# Satisfaction with Sebetralstat for HAE Attacks Stratified by LTP Use and Previous On-demand Treatments

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## Background

- Global hereditary angioedema (HAE) guidelines recommend early use of on-demand treatment upon recognition of an HAE attack to reduce morbidity and prevent mortality[1-4]
- Until recently, available on-demand treatments were only administered parenterally (via intravenous infusion or subcutaneous injection); the burden associated with parenteral administration often results in delayed treatment[5]
- Sebetralstat, an oral, on-demand plasma kallikrein inhibitor, was recently approved for the treatment of HAE attacks in patients aged ≥12 years[6]

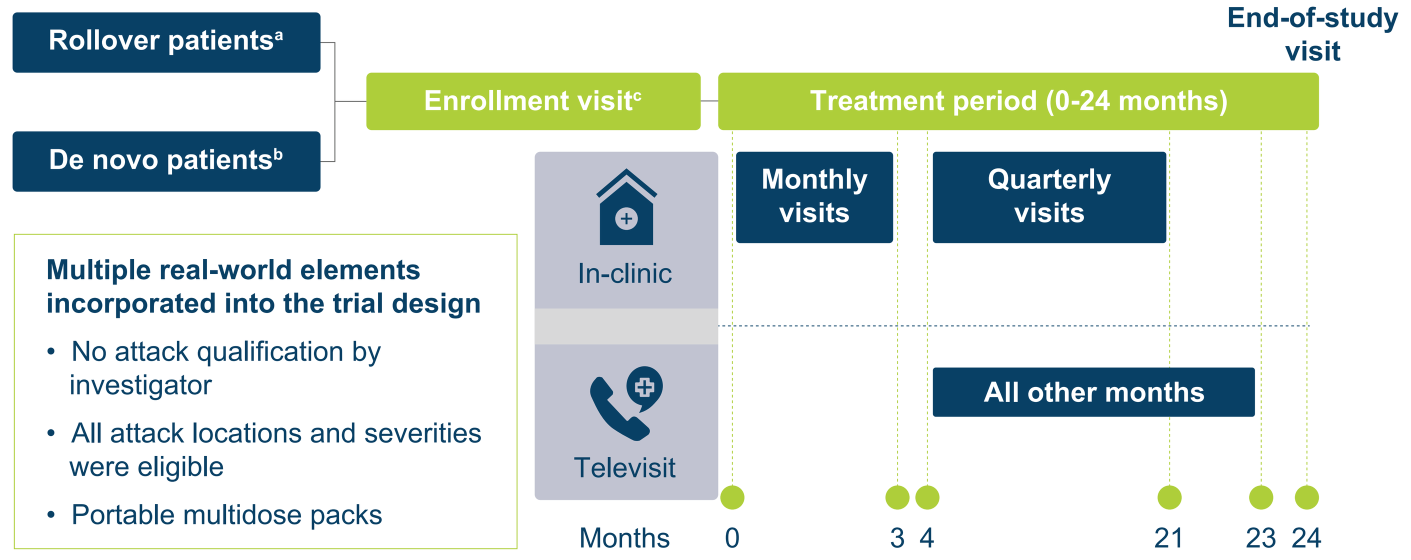
## Objective

- To assess treatment satisfaction with sebetralstat in subgroups of participants in KONFIDENT-S based on long-term prophylaxis (LTP) use and prior conventional injectable on-demand treatment

## Methods

- KONFIDENT-S is an ongoing, 2-year, multicenter, open-label extension trial (NCT05505916; EudraCT: 2021-001176-42; **Figure 1**)
  - Eligible patients were aged ≥12 years with HAE due to C1-inhibitor deficiency (HAE-C1INH) and had ≥2 documented attacks within 3 months before enrollment, or had completed the phase 3 KONFIDENT trial (NCT05259917)
  - Patients using LTP were eligible to participate, provided they had been on a stable dose regimen of a protocol-allowed LTP for ≥3 months. A protocol amendment after study initiation allowed participants to start, stop, or change LTP agents during the trial (at investigator discretion)
  - If preferred by the participant, HAE attacks could be treated with conventional injectable on-demand treatment instead of with sebetralstat
- Treatment satisfaction was assessed 24 hours after the first dose of sebetralstat for each attack using a 7-point Likert scale (**Figure 2**)
  - No dissatisfaction was defined as a score of either neutral (0) or satisfied (+1, +2, or +3)

### Figure 1. KONFIDENT-S OLE Trial Design




NCT05505916, EudraCT: 2021-001176-42.
[a]Completed the phase 3 KONFIDENT trial.
[b]All other patients, including those who participated in the phase 2 trial.
[c]For de novo patients, the enrollment visit was a screening visit.

