Satisfaction with Sebetralstat for HAE Attacks in Patients Switching from Parenteral On-demand Treatments in KONFIDENT-S

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Rationale

- Global hereditary angioedema (HAE) guidelines recommend the early use of on-demand treatment upon recognition of an HAE attack to reduce morbidity and prevent mortality[1,2]
- Until recently, available on-demand treatments were only administered parenterally (via intravenous infusion or subcutaneous injection), which has been previously shown to delay treatment[3]
- Sebetralstat, an oral, on-demand plasma kallikrein inhibitor, was recently approved for the treatment of HAE attacks in patients aged ≥12 years[4-6]
- Here, we present interim findings from the KONFIDENT-S open-label extension trial on time to beginning of symptom relief and treatment satisfaction from patients who switched from icatibant, plasma-derived C1-inhibitor (pdC1INH), recombinant C1-inhibitor (rC1INH), or multiple parenteral on-demand treatments to oral sebetralstat

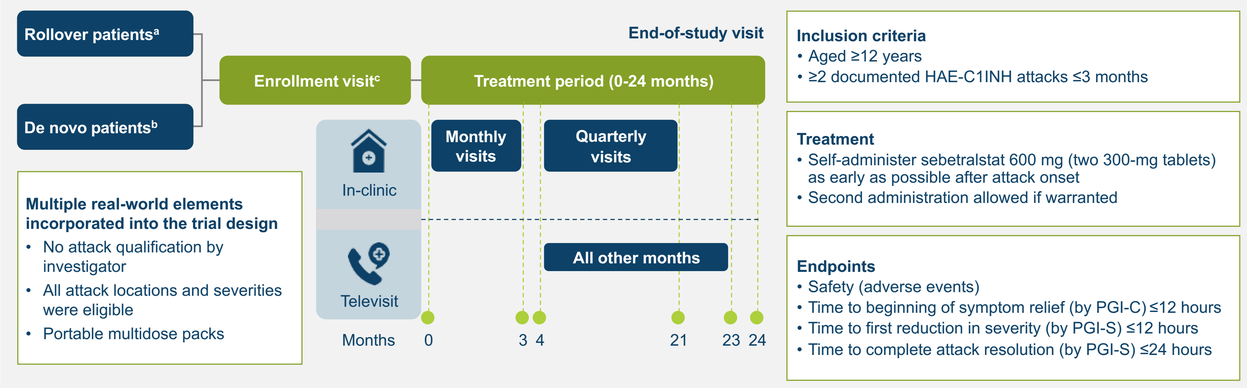
Methods

- KONFIDENT-S is an ongoing, 2-year, multicenter, open-label extension trial (NCT05505916, EudraCT: 2021-001176-42) (**Figure 1**)
  - Eligible patients aged ≥12 years with HAE due to C1-inhibitor deficiency (HAE-C1INH) and ≥2 documented attacks within 3 months before enrollment or had completed the phase 3 KONFIDENT trial (NCT05259917)
  - Patients using long-term prophylactic (LTP) were eligible to participate, provided they had been on a stable dose regimen of a protocol-allowed LTP for ≥3 months before enrollment
- All attacks that included satisfaction data as of September 14, 2024 were included in this assessment

KONFIDENT-S endpoints evaluated

- Time to beginning of symptom relief defined as at least "a little better" at 2 consecutive time points within 12 hours of the first dose, measured by the Patient Global Impression of Change (PGI-C)
- Treatment satisfaction was assessed 24 hours after the first dose of sebetralstat for each attack on a 7-point Likert scale (**Figure 2**)

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 is a screening visit.
HAE-C1NH, hereditary angioedema due to C1 inhibitor deficiency; OLE, open-label extension; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity.

Figure 2. Treatment satisfaction rating (7-point Likert scale)

Overall, how satisfied were you with sebetralstat therapy for this HAE attack?

−3	−2	−1	0	1	2	3
Dissatisfied			Neutral	Satisfied		

Results

Table 1. Baseline characteristics (N=107)

	Previously used on-demand treatment			
	Icatibant (n=47)	pdC1INH (n=18)	rC1INH (n=2)	Multiple treatments[a] (n=40)
Age, median (IQR), years	35 (21.0–47.0)	19 (15.0–36.0)	34 (25.0–44.0)	41 (31.5–52.5)
Sex, female, n (%)	29 (61.7)	13 (72.2)	2 (100)	30 (75.0)
White race, n (%)	35 (74.5)	12 (66.7)	2 (100)	30 (75.0)
BMI, median (IQR), kg/m²	25.6 (22.0–30.0)	23.6 (19.8–30.0)	25.4 (19.5–31.2)	25.1 (23.0–30.5)
Type of HAE-C1INH				
Type 1	42 (89.4)	17 (94.4)	2 (100)	37 (92.5)
Type 2	5 (10.6)	1 (5.6)	0	3 (7.5)
Treatment, n (%)				
On-demand only	33 (70.2)	12 (66.7)	1 (50.0)	33 (82.5)
LTP	14 (29.8)	6 (33.3)	1 (50.0)	7 (17.5)

Data cutoff: September 14, 2024.
[a]Patients reported using >1 conventional on-demand treatment at screening.
BMI, body mass index; HAE-C1NH, hereditary angioedema due to C1 inhibitor deficiency; IQR, interquartile range; LTP, long-term prophylaxis; pdC1INH, plasma-derived C1-inhibitor; rC1INH, recombinant C1-inhibitor.

