JOURNAL OF CLINICAL MEDICINE OF KAZAKHSTAN (E-ISSN 2313-1519)
Original Article DOI: https://doi.org/10.23950/jcmk/18883

Effectiveness and Safety of Lanadelumab in the Treatment of Patients with Hereditary Angioedema in Routine Clinical Practice in the Russian Federation

Tatiana Nekrasova[1], Liubov Aleshina[2], Elena Bobrikova[3], Ekaterina Viktorova[4], Elena Volkova[5], Elena Gracheva[6], Darya Demina[7], Olga Ivanitskaya[8], Marina Karakina[9], Natalia Kuzmenko[4], Irina Lyulyu[10], Irina Manto[11], Nikolay Nazarov[1], Dar'ya Fomina[3,12], Anna Shcherbina[4], Tatiana Latysheva[1], Elena Latysheva[1]

[1]Department of Immunopathology, National Research Center – Institute of Immunology Federal Medical-Biological Agency of Russia, Moscow, Russia
[2]Department of Clinical Immunology and Allergology, Saratov State Medical University named after V.I. Razumovsky, Saratov, Russia
[3]Moscow City Research and Practical Center of Allergy and Immunology, City Clinical Hospital 52, Moscow Healthcare Department, Moscow, Russia
[4]Department of Clinical Immunology, Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, Moscow, Russia
[5]Department of Allergology and Immunology, Smolensk Clinical Hospital №1, Regional Center of Allergology and Immunology, Smolensk, Russia
[6]Counselling outpatient clinic, Vologda regional clinical hospital, Vologda, Russia
[7]Department of Allergology, Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russia
[8]Department of Clinical Medicine, Murmansk Arctic University, Murmansk, Russia
[9]Consultative and diagnostic department, Sverdlovsk Regional Clinical Hospital, Ekaterinburg, Russia
[10]Department of Pulmonology, Republican Hospital named after V.A. Baranov, Petrozavodsk, Republic of Karelia, Russia
[11]Clinical and diagnostic department, DOCMED clinic, Moscow, Russia
[12]Department of Clinical Immunology and Allergy, The First Sechenov State Medical University, Moscow, Russia

Received: 2025-07-30.
Accepted: 2026-06-25.

J Clin Med Kaz 2026; 23(4): 14-24

Corresponding author:
Tatiana Nekrasova.
E-mail: loriley@mail.ru.
ORCID: 0009-0002-4837-6624.

Abstract

Background: Hereditary angioedema (HAE) caused by C1 inhibitor deficiency is a rare condition marked by recurrent swelling of the skin and mucous membranes. This study evaluated the effectiveness and safety of lanadelumab in routine clinical practice in Russia (IISR-2021-200085).

Methods: A prospective cohort of 30 individuals with HAE was observed. Most patients were women (87%), with a mean age of 34 years; Seventeen percent of participants were adolescents. Prior to initiating lanadelumab, 16 patients (53%) had been receiving long-term prophylaxis, which was discontinued once lanadelumab was started. Treatment outcomes were assessed by comparing attack frequency, medication use for acute events, disease control scores, and quality of life before and after lanadelumab therapy.

Results: Before treatment, patients reported an average of 8.6 attacks per month. After 6 months of lanadelumab treatment, the mean attack frequency was reduced to 0.5 per month ($p < 0.001$). Use of acute therapies decreased from 4.73 to 0.43 doses per month ($p < 0.001$). Disease control improved substantially, and quality-of-life scores improved from 58.2 to 25.3 points ($p < 0.001$). No significant lanadelumab-related adverse events were observed.

Conclusion: In routine clinical practice, lanadelumab proved highly effective in reducing attack rates, enhancing disease control, and improving quality of life in patients with hereditary angioedema. The therapy was well tolerated, with no serious safety concerns identified. These findings reinforce lanadelumab as a reliable long-term prophylactic option for hereditary angioedema management.

Keywords: hereditary angioedema, HAE, angioedema, C1-inhibitor, bradykinin, lanadelumab.

Introduction

Hereditary angioedema (HAE) due to C1-esterase inhibitor (C1-INH) deficiency is characterized by recurrent, unpredictable episodes of localized swelling of the skin and mucous membranes, episodes of severe abdominal pain (abdominal attacks). The disease follows an autosomal dominant inheritance pattern and is most commonly linked to mutations in the SERPING1 gene, leading either to reduced levels of C1-INH enzyme (type I HAE) or to impaired C1-INH activity (type II HAE) [1–3].

HAE attacks vary widely in severity and frequency, significantly impairing patients' physical, psychological, and social functioning—even during symptom-free intervals. Laryngeal edema can be life-threatening, while abdominal attacks are intensely painful and often result in unnecessary surgical or diagnostic procedures. Unlike mast cell–mediated angioedema, HAE attacks do not respond to antihistamines or corticosteroids.

Long-term prophylaxis (LTP), short-term prophylaxis (STP), and acute attack management form the basis of HAE treatment. Earlier options such as danazol, progestins, tranexamic acid, and fresh frozen plasma were repurposed from other indications but demonstrated partial effectiveness in HAE. The advent of targeted therapies, including icatibant and plasma-derived or recombinant C1-INH (administered subcutaneously or intravenously), has significantly altered the prognosis and quality of life for patients. However, individuals with frequent attacks continue to require effective and well-tolerated long-term preventive therapy. Existing prophylactic agents have limitations: attenuated androgens are associated with significant adverse effects, intravenous C1-INH requires frequent administration (off-label for LTP, licensed in Russia for treatment of acute HAE attacks), and antifibrinolytics and progestins are effective only in selected cases [4]. This underscores the need for more effective and safer options for prophylaxis.

Lanadelumab is a fully human monoclonal antibody (IgG1/κ) that inhibits the activity of plasma kallikrein (IgG1/κ-light chain). It is administered subcutaneously at a recommended starting dose of 300 mg every two weeks, with the option to extend the interval to every four weeks in well-controlled patients (no HAE attacks) [5–7]. Lanadelumab combines high efficacy, a favorable safety profile, and convenient administration, representing a major advance in the management of HAE.

International WAO/EAACI guidelines position lanadelumab as a first-line prophylactic treatment for HAE [8]. In Russia, expert consensus and updated federal clinical guidelines also endorse its use in patients with high disease activity, frequent attacks, or inadequate response or contraindications to other preventive therapies [9,10].

Its efficacy and safety have been confirmed in the multicenter randomized double-blind, placebo-controlled phase III clinical trial HELP (Hereditary Angioedema Long-term Prophylaxis), which enrolled 125 patients [11], and subsequently in the open-label HELP OLE extension study [7]. Additional evidence has emerged from non-interventional studies such as EMPOWER/ENABLE, which evaluated lanadelumab prophylaxis in adolescents [12].

Nonetheless, given that clinical trial populations are highly selected, the short period of use of lanadelumab, the data from clinical trials may not reflect the variability of routine practice. Real-world data are therefore crucial to confirm the drug's effectiveness across diverse patient groups. Although several small cohort studies have been conducted internationally [13–16], due to the disease's rarity, all studies were conducted on limited patient samples and no published data have addressed the use of lanadelumab in the Russian population. Key aspects of lanadelumab administration in real-world practice remain to be defined:

1. transitioning patients from previous LTP regimens to lanadelumab.
2. The role of STP in patients achieving complete symptom control on lanadelumab.
3. Strategies for extending injection intervals once remission is achieved.
4. Defining the maximum safe dosing interval.
5. Duration of disease control after treatment discontinuation.
6. The feasibility of dose reduction in patients with sustained remission.

Given these gaps, we initiated a two-year, non-interventional, retrospective/prospective study to assess the long-term effectiveness and safety of lanadelumab in routine clinical practice in Russia. This article reports interim study results.