### Figure 2. Treatment Satisfaction Rating (7-point Likert Scale)

| –3 | –2 | –1 | 0 | +1 | +2 | +3 |
|---|---|---|---|---|---|---|
| Extremely dissatisfied | Very dissatisfied | Dissatisfied | Neutral | Satisfied | Very satisfied | Extremely satisfied |

## Results

### Participants and Attacks

- As of September 30, 2025, 115 participants in KONFIDENT-S provided satisfaction data for 1593 attacks treated with sebetralstat (**Table 1**; **Table 2**)
  - Of these, 85 participants were receiving on-demand treatment only (1227 attacks) and 30 participants were receiving LTP + on-demand treatment (366 attacks)
  - Among those receiving LTP, 27 participants received a plasma kallikrein inhibitor (berotralstat or lanadelumab; 314 attacks) and 3 received C1INH (52 attacks)

### Table 1. Participant Demographics[a]

| | Overall N=115 | On-demand only n=85 | LTP + on-demand n=30 |
|---|---|---|---|
| **Age, median (IQR), years** | 36.0 (22.0-49.0) | 35.0 (20.0-47.0) | 44.0 (28.0-56.0) |
| **Sex, female, n (%)** | 78 (67.8) | 55 (64.7) | 23 (76.7) |
| **Race, White, n (%)** | 86 (74.8) | 65 (76.5) | 21 (70.0) |
| **BMI, median (IQR), kg/m²** | 25.1 (22.3-30.0) | 24.4 (22.1-28.0) | 26.2 (24.2-31.3) |
| **HAE-C1INH-Type1, n (%)** | 106 (92.2) | 80 (94.1) | 26 (86.7) |

[a]For participants with treatment satisfaction data available.
Data cutoff: September 30, 2025.
BMI, body mass index; HAE-C1NH-Type1, hereditary angioedema due to C1 inhibitor deficiency; IQR, interquartile range; LTP, long-term prophylaxis.

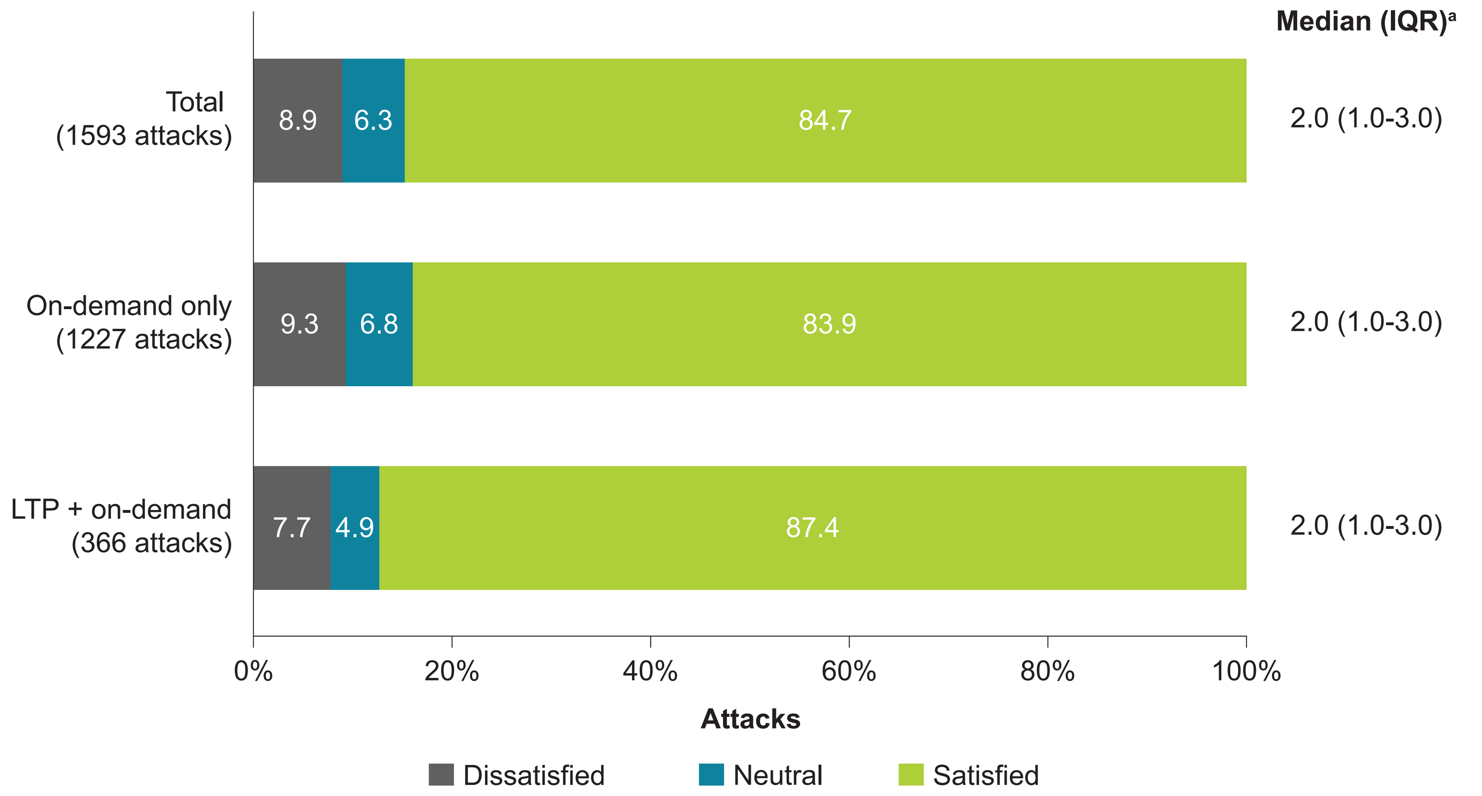
### Table 2. Attack Characteristics in Sebetralstat-treated Attacks

