Sebetralstat for On-demand Treatment of HAE in Pediatric (2-11y) Patients: Interim Results from KONFIDENT-KID

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Presented at the American College of Allergy, Asthma & Immunology Annual Scientific Meeting; November 6-10, 2025; Orlando, FL, USA.

Disclosures

- Dr Adil Adatia reports receiving grants from Astria, BioCryst, CSL Behring, Ionis, KalVista Pharmaceuticals, Octapharma, Pharvaris, and Takeda; receiving consulting fees, payments or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events, and support for attending meetings and/or travel from BioCryst, CSL Behring, KalVista Pharmaceuticals, Pharvaris, and Takeda
- Dr Adil Adatia is a research committee member of Canadian Hereditary Angioedema Network (voluntary)

Background

- Approximately 40% of patients with HAE experience their first attack by age of 5, with potential age of onset as early as infancy[1,2]
- Earlier onset is associated with more severe course of disease and increased attack burden[1]
  - Children with HAE attacks experience significant anxiety, social isolation, and academic disruption[2,3] and there is a multifaceted psychosocial impact on their caregivers[3-5]
- On-demand options for children with HAE require IV infusion or SC injection and are associated with substantial burden, including anxiety and pain, leading to treatment avoidance, denial or delays[5,6]
  - HAE in children (<12 years old) is primarily managed with on-demand treatment
  - Only IV pdC1INH is approved in the US[7,a]
- 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, UK, and EU[8-10]

[a]In the EU, additional approved treatment options in children aged 2 years and older include IV rhC1INH, IV pdC1INH, and SC icatibant.[11-13]

EU, European Union; HAE, hereditary angioedema; HAE-CINH, hereditary angioedema with C1INH deficiency; IV, intravenous; SC, subcutaneous; SmPC, summary of product characteristics; pdC1INH, plasma-derived C1 inhibitor; PI, prescribing information; rhC1INH, recombinant human C1 inhibitor; UK, United Kingdom; US, United States.

1. Tachdjian R et al. *Clin Pediatr (Phila)*. 2023;62(9):973-980. 2. Pagnier A et al. *Pediatr Allergy Immunol*. 2024;35(12):e14268. 3. Piotrowicz-Wójcik K et al. *Children (Basel)*. 2024;11(2):237. 4. Lo SH et al. *PharmacoEconomics Open*. 2022;6(2):231-239. 5. Martinez-Saguer I et al. *Ann Allergy Asthma Immunol*. 2023;131(5):S36-S37. 6. Tachdjian R et al. *J Allergy Clin Immunol*. 2023;2(suppl):Ab133. 7. Berinert (C1 esterase inhibitor [human]). PI. CSL Behring; 2022. 8. Ekterly (sebetralstat). PI. KalVista Pharmaceuticals; 2025. 9. Ekterly (sebetralstat). SmPC (UK). KalVista Pharmaceuticals; 2025. 10. Ekterly (sebetralstat). SmPC (EU). KalVista Pharmaceuticals; 2025. 11. Ruconest 2100 Units powder for solution for injection. SmPC. Pharming Group N. V. The Netherlands; 2015. 12. Cinryze 500 IU powder and solvent for solution for injection. SmPC. Takeda Manufacturing AG; 2022. 13. Firazyr (icatibant). SmPC (EU). Takeda Pharmaceuticals; 2025.

