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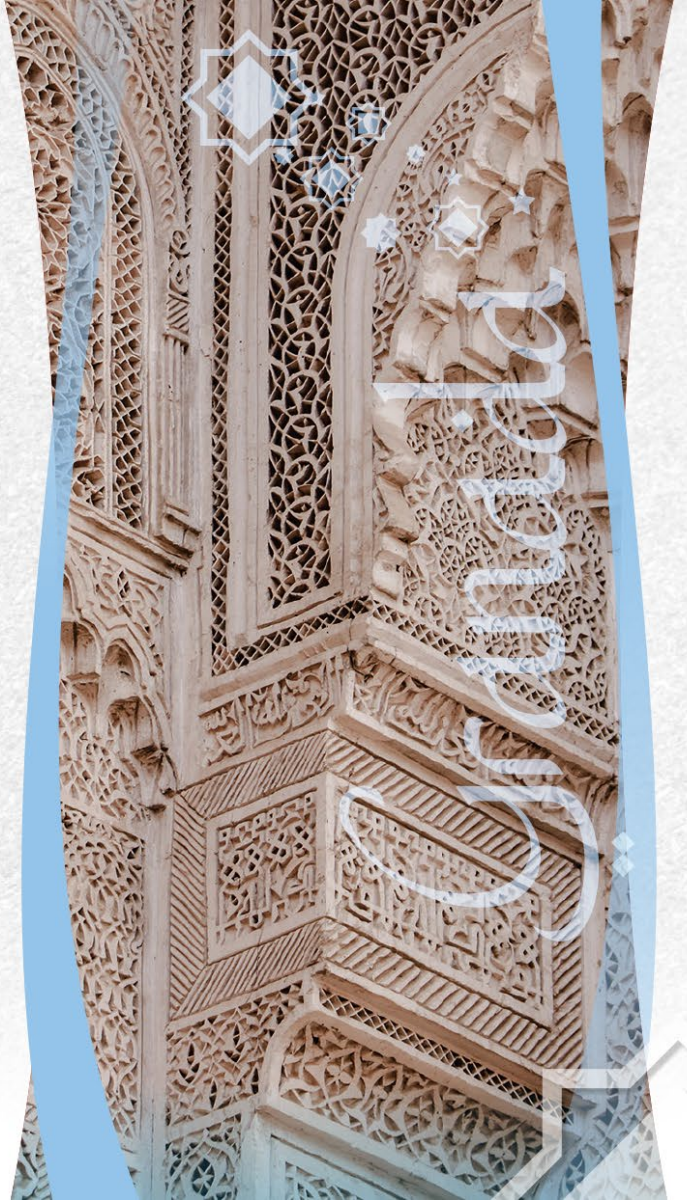

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Sebetralstat for On-demand Treatment of Hereditary Angioedema Attacks in European Participants: Interim Analysis from KONFIDENT-S

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Disclosures

- Dr Guilarte has received grants, honoraria, payment for expert testimony, meeting/travel support, and/or served on advisory boards for BioCryst, CSL Behring, Instituto de Salud Carlos III, KalVista Pharmaceuticals, Novartis, Otsuka Pharmaceuticals, Pharvaris, and Takeda. This study was funded by KalVista Pharmaceuticals

Background and Objective

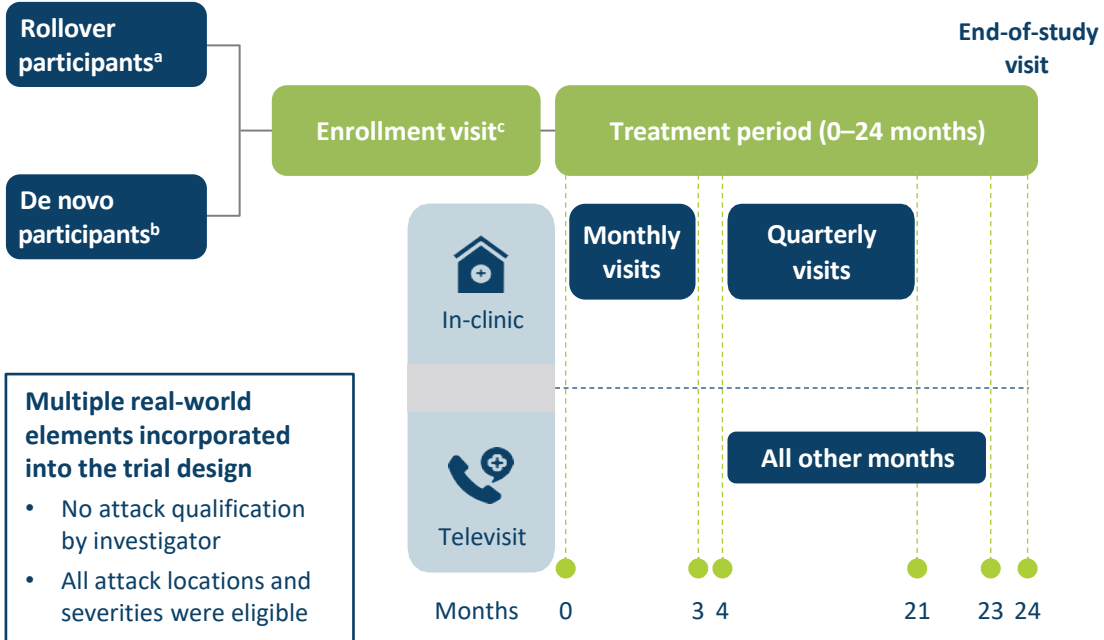
- Sebetralstat—an oral plasma kallikrein inhibitor—was recently approved in the EU for the on-demand treatment for HAE attacks in adults and adolescents aged ≥12 years[1,2]
- In the phase 3 KONFIDENT trial in patients with HAE, sebetralstat compared with placebo resulted in shorter times to beginning of symptom relief, reduction in attack severity, and complete attack resolution; sebetralstat was well tolerated[3]