Aim of the study: The objective of this study was to evaluate the long-term effectiveness and safety of lanadelumab as prophylactic therapy in patients with hereditary angioedema (HAE) caused by C1-esterase inhibitor (C1-INH) deficiency under routine clinical practice conditions in the Russian Federation.

Methods

Study Design

This study was designed as a non-interventional, retro-prospective study involving patients with hereditary angioedema (HAE) caused by C1-esterase inhibitor (C1-INH) deficiency who started lanadelumab therapy in accordance with current usage

guidelines. A total of 30 patients were enrolled, with planned follow-up over a 24-month period. The present article reports interim results based on data collected at multiple time points.

Eligibility Criteria

Inclusion criteria comprised patients aged ≥12 years with a confirmed diagnosis of HAE caused by C1-INH deficiency [3]. Written informed consent was obtained from all participants or their legal representatives. The decision to prescribe lanadelumab had to be made independently of study enrollment, and lanadelumab had to be prescribed in accordance with the drug's instructions for use. The data on disease activity during the preceding six months were required. For retrospective inclusion, patients were additionally required to have complete medical records documenting angioedema attacks, adverse events, and interventions from the initiation of lanadelumab.

Exclusion criteria included absence of informed consent, contraindications to lanadelumab as defined in the product labeling, pregnancy or lactation, and concurrent participation in other interventional clinical trials.

Terms and Conditions

The study was conducted across multiple expert centers in the Russian Federation, including institutions within the ACARE international network: the NRC "Institute of Immunology" (FMBA of Russia, Moscow) and the Allergy and Immunology Center of Moscow City Clinical Hospital No. 52. Additional participating sites included the Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, V.I. Razumovsky Saratov State Medical University, "Vologda Regional Clinical Hospital" and Murmansk

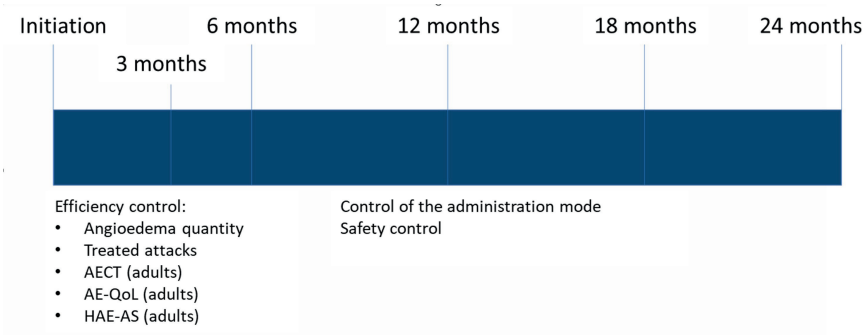

Figure 1 – Study Design

Arctic University, Murmansk ,V.A. Baranov Republic Hospital of Petrozavodsk, Regional Center of Allergology and Immunology of Smolensk, Clinical hospital № 1 of Sverdlovsk region.

Data Sources

Retrospective data were obtained from medical records, while prospective data were collected during scheduled follow-up visits in accordance with the study protocol. All information was recorded in standardized individual registration cards (IRC). Retrospective PRO (patient-reported outcome) data were extracted from routinely maintained patient diaries/PROM records.

Study Duration

The study started in December 2021 and is ongoing. Each patient is to be followed for a total of 24 months. Assessments are conducted at baseline and subsequently at 3, 6, 12, and 24 months, unless participation is discontinued earlier (Figure 1).

Medical Intervention

Patients included in this non-interventional study had been prescribed lanadelumab as part of standard clinical care. The first 16 patients that were enrolled retrospectively in December 2021 were already receiving lanadelumab therapy, with comprehensive medical records available for each patient, which enabled the integration of retrospective data with prospective observations. 14 additional patients were prospectively included between December 2021 and October 2022. All patients continued prospective follow-up after enrollment.

Effectiveness and safety were assessed using PRO tools filled out at control points. Evaluated variables included attack frequency, anatomical location and severity of angioedema episodes (mild: temporary or minor discomfort; moderate: partial activity limitation; severe: significant activity limitation requiring assistance), use of AE management medications, adverse events, and other medical interventions.

The following validated PRO instruments were employed (Table 1):

1) AE-QoL (Angioedema quality of life Questionnaire) [17];
2) AAS28 (Angioedema Activity Score 28) [18];
3) HAE-AS (HAE Activity Score) [19];
4) AECT (Angioedema Control test) [20].

The Primary Outcome of the Study

The primary endpoint was change in disease activity before and during lanadelumab therapy. Additional objectives included evaluation of an algorithm for extending dosing intervals, analysis of medical interventions and adverse events during treatment, and assessment of patient self-administration.

Table 1 Comparative analysis of instruments for assessing hereditary angioedema severity [20, 21]

	AAS28	HAE-AS	AECT	AE-QoL
Title	Angioedema activity score 28	HAE activity score	Angioedema control test	Angioedema quality of life
Evaluation period	4 weeks	6 months	4 weeks / 3 months	4 weeks
Completion method	Prospective	Retrospective	Retrospective	Retrospective
Parameter Assessed	Frequency and duration of angioedema episodes	Frequency and duration of angioedema episodes	Disease control	Impact on quality of life

Subgroup Analysis

No predefined subgroup analyses were conducted.

Outcome Documentation

Medical records covering 6 months prior to lanadelumab initiation and the treatment period of 24 months were analyzed. All relevant data were transferred to IRCs (individual registration cards) and stored electronically (Microsoft Excel).

Ethical Review

The study protocol was reviewed and approved by the local ethics committee of the NRC "Institute of Immunology" FMBA of Russia, Protocol No. 12, dated June 12, 2021.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (USA), RStudio (USA), and Microsoft Excel (USA). Data are presented as descriptive summaries, tables, and graphical representations. Continuous variables with non-normal distributions are presented as median (Q1; Q3), while categorical variables are presented as counts and percentages.

At the initial stage of statistical analysis, group comparisons were performed using the Friedman test (Friedman ANOVA) and Kendall's coefficient of concordance (W). Statistical significance was defined as $p < 0.05$. In cases where statistical significance was identified, pairwise comparisons were subsequently conducted using the Wilcoxon signed-rank test, with p-values adjusted according to the Benjamini–Hochberg method to control for multiple comparisons.

List of abbreviations

HAE — hereditary angioedema

HAE-PLG — HAE with a mutation in the plasminogen gene

HAE-FXII — HAE with a mutation in the coagulation factor 12 (FXII) gene

AE — angioedema
LTP – long-term prophylaxis
STP – short-term prophylaxis
CRF – case report form
PRO – Patient-reported outcome
AE-QoL – Angioedema quality of life
AAS28 – Angioedema activity score 28
HAE-AS – HAE activity score
AECT – Angioedema control test

Results

A total of 30 patients were enrolled in the study, comprising 26 (87%) female and 4 (13%) male individuals. The mean age at initiation of lanadelumab therapy was 33,96 years (range: 13–70 years; median: 32.5 years). 25 patients (83%) were adults, while the remaining 5 participants (17%) were adolescents between 12 and 17 years of age. With respect to HAE subtype, 28 individuals (93%) had type I HAE, and 2 patients (7%) were diagnosed with type II HAE. The mean body mass index (BMI) across the cohort was 26.12 kg/m². Supplementary Table S1 contains a detailed characterization of the study cohort.

At the time of interim analysis, 26 patients had completed their scheduled follow-up. Data from some visits were unavailable in cases where the injection interval exceeded 40 days. Four patients discontinued early: one due to planning of the pregnancy, two due to confirmed pregnancies, and one patient discontinued therapy at his own request after achieving complete disease control.

