

On-demand Treatment of Hereditary Angioedema Attacks With Sebetralstat in Adolescents: Interim Analysis From KONFIDENT-S

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Key Takeaways

Adolescents treated attacks quickly and reported high satisfaction with oral sebetralstat

RAPID TREATMENT



9 minutes

Median time to treatment

HIGH SATISFACTION



88.9%

Participants satisfied with oral sebetralstat as on-demand treatment

Background

- Hereditary angioedema (HAE) is a rare genetic disease most commonly resulting from a quantitative deficiency or dysfunction in the C1 inhibitor protein (HAE-C1INH)
- Parenteral on-demand therapies for the treatment of HAE attacks can be difficult to administer and are often painful
 - These treatments may be particularly burdensome for adolescents, who may require assistance with treatment, especially if it is administered intravenously
- Due to these challenges, adolescents with HAE often delay or withhold on-demand treatment (mean time to treatment of 7.7 hours) which may result in attack progression and suboptimal outcomes¹
 - Anxiety associated with parenteral administration in adolescents is correlated with increased time to treatment¹
- Sebetralstat, an oral plasma kallikrein inhibitor, has been approved for the treatment of acute attacks in patients ≥12 years old with HAE in the United States and recently received approval from the Medicines and Healthcare products Regulatory Agency
 - Sebetralstat continued to be assessed in a multicenter 2-year open-label extension (OLE) study (KONFIDENT-S [NCT05505916])

Objective

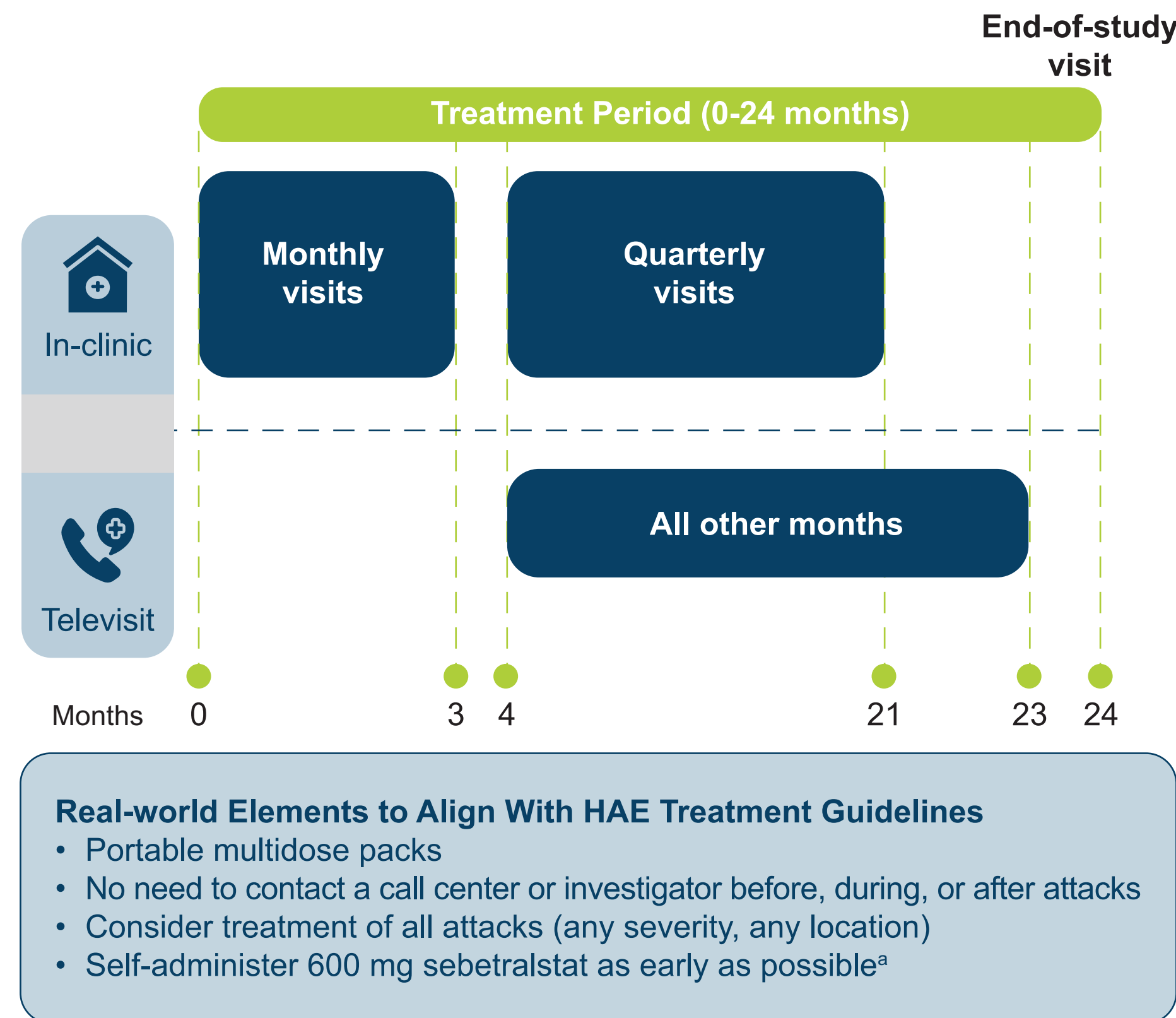
- This prespecified interim analysis of KONFIDENT-S investigated the safety, effectiveness, and treatment satisfaction of oral sebetralstat in adolescents with HAE-C1INH