| | Overall N=1593 | On-demand only n=1227 | LTP + on-demand n=366 |
|---|---|---|---|
| **Baseline severity (PGI-S), n (%)[a]** | | | |
| Mild[b] | 661 (41.5) | 555 (45.2) | 106 (29.0) |
| Moderate | 682 (42.8) | 528 (43.1) | 154 (42.1) |
| Severe/very severe | 249 (15.6) | 143 (11.7) | 106 (29.0) |
| **Primary pooled attack location, n (%)[a]** | | | |
| Mucosal[c] | 671 (42.1) | 459 (37.4) | 212 (57.9) |
| Laryngeal | 28 (1.8) | 11 (0.9) | 17 (4.6) |
| Subcutaneous only[c] | 921 (57.9) | 767 (62.6) | 154 (42.1) |
| **Time to treatment, median (IQR), minutes** | 20.0 (1.0-77.0) | 27.0 (1.0-95.0) | 10.0 (1.0-44.0) |
| **Attacks treated with a second dose, n (%)[d]** | 351 (22.0) | 274 (22.3) | 77 (21.0) |
| **Attacks treated with conventional treatment, n (%)[d]** | 80 (5.0) | 64 (5.2) | 16 (4.4) |

[a]Baseline severity and primary attack location data missing for 1 attack in a participant receiving on-demand treatment only.
[b]Includes attacks with baseline PGI-S rating of 'None': 20 (1.3%) attacks overall; 19 attacks (1.5%) in participants receiving on-demand treatment only; 1 attack (0.3%) in participants receiving LTP + on-demand.
[c]Mucosal: attacks with primary location of "Abdomen" and/or "Larynx/throat"; subcutaneous: other attacks not involving the mucosal locations.
[d]Within 12 hours.
Data cutoff: September 30, 2025.
IQR, interquartile range; LTP, long-term prophylaxis; PGI-S, Patient Global Impression of Severity.