Main Results of the Study

Before initiating lanadelumab, all patients had previously received various forms of long-term prophylactic therapy (Supplementary Table S2). 16 (53%) patients were on LTP regimens at the time of enrollment, which included either tranexamic acid, danazol, progestins, or intravenous C1-INH. Of these, 15 patients discontinued prior prophylaxis upon starting lanadelumab. One patient (patient 29) had been receiving two concurrent prophylactic therapies prior to initiating lanadelumab: desogestrel 0.075 mg daily and tranexamic acid 3000 mg daily. Following the start of lanadelumab, tranexamic acid was discontinued, while desogestrel was continued at 0.075 mg daily as prescribed by her gynecologist for contraceptive purposes."

Among the 16 patients receiving LTP, 8 terminated their prior therapy on the day lanadelumab was initiated. Seven of these individuals remained attack-free, while one had an angioedema episode on day 4, which required treatment with icatibant. The remaining seven patients discontinued their prophylaxis gradually.

In total, 28 of 30 patients (93%) had previously received at least one line of prophylactic therapy. Tranexamic acid was the most frequently used agent but was reported as ineffective in 27 cases. Among these, effectiveness could not be adequately assessed in three patients due to short treatment duration or subtherapeutic dosing secondary to adverse events. Six patients demonstrated a partial response, while 18 had no therapeutic benefit.

Data of the LTP before initiation of lanadelumab treatment are presented in Supplementary Table S2. In total, 28 of 30 patients (93%) had previously received at least one line of long-term prophylactic therapy. Tranexamic acid was the most frequently used agent but was reported as ineffective in 27 cases. Among these, effectiveness could not be adequately assessed in three patients due to short treatment duration or subtherapeutic dosing secondary to adverse events. 6 patients demonstrated a partial response, while 18 had no therapeutic benefit.

Ten patients were previously prescribed danazol. It was partially effective in 4 patients, and 6 patients showed no improvement at all with danazol. Two of the 6 were taking danazol for a short period of time because of side effects, so it was not possible to assess the benefit of the treatment. Ten patients previously received progestins, 4 out of 10 patients had an incomplete response, while in 6 patients the treatment was ineffective. Six patients were treated with intravenous C1 esterase inhibitor, 5 of whom had a suboptimal response and 1 patient did not respond to therapy. Two patients did not receive any of the long-term prophylaxis before lanadelumab therapy (patients 17 and 23).

Ten patients had been treated with danazol. 4 patients reported partial benefit, while 6 patients experienced no clinical improvement. Two of the 6 discontinued danazol early because of adverse effects, precluding assessment of effectiveness.

Ten patients had previously been treated with progestins; 4 out of 10 patients achieved an incomplete response, and in 6 patients the treatment demonstrated no clinical benefit.

Six patients had previously been prescribed intravenous C1-INH as prophylaxis. 5 of these patients showed suboptimal responses, while 1 patient demonstrated no response.

Two patients (patients 17 and 23) had not received any prior LTP before starting lanadelumab.

Patient Self-Injection Ability

At the initiation of lanadelumab therapy, 22 patients (73%), including three adolescents, were trained in self-injection and demonstrated no difficulties with the procedure. During follow-up, an additional six patients successfully transitioned to self-administration. In total, 28 of 30 patients (93%) were able to administer the medication independently. Two patients (patients 2 and 16) were unable to perform injections at home and continued to receive lanadelumab in a clinical setting.

Maintenance of Drug and Regimen Adherence

Among the eight patients receiving lanadelumab at healthcare facilities, three patients experienced deviations from the prescribed regimen owing to factors unrelated to the treatment itself: one patient missed an injection because of a comorbid gout flare, another because of limited clinic availability during public holidays, and a third due to work-related commitments. These patients were not supplied with lanadelumab for home administration, as regional regulations required in-clinic dosing.

All participants initially received lanadelumab 300 mg every 14 days, in line with approved recommendations. In patients who achieved disease control (defined as no HAE attacks for at least three months), dosing intervals were extended. As no standardized protocol exists for interval extension, an algorithm was applied in clinical practice: after three months of remission, the injection interval was extended to 21 days; if remission persisted for a further three months, the interval was extended to 28 days. In selected cases, dosing intervals were prolonged up to four weeks.

Current Regimen Adherence

At the six-month follow-up, injection intervals were analyzed for 29 patients (patient 30 was excluded due to non-adherence to the prescribed regimen). 14 patients (48%) continued the standard 14-day regimen, 8 (27.6%) were on a 21-day interval, and 6 (21.1%) had extended dosing interval to 28–30 days. Notably, one patient successfully extended the interval to 56 days while maintaining complete disease control; this individual subsequently withdrew from the study at their own request due to sustained remission.

Attack Frequency and Treatment Need

The effectiveness of lanadelumab therapy was assessed using the following parameters: the frequency of AE or abdominal attack before and during the treatment period, the need for acute attack treatment drugs, disease activity parameters and quality of life assessed using questionnaires on patient-reported outcome (PRO).

The median monthly attack frequency per patient decreased markedly following initiation of lanadelumab therapy. At baseline, patients experienced a median of 7.0 [5.66–12.0] attacks per month. After 6 months of treatment, this value declined to 2.0 [0.0–5.0], with sustained low attack rates observed at 12, 18, and 24 months (1.0 [0.0–2.0], 1.0 [0.0–2.0], and 1.0 [0.0–4.0], respectively).

A statistically significant difference in median monthly attack frequency across the evaluated time points was identified (Friedman test, p = 0.0004; Kendall's W = 0.317), indicating a moderate effect size.

Pairwise comparisons demonstrated significant reductions in attack frequency between baseline and all subsequent time points, including 6 months (p = 0.0004), 12 months (p = 0.0001), 18 months (p = 0.0001), and 24 months (p = 0.00012).

Reduction in sample size at later time points reflected patient withdrawal: four discontinued therapy, and one was excluded due to irregular drug supply (Figure 2).

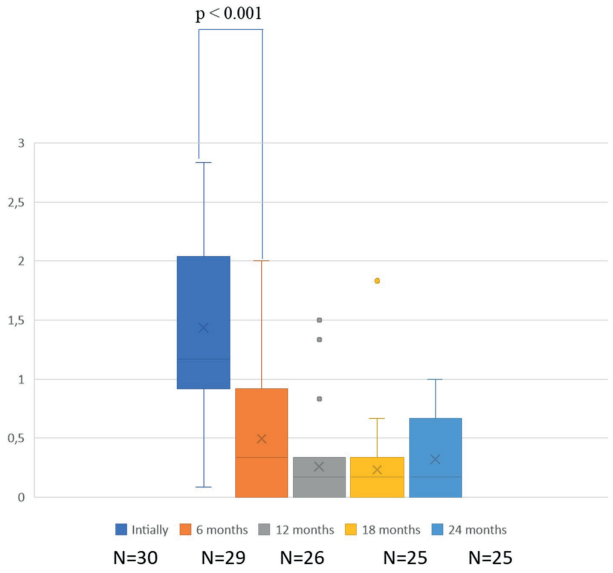

Figure 2 – Median monthly number of attacks per patient prior to and during lanadelumab therapy

A reduction in attack frequency was observed across most anatomical subtypes. Pairwise comparisons between baseline and 6 months demonstrated statistically significant decreases in peripheral attacks (p = 0.0003), abdominal attacks (p = 0.004), and facial attacks (p = 0.009). No statistically significant changes were observed for upper airway attacks (p = 0.286).

When stratified by severity, significant reductions were observed in moderate (p = 0.004) and severe attacks (p = 0.00001), whereas changes in mild attacks did not reach statistical significance (p = 0.586).

By the end of the two-year observation period, 72% of patients reported no severe attacks, 88% reported no upper airway involvement, and 80% reported no abdominal attacks, indicating a marked improvement in overall disease control.