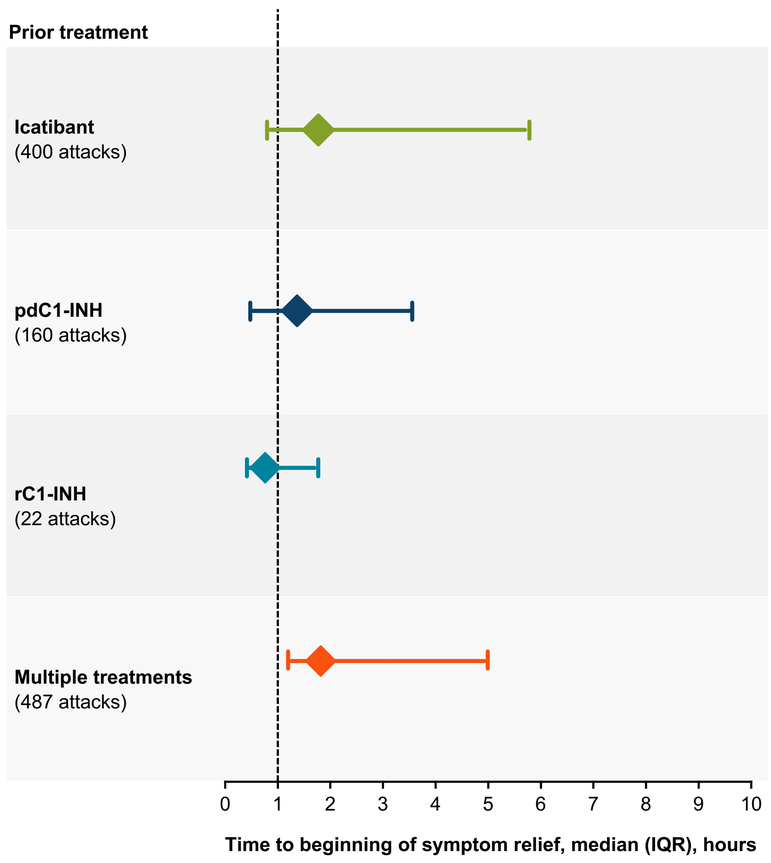
Table 2. Attack characteristics of sebetralstat-treated attacks

	Previously used on-demand treatment			
Attacks	Icatibant (n=409)	pdC1INH (n=167)	rC1INH (n=22)	Multiple treatments (n=491)[a]
Baseline severity (PGI-S), n (%)				
Mild[b]	147 (35.9)	54 (32.3)	3 (13.6)	224 (45.6)
Moderate	165 (40.3)	71 (43.1)	12 (54.5)	234 (47.7)
Severe/very severe	97 (23.7)	41 (24.6)	7 (31.8)	33 (6.7)
Primary pooled attack location, n (%)				
Mucosal[c]	154 (37.7)	98 (58.7)	13 (59.1)	166 (33.8)
Involving the larynx	8 (2.0)	7 (4.2)	0	3 (0.6)
Subcutaneous only[c]	254 (62.1)	69 (43.1)	9 (40.9)	325 (66.2)
Missing	1 (0.2)	0	0	0
Time from attack onset to treatment, median (IQR), minutes	6.0 (1.0–63.0)	6.0 (1.0–39.0)	37.5 (18.0–61.0)	21.0 (1.0–100.0)
Attacks treated with a second dose within 12 hours, n (%)	74 (18.1)	45 (26.9)	6 (27.3)	115 (23.4)
Attacks treated with conventional treatment within 12 hours, n (%)	14 (3.4)	7 (4.2)	0	31 (6.3)

Data cutoff: September 14, 2024.
[a]Icatibant + pdC1INH, n=282; icatibant + pdC1INH + rC1INH, n=124; icatibant + rC1INH, n=51; and pdC1INH + rC1INH, n=34.
[b]Baseline severity was classified as "None" for 4 attacks in the icatibant, 3 in the pdC1INH, and 3 in the multiple treatments.
[c]Mucosal: attacks with primary location of "Abdomen" and/or "Larynx/throat"; subcutaneous: other attacks not involving the mucosal locations. IQR, interquartile range; pdC1INH, plasma-derived C1-inhibitor; PGI-S, Patient Global Impression of Severity; rC1INH, recombinant C1-inhibitor.

