

End of Progression of Attack Manifestations With Oral Deucricitbant Immediate-Release Capsule for On-Demand Treatment of Hereditary Angioedema Attacks in the Phase 3 RAPiDe-3 Trial

Raffi Tachdjian¹, Marc A. Riedl², Philip H. Li³, Adil Adatia⁴, Mauro Cancian⁵, Marcin Stobiecki⁶, Anna Valerieva⁷, Anete S. Grumach⁸, William R. Lumry⁹, Daniel F. Soteres¹⁰, Nicholas Brodyszki¹¹, Natalia L. Fili¹², Roman Haki¹³, Hye-Ryun Kang^{14,15,16,17}, Gul Karakaya¹⁸, Birger Kränke¹⁹, H. Henry Li²⁰, Jonny Peter^{21,22}, Andreas Recke²³, Henriette Farkas²⁴, Paola Triggianese²⁵, Andrea Zanichelli^{26,27}, John Anderson²⁸, Emel Aygören-Pürsün²⁹, Timothy J. Craig^{30,31}, Francesco Giardinio³², Pedro Giavina-Bianchi³³, Sujeong Kim³⁴, Tamar Kinaciyani³⁵, Inmaculada Martinez-Saguer³⁶, Francesca Perego³⁷, Karl V. Sitz³⁸, Maria Staevska⁷, H. James Wedner³⁹, Rafael H. Zaragoza-Urdaz⁴⁰, Ricardo D. Zwiener⁴¹, Asli Gelincik⁴², Francesco Arcoleo⁴³, Rand Arnaut⁴⁴, Alan P. Baptist⁴⁵, Régis Albuquerque Campos⁴⁶, Anthony D. Dorr⁴⁷, Mariana Paes Leme Ferriani⁴⁸, Atsushi Fukunaga⁴⁹, Delphine Gobert⁵⁰, Padmalal Gurugama⁵¹, Michihiro Hide⁵², David I. Hong⁵³, Eisuke Inage⁵⁴, Joshua S. Jacobs⁵⁵, Constance H. Katelaris⁵⁶, Lucy Leeman⁵⁷, Ramón Lleonart⁵⁸, Markus Mager^{59,60}, Michael E. Manning⁶¹, Satoshi Man⁶², Seido Ooka⁶³, Cristina J. Ramos⁶⁴, Jinzhong Liu⁶⁵, Li Zhu⁶⁵, Joan Mendivil⁶⁶, Umar Katbeh⁶⁶, Giorgio Giannattasio⁶⁶, Rafael Crabbé⁶⁷, Ming Yu⁶⁵, Anne Lesage⁶⁸, Peng Lu⁶⁵, Danny M. Cohn⁶⁹