### Treatment Satisfaction

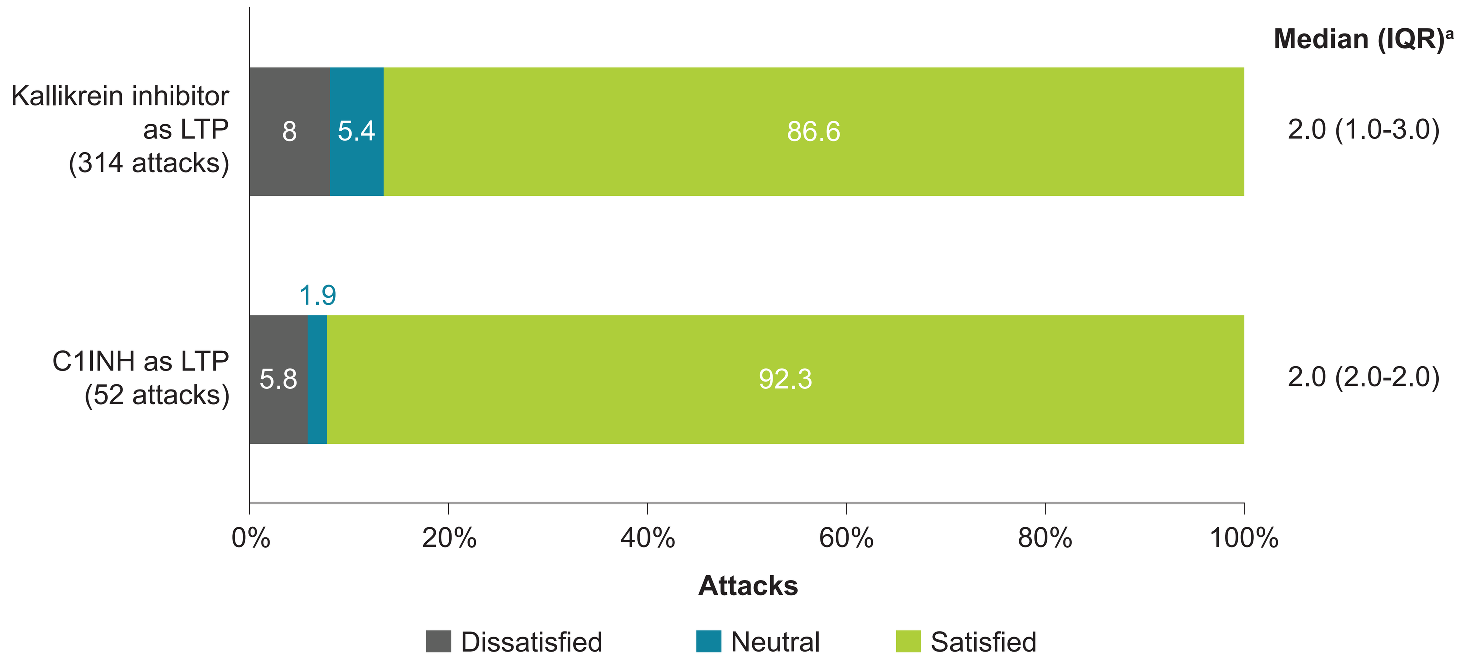
#### Figure 3. Satisfaction With Sebetralstat for Each Attack by LTP Use




[a]Based on the 7-point Likert satisfaction scale, from -3 to +3.
Data cutoff: September 30, 2025.
IQR, interquartile range; LTP, long-term prophylaxis.

- No dissatisfaction was reported in 90.7% and 92.3% of sebetralstat-treated attacks among participants receiving on-demand treatment only and those receiving LTP, respectively (**Figure 3**)
  - Participants reported being very or extremely satisfied with sebetralstat for 65.6% of attacks (63.1% in participants receiving on-demand treatment only and 73.8% in participants receiving LTP + on-demand treatment)