Herein, we present safety and efficacy data from an interim analysis of the European subgroup of KONFIDENT-S, an ongoing, 2-year, open-label extension study of sebetralstat for the on-demand treatment of HAE

HAE, hereditary angioedema.

1. Sebetralstat (EKTERLY) prescribing information. KalVista Pharmaceuticals, Inc. 2025. 2. Sebetralstat (EKTERLY) Summary of Product Characteristics. KalVista Pharmaceuticals (Ireland), Ltd; 2025.
3. Riedl MA, et al. *New Engl J Med.* 2024;391(1):32-43.

KONFIDENT-S OLE Trial Design



Multiple real-world elements incorporated into the trial design

- No attack qualification by investigator
- All attack locations and severities were eligible
- Portable multidose packs

Inclusion criteria

- Age ≥12 years
- ≥2 documented HAE-C1INH attacks ≤3 months

Treatment

- Self-administer sebetralstat 600 mg (2 × 300-mg tablets) as early as possible after attack onset
- Second administration allowed if warranted

Endpoints

- Safety (adverse events)
- Time to beginning of symptom relief (by PGI-C) ≤12 hours
- Time to first reduction in severity (by PGI-S) ≤12 hours
- Time to complete attack resolution (by PGI-S) ≤24 hours

NCT05505916, EudraCT: 2021-001176-42. [a]Completed the phase 3 KONFIDENT trial. [b]All other participants, including those who participated in the phase 2 trial. [c]For de novo participants, 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.

Baseline Characteristics of European Participants with ≥1 Sebetralstat-treated Attack[a]

	Overall n=69
Age, median (IQR), years	35.0 (22.0–48.0)
≥18 years, n (%)	57 (82.6)
Sex, female, n (%)	39 (56.5)
White race, n (%)	64 (92.8)
Patients from Spain, n (%)	3 (4.3)
BMI, median (IQR), kg/m²	25.5 (22.4–30.8)
HAE-C1INH type, n (%)	
Type 1	66 (95.7)
Type 2	3 (4.3)
Treatment, n (%)	
On-demand only	60 (87.0)
LTP	9 (13.0)

Data cutoff: September 14, 2024.
[a]Safety analysis population from 15 European countries. BMI, body mass index; HAE-C1NH, hereditary angioedema due to C1 inhibitor deficiency; IQR, interquartile range; LTP, long-term prophylaxis.

Baseline Attack Characteristics

	Total attacks: N=999[a]
Baseline severity (PGI-S),[b] n (%)	
Mild[c]	355 (35.5)
Moderate	395 (39.5)
Severe/very severe	229 (22.9)
Missing	20 (2.0)
Primary pooled attack location, n (%)	
Mucosal[d]	410 (41.0)
Involving the larynx	23 (2.3)
Subcutaneous only[d]	567 (56.8)
Missing	22 (2.2)
Time from attack onset to treatment, median (IQR), min	16 (1–69)