¹University of California at Los Angeles, Los Angeles, CA, USA; ²University of California San Diego, La Jolla, CA, USA; ³Queen Mary Hospital, University of Hong Kong, Hong Kong SAR, China; ⁴University of Alberta, Edmonton, AB, Canada; ⁵Azienda Ospedale Università di Padova, Padova, Italy; ⁶Jagiellonian University Medical College, Kraków, Poland; ⁷Medical University of Sofia, Sofia, Bulgaria; ⁸Centro Universitario FMABC, São Paulo, Brazil; ⁹AARA Research Center, Dallas, TX, USA; ¹⁰Asthma & Allergy Associates and Research Center, P.C., Colorado Springs; University CO Health Sciences Center, Aurora, CO, USA; ¹¹Children's Hospital, Skåne University Hospital, Lund, Sweden; ¹²Hospital Público Materno Infantil, Salta, Argentina; ¹³St. Anne's University Hospital in Brno and Faculty of Medicine, Masaryk University, Brno, Czech Republic; ¹⁴Seoul National University College of Medicine, Seoul, South Korea; ¹⁵Seoul National University Hospital, Seoul, South Korea; ¹⁶Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul, South Korea; ¹⁷Korean Drug Allergy Research Consortium, Seoul, South Korea; ¹⁸Hacettepe University Faculty of Medicine, Ankara, Türkiye; ¹⁹Medical University of Graz, Graz, Austria; ²⁰Institute for Asthma and Allergy, Chevy Chase, MD, USA; ²¹Groote Schuur Hospital, Cape Town, South Africa; ²²University of Cape Town and Allergy and Immunology Unit, University of Cape Town Lung Institute, Cape Town, South Africa; ²³University of Lübeck, Lübeck, Germany; ²⁴Hungarian Angioedema Center of Reference and Excellence, Semmelweis University, Budapest, Hungary; ²⁵University of Rome Tor Vergata, Rome, Italy; ²⁶Università degli Studi di Milano, Milan, Italy; ²⁷I.R.C.C.S. Policlinico San Donato, Milan, Italy; ²⁸AllerVie Health, Clinical Research Center of Alabama, Birmingham, AL, USA; ²⁹Goethe University Frankfurt, Frankfurt am Main, Germany; ³⁰Penn State University, Hershey, PA, USA; ³¹Vinmec-VinUni Institute of Immunology, Vinmec Hospital, Times City, Vietnam, and Vin University, Hanoi, Vietnam; ³²A.O.U. Policlinico "G. Rodolico-San Marco", Catania, Italy; ³³Prof. Livre Docente Associado - Disciplina de Imunologia Clínica e Alergia da FMUSP, Visiting Professor da Harvard Medical School 2012-14, Editor dos *Arquivos de Asma, Alergia e Imunologia*, Diretor da World Allergy Organization, São Paulo, Brazil; ³⁴School of Medicine, Kyungpook National University Hospital, Daegu, South Korea; ³⁵Medical University of Vienna, Vienna, Austria; ³⁶HZRM Hämophilie Zentrum Rhein Main GmbH, Frankfurt, Germany; ³⁷Istituto Clinico Scientifici Maugeri IRCCS, Milan, Italy; ³⁸Acuro Research, Inc., Little Rock, AR, USA; ³⁹Washington University School of Medicine, St. Louis, MO, USA; ⁴⁰University Pediatric Hospital, San Juan, Puerto Rico; ⁴¹Hospital Universitario Austral, Buenos Aires, Argentina; ⁴²Istanbul University, Istanbul, Türkiye; ⁴³AOR Villa Sofia-Cervello, Palermo, Italy; ⁴⁴King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia; ⁴⁵Henry Ford Health System, Detroit, MI, USA; ⁴⁶Ensino e Terapia de Inovação Clínica AMO, Salvador, Bahia, Brazil; ⁴⁷Barts Health NHS Trust, London, UK; ⁴⁸Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, São Paulo, Brazil; ⁴⁹Osaka Medical and Pharmaceutical University, Takatsuki, Osaka, Japan; ⁵⁰Sorbonne Université, Médecine Interne, Centre de Référence des Angioedèmes à Kinines, Hôpital Saint-Antoine, AP-HP, Paris, France; ⁵¹Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; ⁵²Hiroshima University and Hiroshima City Hospital Organization, Hiroshima, Japan; ⁵³Harvard Medical School and Brigham and Women's Hospital, Boston, MA, USA; ⁵⁴Juntendo University Faculty of Medicine, Tokyo, Japan; ⁵⁵Allergy and Asthma Clinical Research, Walnut Creek, CA, USA; ⁵⁶Campbelltown Hospital and Western Sydney University, Sydney, NSW, Australia; ⁵⁷University Hospitals Plymouth NHS Trust, Plymouth, UK; ⁵⁸Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Spain; ⁵⁹Institute of Allergology, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; ⁶⁰Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany; ⁶¹Allergy, Asthma and Immunology Associates, Ltd., Scottsdale, AZ, USA; ⁶²Juntendo University Hospital, Tokyo, Japan; ⁶³St. Marianna University School of Medicine Hospital, Kanagawa, Japan; ⁶⁴FDI Clinical Research, San Juan, Puerto Rico; ⁶⁵Pharvaris Inc., Lexington, MA, USA; ⁶⁶Pharvaris GmbH, Zug, Switzerland; ⁶⁷RC Consultancy, Bassins, Switzerland; ⁶⁸GrayMatters Consulting, Schilde, Belgium; ⁶⁹Amsterdam Cardiovascular Sciences, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands

Key takeaways

The Phase 3 RAPiDe-3 trial for treatment of attacks in multiple types of hereditary angioedema (HAE) demonstrated that attacks treated with the bradykinin B2 receptor antagonist, deucricitbant immediate-release (IR) capsule, achieved end of progression (EoP) of attack manifestations faster than those treated with placebo.