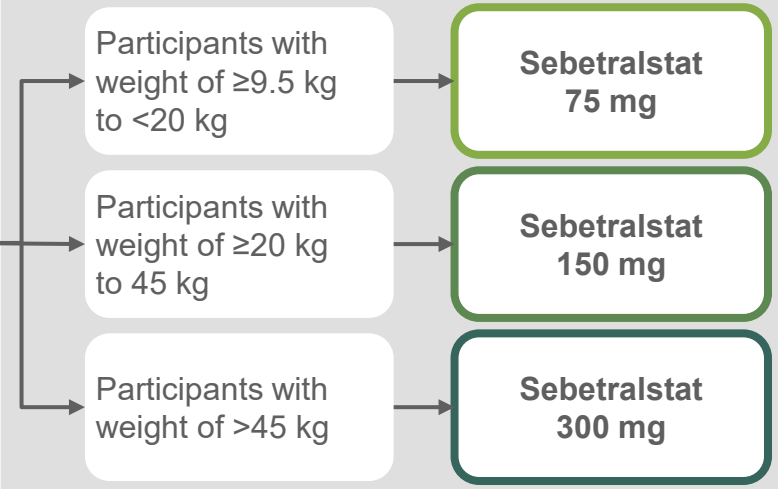
Study Design

The open-label, multicenter phase 3 KONFIDENT-KID trial was designed to evaluate the safety, PK, and efficacy of sebetralstat orally disintegrating tablets (ODT) in children with HAE-C1INH who are 2-11 years old[1]

STUDY POPULATION

- Aged 2-11 years
- Confirmed diagnosis of HAE-C1INH
- ≥1 attack in the past 12 months
- N ~ 36

Treatment algorithm[a,b]



PK assessment at enrollment visit[c]

Treatment of attacks

- **Administration by pediatric participants or caregivers**
- **For up to 1 year**

  OR
- **Until the participant turns 12 years old**

  OR
- **Until trial completion**

PRIMARY OBJECTIVE

- **Safety:** Adverse events

SECONDARY OBJECTIVES

- **PK**
- **Time to beginning of symptom relief:** CaGI-C rating of at least 'A Little Better' for ≥2 time points in a row within 12 hours
- **Time to reduction in severity:** Decrease in CaGI-S rating from baseline for ≥2 time points in a row within 12 hours
- **Time to complete attack resolution:** CaGI-S rating of 'None' within 24 hours

[a]All doses are equivalent to the 300-mg FCT dose in adults; provided as ODT.
[b]Trial was amended in the US to treat with the equivalent of sebetralstat 600 mg.
[c]PK samples were collected at 0.5, 2, and 4 hours. Simulated models were generated based on key parameters from each participant; 500 simulations were ran for each participant.
CaGI-C, Caregiver Global Impression of Change; CaGI-S, Caregiver Global Impression of Severity; FCT, film-coated tablet; PK, pharmacokinetics.
1. ClinicalTrials.gov NCT06467084. Accessed October 9, 2025. https://clinicaltrials.gov/study/NCT06467084.