Methods

Study Design

- Eligible participants were ≥12 years of age with HAE-C1INH and had ≥2 documented attacks within 3 months or had completed the phase 3 KONFIDENT trial⁴ (**Figure 1**)
 - Participants receiving long-term prophylaxis (LTP) were required to be on a stable dose and regimen for ≥3 months immediately before the study
- Participants self-administered sebetralstat 600 mg as early as possible after attack onset
- In this interim analysis, endpoints were assessed in participants 12-17 years old:
 - Time to beginning of symptom relief (Patient Global Impression of Change [PGI-C] rating of at least “A Little Better” for ≥2 consecutive time points) within 12 hours
 - Time to reduction in attack severity (≥1 level decrease on the Patient Global Impression of Severity [PGI-S] for ≥2 consecutive time points) within 12 hours
 - Time to complete attack resolution (PGI-S rating of “None”) within 24 hours
 - Safety assessed by adverse event monitoring
 - Treatment satisfaction assessed 24 hours after treatment of each attack on a 7-point scale from extremely dissatisfied (-3) to extremely satisfied (+3); participant satisfaction was defined as mean satisfaction rating >0

Figure 1. KONFIDENT-S Study Design



*Participants were instructed to treat their attacks involving the larynx immediately with conventional on-demand therapy if the attack symptoms worsened after the initial sebetralstat administration.

HAE, hereditary angioedema.

Results

Participant and Attack Characteristics

- 23 participants experienced HAE attacks during the study period from October 21, 2022, to September 14, 2024 (data cutoff; **Table 1**)
- Adolescents treated a median of 8.0 attacks (interquartile range [IQR], 2.0-28.0 attacks; range, 1-61 attacks)

Table 1. Participant Demographics

	Adolescents n=23
Age, mean (range), years	14.6 (12-17)
Sex, female, n (%)	15 (65.2)
Race, n (%) ^a	
White	16 (69.6)
Asian	1 (4.3)
Other or Multiple	3 (13.0)
BMI, mean (range), kg/m ²	22.9 (16.2-35.6)
HAE-C1INH-Type 1, n (%)	22 (95.7)
Current treatment regimen, n (%)	
On-demand only ^b	18 (78.3)
Icatibant ^c	10 (43.5)
C1INH ^c	7 (30.4)
On-demand ^d + LTP	5 (21.7)
Targeted kallikrein-inhibiting agent ^e	5 (21.7)
Time since diagnosis, median (IQR), years	10.0 (6.0-12.7)

^aNot reported, 3 participants (13.0%).

^bUnknown, 2 participants (8.7%); includes 1 participant who used tranexamic acid as on-demand therapy.

^cIncludes 2 participants who used C1INH and/or icatibant as on-demand therapy.

^dOn-demand therapy was icatibant for 3 participants and C1INH for 2 participants.

^eLTP therapy was lanadelumab for 1 participant and berotralstat for 4 participants.

IQR, interquartile range; LTP, long-term prophylaxis.