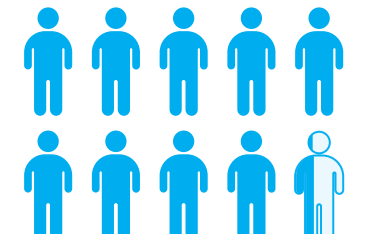
EoP of HAE attack manifestations

was measured in the RAPiDe-3 trial for the first time as a pre-specified endpoint in an HAE on-demand trial



17.47 minutes

Median time to EoP of attack manifestations in participants taking deucricitbant IR



>90%

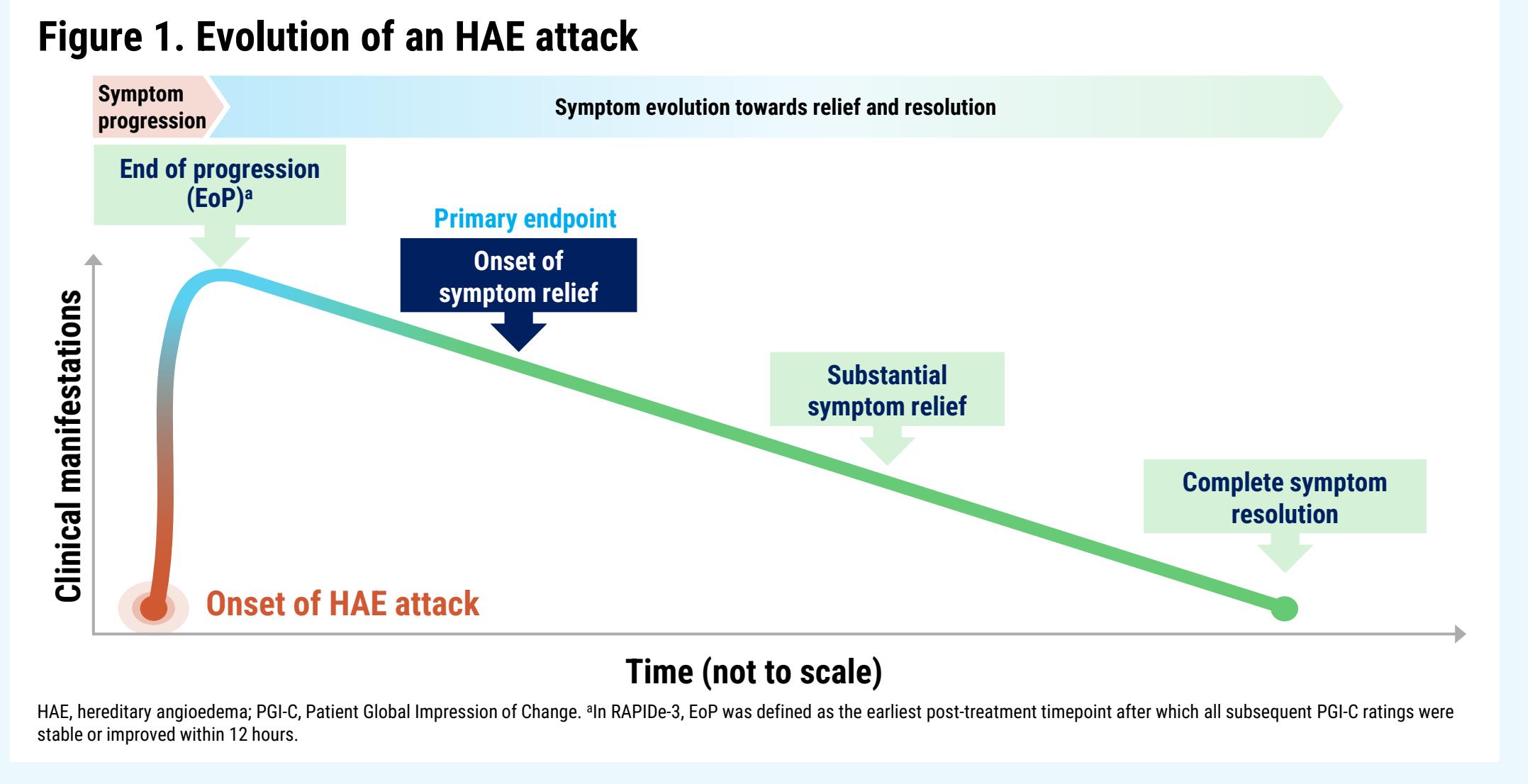
of participants taking deucricitbant achieved EoP of attack manifestations in 12 hours

This presentation includes data for an investigational product not yet approved by regulatory authorities.