A statistically significant reduction in the use of on-demand therapy was observed as early as 3 months after initiation of lanadelumab (p = 0.0001). This reduction remained stable throughout subsequent follow-up visits, indicating sustained disease control and decreased treatment burden. (Figure 3).

No significant differences were observed in the use of on-demand therapy at subsequent control points (6, 12, 18, and 24

Table 2 Median monthly HAE attack frequency

Time frame	Monthly frequency of HAE attack types	Median	Q1 (first quartile)	Q3 (third quartile)
Before lanadelumab treatment (30 patients)	Peripheral angioedema	4	2	5
	Abdominal attacks	3	2	5
	Face	0	0	1
	Upper airways	0	0	0,5
	mild	0	0	2
	moderate	3	1	5
	severe	4	2	5
	total	7	5,66	12
After 6 months of lanadelumab treatment (29 patients)	Peripheral angioedema	0	0	1
	Abdominal attacks	1	0	2
	Face	0	0	0
	Upper airways	0	0	0
	mild	0	0	2
	moderate	1	0	2
	severe	0	0	0
	total	2	0	5
After 12 months of lanadelumab treatment (26 patients)	Peripheral angioedema	0	0	1
	Abdominal attacks	0	0	1
	Face	0	0	0
	Upper airways	0	0	0
	mild	0	0	0
	moderate	0	0	1
	severe	0	0	0
	total	1	0	2
After 18 months of lanadelumab treatment (25 patients)	Peripheral angioedema	0	0	1
	Abdominal attacks	0	0	1
	Face	0	0	0
	Upper airways	0	0	0
	mild	0	0	0
	moderate	0	0	1,5
	severe	0	0	0,5
	total	1	0	2
After 24 months of lanadelumab treatment (25 patients)	Peripheral angioedema	0	0	1
	Abdominal attacks	0,5	0	1,5
	Face	0	0	0
	Upper airways	0	0	0
	mild	0	0	1
	moderate	0	0	1,5
	severe	0	0	1
	total	1	0	4

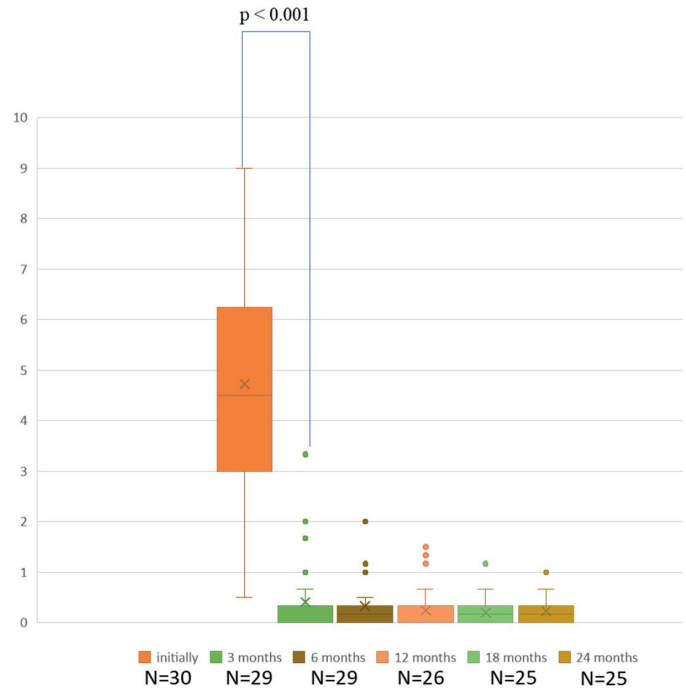

Figure 3 – Monthly use of on-demand medication per patient

months) compared with the third month, indicating sustained reduction in treatment need over time.

Patient-Reported Outcome (PRO) Values

The Angioedema Control Test (AECT) scores demonstrated a statistically significant improvement following initiation of lanadelumab therapy. Median AECT score increased from 5 (5;7) at baseline to 14 (13;16) after 3 months ($p < 0.00001$).

This improvement was sustained throughout the follow-up period, with median values of 15 (12;16) at 6 months, 16 (14;16) at 12 months, 15 (12;16) at 18 months, and 15 (12;16) at 24 months (Figure 4).

A statistically significant difference in AECT scores across all time points was observed (Friedman test, $p = 0.00001$; Kendall's $W = 0.51$), indicating a strong effect size. Pairwise comparisons confirmed significant differences between baseline and all subsequent visits (all $p < 0.00001$).

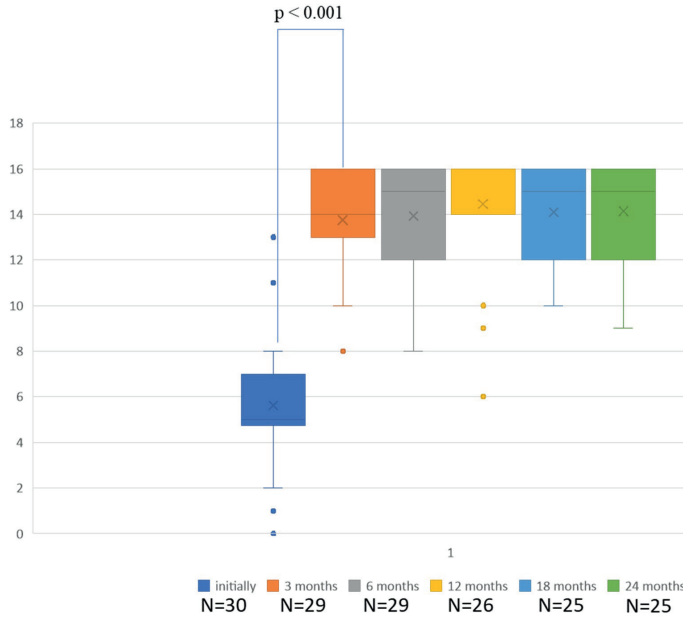

Figure 4 – AECT-based assessment of disease control prior to and during lanadelumab treatment

Improvement in Quality of Life

The Angioedema Quality of Life Questionnaire (AE-QoL) scores showed a marked improvement after initiation of lanadelumab therapy. Median AE-QoL score decreased from 60 (53;66) at baseline to 21 (9;40) after 3 months ($p = 0.0004$), indicating a substantial reduction in disease burden.

This improvement was maintained over time, with median values of 24.5 (11;38) at 6 months, 17 (9;25) at 12 months, 22 (7;29) at 18 months, and 22 (9;28) at 24 months.

Overall, AE-QoL scores differed significantly across time points (Friedman test, $p = 0.00001$; Kendall's $W = 0.51$), with significant pairwise differences between baseline and all subsequent visits (Figure 5).

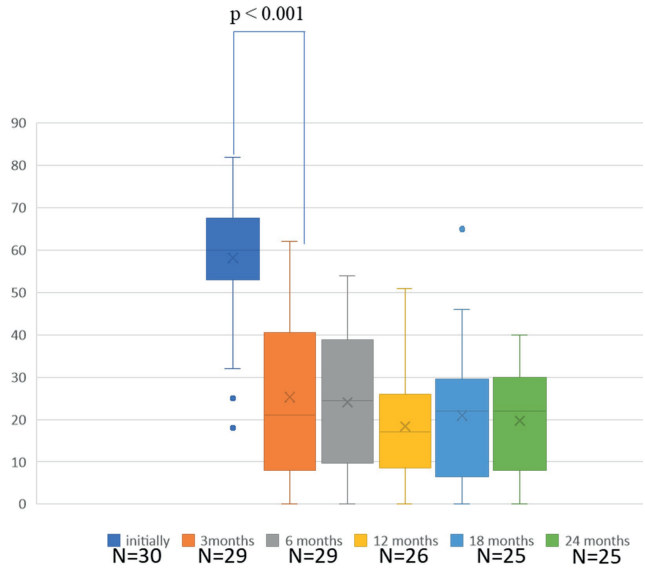

Figure 5 – AE-QoL scores prior to and during lanadelumab therapy

Notably, lower scores indicate less impairment, with reductions reflecting a clinically meaningful improvement in health-related quality of life.

