Attack-Free Status of Patients With Hereditary Angioedema (HAE) During Extended Treatment With Lanadelumab in the HELP OLE Study

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Background

- Hereditary angioedema (HAE) is a rare disease characterized by recurrent, unpredictable, and potentially life-threatening attacks of swelling of subcutaneous and submucosal tissues.[1]
- Lanadelumab is a fully human monoclonal antibody[2] approved in several countries for the prevention of HAE attacks.*
  - In the phase 3 HELP Study (NCT02586805), ~44% of patients were attack free during 26 weeks (182 days) of treatment with lanadelumab 300 mg administered every 2 weeks (q2wks). 77% were attack free during steady state (days 70–182).[3]
- Patients who completed the HELP Study (rollovers) and patients who did not participate in the HELP Study (nonrollovers) were enrolled in the ongoing HELP open-label extension (OLE; NCT02741596).[4]
  - Patients will receive lanadelumab 300 mg q2wks for up to 33 months in the HELP OLE.

Objective

- Patient attack-free status was evaluated in this interim analysis of data from the HELP OLE.

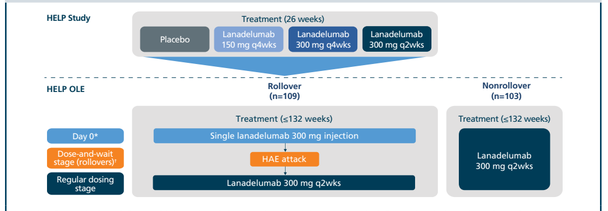
Methods

Patients
- Males and females ≥12 years of age with confirmed HAE type 1/2.
  - Rollover patients had a baseline attack rate of ≥1 attack/4 weeks during the run-in period of the HELP Study.
  - Nonrollover patients had a baseline attack rate of ≥1 attack/12 weeks as derived from patient-reported attack history.

Treatments
- Rollover patients continued immediately into the HELP OLE after completing HELP (**Figure 1**).
  - Patients received their first lanadelumab 300 mg dose on day 0 then underwent a dose-and-wait stage.
  - Patients received their second lanadelumab dose after the first attack, followed by 300 mg q2wks (regular dosing stage).
- Nonrollover patients received lanadelumab 300 mg q2wks starting on day 0.

Analysis
- Analyses were performed using the safety population.
- The treatment period analyzed for rollover patients was the regular dosing stage.
- The treatment period for nonrollover patients started on day 0.
- Attack rates during the treatment period were compared with baseline.
- Data collected up to August 31, 2018, were analyzed.

Figure 1: Design of the HELP OLE



HAE = hereditary angioedema; OLE = open-label extension; q2wks = every 2 weeks; q4wks = every 4 weeks. Rollover patients had a run-in attack rate of ≥1 in 4 weeks in the HELP Study; nonrollover patients had a baseline attack rate of ≥1 in 12 weeks. *For rollover patients, day 0 of the OLE coincided with week 26, day 182 of the HELP Study. For nonrollover patients, the first dose was administered on day 0. †Regardless of when the first HAE attack occurred, there was a minimum of 10 days between the first and the second open-label dose.

Results

Patient disposition and baseline characteristics

- 212 patients were enrolled in the study (n=109 rollovers and n=103 nonrollovers; **Table 1**).
  - Mean (range) time on study was 19.7 (0–26.1) months.
    - For rollovers, mean (range) time in the regular dosing stage was 18.5 (3.1–21.4) months.
  - 91.0% of patients completed ≥12 months on study.
  - 39.2% of patients (including 50.5% of rollovers) had a baseline attack rate ≥3 attacks/4 weeks.

Table 1: Patient demographics and baseline characteristics

Characteristic	Rollovers n=109	Nonrollovers n=103	Total N=212
Mean (range) age, years	41.9 (13–74)	39.5 (12–76)	40.7 (12–76)
Female, n (%)	75 (68.8)	68 (66.0)	143 (67.5)
White, n (%)	99 (90.8)	99 (96.1)	198 (93.4)
Mean ± SD BMI, kg/m²	28.28 ± 6.84	28.42 ± 7.52	28.35 ± 7.16
History of laryngeal attacks, n (%)	67 (61.5)	63 (61.2)	130 (61.3)
History of LTP use, n (%)	62 (56.9)	63 (61.2)	125 (59.0)
Mean ± SD baseline attack rate, attacks/4 weeks	3.52 ± 2.48	2.55 ± 2.75	3.05 ± 2.66
Baseline attack rate group, attacks/4 weeks, n (%)			
<1	0	25 (24.3)	25 (11.8)
1 to <2	35 (32.1)	39 (37.9)	74 (34.9)
2 to <3	19 (17.4)	11 (10.7)	30 (14.2)
≥3	55 (50.5)	28 (27.2)	83 (39.2)
Time on study, months, n (%)*			
≥12	99 (90.8)	94 (91.3)	193 (91.0)
≥24	21 (19.3)	6 (5.8)	27 (12.7)

BMI = body mass index; LTP = long-term prophylaxis.
*The start of exposure was defined as the first dose date.