Background

- Hereditary angioedema (HAE):** a condition characterized by excess bradykinin, which activates bradykinin B2 receptors causing increased fluid migration from the blood vessels to the surrounding tissues. HAE causes recurrent and unpredictable episodes of painful angioedema attacks affecting multiple locations in the body with varying degrees of severity.¹
- Unmet need:** an unmet need remains for additional orally administered treatments combining ease of administration, rapid and sustained effects, and a well-tolerated safety profile.^{2,4}
- End of progression (EoP):** defined as the earliest post-treatment timepoint after which attack manifestations stop worsening further, which marks the earliest evidence of treatment effects.²
 - It may serve as a clinically meaningful indicator of attacks starting to evolve to relief and resolution.²
 - Achieving EoP can also offer psychological reassurance by reducing the uncertainty associated with HAE attack escalation.
- Time to EoP as an outcome to measure treatment efficacy:** recommended for inclusion by the Acute Treatment Outcomes in Hereditary Angioedema (AURORA) consensus project.
 - The AURORA project brought together patients, clinicians, researchers, industry representatives, and regulatory stakeholders to develop a set of core outcomes recommended for inclusion in clinical trials of on-demand treatments for HAE attacks.²
 - 95% of participants agreed that time to EoP should be included as one of the five core outcomes as it represented the earliest sign of treatment effects.²
- Oral deucricitbant:** a selective bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of bradykinin-mediated angioedema attacks.⁵⁻¹²

Background



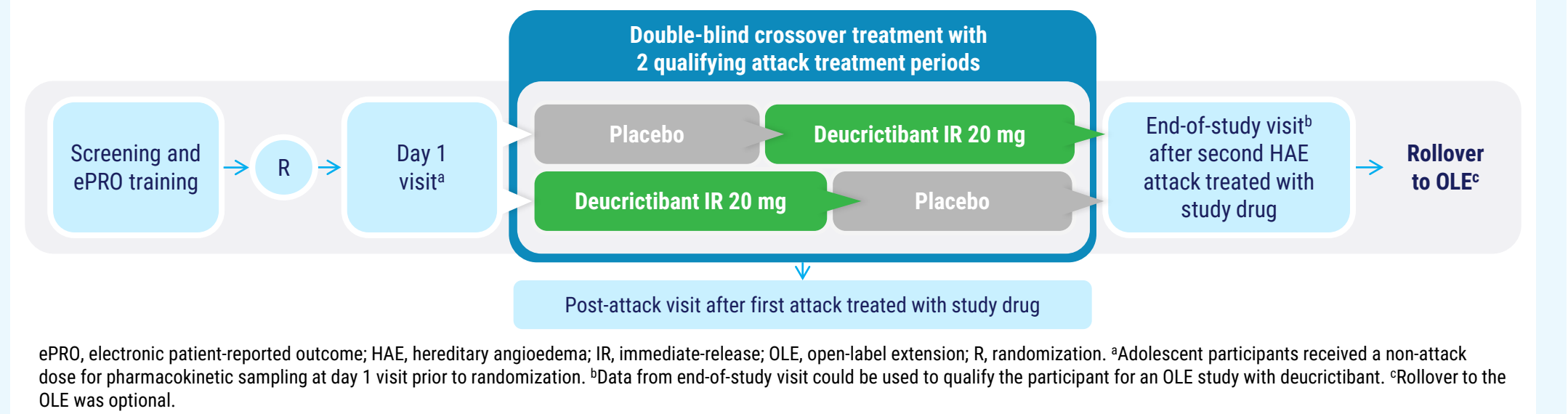
Objective

To evaluate the time to EoP of attack manifestations as a pre-specified outcome aimed to document initial or earliest clinical evidence of acute attack manifestations stopping to worsen and starting to evolve towards relief and resolution following on-demand treatment with deucricitbant immediate-release (IR) versus placebo in adolescents and adults with HAE.

Methods

- RAPiDe-3 (NCT06343779)*:** a global, Phase 3, randomized, double-blind, placebo-controlled, crossover trial.
- Participants:** adolescents (aged ≥12 to <18 years) and adults (aged ≥18 to ≤75 years) with HAE-C1INH type 1 or 2, or HAE with normal C1 inhibitor (HAE-nC1INH). Participants on long-term HAE prophylaxis were also enrolled.
- Study drugs:** participants self-administered deucricitbant IR capsule 20 mg or placebo to treat two qualifying attacks in a crossover design. Qualifying attacks were defined as either a non-laryngeal attack with at least one symptom item score of ≥20 on the Angioedema syMptom Rating scAle (AMRA) assessment, or a non-severe laryngeal attack without breathing difficulties or stridor.
- Analysis set:** primary efficacy analysis included all randomized participants who had two attacks treated with study drug in accordance with the crossover design.

