

# On-demand Treatment Patterns of Hereditary Angioedema Attacks with Sebetralstat in the KONFIDENT-S Study

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## Background

- International treatment guidelines recommend that all hereditary angioedema (HAE) attacks, regardless of severity or location, are considered for treatment with on-demand therapy<sup>1,2</sup>
- People living with HAE who delay or withhold on-demand treatment report increased morbidity and diminished quality of life<sup>3,4</sup>
- In prospective observational real-world studies, only 50% to 79% of HAE attacks were treated when the only treatment options that were available required subcutaneous or intravenous injection<sup>5-7</sup>
  - Administration by injection can introduce significant barriers (eg, storing/carrying injection-related paraphernalia, potential pain and injection site reactions, finding a discreet and hygienic location) that result in delay or withholding of treatment<sup>8-11</sup>
- Sebetralstat, an oral plasma kallikrein inhibitor, has recently been approved for on-demand treatment of HAE attacks in patients ≥12 years old in the US, Europe, Japan and other countries<sup>12-15</sup>

## Objective

- This analysis evaluated treatment patterns among participants experiencing HAE attacks in the open-label KONFIDENT-S study

## Methods

### KONFIDENT-S Study Design

- The ongoing, open-label extension KONFIDENT-S study (NCT05505916, EudraCT: 2021-001176-42) enrolled adults and adolescents (aged ≥12 years) with a confirmed diagnosis of type 1 or type 2 hereditary angioedema due to C1 inhibitor deficiency (HAE-C1INH)
  - Participants must have either completed the KONFIDENT trial (rollover) or have experienced ≥2 documented attacks within 3 months (*de novo*)
  - Patients receiving long-term prophylaxis (LTP) must have been on a stable dose and regimen for ≥3 months immediately before and during the study

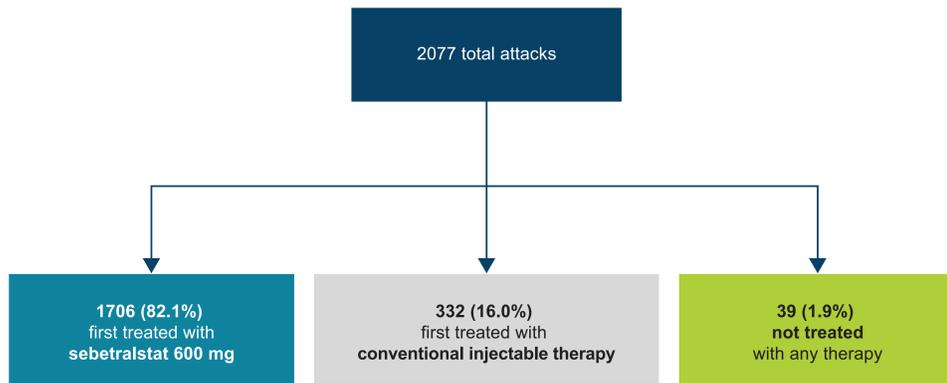
### Study Treatment

- Participants were instructed to self-administer a single 600-mg dose of sebetralstat as early as possible for each attack
  - All attack severities and locations were eligible
  - No attack qualification by investigators was required
  - Participants were provided portable wallets of blistered tablets
- If warranted, a second administration of sebetralstat was permitted ≥3 hours after the first administration
- Conventional injectable on-demand treatment could be used after sebetralstat administration if symptoms were deemed severe enough by the participant
- If preferred by the participant, HAE attacks in KONFIDENT-S could be treated with conventional injectable on-demand treatment instead of with sebetralstat

## Results

- As of September 14, 2024, 134 participants reported experiencing 2077 attacks of which 98.1% were treated
  - In total, 1706 (82.1%) attacks were treated with sebetralstat and 332 (16.0%) were treated with conventional injectable on-demand therapy (Figure 1)
  - Untreated attacks were slightly more likely to affect subcutaneous tissues (vs. abdominal; OR, 1.24) or to occur in participants initially using on-demand treatment only (vs. participants receiving LTP; OR, 1.25)

Figure 1. Proportion of HAE Attacks Treated in KONFIDENT-S



Data cutoff date: September 14, 2024.

- Sebetralstat treatment was preferred across patient subpopulations and types of attacks (Tables 1-2)

Table 1. Treatment Pattern by Population

Characteristic, n (%)	Participants who treated ≥1 attack with sebetralstat N = 134	Participants who treated ≥1 attack with conventional injectable treatment n = 72	Participants with ≥1 untreated attack n = 19
<b>By sex</b>			
Female	87 (64.9)	51 (70.8)	11 (57.9)
Male	47 (35.1)	21 (29.2)	8 (42.1)
<b>By age group</b>			
Adolescents (12 to <18 years)	23 (17.2)	8 (11.1)	2 (10.5)
Adults (≥18 years)	111 (82.8)	64 (88.9)	17 (89.5)
<b>By treatment paradigm</b>			
On-demand only	99 (73.9)	51 (70.8)	15 (78.9)
On-demand + LTP	35 (26.1)	21 (29.2)	4 (21.1)
<b>By region</b>			
Europe	69 (51.5)	39 (54.2)	9 (47.4)
North America	30 (22.4)	14 (19.4)	4 (21.1)
Rest of world <sup>a</sup>	35 (26.1)	19 (26.4)	6 (31.6)

<sup>a</sup>Rest of world includes Australia, Canada, Israel, Japan, New Zealand, Saudi Arabia, and South Africa.  
Data cutoff date: September 14, 2024.

