Poster ID: 11

On-demand Oral Sebetralstat for Hereditary Angioedema Attacks in Children Aged 2-11: Interim Analysis of KONFIDENT-KID

Emel Aygören-Pürsün,[1] Adil Adatia,[2] John Anderson,[3] Shira Benor,[4] Mélisande Bourgoin-Heck,[5] Mauro Cancian,[6] Bob Geng,[7] Eisuke Inage,[8] Aharon Kessel,[9] Majed Koleilat,[10] H. Henry Li,[11] Michael E. Manning,[12] Heloise Reumaux,[13] Raffi Tachdjian,[14] Paola Triggianese,[15] Andrea Zanichelli,[16,17] Erik Hansen,[18] Ya-Hsiu Chuang,[18] Matthew Iverson,[18] Michael D. Smith,[18] Paul K. Audhya,[18] H. James Wedner[19]

[1]University Hospital Frankfurt, Goethe University Frankfurt, Frankfurt, Germany; [2]University of Alberta, Edmonton, Alberta, Canada; [3]Allervie Clinical Research, Cullman, AL, USA; [4]Tel Aviv Sourasky Medical Center – Ichilov, Tel Aviv, Israel; [5]Trousseau Hospital Sorbonne Université AP HP, Paris, France; [6]Azienda Ospedale Università di Padova, Padova, Italy; [7]University of California – San Diego, La Jolla, CA, USA; [8]Juntendo University Hospital, Tokyo, Japan; [9]Bnai Zion Medical Center, Haifa, Israel; [10]Deaconess Clinic Allergy, Evansville, IN, USA; [11]Institute for Asthma and Allergy, Wheaton, MD, USA; [12]Allergy, Asthma and Immunology Associates, Ltd., Scottsdale, AZ, USA; and University of Arizona College of Medicine-Phoenix, Scottsdale, AZ, USA; [13]Hôpital Jeanne de Flandre, Lille, France; [14]University of California, Los Angeles School of Medicine, Los Angeles, CA, USA; [15]Policlinico Universitario Tor Vergata, Department of Biomedicine and Prevention, Rome, Italy; [16]Department of Biomedical Sciences for Health, University of Milan, Milan, Italy; [17]Operative Unit of Medicine, Angioedema Center, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy; [18]KalVista Pharmaceuticals, Framingham, MA, USA; [19]John T. Milliken Department of Medicine, Washington University School of Medicine, St. Louis, MO, USA

Background

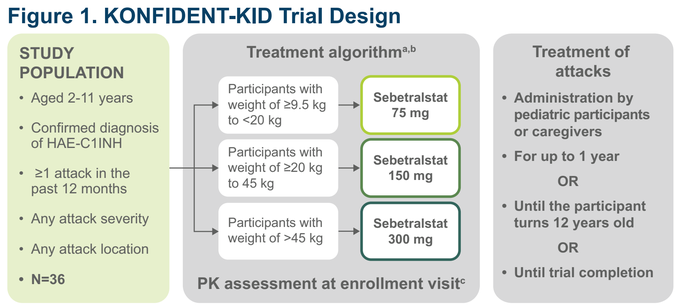
- Approximately 50%-75% of patients with hereditary angioedema (HAE) experience their first attack by the age of 12[1,2]
- Children with HAE attacks experience significant anxiety, social isolation, and academic disruption.[1,3] Their caregivers also experience a multifaceted psychosocial impact[3-5]
- On-demand HAE treatment options for children require injection and are associated with substantial burden, including anxiety and pain, leading to treatment avoidance, denial, or delays[5-10]
- Sebetralstat, an oral plasma kallikrein inhibitor, is currently only approved for on-demand treatment of HAE attacks in patients ≥12 years old in the EU, US, and other countries[11-13]

Objective

- This ongoing open-label, international, multicenter phase 3 KONFIDENT-KID trial was designed to evaluate the safety, pharmacokinetics (PK), and effectiveness of sebetralstat orally disintegrating tablets (ODTs) in children (2-11 years) with hereditary angioedema with C1INH deficiency (HAE-C1INH)

Methods

Figure 1. KONFIDENT-KID Trial Design



[a]All doses provide equivalent exposure as 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 after a single administration of sebetralstat.
FCT, film-coated tablet; HAE-C1INH, hereditary angioedema with C1INH deficiency; ODT, orally disintegrating tablet; PK, pharmacokinetics.

Trial Design

- The trial design of the phase 3 KONFIDENT-KID trial (NCT06467084) is shown in **Figure 1**

Objectives

- The primary objective was to evaluate the safety of sebetralstat in this patient population
- Secondary objectives were to assess PK and effectiveness
- Effectiveness endpoints were assessed using Caregiver Global Impression of Change (CaGI-C) and Severity (CaGI-S)
  - Time to beginning of symptom relief was defined as CaGI-C ratings of at least 'A Little Better' for ≥2 time points in a row within 12 hours
  - Time to reduction in attack severity was defined as a decrease in CaGI-S rating from baseline for ≥2 time points in a row within 12 hours
  - Time to complete attack resolution was defined as a CaGI-S rating of 'None' within 24 hours

Results

Participant Demographics

- As of December 15, 2025, 36 pediatric participants were enrolled in KONFIDENT-KID (**Table 1**)

Table 1. 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	4.7 (4-5)	7.9 (6-11)	9.2 (8-10)	7.8 (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	19.1 (18.8-19.5)	29.8 (21.0-44.4)	55.1 (48.5-72.3)	33.1 (18.8-72.3)
HAE-C1INH-Type 1, n (%)	3 (100)	24 (88.9)	6 (100)	33 (91.7)

[a]No participants 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: December 15, 2025.
HAE-CINH, hereditary angioedema with C1INH deficiency; ODT, orally disintegrating tablet.

