

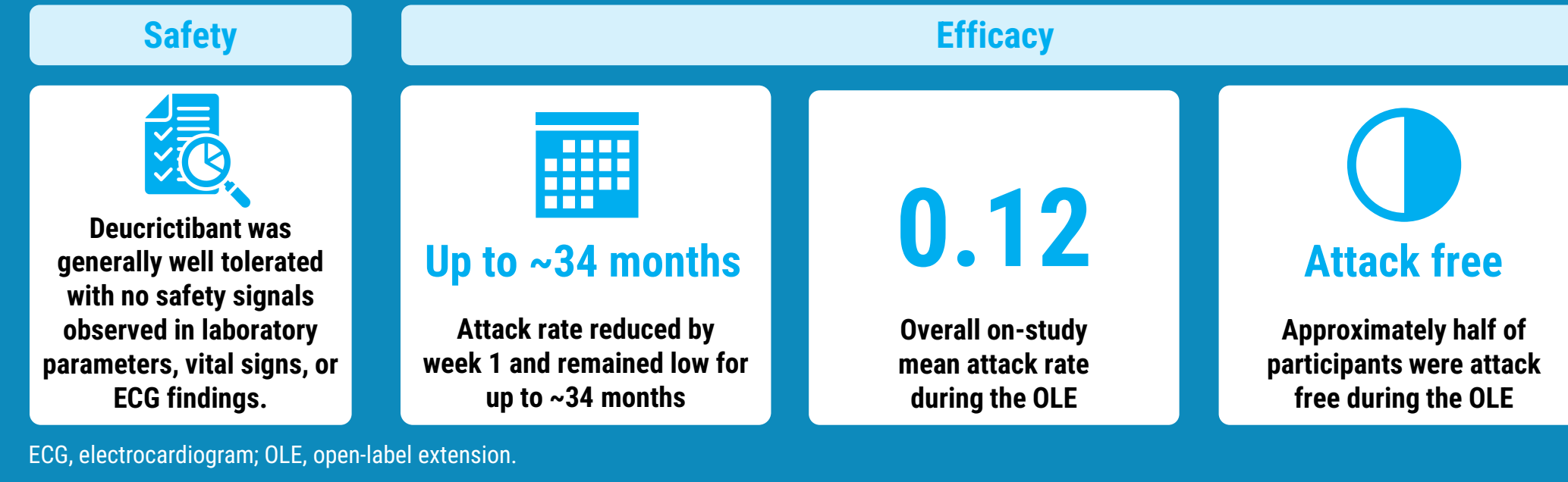
Long-Term Safety and Efficacy of Oral Deucricitbant for Prophylaxis in Hereditary Angioedema: Final Results of the Phase 2 CHAPTER-1 Open-Label Extension Study

John Anderson¹, Francesco Arcoletto², Mauro Cancian³, Hugo Chapdelaine⁴, Niall Conlon⁵, Efrem Eren⁶, Mark Gompels⁷, Sofia Grigoriadou⁸, Maria D. Guarino⁹, Padmalal Gurugama¹⁰, Sorena Kiani-Alikhan¹¹, Tamar Kinacian¹², Markus Magerl^{13,14}, Michael E. Manning¹⁵, Marcin Stobiecki¹⁶, Michael D. Tarzi¹⁷, Anna Valerieva¹⁸, H. James Wedner¹⁹, William H. Yang²⁰, Andrea Zanichelli^{21,22}, Rafael Crabbé²³, Susan Mulders²⁴, Jonathan Levy²⁵, Ulrich Freudensprung²⁶, Umar Katbeh²⁶, Jochen Knolle²⁷, Anne Lesage²⁸, Peng Lu²⁵, Emel Ayygören-Pürsün²⁹, Marc A. Riedl³⁰