Table 2. Sebetralstat-treated Attack Characteristics

	Sebetralstat-treated Attacks n=369
Baseline pooled primary attack n (%) ^a	
Mucosal	162 (43.9)
Laryngeal	8 (2.2)
Subcutaneous	198 (53.7)
Baseline PGI-S rating, n (%) ^b	
Mild ^c	97 (26.3)
Moderate	129 (35.0)
Severe/Very severe	135 (36.6)

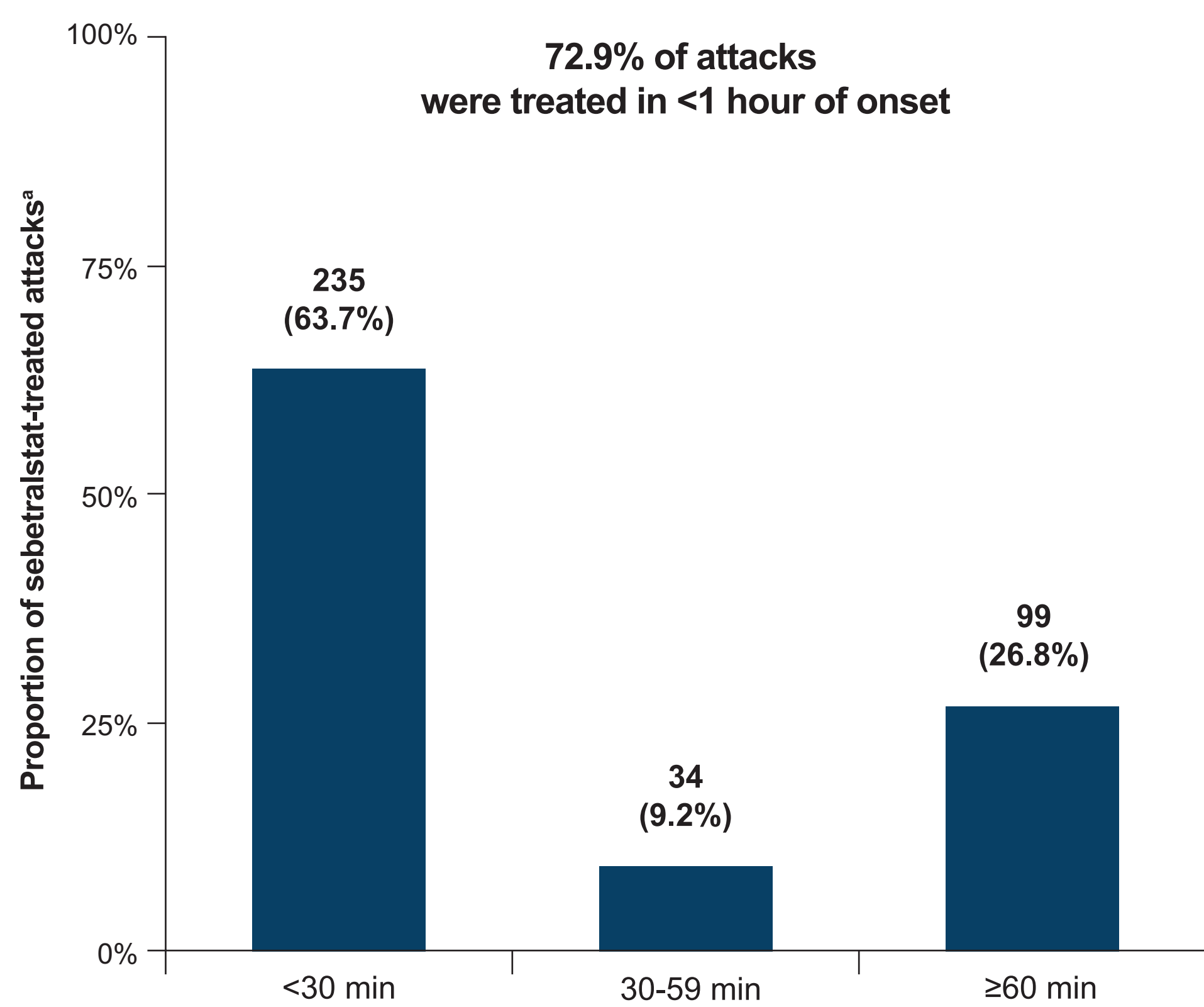
^aMissing: 9 (2.4%).

^bMissing: 8 (2.2%).

^cIncludes PGI-S rating “None”: 17 (4.6%).

PGI-S, Patient Global Impression of Severity.