The Hereditary Angioedema Activity Score (HAE-AS) decreased significantly following initiation of lanadelumab therapy. Median values declined from 15.5 (13;18) at baseline to 4 (1;5) at 6 months ($p = 0.0003$).

Further reductions were observed at 12 months (2 (0;4)), 18 months (2 (1;5)), and 24 months (4 (1;5)), indicating sustained suppression of disease activity over time.

HAE-AS scores differed significantly across time points (Friedman test, $p = 0.00001$; Kendall's $W = 0.55$), with significant differences between baseline and all subsequent follow-up visits (Figure 6, see the next page).

Impact of Medical, Dental, and Cosmetic Interventions

During the observation period, 18 patients (60%) underwent a total of 43 medical, dental, or cosmetic interventions that carried the potential to trigger HAE attacks. Of these, 36 procedures were performed without short-term prophylaxis (STP). Only three interventions (two performed with STP and one without) were followed by angioedema episodes, all occurring after minimally invasive procedures (conization of the cervix and removal of a uvular papilloma). Details are presented in Table 3.

Dental procedures were the most common (n = 28), followed by esophagogastroduodenoscopy (n = 5), cosmetic procedures (n = 5), minimally invasive gynecological or ENT interventions (n = 2), and surgical operations (n = 3) (Table 3). The majority were carried out safely, suggesting that

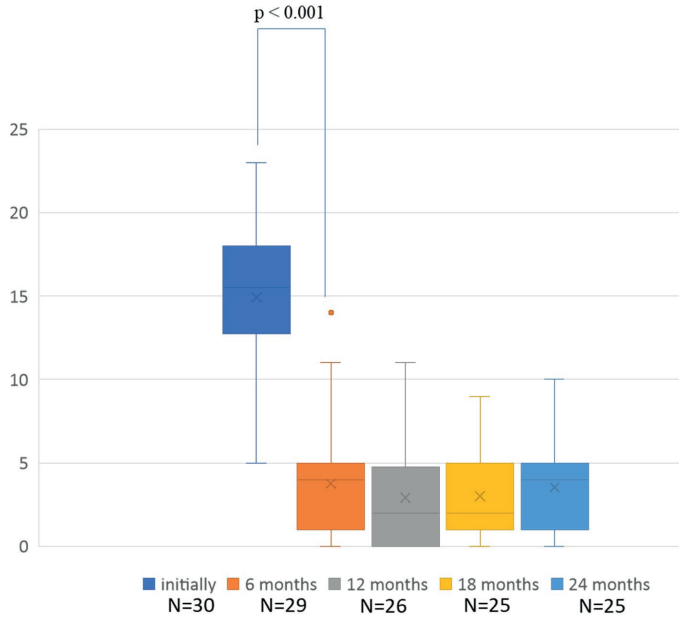

Figure 6 – HAE-AS score prior to and during lanadelumab therapy.

Table 3 Medical, dental, and cosmetic procedures performed during the 24-month period following initiation of lanadelumab therapy

Type of procedure	Number of procedures	Prior to short-term prophylaxis therapy (C1-inhibitor 1000 IU IV)	Angioedema
Dental procedures	28	2	0
Esophagogastroduodenoscopy	5	2	0
Cosmetic procedures	5	0	0
Minimally invasive procedures (cervical conization and excision of uvular papilloma)	2	0	2
Surgical procedures	3	3	1

Table 4 Reported adverse events

Adverse events after lanadelumab administration	Patient	Severity	Association with the drug	Outcome	Note
Small papular rash appearing the day following the injection	07	Mild	Probably related	Continues and reappears	-
Hyperemia at the injection site	15	Mild	Probably related	Reappears	-
Uterine bleeding	22	Severe (hospitalization)	Not related	Hospitalization	Probably due to tranexamic acid discontinuation
Headache on the day of injection	02	Mild	Probably related	Reappears	-

lanadelumab therapy may reduce the need for routine STP in certain patients with stable disease control, although access to on-demand medication remains essential.

Adverse Events

During the observation period, four adverse events were documented. Three were considered likely related to lanadelumab administration, while one was unrelated. All treatment-related adverse events were classified as mild and corresponded to reactions described in the instructions for use. A single serious adverse event was recorded in Patient 22, who experienced uterine bleeding requiring hospitalization. This event was not attributed to lanadelumab and was considered most likely secondary to discontinuation of tranexamic acid. Importantly, no treatment-related serious adverse events occurred during the study, and none of the reported adverse events led to therapy discontinuation (Table 4).

Discussion

The study demonstrated the effectiveness of lanadelumab as a long-term prophylactic therapy in patients with HAE caused by C1-esterase inhibitor deficiency. A substantial reduction in attack frequency, a marked decrease in the need for on-demand medication, and significant improvements in patients' quality of life were observed. Moreover, the favorable safety profile of lanadelumab was confirmed by the absence of treatment-related serious adverse events.

The efficacy and safety of lanadelumab have previously been established in a double-blind, randomized clinical trial, which identified 300 mg administered subcutaneously every 14 days as the optimal dosing regimen [5]. Real-world experience with lanadelumab has since been documented in several countries, including Canada, Germany, France, and the United Kingdom [13,15,22–23]. However, data from prolonged observation periods under routine clinical practice conditions remain limited. The present study addresses this gap by providing long-term real-world evidence from a Russian cohort undergoing lanadelumab prophylaxis.

The predominance of female patients (87%) in our cohort is noteworthy and consistent with demographic patterns observed in other real-world studies, where women represented 75% of participants in Canada, 72.6% in the United Kingdom, 68.8% in France, and 55.6% in Germany [8,15,23]. This imbalance may reflect both increased occurrence of HAE among females and the limitations associated with attenuated androgens, which are more frequently discontinued or avoided in women due to adverse effects [8]. However, danazol is an effective drug for long-term prophylaxis, generally better tolerated by male patients [24].

The majority of patients enrolled in this study (97%) were diagnosed with type I HAE. This predominance is influenced by natural distribution of type I and II in population of HAE patients.

The sustained reduction in attack frequency and improvement in disease control observed in our cohort, as well as in Canadian, British, French, and German real-world cohorts, highlights an important conclusion: lack of effectiveness of previous prophylactic therapies does not predict the ineffectiveness of lanadelumab.

Transitioning patients from prior long-term prophylactic regimens to lanadelumab remains a clinical challenge for which standardized guidance is currently lacking. In our cohort, one patient experienced uterine bleeding after discontinuing

tranexamic acid, illustrating the potential complexities associated with withdrawing prior therapies – particularly antifibrinolytics. Additional data are therefore needed to inform safe and effective strategies for tapering or discontinuing tranexamic acid. A similar discontinuation problem exists for attenuated androgens, prompting the initiation of the SHAERPA study, which aims to generate evidence-based recommendations for the discontinuation of danazol and related agents. Importantly, subgroup analyses by Fain et al. [15] indicate that the type or effectiveness of previous prophylactic therapy does not influence the subsequent therapeutic response to lanadelumab.