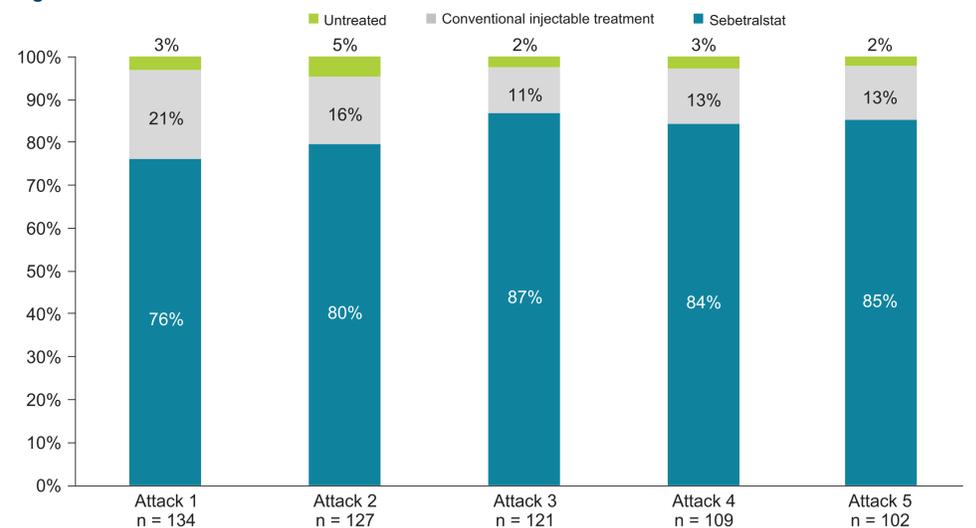
Table 2. Treatment Pattern by Attack Location and Severity

Characteristic, n (%)	All attacks N = 2077	Attacks treated with sebetralstat n = 1706	Attacks treated with conventional injectable treatment n = 332	Untreated attacks n = 39
<b>By location<sup>a</sup></b>				
Mucosal <sup>b</sup>	825 (39.7)	675 (39.6)	136 (41.0)	14 (35.9)
Subcutaneous <sup>b</sup>	1087 (53.3)	954 (55.5)	110 (33.1)	23 (59.0)
<b>By severity<sup>c</sup></b>				
Mild <sup>d</sup>	718 (34.6)	618 (36.2)	84 (25.3)	16 (41.0)
Moderate	793 (38.2)	685 (40.2)	97 (29.2)	11 (28.2)
Severe/very severe	400 (19.3)	330 (19.3)	60 (18.1)	10 (25.6)

<sup>a</sup>Attacks with missing location data: All attacks, 165 (7.9%); Attacks treated with sebetralstat, 77 (4.5%); Attacks treated with conventional injectable treatment, 86 (25.9%); Untreated attacks, 2 (5.1%).  
<sup>b</sup>Mucosal attacks were defined as those with primary location of 'Abdomen' and/or 'Larynx/Throat.' Subcutaneous attacks were defined as not involving the mucosal locations.  
<sup>c</sup>Attacks with missing PGI-S rating: All attacks, 166 (8.0%); Attacks treated with sebetralstat, 73 (4.3%); Attacks treated with conventional injectable treatment, 91 (27.4%); Untreated attacks, 2 (5.1%).  
<sup>d</sup>Includes attacks with PGI-S rating of 'None.'  
Data cutoff date: September 14, 2024.

- Across the first 5 attacks treated by participants in the KONFIDENT-S study, sebetralstat was consistently used to treat 76.1% to 86.8% of attacks (Figure 2)

Figure 2. Initial Treatment Choice for First 5 Attacks



n represents the number of participants.  
Data cutoff date: September 14, 2024.

## Conclusions

- The availability of oral sebetralstat has shifted on-demand treatment patterns in KONFIDENT-S, likely due to the reduced barriers of treatment, leading to increased willingness of participants to treat attacks
- Consistent with the treatment guideline recommendation that all attacks should be considered for treatment, 98.1% of HAE attacks were treated in the KONFIDENT-S study
  - Participants treated more mild and subcutaneous attacks than previously reported values for injectable on-demand treatments<sup>3,6,7</sup>
  - Of those attacks left untreated, more were likely to be subcutaneous (versus mucosal) or occurred in participants not receiving LTP (versus those receiving LTP)
  - Initial conventional injectable treatment use was most common among attacks that occurred in the beginning of the study
- Across the first 5 attacks treated by participants in the KONFIDENT-S study, preference for sebetralstat was high and increased after the initial attack was treated

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