20. DEUTSCHER ALLERGIE KONGRESS

Wirksamkeit von Sebetralstat zur bedarfsweisen Behandlung von mukosalen hereditären Angioödem-Attacken: Zwischenanalyse aus KONFIDENT-S

Emel Aygören-Pürsün,[1] Inmaculada Martinez-Saguer,[2] Jonathan A. Bernstein,[3] Danny M. Cohn,[4] Vesna Grivcheva-Panovska,[5] William R. Lumry,[6] Marc A. Riedl,[7] Andrea Zanichelli,[8,9] Laurence Bouillet,[10] Ya-Hsiu Chuang,[11] Michael D. Smith,[11] Christopher M. Yea,[11] Paul K. Audhya,[11] Henriette Farkas,[12] Petra Staubach,[13] Markus Magerl[14,15]

[1]University Hospital Frankfurt, Goethe University Frankfurt, Frankfurt, Germany; [2]HZRM Hämophilia Center Rhein Main, Frankfurt, Germany; [3]University of Cincinnati College of Medicine and Bernstein Clinical Research Center, Cincinnati, OH, USA; [4]Amsterdam University Medical Center, University of Amsterdam, Amsterdam, Netherlands; [5]University Clinic of Dermatology, School of Medicine, University Saints Cyril and Methodius, Skopje, North Macedonia; [6]AARA Research Center, Dallas, TX, USA; [7]University of California, San Diego, La Jolla, CA, USA; [8]Operative Unit of Medicine, Angioedema Center, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy; [9]Department of Biomedical Science for Health, University of Milan, Milan, Italy; [10]French National Reference Center for Angioedema (CREAK), Grenoble Alpes University, Grenoble, France; [11]KalVista Pharmaceuticals, Salisbury, United Kingdom, and Framingham, MA, USA; [12]Hungarian Angioedema Center of Reference and Excellence, Semmelweis University, Budapest, Hungary; [13]Department of Dermatology, University Medical Center, Mainz, Germany; [14]Institute of Allergology, Charité-Universitätsmedizin Berlin, corporate member of Freie Universitätsmedizin Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; [15]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany

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Background

- Mucosal attacks (eg, affecting the abdomen or larynx) may progress rapidly and are associated with substantial morbidity in people living with HAE[1-3]
- Sebetralstat, an oral plasma kallikrein inhibitor, has been approved for the treatment of acute HAE attacks in patients ≥12 years old in the US, UK, and EU[4-6]

The objective of this interim analysis was to assess the safety and effectiveness of sebetralstat in mucosal attacks in the KONFIDENT-S OLE study

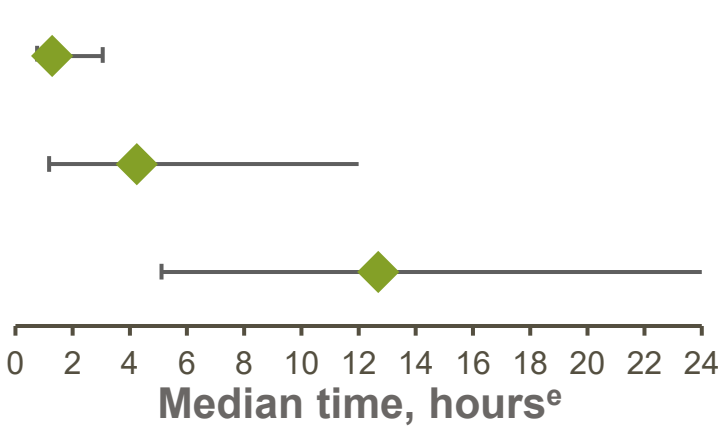
KONFIDENT-S: NCT05505916; EudraCT: 2021-001176-42.