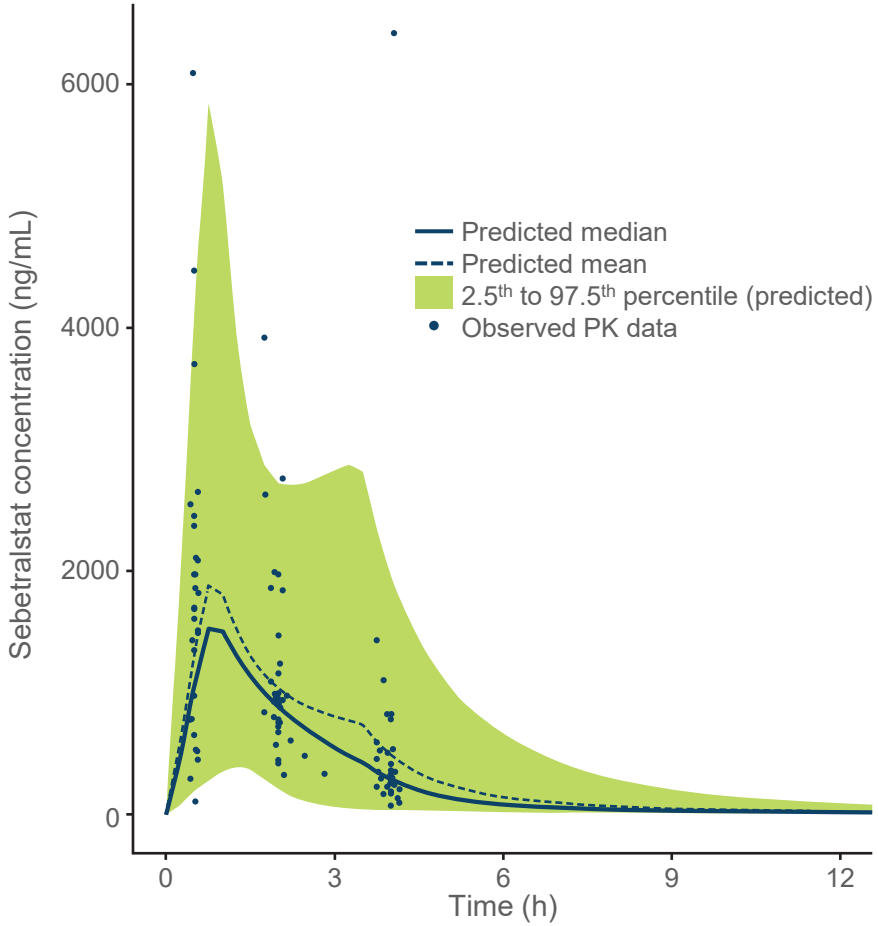
Participant Demographics

	Participants in sebetralstat ODT dosing group[a]			
	75 mg n=3	150 mg n=27	300 mg n=6	All participants N=36
Age, mean (range), years	5.0 (4-5)	8.0 (6-11)	9.5 (8-10)	8.0 (4-11)
Sex, male, n (%)	1 (33.3)	14 (51.9)	3 (50.0)	18 (50.0)
Race, n (%)				
White	3 (100)	20 (74.1)	3 (50.0)	26 (72.2)
Other[b]	0	3 (11.1)	2 (33.3)	5 (13.9)
Not reported	0	4 (14.8)	1 (16.7)	5 (13.9)
Weight, mean (range), kg	19.4 (19.0-19.5)	28.0 (20.2-43.2)	50.6 (47.2-70.0)	28.8 (19.0-70.0)
HAE-C1INH-Type 1, n (%)	3 (100)	24 (88.9)	5 (83.3)	32 (88.9)

[a]No participants have received 600 mg sebetralstat.
[b]Includes Asian (n=2; 5.6%), Black or African American (n=1; 2.8%), American Indian/Native Alaskan (n=1; 2.8%), other (n=1, 2.8%).
Data cutoff date: September 15, 2025.
ODT, orally disintegrating tablet.

Part 1: Pharmacokinetics

Population PK Predicted and Observed Pediatric Exposures



- Observed sebetralstat plasma concentrations reliably fit within predicted exposures

- Sebetralstat concentrations in pediatric participants 30 minutes post-dose were comparable to plasma concentrations in adults following a 300-mg FCT dose
  - Pediatric C_{30} (geomean): 1364 ng/mL
  - Adult C_{30} (geomean): 1810 ng/mL[a]

[a]Data on file. KalVista Pharmaceuticals, Inc.
Data cutoff date: June 5, 2025.
C_{30}, plasma concentration 30 minutes after dosing.

Attack Characteristics

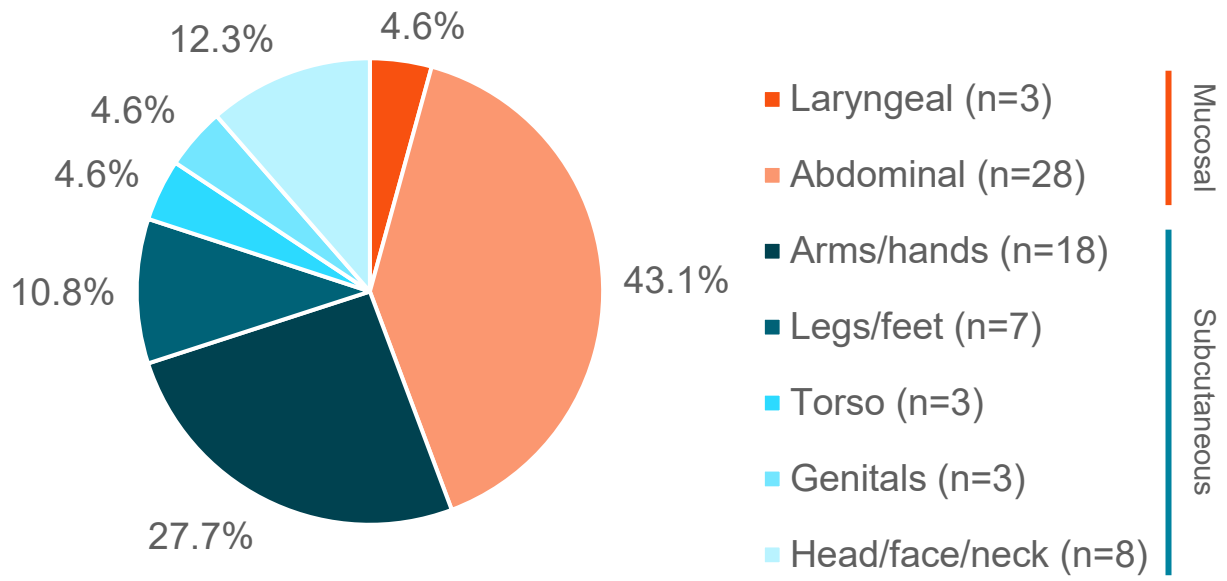
- Participants treated a mean of **0.8 (SD, 0.56) attacks/month** with sebetralstat ODT