Lanadelumab is intended for self-administration according to established guidelines. In our study, 28 of 30 patients were successfully trained to self-inject the medication. All individuals who undertook self-administration performed the procedure correctly on the first attempt and continued to do so reliably thereafter. Among patients administering the drug at home, only one deviation from the prescribed dosing schedule occurred (a missed injection day), excluding cases related to drug-supply issues. By contrast, three deviations were recorded among patients receiving injections exclusively in medical facilities. These findings underscore the practical advantages of self-administration. Nevertheless, the adoption of flexible, patient-directed dosing regimens requires ongoing clinical monitoring to assess disease activity and quality of life, ensuring timely adjustment of treatment plans. Administration in healthcare settings, while necessary for some patients, may increase the likelihood of regimen interruptions due to factors such as appointment availability and institutional workflows, which may adversely impact therapeutic consistency.

A group of researchers from France analyzed patients' attitudes toward training in self-administration and toward ease of administration in a cohort of patients. In a French cohort, the majority of patients (71%, n = 54) reported that training in self-administration was very easy, with a mean difficulty score of 8.8 on a 10-point scale (1 = very difficult; 10 = very easy). Satisfaction with the ease of lanadelumab administration remained consistently high throughout follow-up, with mean scores of 8.1 at one month and 8.7 at six months (1 = not at all satisfied; 10 = very satisfied) [15].

The approved dosing regimen for lanadelumab recommends administration of 300 mg every 14 days, with the option to extend the interval to 28 days in patients achieving stable disease control (according to the official usage guidelines). Real-world evidence has demonstrated even greater flexibility, with some studies reporting successful interval extensions to 30 days and, in selected cases, up to 90 days [15]. Despite these observations, no standardized protocol for extending dosing intervals has yet been established. Buttgereit et al. proposed a pragmatic approach in which the first three injections are administered at 14-day intervals, followed by incremental 3-day extensions contingent upon sustained remission. This method allowed for individualized adjustment of the dosing interval for each patient. A study by Inmaculada Martinez-Saguer accessed the number of patients in the cohort able to extend the injection intervals for more than 17 days. Among 106 patients treated for no less than four months, 33 patients (31 %) administered lanadelumab with extended injection intervals (more than 17 days between injections). The average period of lanadelumab therapy before an attempt to extend the injection interval was 110 +/- 91 days. The proportion of patients with extended interval regimens increased to 48 % (among 44 patients receiving therapy for 12 months) after 12 months of lanadelumab therapy (Table 1). The average period of lanadelumab therapy before an attempt to extend the injection interval was 144 +/- 95 days. However, In Maculada Martinez-Saguer give no details on their approach to injection interval extension. [25] A group of researchers from Great Britain also analyzed the injection intervals in their cohort of patients. In a cohort of 60 patients, half (n = 30) were able to extend the dosing interval to at least three weeks. Among these, 27 patients transitioned to a 28-day regimen, and one patient successfully extended the interval to five weeks. The authors note that it took an average of 15.2 ± 12.1 weeks to extend the interval, but give no details on their approach to interval extension [13].

In another study, all patients were initially prescribed the standard lanadelumab regimen of 300 mg every 14 days. Dose adjustment was planned for a control visit 6 months. However, in two patients, the intervals were extended after 3 months due to severe pain at the injection sites. After 6 months of therapy, 10 of 39 remaining participants continued therapy with extended administration regimen: 3 patients received injections every 3 weeks and 6 patients – every 4 weeks. The extension of injection intervals was driven by good disease control, painful injections or by patient request. In contrast, in one instance the injection interval was reduced to 1 week, but the authors did not disclose the details of this clinical decision in the article [15].

In our study, interval extension was initiated after the first six injections. This strategy was based on the pharmacokinetic profile of lanadelumab, as steady-state concentrations are typically achieved by approximately day 70, aside from cases involving deviations from the recommended dosing schedule. A three-month period was also considered adequate for evaluating both therapeutic effectiveness and potential adverse effects. Thus, dosing intervals were extended by seven days in patients who achieved complete remission, followed by an additional seven-day extension if remission persisted, allowing for a final interval of 28 to 30 days. Considering the cost of therapy, the possibility of optimizing lanadelumab administration regimen by extending the injection intervals without diminishing the therapy effectiveness is of great pharmacoeconomic importance. We have developed a scheme for optimizing lanadelumab administration regimen based on our own observations and on literature data (Figure 7).

A primary aim of our study was to evaluate the effectiveness of lanadelumab as a long-term prophylactic therapy in routine clinical practice in the Russian Federation. The median monthly attack frequency per patient decreased from 7.0 (5.66; 12.0) attacks at baseline to 2.0 (0.0; 5.0) after 6 months of therapy. These findings are consistent with the results of the randomized

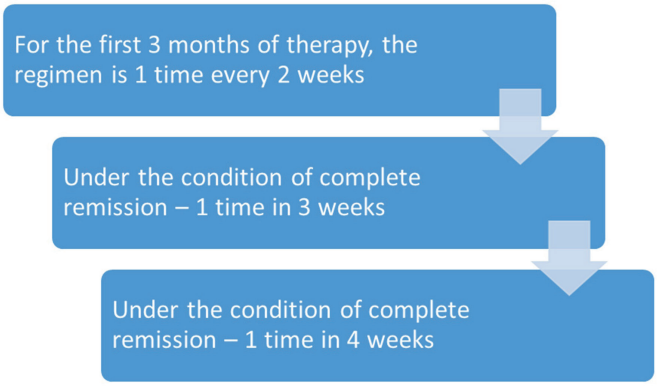

Figure 7 – Standardized protocol for extending lanadelumab dosing intervals

HELP (Hereditary Angioedema Long-term Prophylaxis) trial, which demonstrated a marked reduction in attack frequency among patients receiving lanadelumab prophylaxis [5]. Direct numerical comparison should be interpreted with caution because the present study reports median values, whereas the HELP trial reported mean attack rates. Furthermore, our cohort had a higher baseline disease burden and was evaluated under real-world clinical practice conditions, including individualized extension of dosing intervals in selected patients. Despite these differences, both studies demonstrated substantial and sustained reductions in HAE attack frequency during lanadelumab treatment.

A marked reduction was also observed in attacks of greater clinical severity. The median frequency of severe attacks decreased from 4 (2; 5) attacks per month at baseline to 0 (0; 0) after 6 months of therapy, while the median frequency of moderate attacks decreased from 3 (1; 5) to 1 (0; 2) attacks per month. These findings are directly comparable with those of the HELP trial, as both studies applied the same criteria for attack severity classification. In the HELP study, the combined rate of moderate and severe attacks after 6 months of treatment averaged 0.20 attacks per month in patients receiving lanadelumab every four weeks and 0.32 attacks per month in those receiving lanadelumab every two weeks [5].

Similarly, real-world data from France demonstrated a low attack burden during lanadelumab prophylaxis, with a mean monthly attack frequency of 0.16 attacks per patient among individuals receiving the standard 300 mg every-14-days regimen [15].

The need for on-demand treatment decreased significantly as early as the third month of therapy ($p = 0.0001$) and remained low throughout follow-up. This finding is consistent with the results of the HELP trial, in which the mean frequency of attacks requiring on-demand treatment was 0.26 attacks per month among patients receiving lanadelumab every 14 days and 0.53 attacks per month among those receiving lanadelumab every 28 days [5].

Lanadelumab's proven to be highly effective already at the 3 months visit. Heightened disease control remained consistent throughout the following months of therapy. This finding is crucial for real-world clinical practice, when the patient does not have strict selection criteria for comorbidities, concomitant medication and other characteristics that may be the exclusion criteria in the clinical trials.

These findings suggest meaningful long-term advantages despite the high cost of lanadelumab, including a reduction in expenditures associated with on-demand medications, missed workdays, medical consultations, and hospitalizations. It is also conceivable that the improved disease control achieved with lanadelumab may reduce the cost of short-term prophylaxis and, importantly, enhance the safety of urgent invasive procedures that could otherwise pose life-threatening risks in the absence of adequate prophylactic measures. Nevertheless, these potential economic and clinical benefits require further investigation and more comprehensive validation.