Figure 2. RAPiDe-3 trial design⁷



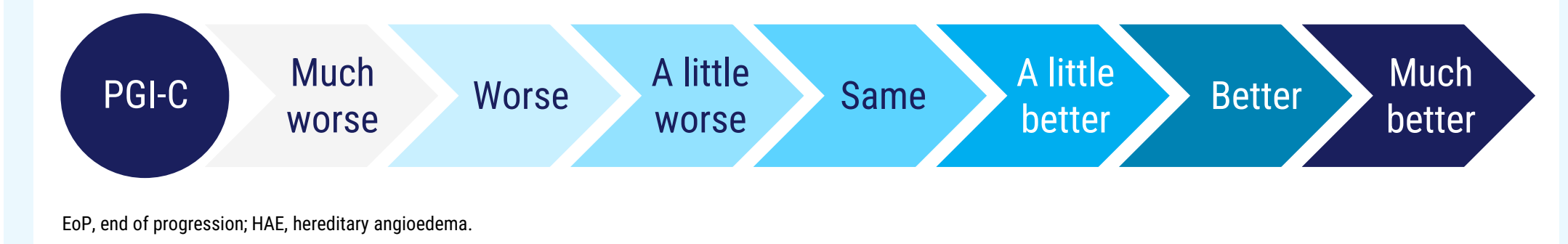
Methods

Table 1. Assessment of time to EoP of HAE attack manifestations	
Parameter	Details
Time to EoP of attack manifestations	The time to the earliest post-treatment timepoint after which all subsequent PGI-C scale ratings were stable or improved within 12 hours
Instrument	PGI-C
Type of analysis	Pre-specified secondary endpoint (5th in the hierarchical testing order) ⁷
Window for endpoint assessment	Baseline to 12 (+1) hours

EoP, end of progression; HAE, hereditary angioedema; PGI-C, Patient Global Impression of Change.

Figure 3. Scale used to assess time to EoP of HAE attack manifestations

Patient Global Impression of Change (PGI-C)¹³: a tool that uses a seven-point Likert response scale to assess the change in HAE attack manifestations since starting study treatment compared with pre-treatment.



