Impact of Long-Term Prophylaxis Adherence in Hereditary Angioedema Patients: Results of a Claims Database Analysis

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Introduction

- Most patients with hereditary angioedema (HAE) in the US are treated with long-term prophylaxis (LTP), which requires parenteral regimens or daily oral dosing[1]
- Despite receiving LTP, patients with HAE still need access to on-demand treatments per clinical treatment guideline recommendations[2]
- There have been no new commercialized on-demand treatments over the past decade, and real-world data on on-demand treatment use among LTP users and LTP refill patterns is limited[2,3]

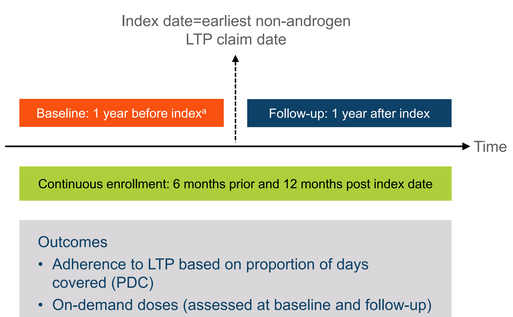
Objective

- To characterize LTP adherence and patterns of on-demand treatment refills using a large national administrative claims database

Methods

- Eligible commercially insured patients from the IQVIA PharMetrics® Plus Database (January 2016–September 2023) who had ≥1 claim for non-androgen LTP, with ≥6 months of continuous enrollment before and ≥12 months after the index date (first non-androgen LTP claim) were included (**Figure 1**)
- Patients with multiple LTP claims on index date or with annualized claim amount more than mean ±3 times the standard deviation (SD; ie, outliers) were excluded

Figure 1. Longitudinal retrospective study design



Outcomes
- Adherence to LTP based on proportion of days covered (PDC)
- On-demand doses (assessed at baseline and follow-up)

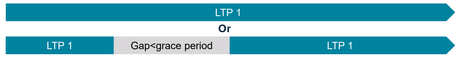
LTP, long-term prophylaxis.

[a]For patients with a baseline period shorter than 364 days, these data are annualized; for patients with baseline period 364 days or longer, the entire 12-month period is considered without annualization.

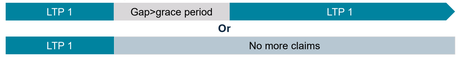
- Patients were classified into the following cohorts: no/minimal refill gaps, with refill gaps, or switchers (**Figure 2**)

Figure 2. LTP patient cohort definitions

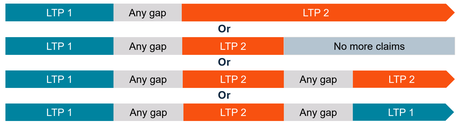
No/minimal refill gaps: Patients with no prescription gap >60 days for lanadelumab or >30 days for other LTPs



With refill gaps: Patients who discontinued their LTP or had ≥1 gap between refills >60 days for lanadelumab or >30 days for other LTPs



Switchers: Patients with ≥1 non-index LTP claim during the 12-month follow-up, regardless of gaps between treatments or whether patients return to index treatment



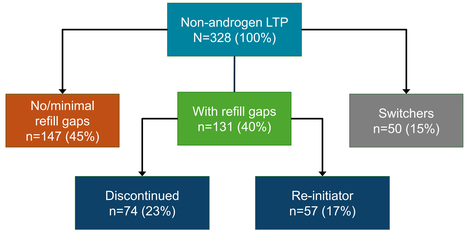
LTP, long-term prophylaxis.
LTP 1 is the LTP at index date; LTP 2 is any non-index LTP.

- PDC was calculated as the percentage of days covered by index LTP prescription fills during follow-up for both the cohorts with refill gaps and without (ie, no/minimal refill gaps). A high PDC percentage signifies good adherence to chronic treatment regimens, commonly accepted with a threshold of 80%[4]
- Annualized mean on-demand claims were evaluated 12 months before and after index date

Results

- Most enrolled patients (N=328) were female (230/328; 70%) with a mean (SD) age at index date of 41.1 (15.6) years
- At enrollment the most common LTP used by patients was subcutaneous (SC) lanadelumab injection 42.1% (138/328), followed by (29.6%) 97/328 taking SC C1 esterase inhibitor (C1INH), 16.5% (54/328) taking intravenous C1INH, and 11.9% (39/328) taking oral berotralstat
- LTP users were distributed almost equally across the 2 cohorts with no/minimal refill gaps, and those with refill gaps, followed by about a sixth that were switchers (**Figure 3**)

Figure 3. Patient cohort populations



LTP, long-term prophylaxis.

- Mean PDC among those patients with minimal or no refill gaps was 93% compared with 42% among those with refill gaps (**Table 1**)

Table 1. Mean PDC by cohort

Cohort	N	Mean days covered	Mean PDC
No/minimal refill gaps	147	339	93%
With refill gaps	131	155	42%
Discontinued	74	105	29%
Re-initiator	57	220	60%

PDC, proportion of days covered.