Figure 2. Time From Attack Onset to Sebetralstat Administration

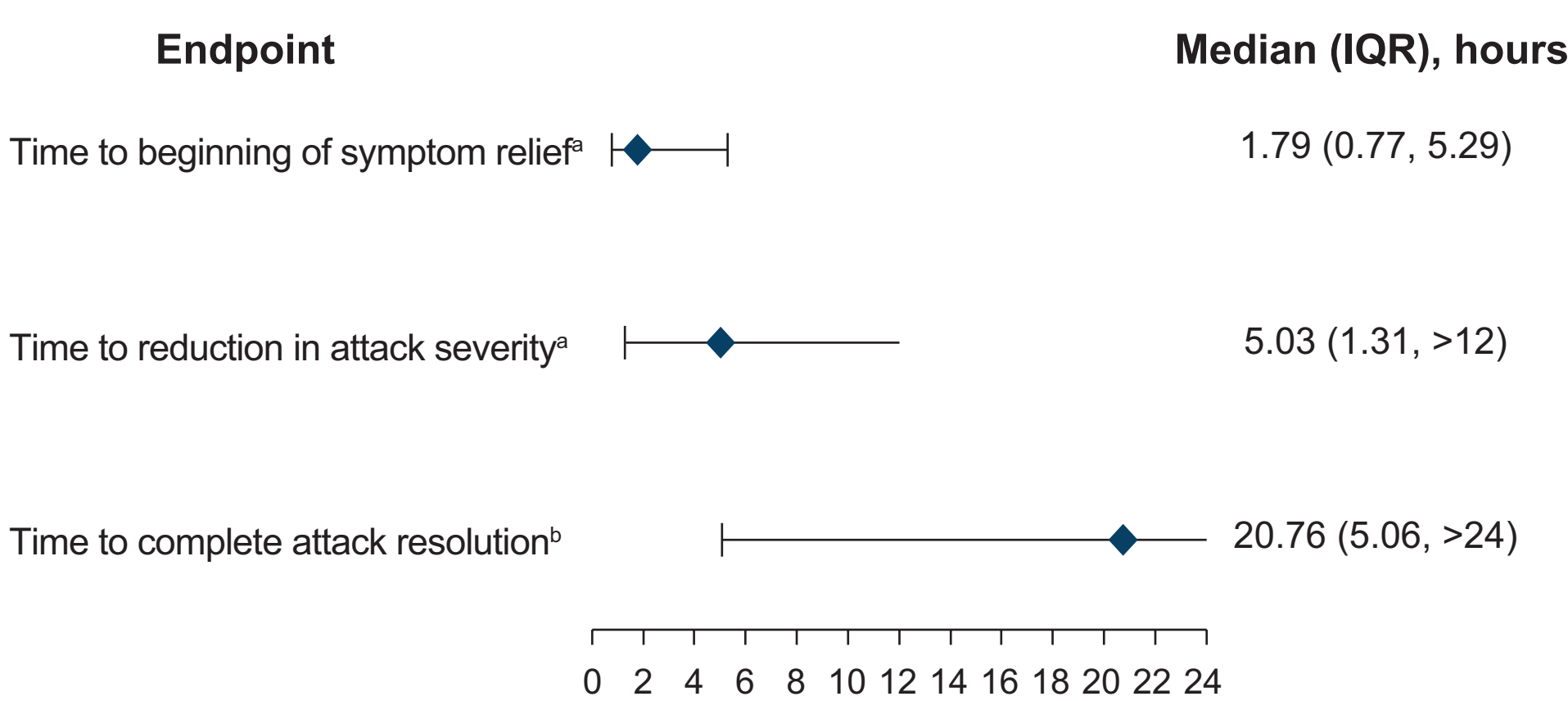


*Missing: 1 (0.3%).

- The median time from attack onset to treatment was 9 minutes (IQR, 1.0-70.0 minutes; **Figure 2**)

Effectiveness

Figure 3. Effectiveness Endpoints



^aWithin 12 hours.