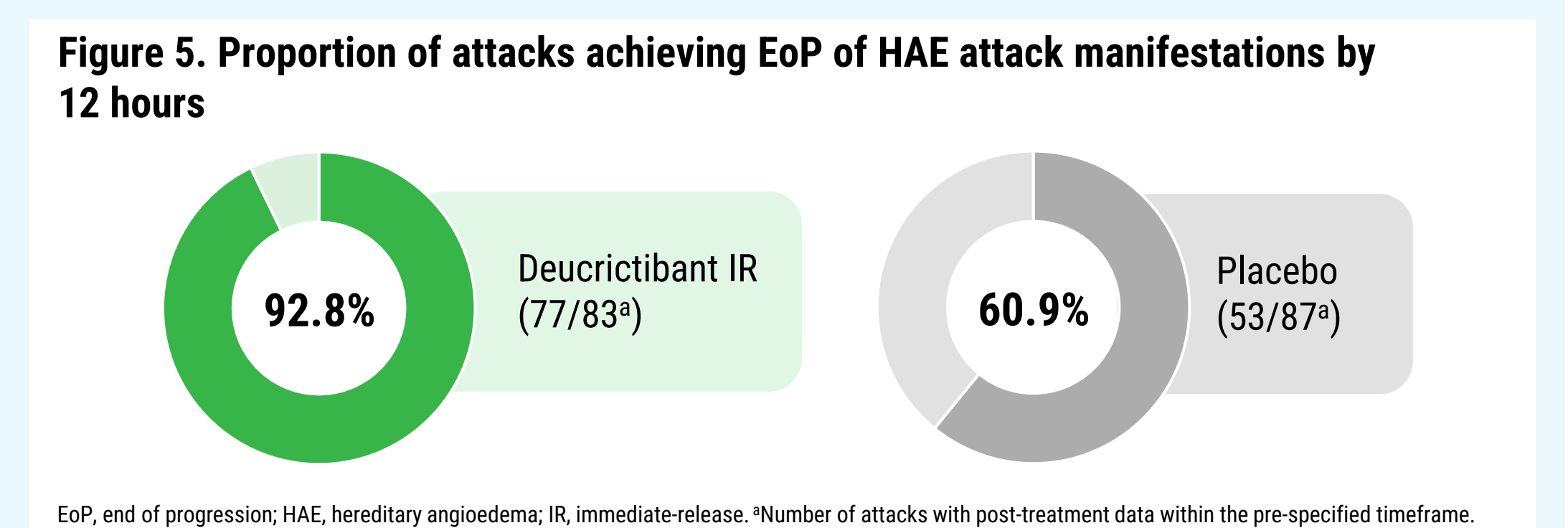
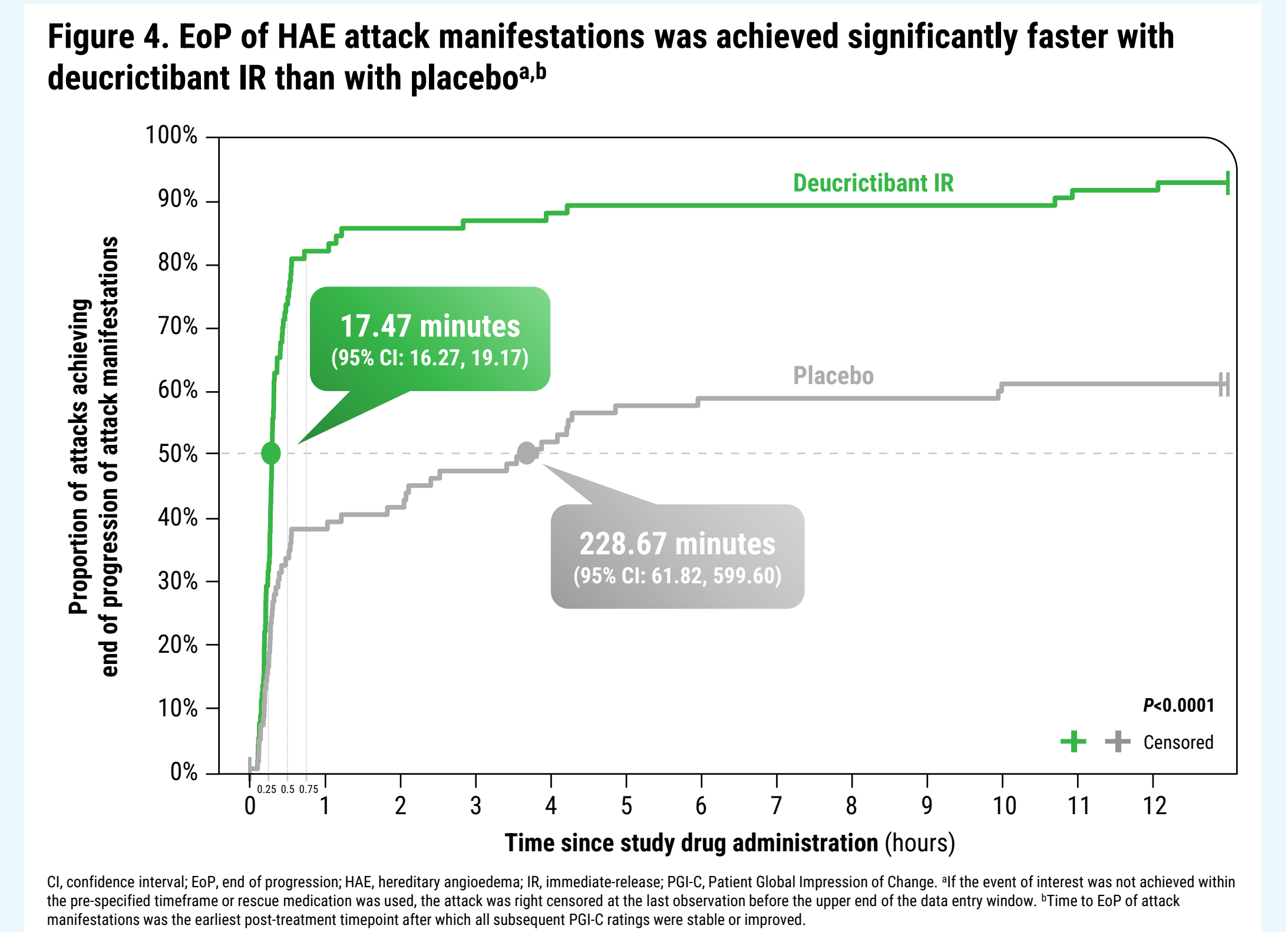
Results