¹AllerVie Health, Clinical Research Center of Alabama, Birmingham, AL, USA; ²AOR Villa Sofia-Cervello, Palermo, Italy; ³Azienda Ospedale Università di Padova, Padua, Italy; ⁴CHU de Montréal, Université de Montréal, Montréal, QC, Canada; ⁵St. James's Hospital and Trinity College, Dublin, Ireland; ⁶University Hospital Southampton NHS Foundation Trust, Southampton, UK; ⁷North Bristol NHS Trust, Bristol, UK; ⁸Barts Health NHS Trust, London, UK; ⁹U.O.C. Allergologia Ospedale di Civitanova Marche, Civitanova Marche, Italy; ¹⁰Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; ¹¹Royal Free London NHS Foundation Trust, London, UK; ¹²Medical University of Vienna, Vienna, Austria; ¹³Charité-Universitätsmedizin Berlin, Institute of Allergy, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; ¹⁴Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany; ¹⁵Allergy, Asthma and Immunology Associates, Ltd., Scottsdale, AZ, USA; ¹⁶Jagiellonian University Medical College, Krakow, Poland; ¹⁷University Hospitals Sussex NHS Foundation Trust, Brighton, UK; ¹⁸Medical University of Sofia, Sofia, Bulgaria; ¹⁹Washington University School of Medicine, St. Louis, MO, USA; ²⁰University of Ottawa, Ottawa, ON, Canada; ²¹Università degli Studi di Milano, Milan, Italy; ²²I.R.C.C.S., Policlinico San Donato, Centro Angioedema, UO Medicina, Milan, Italy; ²³RC Consultancy, Bassins, Switzerland; ²⁴Mulders Clinical Consulting, Groesbeek, Netherlands; ²⁵Pharvaris Inc., Lexington, MA, USA; ²⁶Pharvaris GmbH, Zug, Switzerland; ²⁷JCK Consult, Frankfurt, Germany; ²⁸GrayMatters Consulting, Schilde, Belgium; ²⁹Goethe University Frankfurt, Department of Pediatrics, Frankfurt am Main, Germany; ³⁰University of California San Diego, La Jolla, CA, USA

Key takeaways

Final data from the completed open-label extension (OLE) of the Phase 2 CHAPTER-1 study investigating daily oral deucricitbant administration provide first evidence on the long-term safety and efficacy of bradykinin B2 receptor antagonism for prophylaxis against bradykinin-mediated angioedema attacks.



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

Background

- Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.¹
- Unmet need:** additional prophylactic treatments offering injectable-like efficacy[™], a well-tolerated profile, and ease of administration.²⁻⁵
- Oral deucricitbant:** a selective, investigational, bradykinin B2 receptor antagonist under development for prophylaxis and on-demand treatment of bradykinin-mediated attacks.⁶⁻¹⁶

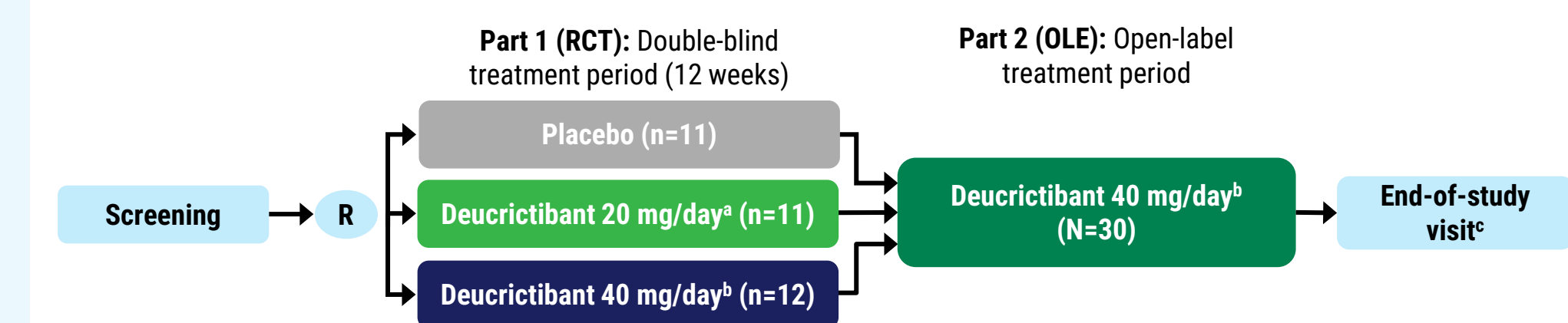
Objective

To evaluate the safety and efficacy of deucricitbant for long-term prophylaxis of HAE attacks in adults in the open-label extension (OLE) of the CHAPTER-1 study.¹²