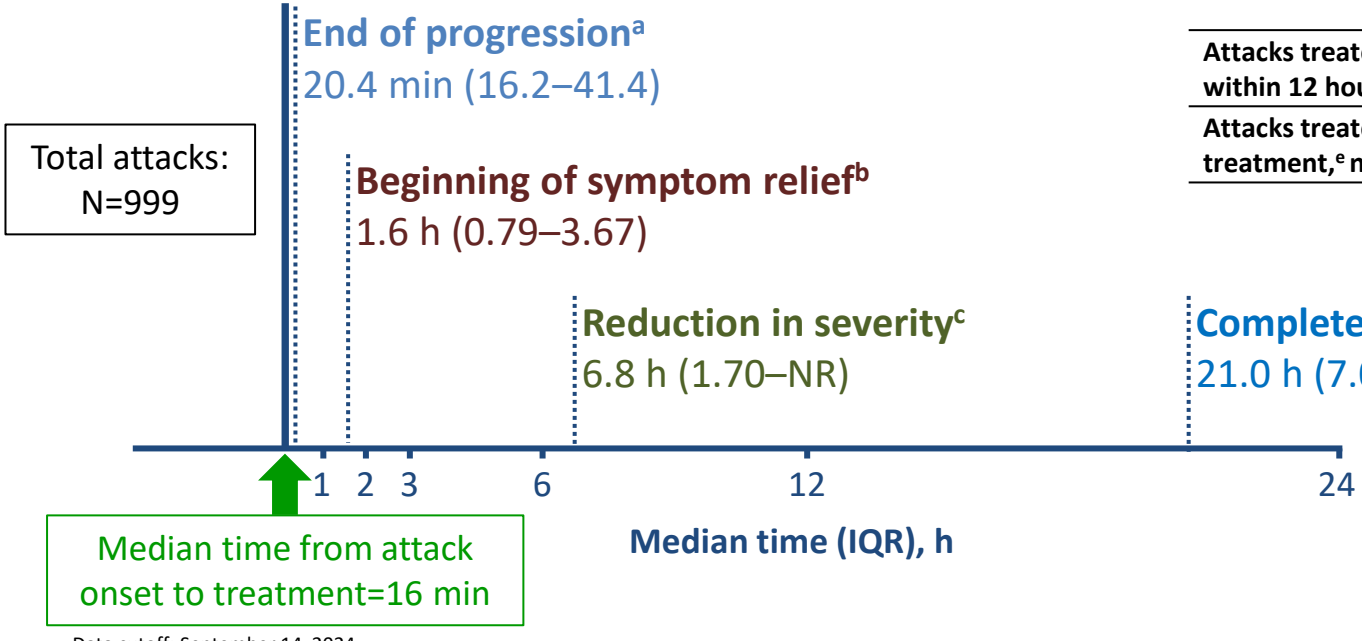
Data cutoff: September 14, 2024.
[a]Twenty-one attacks occurred in patients from Spain. [b]PGI-S score was transformed into numeric values: 0=none, 1=mild, 2=moderate, 3=severe, 4=very severe. [c]'None' was reported for 12 attack (1.2%). [d]Mucosal: attacks with primary location of "Abdomen" and/or "Larynx/Throat"; subcutaneous: other attacks not involving the mucosal locations. IQR, interquartile range; PGI-S, Patient Global Impression of Severity.

Safety

Participants experiencing TEAE, n (%)	Total N=69
Any TEAE	40 (58.0)
Treatment related[a]	6 (8.7)
Any TEAE within 3 days of sebetralstat administration	27 (39.1)
Any grade ≥3 TEAE	6 (8.7)
Treatment related	0
Any serious TEAE	6 (8.7)
Treatment related	0
Any TEAE leading to hospitalization	5 (7.2)
Any TEAE leading to study discontinuation	2 (2.9)
Any TEAE leading to death	0

Data cutoff: September 14, 2024.
[a]Six patients reported treatment-related TEAEs, including headache (n=3), influenza-like illness (n=3), vomiting (n=3), skin burning sensation (n=2), myalgia (n=2), and tremor (n=1).
TEAE, treatment-emergent adverse event.