Table 2. Participant baseline demographics and disease characteristics	
Participant characteristics	All randomized participants (N=134)
Age in years, mean (SD)	39.0 (14.7)
Sex: Female, n (%)	76 (56.7)
Years since HAE diagnosis, mean (SD)	17.7 (13.0)
Number of attacks within 3 months before screening, mean (SD)	4.4 (3.3)
HAE type, n (%)	
HAE-C1INH-type 1	118 (88.1)
HAE-C1INH-type 2	10 (7.5)
Unspecified type 1 or 2 ^a	2 (1.5)
HAE-nC1INH ^b	4 (3.0)
Current long-term prophylaxis use, n (%) ^c	31 (23.1)

HAE, hereditary angioedema; HAE-C1INH-type 1, hereditary angioedema type 1; HAE-C1INH-type 2, hereditary angioedema type 2; HAE-nC1INH, hereditary angioedema with normal C1 inhibitor; SD, standard deviation. ^aHAE type not specified by participant at baseline. ^bIncluded participants with HAE-nC1INH associated with a documented genetic variant. ^cLong-term prophylaxis medication included lanadelumab (13 [9.7%]), eotizerstat (8 [6.0%]), complement C1 esterase inhibitor (6 [4.5%]), and other (4 [3.0%]).

Results

- A total of 134 eligible participants (10 [7.5%] adolescents, 4 [3.0%] with HAE-nC1INH) were enrolled and randomized at 59 sites across 24 countries on six continents.
- The primary efficacy analysis set included 88 participants with paired attacks; 113 participants had at least one attack treated with study drug.



References

- Busse PJ, et al. *N Engl J Med*. 2020;382:1136-48. **2.** Petersen RS, et al. *J Allergy Clin Immunol Pract*. 2024;12(6):1614-21.
- Betschel SD, et al. *Allergy Asthma Clin Immunol*. 2025;21:25. **4.** Valerieva A, et al. *Clin Transl Allergy*. 2024;14:e12391.
- Maurer M, et al. *Lancet Haematol*. 2026;13(4):e200-14. **6.** RAPiDe-2. <https://clinicaltrials.gov/study/NCT05396105>. Accessed August 31, 2026. **7.** Riedl MA, et al. *Lancet*. 2026; In press. **8.** Aygören-Pürsün E, et al. *Lancet Haematol*. 2026;13(4):e215-26. **9.** CHAPTER-3. <https://clinicaltrials.gov/study/NCT0669754>. Accessed August 31, 2026.
- CHAPTER-4. <https://clinicaltrials.gov/study/NCT06679881>. Accessed August 31, 2026. **11.** CREAATE. <https://clinicaltrials.gov/study/NCT07266805>. Accessed August 31, 2026. **12.** Covella B, et al. *Future Pharmacol*. 2024;4(1):41-53. **13.** Cohn DM, et al. *Clin Transl Allergy*. 2023;13(9):e12288.