Pharmacokinetics

- Sebetralstat concentrations in all pediatric participants 30 minutes post-dose were comparable to plasma concentrations in adults following a 300-mg FCT dose, with a C_{30} (geomean) of 1364 ng/mL in pediatric participants and 1810 ng/mL in adults[14]

Attack Characteristics

- Sebetralstat was administered as treatment for 172 attacks in 33 participants (**Table 2**)
  - Participants had a median of 4 total attacks; mean of 0.70 (SD, 0.45) attacks per month
- At the time of treatment, most attacks (88.9%) were still mild or moderate in severity

Table 2. Baseline Attack Characteristics

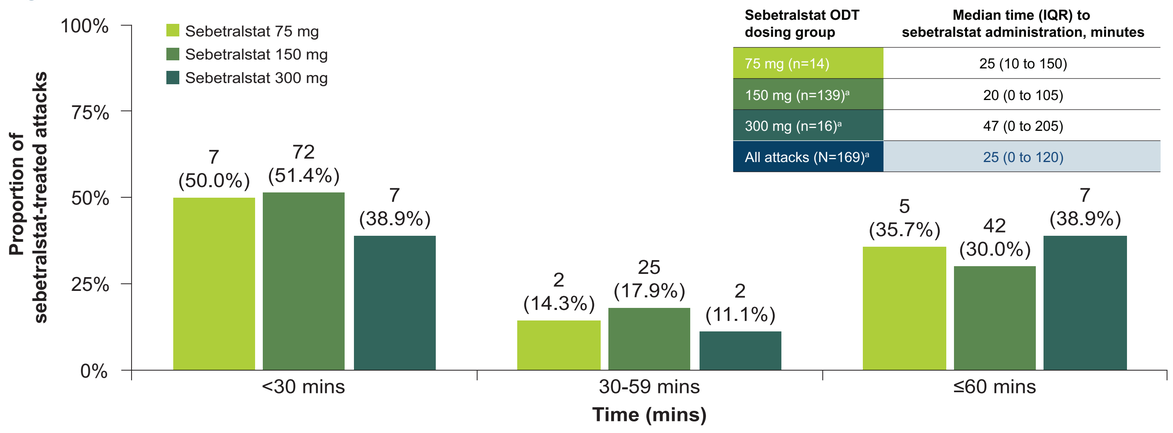
	Attacks in sebetralstat ODT dosing group			
	75 mg n=14	150 mg n=140	300 mg n=18	All attacks N=172
Severity, n (%)[a,b]				
Mild[c]	5 (35.7)	46 (32.9)	11 (61.1)	62 (36.0)
Moderate	9 (64.3)	78 (55.7)	4 (22.2)	91 (52.9)
Severe	0	9 (6.4)	0	9 (5.2)
Very Severe	0	1 (0.7)	0	1 (0.6)
Pooled primary attack location, n (%)[b]				
Laryngeal	0	3 (2.1)	1 (5.6)	4 (2.3)
Abdominal only	7 (50.0)	50 (35.7)	2 (11.1)	59 (34.3)
Subcutaneous only	7 (50.0)	77 (55.0)	10 (55.6)	94 (54.7)
Abdominal and subcutaneous	0	4 (2.9)	2 (11.1)	6 (3.5)

[a]Assessed by CaGI-S.
[b]Missing for 9 (5.2%) attacks as of this interim data cutoff.
[c]Includes attacks with baseline CaGI-S rating of 'None': 2 (1.4%) attacks in 150-mg group and 5 (27.8%) attacks in 300-mg group.
Data cutoff date: December 15, 2025.
ODT, orally disintegrating tablet.

Time to Treatment

- Across all attacks, the median (IQR) time to treatment was 25 minutes (0-120) (**Figure 2**)
  - 67% of attacks were treated in <1 hour after onset

Figure 2. Time from Attack Onset to Sebetralstat ODT Administration[a,b]



Sebetralstat ODT dosing group	Median time (IQR) to sebetralstat administration, minutes
75 mg (n=14)	25 (10 to 150)
150 mg (n=139)[a]	20 (0 to 105)
300 mg (n=16)[a]	47 (0 to 205)
All attacks (N=169)[a]	25 (0 to 120)

[a]Data missing for 1 (0.7%) attack in the 150-mg group and 2 (11.1%) attacks in the 300-mg group.
[b]Caregiver or child could administer treatment.
Data cutoff date: December 15, 2025.
IQR, interquartile range; ODT, orally disintegrating tablet.