- Overall (N=328), 67.1% (220/328) of LTP users had ≥1 post-index on-demand claim with a median (interquartile range) of 9.0 (3–20.3) doses at follow-up
  - Mean (SD) annualized on-demand doses post-LTP (ie, follow-up) decreased significantly for the no/minimal refill gap cohort (P=0.001), remained the same for the cohort with refill gaps (P=0.769), and increased in the switchers cohort (P=0.12) (**Table 2**)
- A reduction in on-demand doses was more likely among patients with no/minimal refill gaps than patients with refill gaps (odds ratio [95% CI]: 1.43 [1.24–1.65]) or those who had switched LTP therapies (odds ratio [95% CI]: 2.04 [1.60–2.60])

Table 2. On-demand dose count by patient cohort

	Overall LTP (N=328)		No/minimal refill gaps (n=147)		With refill gaps (n=131)		Switchers (n=50)	
Parameter	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
N (%) patients with ≥1 on-demand dose	207 (63.1%)	220 (67.1%)	96 (65.3%)	95 (64.6%)	75 (57.3%)	84 (64.1%)	36 (72.0%)	41 (82.0%)
Annualized number of on-demand doses, Mean (SD)								
All patients	13.1 (21.5)	11.8 (19.7)	13.6 (22.5)	8 (13.5)	10.5 (17.4)	11.5 (19.8)	18.5 (26.8)	23.9 (28.4)
Patients with ≥1 on-demand dose	20.8 (24.0)	(17.7) (21.8)	20.8 (25.1)	12.4 (15.2)	18.3 (19.7)	18.0 (22.3)	25.7 (28.7)	29.2 (28.8)
Annualized number of on-demand doses, Median (IQR)								
All patients	3.0 (0–15.5)	3.0 (0–12.0)	3 (0–15.8)	3 (0–9.5)	3 (0–14.2)	3 (0–12)	6.5 (0–21.1)	12 (3.0–35.3)
Patients with ≥1 on-demand dose	11.2 (4.0–27.2)	9.0 (3–20.3)	11.6 (3–27.1)	6 (3–12)	11.1 (4.3–27)	9.4 (3–21)	2.0 (5.8–35.0)	18.0 (9.0–42.0)

IQR, interquartile range; LTP, long-term prophylaxis; SD, standard deviation.

Conclusions

- **In this commercial claims analysis, 23% of patients with HAE who initiated LTP discontinued and 17% switched to at least one non-index LTP within the first year**
- **Among patients (45%) with no/minimal gaps in between refills, PDC was 93%, whereas PDC was 42% among those with refill gaps**
- **Within 1 year of LTP initiation, there was a significant decrease in on-demand doses in patients with no/minimal refill gaps. On-demand doses did not decrease in patients with refill gaps**
- **Despite the continued need for ready access to on-demand therapy among patients receiving LTP, only (67.1%) of patients had at least 1 claim for on-demand therapy**
- **Greater focus may be necessary on monitoring LTP effectiveness and adherence as well as ensuring ready access to on-demand treatment for patients receiving LTP**

Acknowledgments

Medical writing support was provided by Tarah M. Connolly, PhD, of Oxford PharmaGenesis Inc., Newtown, PA and funded by KalVista Pharmaceuticals, Inc.

Disclosures

Raffi Tachdjian has served on Advisory Boards for Astria, BioCryst, CSL Behring, Ionis, KalVista, Pharming, and Takeda; received research support from Astria, BioCryst, CSL Behring, Ionis, KalVista, Pharming, Pharvaris, and Takeda; and had received honoraria for lectures from BioCryst, CSL Behring, Pharming, and Takeda.

Daniel Soteres has served on Advisory Boards for BioCryst, CSL Behring, KalVista, Pharming, and Takeda; received research support from Astria, BioCryst, Ionis, KalVista, Pharming, Pharvaris, and Takeda; and had received honoraria for lectures from BioCryst, CSL Behring, Pharming, and Takeda.

Maeve O'Connor is a speaker/consultant/advisor or researcher for KalVista, Pharming, CSL, GSK, Blueprint, TEVA, AZ, Sanofi, Grifols, and AbbVie; and Chief Medical Officer of the CIIC.

Chirag Maheshwari received consulting fees from KalVista.

Paul Audhya is an employee of KalVista Pharmaceuticals.

Alice Wang is an employee of KalVista Pharmaceuticals.

Timothy Craig received research support and was a consultant for CSL Behring, Ionis, Takeda, BioCryst, BioMarin, KalVista, Pharvaris, Intellia, and Astria; received speaker fees from CSL Behring and Takeda, and travel support from CSL Behring, Takeda, and BioCryst.

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Presented at the Western Society of Allergy, Asthma & Immunology (WSAAI) Annual Meeting; February 9–13, 2025; Kohala Coast, Hawaii, HI, USA