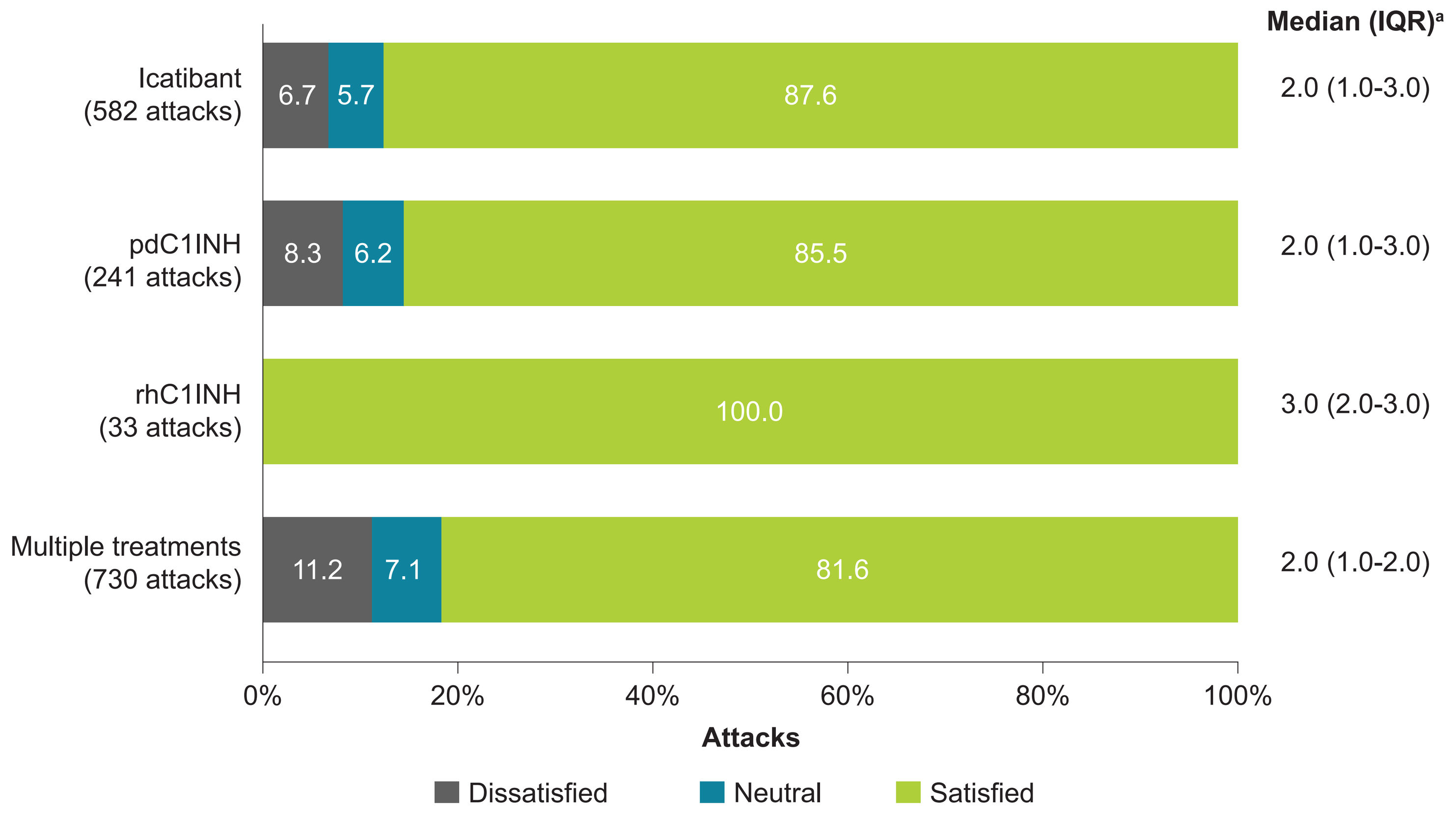
#### Figure 4. Satisfaction With Sebetralstat for Each Attack by LTP Mechanism of Action




[a]Based on the 7-point Likert satisfaction scale, from -3 to +3.
Data cutoff: September 30, 2025.
C1INH, C1 inhibitor; IQR, interquartile range; LTP, long-term prophylaxis.

- No dissatisfaction was reported in 92.0% of sebetralstat-treated attacks among participants receiving a kallikrein-inhibiting LTP agent and in 94.2% of attacks among participants receiving C1INH as LTP (**Figure 4**)
  - Participants reported being very or extremely satisfied with sebetralstat for 72.3% of attacks in those receiving kallikrein-inhibiting LTP and 82.7% of attacks in those receiving C1INH as LTP

#### Figure 5. Satisfaction With Sebetralstat for Each Attack by Previously Used On-demand Treatment




[a]Based on the 7-point Likert satisfaction scale, from -3 to +3.
Data cutoff: September 30, 2025.
IQR, interquartile range; pdC1INH, plasma-derived C1 inhibitor; rhC1INH, recombinant human C1 inhibitor.

- For participants who switched from icatibant, pdC1INH, rhC1INH, and multiple on-demand treatments, no dissatisfaction was reported for 93.3%, 91.7%, 100%, and 88.8% of attacks treated with sebetralstat, respectively (**Figure 5**)
  - Participants reported being very or extremely satisfied with sebetralstat for 70.3%, 68.9%, 94.0%, and 59.7% of attacks in those who switched from icatibant, pdC1INH, rhC1INH, and multiple on-demand treatments, respectively

## Conclusions

- **Overall, the median satisfaction score for attacks treated with sebetralstat was 2.0, with participants being very or extremely satisfied for 65.6% of attacks**
- **No dissatisfaction was reported for the majority of attacks treated with sebetralstat (88.8%-100%), regardless of LTP use, LTP regimen, or prior on-demand therapy used**

### References

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