Timing of Efficacy Outcomes of Sebetralstat-treated Attacks



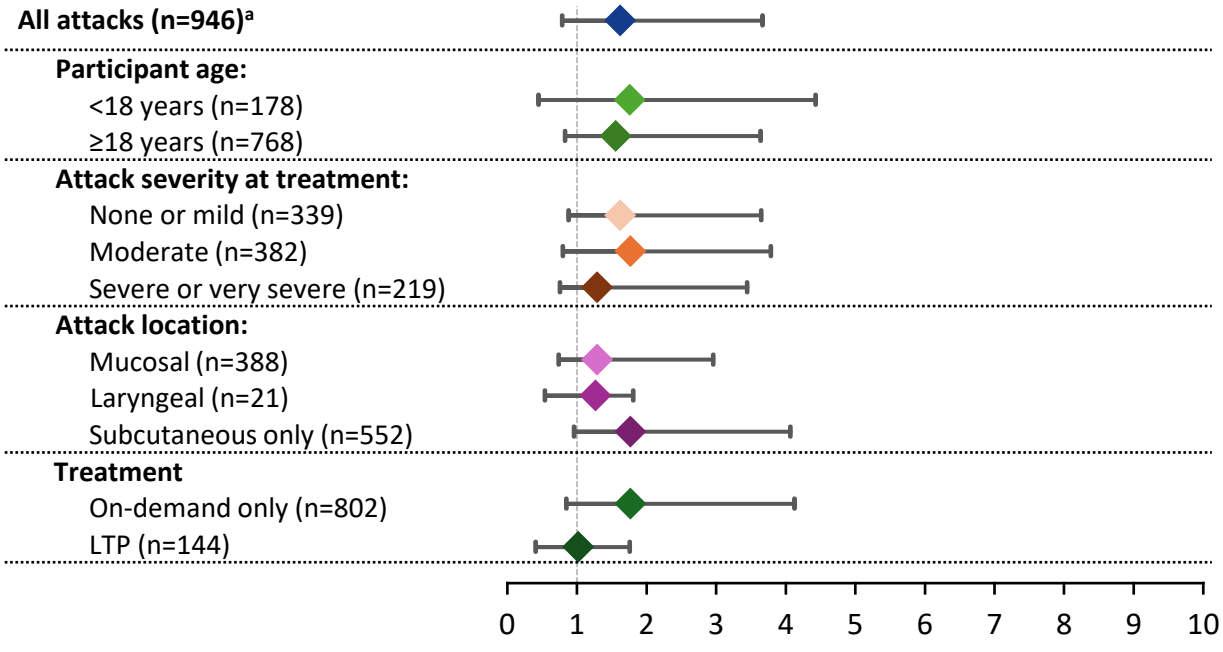
	Total attacks: N=999
Attacks treated with a second dose within 12 hours, n (%)	174 (17.4)
Attacks treated with conventional treatment,[e] n (%)	60 (6)

Data cutoff: September 14, 2024.

[a]End of progression was analyzed post hoc as the time when the worst HAE attack severity was recorded within 4 hours on the PGI-S scale for attacks treated with sebetralstat. [b]Defined as a PGI-C rating of at least "A little better" for ≥2 consecutive time points (with missing data entries in between) within 12 hours of the first dose of sebetralstat (7-point scale: "Much worse," "Worse," "A little worse," "No change," "A little better," "Better," "Much better"). [c]Defined as a ≥1-level decrease on the PGI-S scale for ≥2 consecutive time points within 12 hours of the first dose of sebetralstat. [d]Defined as a PGI-S rating of "None" (ie, no symptoms) within 24 hours of the first dose of sebetralstat. [e]Received conventional medicine within 12 hours of the first dose of sebetralstat.

HAE, hereditary angioedema; IQR, interquartile range; NR, not reached; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity.

Time to Beginning of Symptom Relief in Subgroups



Data cutoff: September 14, 2024.
Diamonds are the medians met within time window. Error bars are IQR.
[a]Excluding attacks that lacked post-baseline assessments. [b]Defined as a PGI-C rating of at least "A little better" for 2 consecutive time points within 12 hours of the first dose of sebetralstat.
IQR, interquartile range; LTP, long-term prophylaxis; PGI-C, Patient Global Impression of Change.

Conclusions

- In KONFIDENT-S, sebetralstat enabled early treatment of HAE attacks in European participants (median time, 16 min)
- Sebetralstat resulted in rapid end of attack progression, early symptom relief, reduction in attack severity, and attack resolution, consistent with data reported in the KONFIDENT trial
- Median time to beginning of symptom relief was consistent across all subgroups, including by age, attack severity at onset, attack location at onset, and LTP use
- Sebetralstat was well tolerated, and safety results were consistent with the phase 3 KONFIDENT trial[1]

1. Riedl MA et al. *New Engl J Med.* 2024;391(1):32-43. HAE, hereditary angioedema; LTP, long-term prophylaxis.

Acknowledgments

- The authors thank the people living with HAE and their families; the US Hereditary Angioedema Association (HAEA), HAE International (HAEi), and member organizations; and the investigator teams who contributed to the international KONFIDENT-S trial
- Medical writing and editorial support for the development of this presentation, under the direction of the authors, was provided by Sara Thier, PhD, MPH, and Kathleen A. Blake, PhD, Ashfield MedComms (US), an Inizio company, and was funded by KalVista Pharmaceuticals