Methods

- CHAPTER-1 (NCT05047185)*:** a two-part, Phase 2 study.^{12,15}
 - Part 1 randomized controlled trial (RCT) and Part 2 OLE were completed.
- Eligibility:** adults diagnosed with HAE-1/2, not receiving other prophylactic treatments at screening, and with a pre-specified minimum number of attacks in the 3 months prior to screening.

Figure 1. CHAPTER-1 study design



IR, immediate-release; OLE, open-label extension; R, randomization; RCT, randomized controlled trial. n = number of participants randomized in each treatment group in the RCT. N = number of participants. *Deucricitbant IR capsule, 10 mg twice daily. †Deucricitbant IR capsule, 20 mg twice daily. ‡Twenty-one participants rolled over to the ongoing CHAPTER-4¹⁴ (NCT06679881) OLE in which deucricitbant extended-release tablet is self-administered.

Methods

- Participants:** all 30 participants who completed the RCT continued into the OLE.
 - In the RCT, these 30 participants were randomized to deucricitbant 20 mg/day (n=11) or 40 mg/day (n=10), or placebo (n=9).
- Key OLE objectives:** evaluate the long-term safety (primary objective) and efficacy of deucricitbant for prophylaxis against HAE attacks.

Results

Participants in the OLE

- Thirty participants in the OLE received deucricitbant 40 mg/day for a mean (SD) treatment duration of 22.2 (8.1) months.
 - Maximum deucricitbant exposure during the entire study was 33.8 months.
- Twenty-one participants were on study at the time of CHAPTER-1 study end and all continued into the ongoing CHAPTER-4 OLE (NCT06679881)¹⁴ in which deucricitbant extended-release (XR) tablet, 40 mg, is self-administered. None of the 9 discontinuations in the CHAPTER-1 OLE were reported as treatment-related or associated with an adverse event.

Safety analysis

- Deucricitbant was generally well tolerated, with one treatment-related treatment-emergent adverse event (TEAE) reported: mild, asymptomatic increased gamma-glutamyltransferase (<2 upper limit of normal).
- No clinically significant abnormalities in laboratory parameters, vital signs, or ECG findings.
- No treatment-related severe or serious TEAEs were reported.
- No TEAEs leading to study drug discontinuation, study withdrawal, or death.