Interim Effectiveness

- Effectiveness was assessed for the largest treatment group (81% of attacks), 150 mg (**Table 3**)
- Conventional medication was utilized within 12 hours for 0.7% of attacks (1/140)

Table 3. Interim Effectiveness with Sebetralstat 150 mg

Endpoint	Sebetralstat ODT 150 mg n=140 attacks
Time to beginning of symptom relief within 12 hours, median (IQR), hours	**1.5** (1.0 to 4.0)
Time to reduction in attack severity within 12 hours, median (IQR), hours	**4.0** (1.7 to 10.6)
Time to complete attack resolution within 24 hours, median (IQR), hours	**12.0** (6.0 to 24.0)

Data cutoff date: December 15, 2025.
IQR, interquartile range; ODT, orally disintegrating tablet.

Safety and Tolerability

- There were no serious or treatment-related adverse events (**Table 4**)
- The safety profile was consistent across sebetralstat ODT dosing groups (ie, no dose level–dependent effect)
- There were no reports of difficulty swallowing sebetralstat ODT

Table 4. Safety and Tolerability

Event	All participants[a] N=36
Any TEAE, n (%)	16 (44.4)[b]
Treatment-related	**0**
Serious TEAE, n (%)	0
Severe TEAE, n (%)	0
Any TEAE leading to discontinuation, n (%)	0
Any TEAE leading to death, n (%)	0

[a]Participants who received at least 1 dose of sebetralstat.
[b]Thirty-one events in 16 participants. TEAEs by system organ class: infections and infestations (11 [30.6%]; 15 events); gastrointestinal disorders (5 [13.9%]; 5 events); nervous system disorders (4 [11.1%]; 7 events); eye disorders, injury, poisoning, and procedural complications, skin and subcutaneous tissue disorders, and vascular disorders (all 1 [2.8%]; 1 event each).
Data cutoff date: December 15, 2025.
HAE, hereditary angioedema; ODT, orally disintegrating tablet; TEAE, treatment-emergent adverse event.

Conclusions

- **Children with HAE and their caregivers experience significant burden from HAE attacks and currently available injectable on-demand treatment options[1,6]**
- **KONFIDENT-KID is the largest pediatric trial conducted in HAE to date[10,15-18] and is aligned with treatment guidelines[19]**
- **Attacks occurred in all locations, including the larynx**
  - **Participants had a mean of 0.7 attacks per month**
  - **The median time to treatment was 25 minutes by children or their caregivers**
  - **88.9% of attacks were still mild or moderate 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 (aged 2-11 years) with HAE and their caregivers**

References

1. Pagnier A et al. *Pediatr Allergy Immunol*. 2024;35(12):e14268
2. Pancholy N, Craig T. et al. *Curr Opin Pediatr*. 2019;31(6):863-868
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. Ruconest 2100 Units powder for solution for injection. SmPC. Pharming Group N. V. The Netherlands; 2015
8. Cinryze 500 IU powder and solvent for solution for injection. SmPC. Takeda Manufacturing AG; 2022
9. Firazyr (icatibant). SmPC (EU). Takeda Pharmaceuticals; 2025
10. Berinert (C1 esterase inhibitor [human]). PI. CSL Behring; 2022
11. Ekterly (sebetralstat). PI. KalVista Pharmaceuticals; 2025
12. Ekterly (sebetralstat). SmPC (UK). KalVista Pharmaceuticals; 2025
13. Ekterly (sebetralstat). SmPC (EU). KalVista Pharmaceuticals; 2025
14. Data on file. KalVista Pharmaceuticals, Inc.
15. Schneider L et al. *Pediatr Allergy Immunol*. 2013;24(1):54-60
16. Lumry W et al. *J Pediatr*. 2013;162(5):1017-22
17. Reshef A et al. *Pediatr Allergy Immunol*. 2019;30(5):562-568
18. Farkas H et al. *J Allergy Clin Immunol Pract*. 2017;5(6):1671-1678
19. Farkas H et al. *Allergy*. 2026:1-30

Acknowledgments

We thank the people living with HAE and their families; the US Hereditary Angioedema Association, HAE International, 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 Rachel Hood, PhD, of ApotheCom, San Francisco, CA, USA, and was funded by KalVista Pharmaceuticals.

Disclosures

Dr Emel Aygören-Pürsün declares the following real or perceived conflicts of interest: Receipt of grants/research support: CSL Behring, and Takeda/Shire. Receipt of honoraria or consultation fees: KalVista Pharmaceuticals, Astria, BioCryst, BioMarin Europe, Centogene, CSL Behring, Intellia Therapeutics, Otsuka, Pharming Technologies, Pharvaris, and Takeda/Shire. Participation in sponsored speaker bureau: none. Stock/shareholder: none. Other support: none.

Please scan the QR code to view the poster after the presentation.

Presented at the 2026 Global Angioedema Leadership Conference; March 26-29, 2026; Madrid, Spain

Copyright © 2026 KalVista Pharmaceuticals, Inc. All rights reserved.