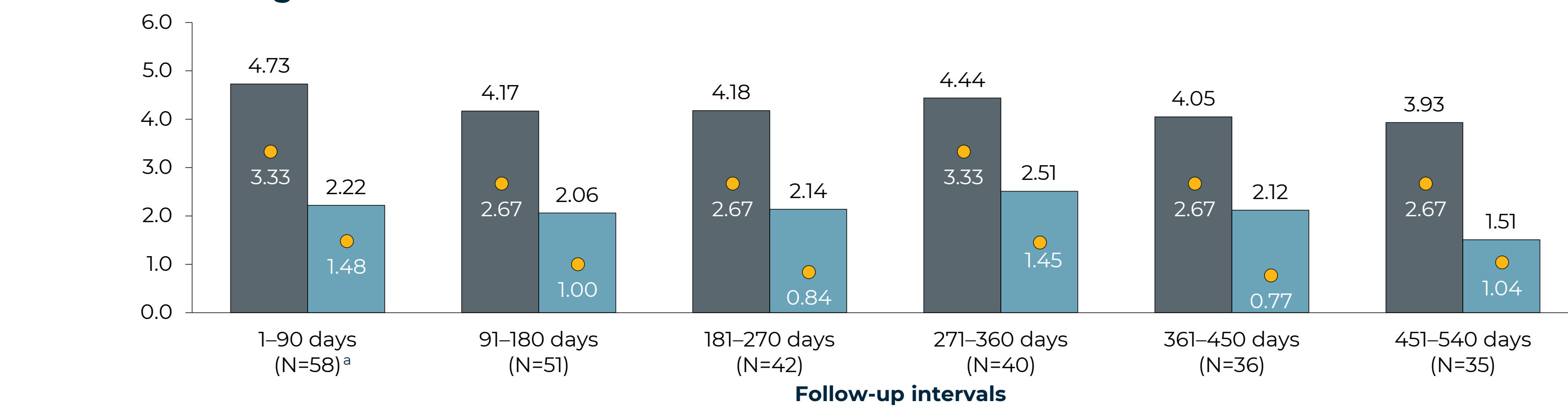
SD, standard deviation. \*The South region includes patients from Puerto Rico and Guam.

Figure 2. LTP Agents used Prior to Switching to Berotralstat<sup>a</sup>

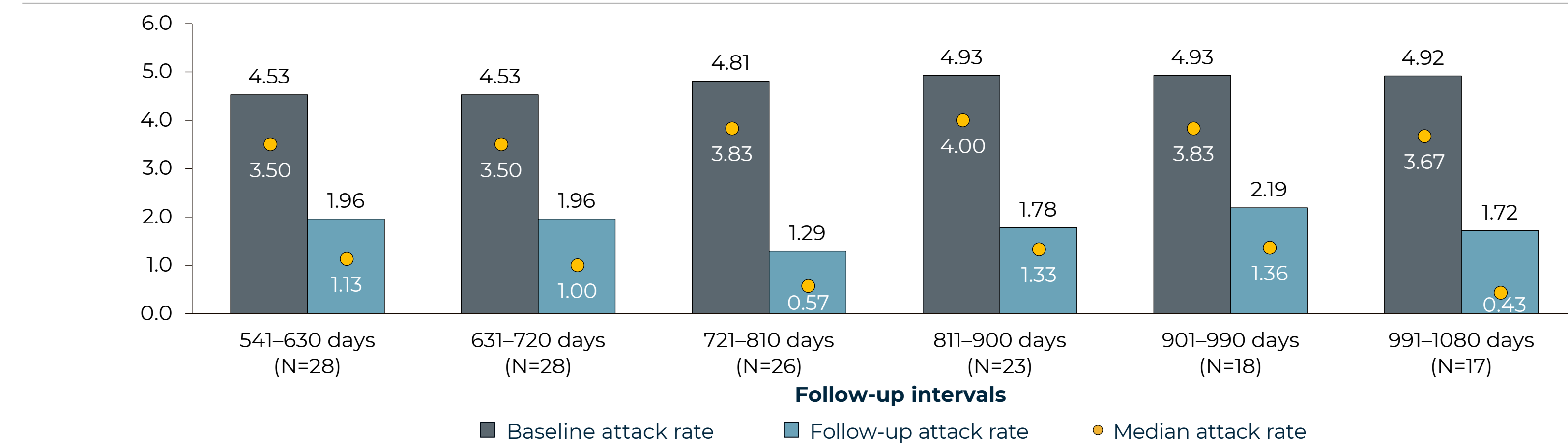


LTP, long-term prophylaxis; SC-pdC1INH, subcutaneous plasma-derived C1 esterase inhibitor. <sup>a</sup>Other attenuated androgens included stanozolol. Multiple LTPs refers to patients with ≥2 LTP agents with the same stop date.