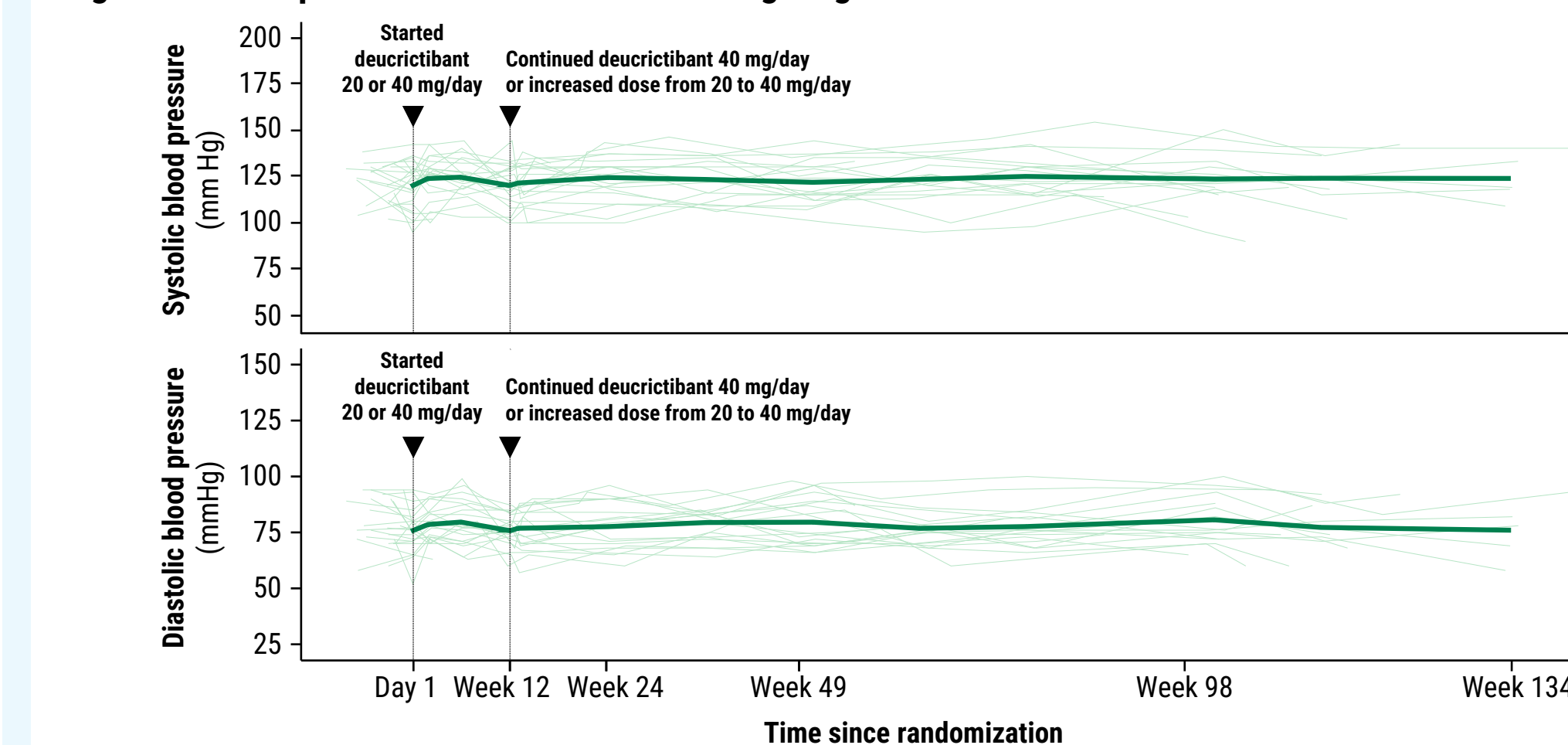
Table 1. Adverse events in the OLE

	Placebo to 40 mg/day ^a (N=9)		20 mg/day ^b to 40 mg/day ^a (N=11)		40 mg/day ^a to 40 mg/day ^a (N=10)		Total (N=30)	
	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n
TEAEs	8 (88.9)	40	8 (72.7)	45	8 (80.0)	25	24 (80.0)	110
Treatment-related TEAEs	0	0	0	0	1 (10.0)	1	1 (3.3)	1
Gamma-glutamyltransferase increased ^c	0	0	0	0	1 (10.0)	1	1 (3.3)	1
Serious TEAEs ^d	0	0	1 (9.1)	2	1 (10.0)	1	2 (6.7)	3
Tendon injury	0	0	0	0	1 (10.0)	1	1 (3.3)	1
Arthritis	0	0	1 (9.1)	1	0	0	1 (3.3)	1
Osteoarthritis	0	0	1 (9.1)	1	0	0	1 (3.3)	1
Treatment-related serious TEAEs	0	0	0	0	0	0	0	0
TEAEs leading to study drug discontinuation, study withdrawal, or death	0	0	0	0	0	0	0	0

IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial; TEAE, treatment-emergent adverse event. TEAE defined as adverse event that started or pre-existing adverse events that worsened during the period between the first study dose in OLE and 4 weeks after the last dose in OLE or the end of study visit, whichever was later. n = number of participants who received ≥1 dose of study treatment in the OLE. ^aDeucricitbant IR capsule, 20 mg twice daily. ^bDeucricitbant IR capsule, 10 mg twice daily. ^cStarted during the RCT, resolved while continuing deucricitbant treatment during the OLE, and recurred by end of the OLE. alanine aminotransferase, aspartate aminotransferase, bilirubin, and alkaline phosphatase (ALP) levels were normal. ^dThree serious TEAEs required reconstruction surgery, hip replacement, or knee replacement. These were not considered treatment-related.