Baseline attack severity[a,b]

Attacks in sebetralstat ODT dosing group

	75 mg n=1	150 mg n=55	300 mg n=9	All attacks N=65
Severity, n (%)				
Mild[c]	1 (100)	16 (29.1)	4 (44.4)	21 (32.3)
Moderate	0	31 (56.4)	4 (44.4)	35 (53.8)
Severe	0	5 (9.1)	0	5 (7.7)
Very Severe	0	0	0	0

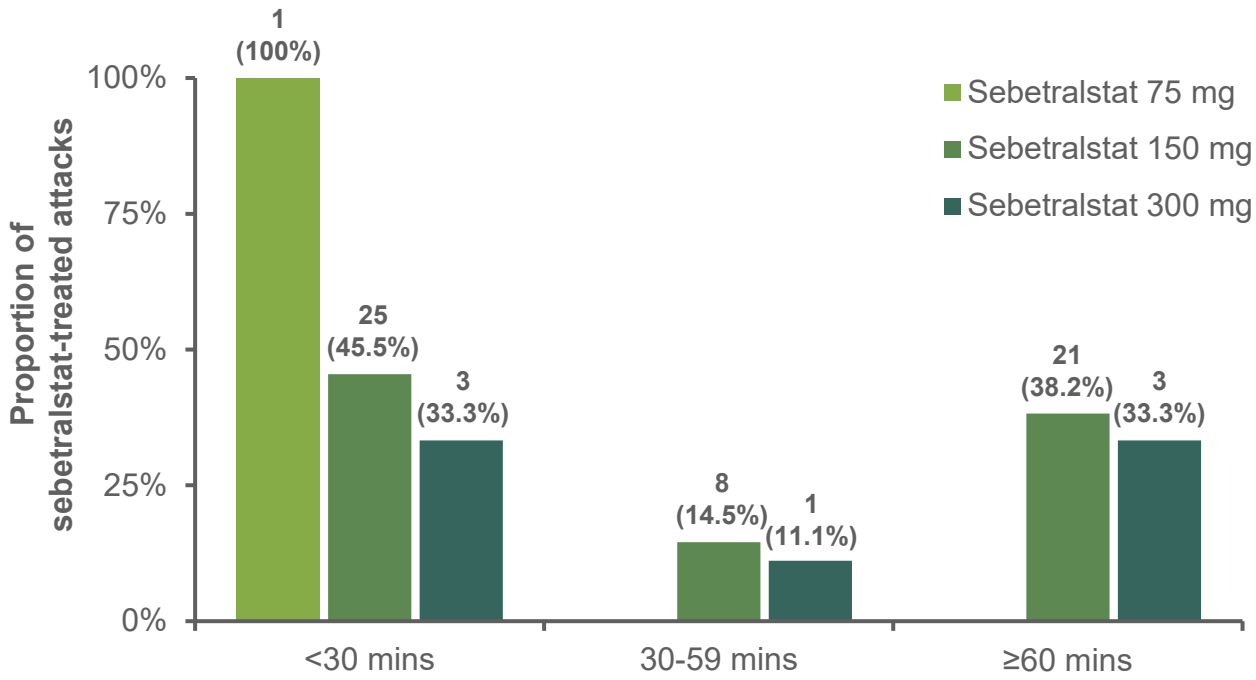
Primary attack location[d]