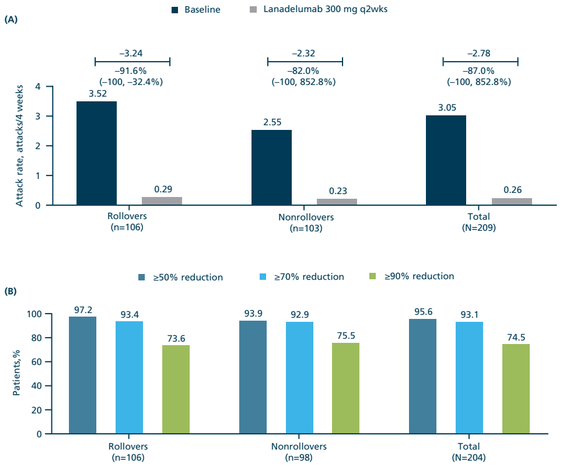
Lanadelumab reduced the rate of HAE attacks

- The attack rate was reduced by an average of 87.0% overall compared with baseline (**Figure 2A**).
- ~93% of patients achieved an attack reduction of ≥70% from baseline, and ~75% of patients achieved a reduction of ≥90% (**Figure 2B**).
- 92.8% of patients achieved an attack rate of <1 attack/month during the treatment period.

Extended attack-free periods during lanadelumab treatment

- On average, patients were attack free for most days during the treatment period.
  - There was a mean (range) of 27.3 (14.4–28.0) attack-free days/4 weeks (97.5% [51.6–100]; **Table 2**).
- The maximum duration of the attack-free period was ≥6 months in 78.0% of patients (6 to <12 months and ≥12 months groups) and ≥12 months in 57.9% of patients (**Figure 3**).
- The mean (range) duration of the attack-free period was 10.40 (0.12–24.61) months.

Figure 2: Reduction in attack rate during lanadelumab treatment in the HELP OLE



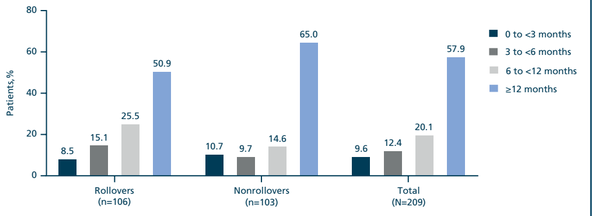
OLE = open-label extension; q2wks = every 2 weeks.
(A) Attack rates were reduced in patients treated with lanadelumab 300 mg q2wks compared with baseline. Values above bars are mean attack rates. Mean change from baseline and mean (minimum, maximum) percentage change from baseline are shown. **(B)** Proportion of patients who achieved an attack rate reduction versus baseline of ≥50%, 70%, and 90%. 3 rollovers who were still in the dose-and-wait period at the time of the data cut, or who discontinued during the dose-and-wait period, were not included in the analyses. Nonrollovers who had a 3-month historical attack rate of 0 were excluded from the responder analysis.

Table 2: Summary of attack-free period

	Rollovers n=106	Nonrollovers n=103	Total N=209
Number of attack-free days/4 weeks			
Mean (SD)	27.3 (1.7)	27.4 (1.8)	27.3 (1.7)
Range	14.4–28.0	15.2–28.0	14.4–28.0
Average duration of attack-free period, months*			
Mean (SD)	9.37 (7.34)	11.47 (8.12)	10.40 (7.78)
Range	0.12–24.61	0.14–24.54	0.12–24.61
Maximum duration of attack-free period, months*			
Mean (SD)	12.21 (6.40)	14.35 (7.34)	13.27 (6.94)
Range	0.50–24.82	0.36–25.29	0.36–25.29

*A month was defined as 28 days.

Figure 3: Maximum duration of attack-free period



3 rollovers who were still in the dose-and-wait period at the time of the data cut, or who discontinued during the dose-and-wait period, were not included in the analysis. For each patient, the maximum duration of attack-free period was derived by taking the maximum of the individual attack-free periods experienced.

Conclusions

- **Patients experienced extended attack-free periods during treatment with lanadelumab 300 mg q2wks.**
  - **~8/10 patients had a maximum duration of attack-free period of ≥6 months.**
  - **~6/10 patients had a maximum duration of attack-free period of ≥12 months.**
- **On average, 97.5% of days each month during treatment were attack free.**
- **These results support the efficacy of lanadelumab over an extended treatment period.**

*Lanadelumab is approved as prophylaxis to prevent attacks of HAE in patients ≥12 years of age in the United States and for the routine prevention of attacks in patients ≥12 years of age in Canada.[5,6] Lanadelumab also was approved in the European Union, Australia, and Brazil for the routine prevention of recurrent attacks of HAE in patients ≥12 years of age,[7,8] and in Switzerland for the long-term prevention of attacks of HAE in patients ≥12 years of age.[9]

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