Results

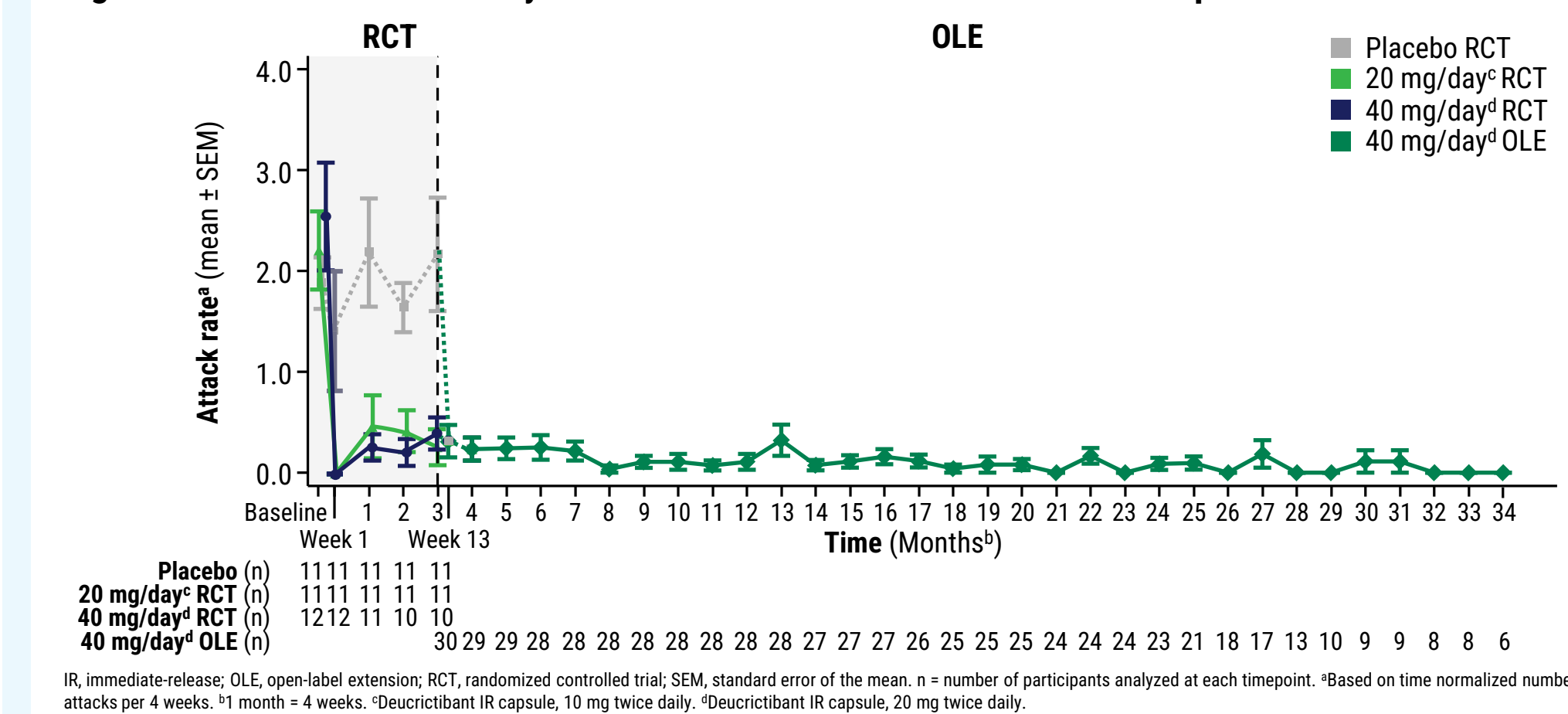
Figure 2. Blood pressure remained stable during long-term treatment with deucricitbant



Thin lines represent individual participant blood pressure. Thick lines represent the group mean blood pressure.