Our study demonstrated a statistically significant improvement in disease control three months after the initiation of lanadelumab therapy, as reflected by the AECT scores (Fig. 4). Notably, this enhanced level of control was maintained between the third and sixth months, indicating that lanadelumab not only achieves rapid stabilization of disease activity but also sustains it over time. Across all assessment points, the proportion of patients achieving high levels of disease control ranged from 89% to 100% according to AECT results.

HAE significantly burdens patients' lives. Highly effective drugs like danazol have been in used for this condition; however, they do not improve patient's overall quality of life given the development of adverse events. Many patients stop LTP in routine life because the burden of the medication intake may disturb even greater than the disease itself. Therefore, upon evaluating the effectiveness of therapy in real-world practice, we paid great attention to assessing quality of life. In our study lanadelumab therapy resulted in a significant enhancement in quality of life after only 3 months, the result comparable to the HELP study and in other cohort studies [5,7,22].

One of the most important practical issues regarding lanadelumab therapy is short-term prophylaxis before invasive interventions. According to the HELP and HELP OLE studies, the number of invasive procedures resulting in HAE attacks was comparable in patients who used short-term prophylaxis and those who did not. In our study, 36 interventions were performed without STP with HAE attack developing only in two instances, while 7 interventions were performed with STP with one following HAE attack. The data obtained is insufficient to advise against STP. However, prolonged observation period may change the approaches to STP in patients receiving lanadelumab with complete control over the disease symptoms and a stable access to acute attack management drugs in sufficient quantities. Regardless, the access to acute attack management drugs is mandatory [6,7].

Our findings confirm that lanadelumab maintains a favorable safety profile, consistent with previously published data [5,7]. All observed adverse events corresponded to those described in the product information and were classified as mild. Importantly, none of these events interfered with patients' ability to perform self-administration.

This study represents the first real-world investigation of lanadelumab use in routine clinical practice in the Russian Federation. The present report summarizes findings from a 24-month observation of 30 patients, demonstrating both the effectiveness and safety of lanadelumab in a real-world setting. In addition to confirming its clinical benefits, our results provide valuable insights into practical aspects of therapy, including strategies for extending dosing intervals, the safety of medical and dental interventions performed during treatment, and the feasibility of home-based self-administration.

Conclusion

Current HAE management guidelines identify the primary therapeutic goals as complete prevention of attacks, sustained disease control, and preservation of patients' quality of life [8]. Lanadelumab—approved globally in 2018 and in Russia in 2021—has demonstrated, through its convenient subcutaneous administration and favorable safety profile, a strong capacity to meet these objectives. Our findings further support its role as an effective and well-tolerated long-term prophylactic option in routine clinical practice.

Study Limitations

As HAE is a rare (orphan) disease, a formal sample size calculation was not possible to perform due to the limited number of available patients. Consequently, all individuals with HAE caused by C1-inhibitor deficiency who met the inclusion criteria were enrolled. While this approach enabled the inclusion of the entire accessible patient population, it inherently restricts the representativeness of the sample and limits the generalizability

of the findings to broader HAE populations beyond the study cohort.

Supplementary materials

The Supplementary information includes:

• Supplementary Table S1. Data about the patients enrolled in the study;

• Supplementary Table S2. Analysis of baseline and prior long-term prophylactic therapies before initiation of lanadelumab.

This supplemental materials have been provided by the authors to give readers additional information about their work.

The file can be accessed using: https://www.editorialpark.com/download/article-supp/768/Supplementary-materials.docx.

Author Contributions: Conceptualization, methodology, supervision – E. L. and T. L.; E. L. and I. M. and E. B. and D. F., E.V. and E. G. and L. A. and D. D. and E. V. and O. I. and M. K. and N. K. and I. L. and N. N. and T. N. — investigation, resources; I. M. — project administration, data curation, validation, formal analysis; E. L. and I. M. — writing – original draft preparation; E. L. and T. L. and A. S. — writing – review and editing. All authors have read and agreed to the published version of the manuscript.

Disclosures: The authors have no conflicts of interest.

Acknowledgments: None.

Funding: This study was supported by an Investigator-Initiated Research grant IISR-2021-200085 from Takeda Pharmaceuticals LLC. The sponsors of this study had no role in the study design, data collection, analysis, interpretation, or preparation of the manuscript.

Data availability statement: All raw data underlying the findings of this study can be obtained from the corresponding author upon reasonable request.

Artificial Intelligence (AI) Disclosure Statement: Artificial intelligence was used to translate and edit the text to improve its readability in English, ensure efficient work under human supervision.

References

1. Aygören-pürsün E, Magerl M, Maetzel A, Maurer M. Epidemiology of Bradykinin-mediated angioedema: a systematic investigation of epidemiological studies. *Orphanet J Rare Dis*. 2018; May 4;13(1): 1–9. https://doi.org/10.1186/s13023-018-0815-5.
2. Cicardi M, Aberer W, Banerji A, Bas M, Bernstein JA, Bork K, Caballero T, Farkas H, Grumach A, Kaplan AP, Riedl MA, Triggiani M, Zanichelli A, Zuraw B; HAWK under the patronage of EAACI (European Academy of Allergy and Clinical Immunology). Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014: May; 69(5):602-616. https://doi.org/10.1111/all.12380.
3. Bliznetz EA, Viktorova EA, Vishneva EA, Dzobava EM, Il'ina NI, Kuzmenko NB, Latysheva EA, Latysheva TV, Manto IA, Namazova-Baranova LS, Nenasheva NM, Pampura AN, Polyakov AV, Selimzianova LR, Shcherbina AY. Hereditary angioedema. Clinical Guidelines (D84.1). *Russian Journal of Allergy.* 2021;18(2):77–114.
4. Li HH, Mycroft S, Christiansen S, Wood DN, Feuersenger H, Pawaskar D, Jacobs I. Subcutaneous C1-esterase inhibitor to prevent hereditary angioedema attacks: Safety findings from the COMPACT trial. *Allergy Asthma Proc*. 2018 Sep 14;39(5):365-370. https://doi.org/10.2500/aap.2018.39.4164.
5. Banerji A, Riedl MA, Bernstein JA, Cicardi M, Longhurst HJ, Zuraw BL, Busse PJ, Anderson J, Magerl M, Martinez-Saguer I, Davis-Lorton M, Zanichelli A, Li HH, Craig T, Jacobs J, Johnston DT, Shapiro R, Yang WH, Lumry WR, Manning ME, Schwartz LB, Shennak M, Soteres D, Zaragoza-Urdaz RH, Gierer S, Smith AM, Tachdjian R, Wedner HJ, Hebert J, Rehman SM, Staubach P, Schranz J, Baptista J, Nothaft W, Maurer M; HELP Investigators. Effect of Lanadelumab Compared With Placebo on Prevention of Hereditary Angioedema Attacks: A Randomized Clinical Trial. *JAMA*. 2018 Nov 27;320(20):2108-2121. https://doi.org/10.1001/jama.2018.16773. Erratum in: *JAMA*. 2019 Apr 23;321(16):1636. https://doi.org/10.1001/jama.2019.4254.
6. Riedl MA, Bernstein JA, Craig T, Banerji A, Magerl M, Cicardi M, Longhurst HJ, Shennak MM, Yang WH, Schranz J, Baptista J, Busse PJ. An open-label study to evaluate the long-term safety and efficacy of lanadelumab for prevention of attacks in hereditary angioedema: design of the HELP study extension. *Clin Transl Allergy.* 2017 Oct 6(7):36. https://doi.org/10.1186/s13601-017-0172-9.
7. Banerji A, Bernstein JA, Johnston DT, Lumry WR, Magerl M, Maurer M, Martinez-Saguer I, Zanichelli A, Hao J, Inhaber N, Yu M, Riedl MA; HELP OLE Investigators. Long-term prevention of hereditary angioedema attacks with lanadelumab: The HELP OLE Study. *Allergy*. 2022 Mar;77(3):979-990. https://doi.org/10.1111/all.15011.
8. Maurer M, Magerl M, Betschel S, Aberer W, Ansotegui IJ, Aygören-Pürsün E, Banerji A, Bara NA, Boccon-Gibod I, Bork K, Bouillet L, Boysen HB, Brodszki N, Busse PJ, Bygum A, Caballero T, Cancian M, Castaldo A, Cohn DM, Csuka D, Farkas H, Gompels M, Gower R, Grumach AS, Guidos-Fogelbach G, Hide M, Kang HR, Kaplan AP, Katelaris C, Kiani-Alikhan S, Lei WT, Lockey R, Longhurst H, Lumry WR, MacGinnitie A, Malbran A, Martinez Saguer I, Matta JJ, Nast A, Nguyen D, Nieto-Martinez SA, Pawankar R, Peter J, Porebski G, Prior N, Reshef A, Riedl M, Ritchie B, Rafique Sheikh F, Smith WB, Spaeth PJ, Stobiecki M, Toubi E, Varga LA, Weller K, Zanichelli A, Zhi Y, Zuraw B, Craig T. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2021 revision and update. *Allergy*. 2022 Jul;77(7):1961-1990. https://doi.org/10.1111/all.15214.
9. Latysheva E, Latysheva T, Bodnya O, Demina D, Kuzmenko N, Fedotova N, Pampura A, Fomina D, Ukhanova O, Sizyakina L, Totolian A, Milichkina A. Resolution on the results of the Council of Experts on the Long-term Prophylaxis of Hereditary Angioedema in Russia [in Russian]. *Russian Journal of Allergy*. 2021; 18(3):126–130.
10. Clinical Guidelines. Hereditary angioedema, [Internet]. 2024 [cited 2023 Aug 12] Avaliable from: https://cr.minzdrav.gov.ru/view-cr/267_2.