[a]Assessed by CaGI-S.
[b]Missing: 3 (5.5%) attacks in 150-mg group and 1 (11.1%) attack in 300-mg group.
[c]Includes attacks with baseline CaGI-S rating of 'None': 1 (1.8%) attack in 150-mg group and 2 (22.2%) attacks in 300-mg group.
[d]Missing: 2 (3.6%) attacks in 150-mg group and 1 (11.1%) attack in 300-mg group.
Data cutoff date: September 15, 2025.
SD, standard deviation.

Time to Treatment

Time from attack onset to sebetralstat ODT administration[a,b]



- The median time to treatment was 30 minutes
- 61.3% of attacks were treated in <1 hour of onset

	Median time (IQR) to sebetralstat administration, minutes
75 mg (n=1)	20 (20 to 20)
150 mg (n=55)[a]	30 (5 to 135)
300 mg (n=9)[a]	50 (0 to 146)
All (N=65)[a]	30 (5 to 135)

[a]Data missing for 1 (1.8%) attack in the 150-mg group and 2 (22.2%) attacks in the 300-mg group.
[b]Caregiver or child could administer treatment.
Data cutoff date: September 15, 2025.
IQR, interquartile range.

Part 2: Interim Efficacy

	Attacks in Sebetralstat ODT Dosing Group		
	75 mg n=1	**150 mg n=55**	**300 mg n=9**
Time to beginning of symptom relief within 12 hours, median (IQR), hours	**NE**	**1.50** (0.50 to 4.00)	**NE** (0.50 to >12)
Time to reduction in attack severity within 12 hours, median (IQR), hours	**NE**	**4.00** (1.50 to >12)	**NE** (1.00 to >12)
Time to complete attack resolution within 24 hours, median (IQR), hours	**NE**	**12.00** (8.00 to 24.00)	**18.00** (4.00 to >24)

- Overall, 78.9% attacks achieved beginning of symptom relief within 12 hours[a]
- Conventional medication was utilized within 12 hours for 3.1% of attacks

[a]Includes all attacks with post-baseline values.
Data cutoff date: September 15, 2025.
NE, not estimable.

Safety and Tolerability

	All participants[a] N=26
Any TEAE, n (%)	9 (34.6)
Treatment-related	**0**
Serious TEAE, n (%)	0
Treatment-related	**0**
Severe TEAE, n (%)	0
Treatment-related	**0**
Any TEAE leading to discontinuation, n (%)	0
Any TEAE leading to death, n (%)	0

- No reports of difficulty swallowing sebetralstat ODT

[a]Participants who treated at least 1 HAE attack with sebetralstat.
Data cutoff date: June 5, 2025.
TEAE, treatment-emergent adverse event.

Conclusions: KONFIDENT-KID

- Children with HAE aged 2-11 years have a high unmet need for non-parenteral treatment options
- Observed sebetralstat plasma concentrations reliably fit within predicted exposures
  - Sebetralstat concentrations in children 30 minutes post-dose were comparable to plasma concentrations in adults following a 300-mg dose
- Participants treated a mean of 0.8 attacks/month with sebetralstat
- Sebetralstat enabled early treatment (median: 30 minutes) by participants or their caregivers
  - Attacks occurred in all locations with 32% still mild at time of treatment
- Sebetralstat was generally safe, well tolerated, and demonstrated rapid symptom relief, reduction in severity and complete attack resolution

Sebetralstat ODT has the potential to address high unmet need for children (2-11 years) with HAE and their caregivers

Acknowledgments

- We thank the people living with HAE and their families; the HAEA, HAEi, and member organizations; and the investigator teams who are contributing to the international KONFIDENT-KID trial
- Medical writing assistance was provided under the direction of the authors by Richard W. Davis IV, PhD, of ApotheCom (San Francisco, CA) and was supported by KalVista Pharmaceuticals

HAEA, US Hereditary Angioedema Association; HAEi, HAE International.