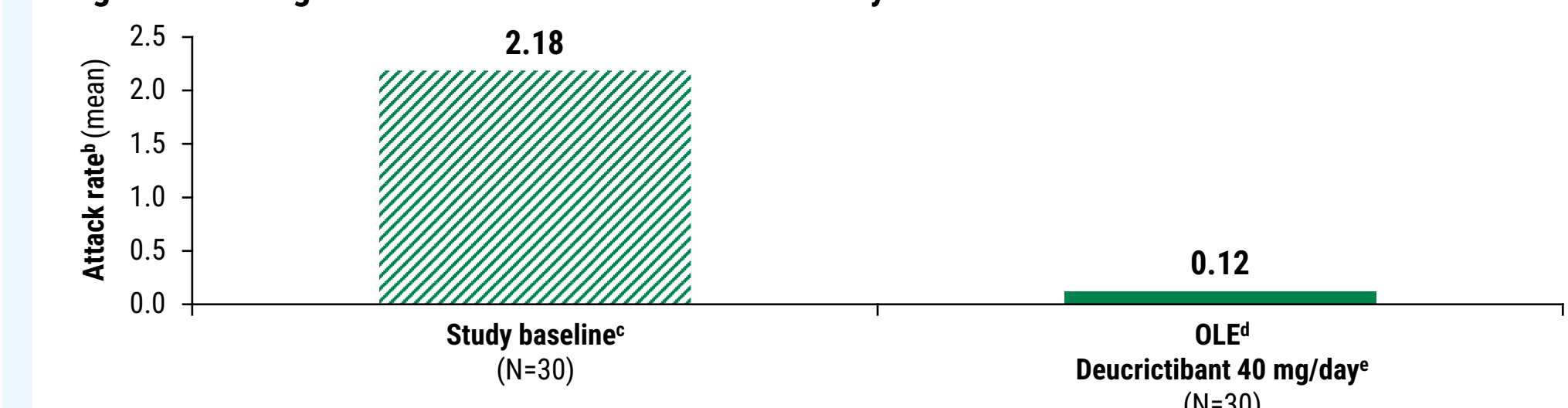
Efficacy analysis

Figure 3. Attack rate reduced by week 1 and week 13 and remained low for up to ~34 months



IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial; SEM, standard error of the mean. n = number of participants analyzed at each timepoint. *Based on time normalized number of attacks per 4 weeks. †1 month = 4 weeks. ‡Deucricitbant IR capsule, 10 mg twice daily. §Deucricitbant IR capsule, 20 mg twice daily.

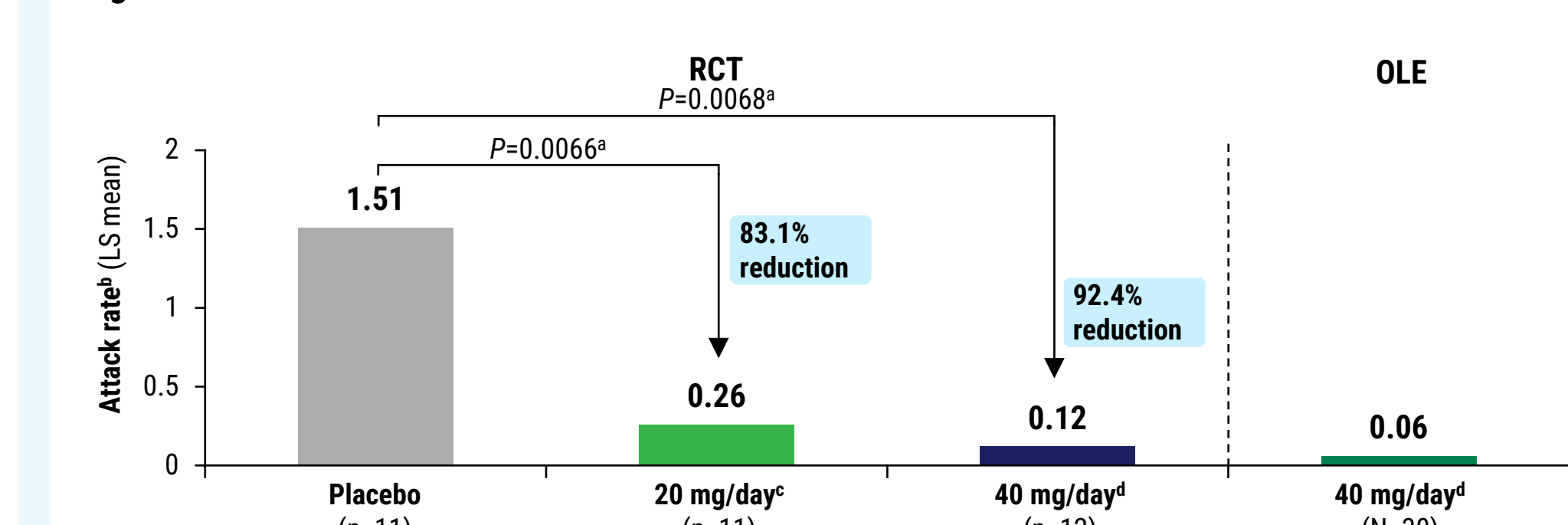
Figure 4. Average of 92.4% attack reduction from study baseline^a



IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants in the OLE. *92.4% is the average participant-level reduction from CHAPTER-1 RCT baseline and excludes one participant with 4 days of OLE treatment and no attacks. †Based on time-normalized number of attacks per 4 weeks. ‡Crude mean attack rate at baseline. §Crude mean attack rate in the OLE. ¶Deucricitbant IR capsule, 20 mg twice daily.

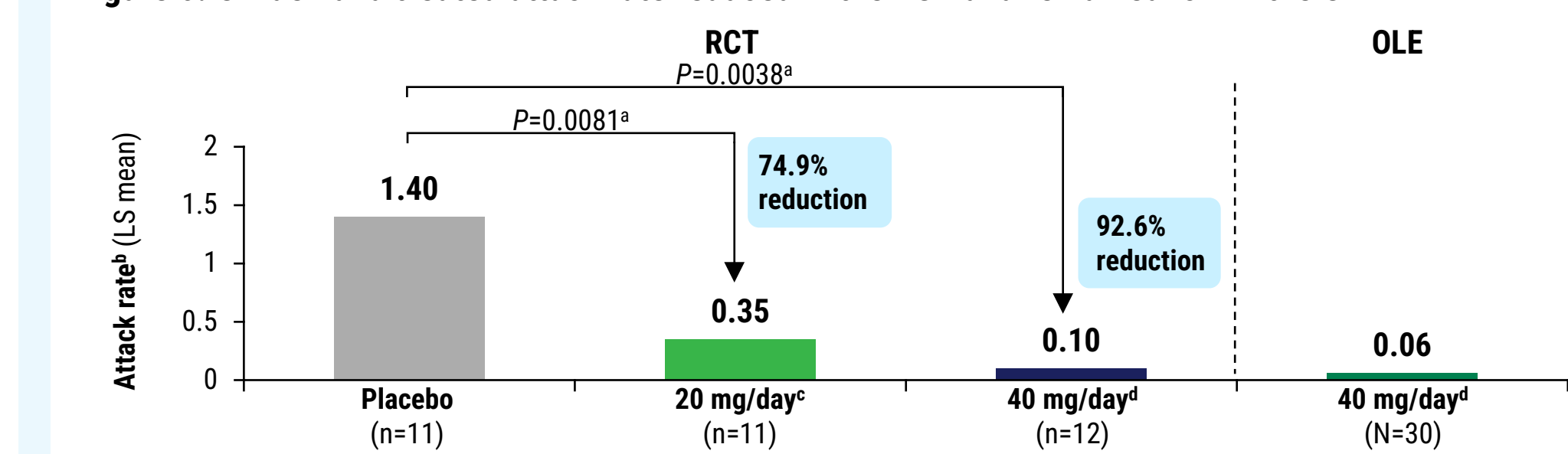
Results

Figure 5. "Moderate and severe" attack rate reduced in the RCT and remained low in the OLE