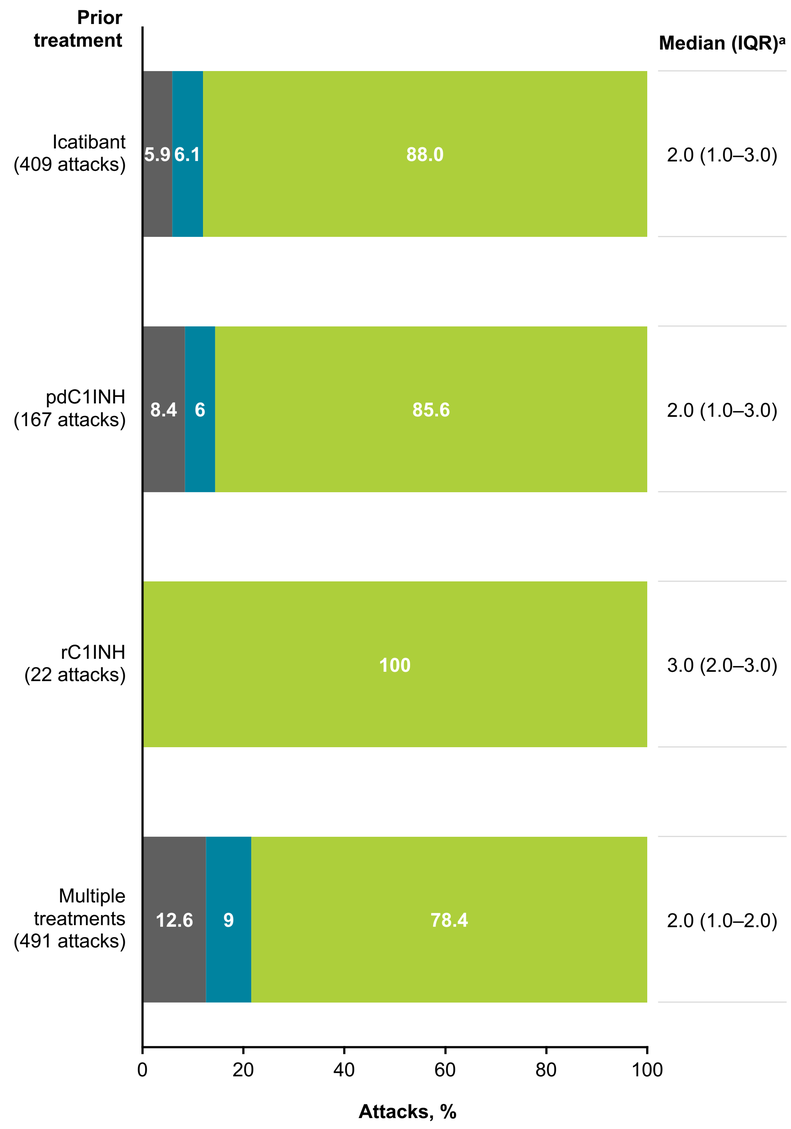
- Across all subgroups (**Table 1**), most attacks were mild (38.5%) or moderate (44.3%; **Table 2**)
- A second dose of sebetralstat was administered within 12 hours of their first dose for a total of 240 attacks (22.0%) across all subgroups
- In total, conventional on-demand treatments were administered for 52 attacks (4.8%) within 12 hours after use of sebetralstat

Figure 3. Time to beginning of symptom relief[a] with sebetralstat by previously used on-demand treatments



Data cutoff: September 14, 2024.
Diamonds are the medians met within time window. Error bars are IQR.
[a]Defined as a PGI-C rating of at least "A little better" for 2 consecutive time points, with missing data entries between consecutive time points within 12 hours of the first dose of sebetralstat.
IQR, interquartile range; pdC1INH, plasma-derived C1-inhibitor, rC1INH, recombinant C1-inhibitor.

Figure 4. Satisfaction with sebetralstat for each attack by previously used on-demand treatments (N=1089)



[a]Based on the 7-point Likert satisfaction scale, from −3 to 3.
IQR, interquartile range; pdC1INH, plasma-derived C1-inhibitor, rC1INH, recombinant C1-inhibitor.

- Time to beginning of symptom relief was similar regardless of which on-demand treatment was previously used (**Figure 3**)
  - Median time to beginning of symptom relief ranged from 0.76 to 1.82 hours across subgroups
- Median satisfaction rating for sebetralstat for all attacks was 2.0 (1.0–3.0) (**Figure 4**)
- No dissatisfaction (ie, neutral or satisfied) was reported for 90.8% of attacks (7.3% neutral; 83.6% satisfied)

Conclusions

- **In this interim analysis of the KONFIDENT-S trial, oral sebetralstat enabled early treatment and resulted in early symptom relief**
- **Patients reported being very satisfied with sebetralstat, regardless of prior parenteral on-demand therapy**

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Disclosures

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