Figure 3. Monthly HAE Attack Rates (Mean and Median) Before and After Berotralstat Initiation Among Patients with HAE-nC1INH who Switched from Another LTP



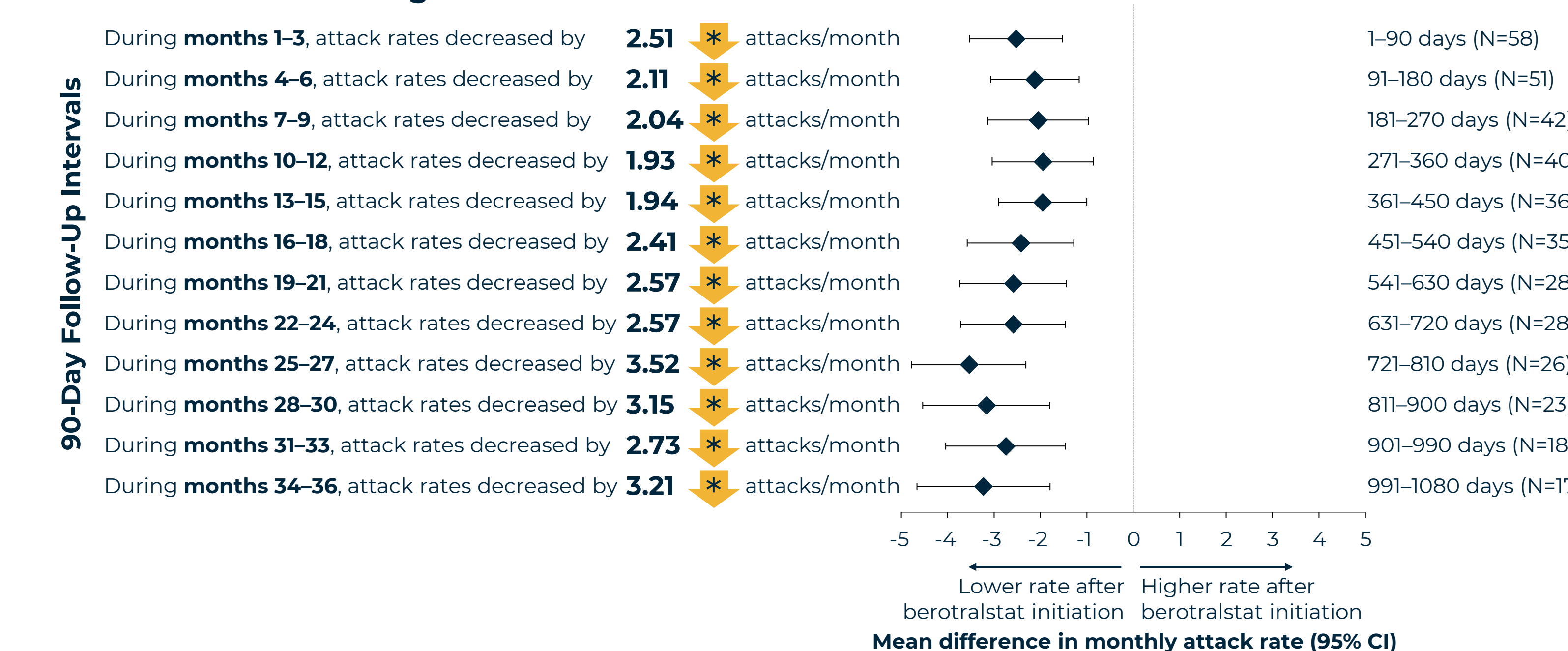
Reasons for sample size change in the next interval, n (%) <sup>b</sup>	1-90 days (N=58) <sup>a</sup>	91-180 days (N=51)	181-270 days (N=42)	271-360 days (N=40)	361-450 days (N=36)	451-540 days (N=35)
Discontinuation	5 (8.6)	6 (11.8)	1 (2.4)	4 (10.0)	0 (0.0)	-
End of study	2 (3.4)	3 (5.9)	1 (2.4)	0 (0.0)	1 (2.8)	-



Reasons for sample size change in the next interval, n (%) <sup>b</sup>	541-630 days (N=28)	631-720 days (N=28)	721-810 days (N=26)	811-900 days (N=23)	901-990 days (N=18)	991-1080 days (N=17)
Discontinuation	1 (3.6)	1 (3.6)	3 (11.5)	0 (0.0)	1 (5.6)	-
End of study	0 (0.0)	1 (3.6)	0 (0.0)	5 (21.7)	0 (0.0)	-

HAE, hereditary angioedema; LTP, long-term prophylaxis; nC1INH, normal C1 esterase inhibitor. <sup>a</sup>The sample size for the 1-90 day interval (N=58) was smaller than the eligible study population (N=59) as 1 patient discontinued and later re-initiated in a subsequent interval. <sup>b</sup>Other reasons for sample size change were no self-assessment of HAE attacks associated with dispensing in interval (0.0%-1.7%), and discontinuation with later re-initiation (0.0%-2.9%).

Figure 4. Comparison of HAE Attack Rates Before and After Berotralstat Initiation using Mean Differences Among Patients with HAE-nC1INH who Switched from Another LTP



CI, confidence interval; HAE, hereditary angioedema; LTP, long-term prophylaxis; nC1INH, normal C1 esterase inhibitor. \* Indicates p<0.05.

## Limitations

- A berotralstat dispensing does not indicate that the medication was consumed or taken as prescribed.
- Prior non-berotralstat LTP start and stop dates were self-reported, which could be subject to recall bias or incomplete reporting.
- IV-pdC1INH could have been used as on-demand therapy or short-term prophylaxis instead of LTP.

## CONCLUSIONS

- Significant and sustained reductions in HAE attacks were observed among patients with HAE-nC1INH who switched to berotralstat from another LTP.
- Most patients who switched from another LTP to berotralstat switched from lanadelumab or SC-pdC1INH.