20. DEUTSCHER ALLERGIE KONGRESS

Sebetralstat for Treatment of HAE Attacks in Patients Receiving Berotralstat: Interim Analysis from the KONFIDENT-S Open-label Study

Markus Magerl,[1,2] Inmaculada Martinez-Saguer,[3] Michael E. Manning,[4,5] Marc A. Riedl,[6] Raffi Tachdjian,[7] H. Henry Li,[8] H. James Wedner,[9] Daniel F. Soteres,[10] James Hao,[11] Michael D. Smith,[11] Paul K. Audhya,[11] Tamar Kinaciyan,[12] Petra Staubach,[13] Emel Aygören-Pürsün[14]

[1]Institute of Allergology, Charité-Universitätsmedizin Berlin, corporate member of Freie Universitätsmedizin Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; [2]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany; [3]HZRM Hämophilia Center Rhein Main, Frankfurt, Germany; [4]Allergy, Asthma and Immunology Associates, Ltd., Scottsdale, AZ, USA; [5]University of Arizona College of Medicine-Phoenix, Scottsdale, AZ, USA; [6]University of California, San Diego, La Jolla, CA, USA; [7]University of California, Los Angeles, School of Medicine, Los Angeles, CA, USA; [8]Institute for Asthma and Allergy, Wheaton, MD, USA; [9]Washington University School of Medicine, St. Louis, MO, USA; [10]Asthma & Allergy Associates, PC, and Research Center, Colorado Springs, CO, USA; [11]KalVista Pharmaceuticals, Salisbury, United Kingdom, and Framingham, MA, USA; [12]Medical University of Vienna, Vienna, Austria; [13]University Medical Center, Mainz, Germany; [14]University Hospital Frankfurt, Goethe University Frankfurt, Frankfurt, Germany

Disclosures: Markus Magerl has received grants, honoraria, and medical writing support from KalVista Pharmaceuticals, CSL Behring, Takeda, Pharming, BioCryst, Novartis, Octapharma, Intellia Therapeutics, and Pharvaris.

Background

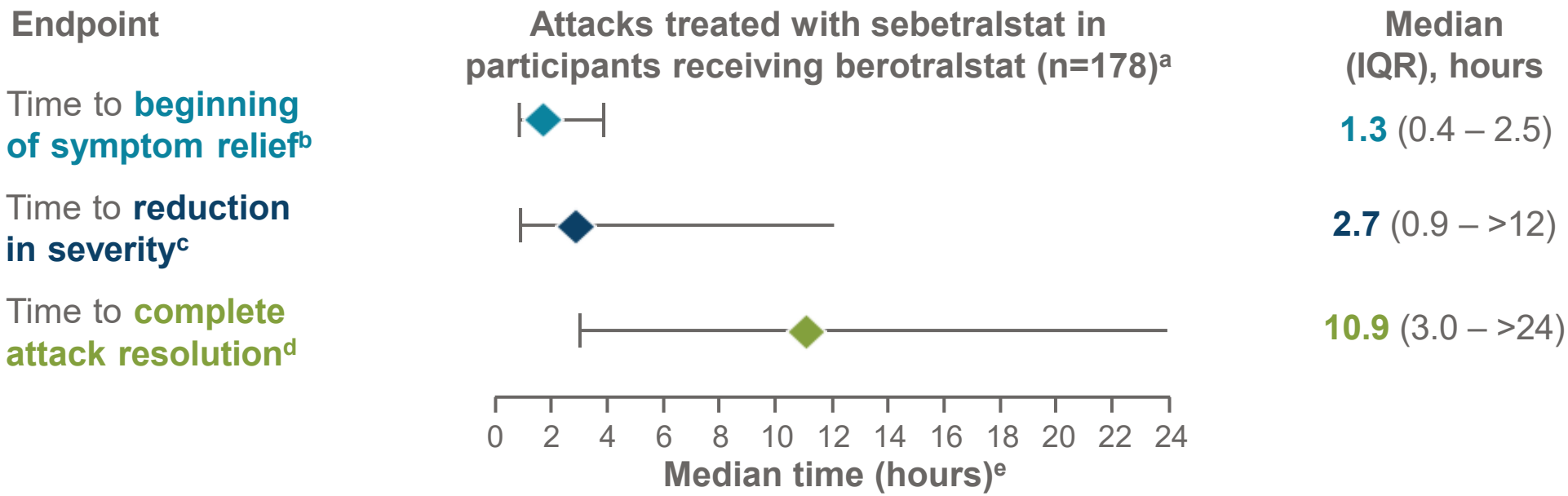
- Patients with HAE report a clear preference for oral compared with parenteral medication[1,2]
- Sebetralstat and berotralstat (both plasma kallikrein inhibitors) are the only approved oral on-demand and non-androgen LTP treatments, respectively
  - Sebetralstat was recently approved for the treatment of acute HAE attacks in patients ≥12 years old in the US, UK, and EU[3-5]