11. Riedl MA, Maurer M, Bernstein JA, Banerji A, Longhurst HJ, Li HH, Lu P, Hao J, Juethner S, Lumry WR; HELP Investigators. Lanadelumab demonstrates rapid and sustained prevention of hereditary angioedema attacks. *Allergy*. 2020 Nov;75(11):2879-2887. https://doi.org/10.1111/all.14416.
12. Tachdjian R, Banerji A, Busse PJ, Agmon-Levin N, Anderson J, Cancian M, Spadaro G, Enciu C, Estepan DN, Khutoryansky N, Jain S, Recke A. Effective long-term prophylaxis with lanadelumab in adolescents with hereditary angioedema: EMPOWER/ENABLE. *Pediatr Allergy Immunol.* 2025 Apr;36(4):e70072. https://doi.org/10.1111/pai.70072.
13. Dorr AD, Chopra C, Coulter TI, Dempster J, Dziadzio M, El-Shanawany T, Garcez T, Gompels M, Herriot R, Jain R, Levi M, Lorenzo L, Makki I, Mapazire E, Murng SHK, Noorani S, Savic S, Steele CL, Symons C, Tarzi M, Yong PFK, Kiani-Alikhan S. Lanadelumab for the prevention of hereditary angioedema attacks: A real-world UK audit. *Allergy*. 2023 May;78(5):1369-1371. https://doi.org/10.1111/all.15620.
14. Martinez-Saguer I, Knop J, Flemming A, Thomann M, Maurer M. Real World treatment patterns of hereditary angioedema with lanadelumab in Germany: A prescription data analysis. *J Dtsch Dermatol Ges.* 2022 Aug;20(8):1127-1129. https://doi.org/10.1111/ddg.14785.
15. Fain O, Du-Thanh A, Gobert D, Launay D, Inhaber N, Boudjemia K, Aubineau M, Sobel A, Boccon-Gibod I, Weiss L, Bouillet L. Long-term prophylaxis with lanadelumab for HAE: authorization for temporary use in France. *Allergy Asthma Clin Immunol.* 2022 Apr 1;18(1):30. https://doi.org/10.1186/s13223-022-00664-4.
16. Iaboni A, Kanani A, Lacuesta G, Song C, Kan M, Betschel SD. Impact of lanadelumab in hereditary angioedema: a case series of 12 patients in Canada. *Allergy Asthma Clin Immunol.* 2021 Jul 23;17(1):78. https://doi.org/10.1186/s13223-021-00579-6.
17. Weller K, Magerl M, Peveling-Oberhag A, Martus P, Staubach P, Maurer M. The Angioedema Quality of Life Questionnaire (AE-QoL) - assessment of sensitivity to change and minimal clinically important difference. *Allergy*. 2016 Aug;71(8):1203-9. https://doi.org/10.1111/all.12900.
18. Weller K, Groffik A, Magerl M, Tohme N, Martus P, Krause K, Metz M, Staubach P, Maurer M. Development, validation, and initial results of the Angioedema Activity Score. *Allergy*. 2013 Sep;68(9):1185-92. https://doi.org/10.1111/all.12209.
19. Forjaz MJ, Ayala A, Caminoa M, Prior N, Pérez-Fernández E, Caballero T; DV-HAE-QoL Study Group. HAE-AS: A Specific Disease Activity Scale for Hereditary Angioedema With C1-Inhibitor Deficiency. *J Investig Allergol Clin Immunol.* 2021 Jun 22;31(3):246-252. https://doi.org/10.18176/jiaci.0479.
20. Weller K, Donoso T, Magerl M, Aygören-Pürsün E, Staubach P, Martinez-Saguer I, Hawro T, Altrichter S, Krause K, Siebenhaar F, Metz M, Zuberbier T, Freier D, Maurer M. Validation of the Angioedema Control Test (AECT)-A Patient-Reported Outcome Instrument for Assessing Angioedema Control. *J Allergy Clin Immunol Pract.* 2020 Jun;8(6):2050-2057.e4. https://doi.org/10.1016/j.jaip.2020.02.038.
21. Bygum A, Busse P, Caballero T, Maurer M. Disease Severity, Activity, Impact, and Control and How to Assess Them in Patients with Hereditary Angioedema. *Front Med (Lausanne).* 2017 Dec 4;(4):1-7. https://doi.org/10.3389/fmed.2017.00212.
22. Buttgereit T, Vera C, Weller K, Gutsche A, Grekowitz EM, Aykanat S, Wahn V, Krüger R, Maurer M, Magerl M. Lanadelumab Efficacy, Safety, and Injection Interval Extension in HAE: A Real-Life Study. *J Allergy Clin Immunol Pract.* 2021 Oct;9(10):3744-3751. https://doi.org/10.1016/j.jaip.2021.04.072.
23. Abuzakouk M, Ghorab O, Al-Hameli H, Salvo F, Grandon D, Maurer M. Using an extended treatment regimen of lanadelumab in the prophylaxis of hereditary angioedema: a single-centre experience. *World Allergy Organ J.* 2022 Jul 12;15(7):100-664. https://doi.org/10.1016/j.waojou.2022.100664.
24. Maurer M, Magerl M. Long-term prophylaxis of hereditary angioedema with androgen derivates: a critical appraisal and potential alternatives. *J Dtsch Dermatol Ges.* 2011 Feb;9(2):99-107. English, German. https://doi.org/10.1111/j.1610-0387.2010.07546.x.
25. Martinez-Saguer I, Knop J, Flemming A, Thomann M, Maurer M. Real World treatment patterns of hereditary angioedema with lanadelumab in Germany: A prescription data analysis. *J Dtsch Dermatol Ges.* 2022 Aug;20(8):1127-1129. https://doi.org/10.1111/ddg.14785.