Long-Term Prophylaxis Compliance for Hereditary Angioedema and the Impact on On-demand Treatment Claims

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Introduction

- Most patients with hereditary angioedema (HAE) in the United States (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 for on-demand treatment use among LTP users and LTP refill patterns are limited[2,3]

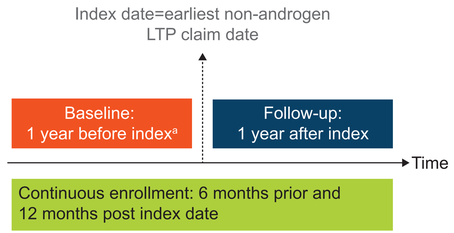
Objective

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

Methods

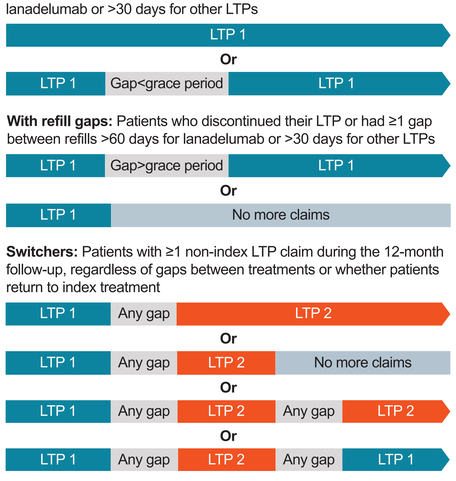
- Eligible commercially insured patients from the IQVIA PharMetrics® Plus Database (January 2016–September 2023) who had ≥1 claim for non-androgen LTP with ≥6 months of continuous enrollment before and ≥12 months after the index date (first non-androgen LTP claim) were included (**Figure 1**)
- Patients with multiple LTP claims on the index date or with an annualized claim amount more than mean ±3 times the standard deviation (SD; ie, outliers) were excluded
- Patients were classified into the following cohorts: no/minimal refill gaps, with refill gaps, or switchers (**Figure 2**)

Figure 1. Longitudinal retrospective study design



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

Figure 2. LTP patient cohort definitions



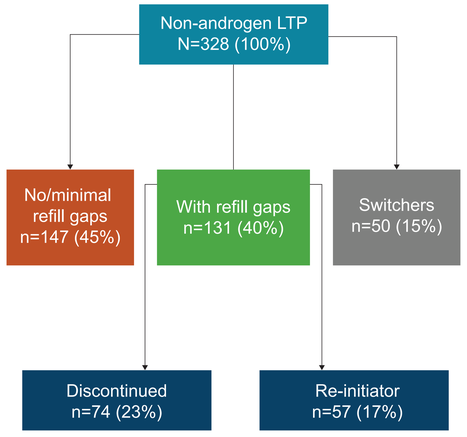
LTP 1 is the LTP at index date; LTP 2 is any non-index LTP.
LTP, long-term prophylaxis.

- Proportion of days covered (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 compliance 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; **Figure 3**) were female (230/328; 70%) with a mean (SD) age at index date of 41.2 (15.6) years
- At enrollment, the most common LTP was subcutaneous (SC) lanadelumab injection (42.1% [138/328]), followed by SC C1 esterase inhibitor (C1INH; 29.6% [97/328]), intravenous C1INH (16.5% [54/328]), and oral berotralstat (11.9% [39/328])

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. Summary of on-demand doses pre- and post-index LTP by LTP cohort

	Number of on-demand doses per patient per year							
	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
All patients								
Mean (SD)	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, n (%)	207 (63.1)	220 (67.1)	96 (65.3)	95 (64.6)	75 (57.3)	84 (64.1)	36 (72.0)	41 (82.0)
Mean (SD)	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)

LTP, long-term prophylaxis; SD, standard deviation.

Discussion

- **This commercial claims analysis found 55% of patients treated with LTP had substantial refill gaps, discontinued, or switched within a year from initiation**
- **Within 1 year of LTP initiation, there was a significant decrease in on-demand doses in patients with no/minimal refill gaps; in patients with refill gaps, on-demand doses did not decrease**
- **Greater focus may be necessary on monitoring LTP effectiveness and compliance as well as ensuring ready access to on-demand treatment for patients receiving LTP**

Lay Summary

- **More than half of the people in the study who started LTP experienced treatment interruptions within a year. These interruptions included missed medication refills, discontinuation of therapy, or transitioning to other treatments**
- **After 1 year, people in the study who consistently refilled their prescribed LTP therapy used slightly fewer on-demand treatment doses. The number of on-demand treatment doses used did not decrease for people who experienced gaps in LTP refills or switched LTP therapies**
- **The study highlights the importance of monitoring whether people living with HAE experience interruptions in LTP treatment, and making sure they have access to on-demand treatment for HAE attacks**

Disclosures
MO 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. **DS** 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. **RT** has served on Advisory Boards for Astria, BioCryst, CSL Behring, Intellia, 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. **CM** received consulting fees from KalVista. **AW** is an employee of KalVista. **PA** is an employee of KalVista. **TC** received research support and was a consultant for ADARx, 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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