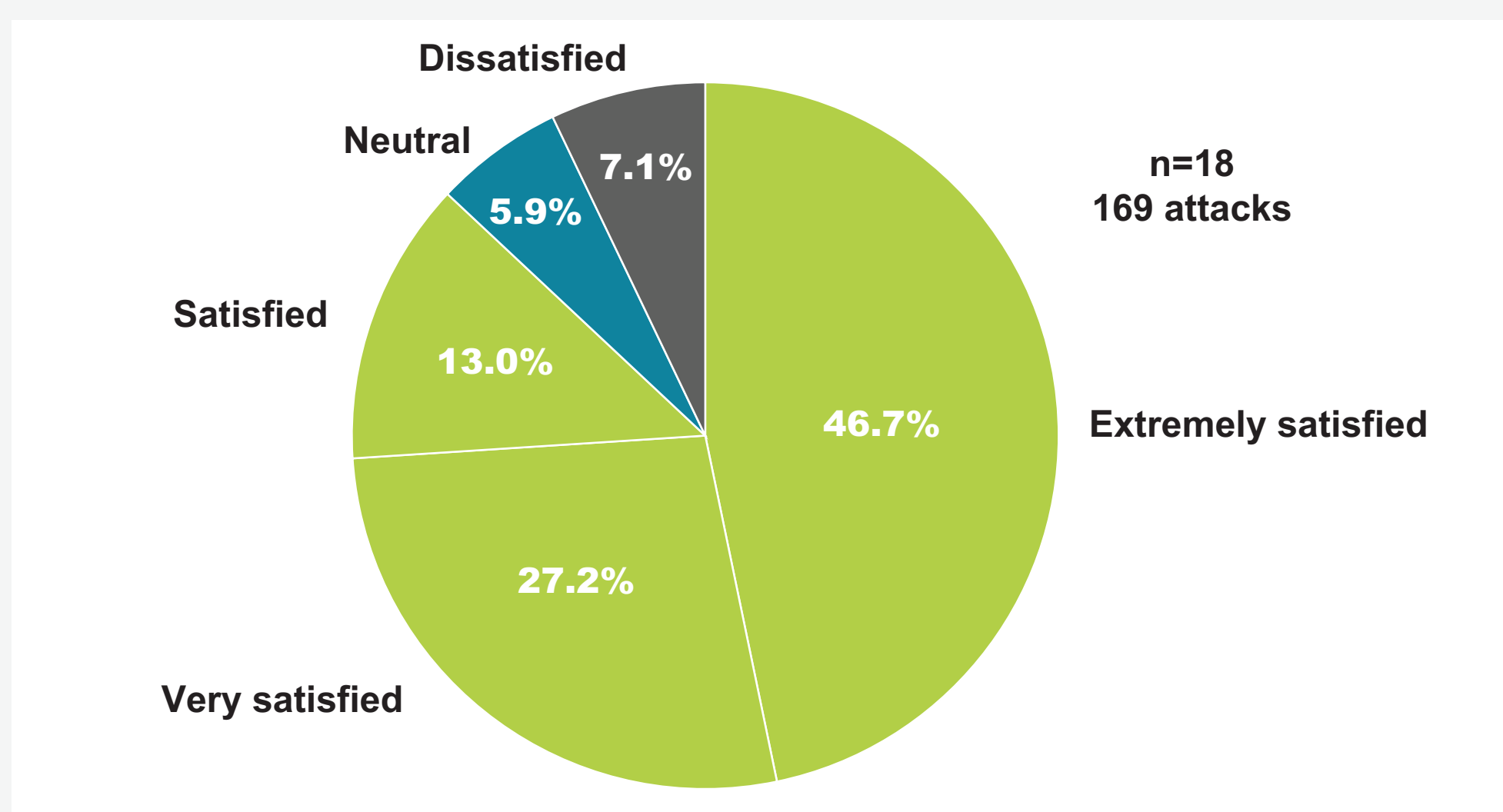
^bWithin 24 hours.

^cError bars display IQR.

IQR, interquartile range.

- Of attacks reaching beginning of symptom relief within 12 hours (80.2%), 93.7% did so before or without an additional sebetralstat administration
- Use of additional treatments within 12 hours included 66 (17.9%) of attacks treated with an additional dose of sebetralstat and 13 (3.5%) of attacks treated with conventional treatment

Figure 4. Treatment Satisfaction



- The median satisfaction score (IQR) for all attacks was 2.0 (1, 3), which corresponds to a rating of very satisfied. On average, 88.9% of adolescent participants were satisfied

Safety

- No participant reported difficulty swallowing sebetralstat in the study

Table 3. Safety

	Adolescents n=23
Any TEAE, n (%)	10 (43.5)
Treatment-related	1 (4.3) ^a
Serious TEAE, n (%)	2 (8.7) ^b
Treatment-related	0
Severe TEAE, n (%)	2 (8.7) ^b
Treatment-related	0
Any TEAE leading to permanent discontinuation, n (%)	0
Any TEAE leading to death, n (%)	0

^aTreatment-related event of tremor occurred in 1 participant.

^b1 instance of hypotension in 1 participant, and 4 instances of laryngeal HAE attacks and 1 instance of abdominal HAE attack in 1 participant (not considered treatment related).

TEAE, treatment-emergent adverse event.

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Disclosures

Sinisa Savic has the following conflicts of interest: Study PI: Novartis, Pharming, KaVista, Celldex, Astria, and CSL Behring; advisory boards, lectures: Novartis, Pharming, Takeda, and CSL Behring; Pharvaris, KaVista, Otsuka, SOBI, GSK, and AstraZeneca; conference travel support: Novartis; and research grants: Takeda, Pharming, Novartis, and CSL Behring.

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