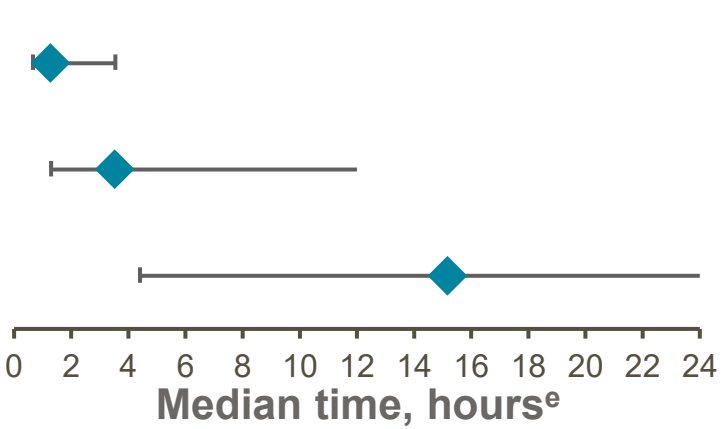
1. De Maat S, et al. *J Thromb Haemost*. 2018;16(11):2349-2351. 2. Bork K, et al. *J Emerg Med*. 2016;50(4):567-580.e1. 3. Bork K, et al. *Am J Gastroenterol*. 2006;101(3):619-627. 4. EKTERLY (sebetralstat) tablets, for oral use. US prescribing information. KalVista Pharmaceuticals, Inc; 2025. 5. EKTERLY (sebetralstat). Summary of Product Characteristics. UK prescribing information. KalVista Pharmaceuticals, Inc; 2025. 6. EKTERLY (sebetralstat). Summary of Product Characteristics. EU prescribing information. KalVista Pharmaceuticals, Inc; 2025.

HAE, hereditary angioedema; OLE, open-label extension.

Effectiveness of Sebetralstat

Endpoint	Laryngeal Attacks (n=32)[a]	Median (IQR), hours	Abdominal Attacks (n=533)[a]	Median (IQR), hours
Time to beginning of symptom relief[b]		1.29 (0.76 – 3.02)		1.27 (0.76 – 3.54)
Time to reduction in attack severity[c]		4.25 (1.22 – >12)		3.52 (1.26 – >12)
Time to complete attack resolution[d]		12.69 (5.11 – >24)		15.17 (4.46 – >24)





- The median (IQR) time from attack recognition to sebetralstat administration was **11.5 minutes (1.0 – 34.0)** for laryngeal and **20.0 minutes (1.0 – 61.0)** for abdominal attacks
- Sebetralstat showed similar effectiveness as an on-demand treatment for both laryngeal and abdominal attacks

[a]Out of a total of 1706 attacks (laryngeal, 1.9%; abdominal, 31.2%). [b]Defined as a PGI-C rating of at least "A Little Better" for 2 consecutive time points within 12 hours (with missing data entries between consecutive time points). [c]Defined as a decrease in the PGI-S rating for 2 consecutive time points within 12 hours. [d]Defined as a PGI-S rating of "None" within 24 hours. [e]Error bars display IQR.
Data cutoff date of September 14, 2024. IQR, interquartile range; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity.

Effectiveness of Sebetralstat

	Laryngeal Attacks n=32[a]	Abdominal Attacks n=533[a]
Attacks treated with an additional dose within 12 hours, n (%)	4 (12.5)	95 (17.8)
Proportion of attacks reaching beginning of symptom relief within 12 hours before or without an additional dose[b]	96.0%	95.8%
Attacks treated with conventional treatment within 12 hours, n (%)	3 (9.4)	43 (8.1)

Most mucosal attacks achieved beginning of symptom relief before or without a second dose of sebetralstat

[a]Out of a total of 1706 attacks (laryngeal, 1.9%; abdominal, 31.2%). [b]Among the attacks that reached this endpoint (89.3% of laryngeal attacks; 85.7% of abdominal). Data cutoff date of September 14, 2024. n, number of attacks.

Safety of Sebetralstat

	Laryngeal Attacks n=16	Abdominal Attacks n=102
Any TEAE, n (%)	7 (43.8)	36 (35.3)
Treatment-related	**1 (6.3)[a]**	**6 (5.9)[a,b]**
Serious TEAE, n (%)	2 (12.5)[c]	2 (2.0)
Treatment-related	**0**	**0**
Severe TEAE, n (%)	3 (18.8)	2 (2.0)
Treatment-related	**0**	**0**
Any TEAE leading to permanent discontinuation, n (%)	1 (6.3)	2 (2.0)
Any TEAE leading to death, n (%)	0	0

Sebetralstat was well tolerated as treatment for mucosal attacks.
No participants reported difficulty swallowing sebetralstat.

[a]Nausea and vomiting (grade 2) occurred in the same participant, who experienced a laryngeal and abdominal attack. [b]Flu-like symptoms, cutaneous burning, diarrhea (3 events), headaches, myalgia (bilateral arm and bilateral leg [1 event each]; all grade 2), and vomiting (2 events, grade 1) occurred in 6 participants, who experienced an abdominal attack only. [c]Serious AEs resulting in hospitalization (but considered unrelated to treatment): 1 event of grade 3 viral meningitis in 1 participant and 2 events of laryngeal HAE attack in 1 participant.
Data cutoff date of September 14, 2024. n, number of participants; TEAE, treatment-emergent adverse event.