This interim analysis of KONFIDENT-S examined the safety and effectiveness of oral sebetralstat to treat HAE attacks in participants receiving oral berotralstat as LTP

KONFIDENT-S: NCT05505916; EudraCT: 2021-001176-42. Data cutoff date: September 14, 2024.

1. Radojicic C, et al. *Allergy Asthma Proc*. 2021;42(3):S4-S10. 2. Geba D, et al. *J Drug Assess.* 2021;10(1):51-56. 3. Ekterly (sebetralstat). Prescribing information. KalVista Pharmaceuticals, Inc; 2025. 4. Ekterly (sebetralstat). Summary of product characteristics (UK). KalVista Pharmaceuticals, Inc; 2025. 5. Ekterly (sebetralstat). Summary of product characteristics (EU). KalVista Pharmaceuticals, Inc; 2025. HAE, hereditary angioedema; LTP, long-term prophylaxis.

Effectiveness of Sebetralstat



- The median (IQR) time from attack recognition to sebetralstat administration in participants receiving berotralstat was **20.0 minutes (IQR, 1.0 – 67.0)**
- Sebetralstat provided early symptom relief, reduction in severity, and complete attack resolution in participants experiencing attacks while on berotralstat

[a]Out of a total of 1706 attacks (10.4%). [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: September 14, 2024. IQR, interquartile range; n, number of attacks; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity.

Effectiveness of Sebetralstat

	Attacks treated with sebetralstat in participants receiving berotralstat n=178[a]
Attacks treated with an additional dose within 12 hours, n (%)	38 (21.3)
Proportion of attacks reaching beginning of symptom relief within 12 hours before or without an additional dose[b]	92.1%
Attacks treated with conventional treatment within 12 hours, n (%)	8 (4.5)

Most attacks achieved the beginning of symptom relief before or without an additional dose of sebetralstat

[a]Out of a total of 1706 attacks (10.4%). [b]Among the attacks that reached this endpoint (78.1%).
Data cutoff date: September 14, 2024. n, number of attacks.

Safety of Sebetralstat

	Participants receiving berotralstat n=16
Any TEAE, n (%)	12 (75.0)
Treatment-related	**3 (18.8)[a]**
Serious TEAE, n (%)	3 (18.8)
Treatment-related	**0**
Severe TEAE, n (%)	3 (18.8)
Treatment-related	**0**
Any TEAE leading to permanent discontinuation, n (%)	1 (6.3)
Treatment-related	**1 (6.3)[b]**
Any TEAE leading to death, n (%)	0

Sebetralstat was generally well tolerated, and no new safety signals were observed in participants receiving LTP with berotralstat

[a]Six TEAEs in 3 participants were considered treatment related: myalgia (2 events), arthralgia (1 event), headache (1 event), nausea (1 event), and vomiting (1 event). [b]One participant discontinued the study due to treatment-related TEAEs of nausea and vomiting, which occurred during an attack involving the abdomen and the larynx/throat. Data cutoff date: September 14, 2024. n, number of participants; TEAE, treatment-emergent adverse event.