DOI: R.T.M.: AstraZeneca, Astria, BioCryst, CSL Behring, GlaxoSmithKline, Grifols, Intellia, Ionis, KalVista, Lilly, Novartis, Pharming, Pharvaris, Sanofi/Regeneron, Takeda; M.A.R.: ADARx, Astria, BioCryst, BioMarin, CellClex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi/Regeneron, Takeda; P.H.L.: Astria, BioCryst, CSL Behring, KalVista, Novartis, Pharvaris, Takeda; A.A.: Astria, BioCryst, CSL Behring, Intellia, Ionis, KalVista, Otsuka, Pharming, Pharvaris, Sobri, Takeda, UCB; M.Sto.: BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda; A.V.: AstraZeneca, Astria, Berlin-Chemie/Menarini Group, CSL Behring, Ewopharma, Ionis, KalVista, Novartis, Organon, Pharming, Pharvaris, Shire/Takeda, SOBI, Stallergenes Greer, Teva; A.S.G.: AstraZeneca, Astria, BioMarin, Brazilian research Entity (CNPq), Catalist, CSL Behring, Exeltis, KalVista, Kedrion, Multicare, Pharvaris, Pinte Pharma, Takeda, The Binding Site; W.R.L.: AstraZeneca, Astria, BioCryst, BioMarin, CSL Behring, Fresenius-Kabi, GlaxoSmithKline, Grifols, Intellia, Ionis, KalVista, Magellan, Optinose, Pharming, Pharvaris, Regeneron, Sanofi, Takeda, Teva; D.F.S.: BioCryst, CSL Behring, Intellia, Ionis, KalVista, Pharvaris, Takeda; N.B.: none to report; N.L.F.: Bago, CSL Behring, Pinte Pharma, Sanofi, Takeda, Director of HAE committee for AAeIC; R.H.: BioCryst, CSL Behring, Genesis Pharma, KalVista, Pharming, Pharvaris, Takeda; H.R.K.: Astria, BioCryst, CSL Behring, KalVista, Pharvaris, Takeda; G.K.: CSL Behring, Er-kim ilac, Ionis, Pharvaris, Polifarma, Takeda, Vem ilac; B.K.: Pharvaris; H.H.L.: BioCryst, CSL Behring, Intellia, Ionis, KalVista, Otsuka, Pharming, Pharvaris, Takeda; J.A.: Astria, BioCryst, CSL Behring, Intellia, Ionis, KalVista, Otsuka, Pharming, Pharvaris, Takeda; J.A.: Astria, BioCryst, CSL Behring, Intellia, Ionis, KalVista, Otsuka, Pharming, Pharvaris, Takeda; E.A.-P.: Astria, BioCryst, BioMarin, CSL Behring, Intellia, KalVista, Otsuka, Pharming, Pharvaris, Takeda; J.C.: ADARx, ARGO, Astria, BioCryst, BioMarin, CSL Behring, GlaxoSmithKline, Grifols, Intellia, Ionis, KalVista Pharma, Pharvaris, Takeda, Director of ACARE International Hereditary Angioedema Center, member of the Medical Advisory Board for the HAE; A.F.B.: BioCryst, CSL Behring, Ionis, KalVista, Otsuka, Pharming, Pharvaris, Takeda; P.G.-B.: CSL Behring, Pharvaris, Pinte Pharma, Takeda, participates in the World Allergy Organization and Associação Brasileira de Alergia e Imunologia; S.K.: none to report; T.K.: ADARx, Astria, BioCryst, CSL Behring, KalVista, Otsuka, Pharming, Pharvaris, Takeda; M.P.L.F.: Pharvaris, Pinte Pharma, Takeda; A.F.: BioCryst, CSL Behring, Kaken, KalVista, Pharvaris, Takeda, Torii Pharmaceutical Comp. Ltd., is a committee chair for Japanese Dermatological Association Urticaria Treatment Guidelines 4th Edition; Creation; D.B.: Astria, BioCryst, CSL Behring, Ionis, KalVista, Otsuka, Pharming, Takeda; P.G.: BioCryst, CSL Behring, KalVista, Otsuka, Pharming, Takeda, Torii Pharmaceuticals; D.J.H.: KalVista, Pharming, Takeda, Torii Pharmaceuticals; E.L.: BioCryst, CSL Behring, Kaco Corporation, KalVista Japan, Pharvaris, Takeda, Torii Pharmaceuticals; J.S.J.: BioCryst, CSL Behring, Cycle Pharma, Intellia, Ionis, KalVista, Pharming, Pharvaris, Takeda; C.H.K.: AstraZeneca, CSL Behring, GlaxoSmithKline, Novartis, Pebbles trial, Pharvaris, Sanofi, Takeda; L.L.: BioCryst, CSL Behring, Novartis, Takeda; R.L.: BioCryst, CSL Behring, Ionis, KalVista, Otsuka, Pharming, Pharvaris, Takeda; M.M.: Argo, Astria, BioCryst, Intellia, KalVista, Octapharma, Otsuka, Pharvaris, Takeda; M.E.M.: AstraZeneca, Astria, BioCryst, Blueprint, CellClex, Cogent, CSL Behring, GlaxoSmithKline, Intellia, Ionis, KalVista, Merck, Novartis, Pharming, Pharming, Regeneron, Takeda, Teva; S.M.: none to report; S.O.: none to report; C.J.R.: Amgen, GlaxoSmithKline, Pfizer, Pharvaris, Sanofi, Takeda; J.L., L.Z., J.M., J.K., G.G., M.Y., P.L.: employees of Pharvaris, holds stocks in Pharvaris; R.C.: employee of RC Consultancy and consultant to Pharvaris, holds stocks in Pharvaris; A.L.: employee of GrayMatters Consulting and consultant to Pharvaris, holds stocks/stock options in Pharvaris; advisor to Kosa Pharma; D.M.C.: ADARx, Astria Therapeutics, BioCryst, CSL Behring, Gentili Neopharma, Intellia, Ionis, KalVista, Otsuka, Pharvaris, Takeda, is a Regional Medical Advisory Panel Member for HAE Central Eastern Europe and the Benelux.

Acknowledgments: Medical writing services were provided by Natasha Drissi, PhD, of Envision Medical Communications, and funded by Pharvaris.