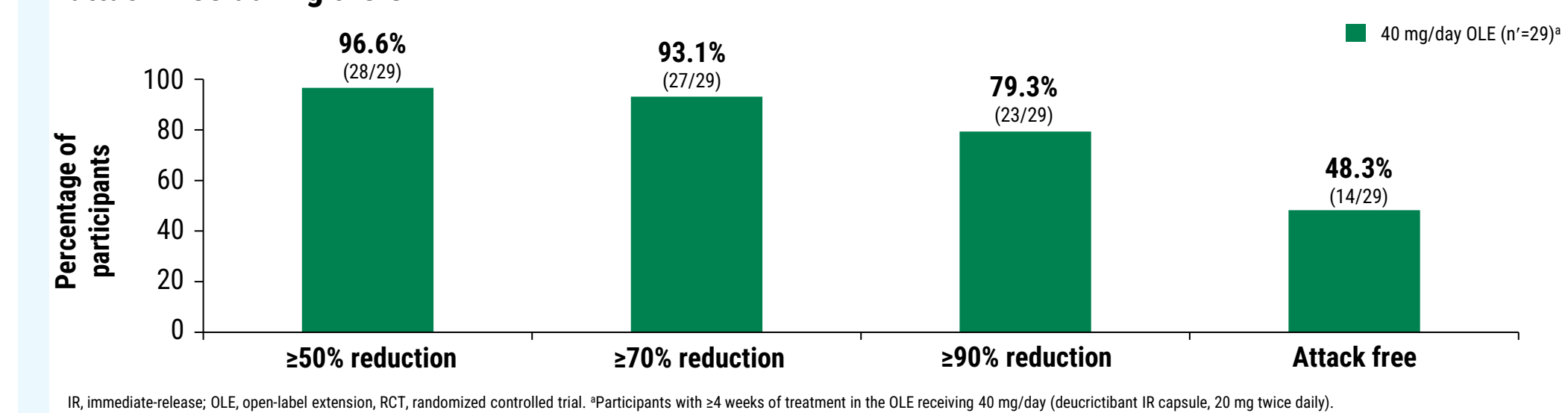
IR, immediate-release; LS, least squares; OLE, open-label extension; RCT, randomized controlled trial. n = number of participants randomized in each treatment group in the RCT. N = number of participants in the OLE. LS mean estimates of attack rate are based on Poisson regression models adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. *The P-values in this figure are nominal. †Based on time-normalized number of attacks per 4 weeks. ‡Deucricitbant IR capsule, 10 mg twice daily. §Deucricitbant IR capsule, 20 mg twice daily.

Figure 6. On-demand treated attack rate reduced in the RCT and remained low in the OLE



IR, immediate-release; LS, least squares; OLE, open-label extension; RCT, randomized controlled trial. n = number of participants randomized in each treatment group in the RCT. N = number of participants in the OLE. LS mean estimates of attack rate are based on Poisson regression models adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. *The P-values in this figure are nominal. †Based on time-normalized number of attacks per 4 weeks. ‡Deucricitbant IR capsule, 10 mg twice daily. §Deucricitbant IR capsule, 20 mg twice daily.

Figure 7. Attack rate reduced relative to RCT study baseline with approximately half of participants attack free during the OLE



IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. *Participants with ≥4 weeks of treatment in the OLE receiving 40 mg/day (deucricitbant IR capsule, 20 mg twice daily).

References

- Busse PJ, et al. *N Engl J Med*. 2020;382:1136-48. 2. Bouillet L, et al. *Allergy Asthma Proc*. 2022;43:406-12. 3. Covello B, et al. *Future Pharmacol*. 2024;4:41-53. 4. Center for Biologics Evaluation and Research. The voice of the patient – hereditary angioedema. US Food and Drug Administration; May 2018. Accessed January 7, 2026. <https://www.fda.gov/media/113509/download>. 5. Betschel SD, et al. *J Allergy Clin Immunol Pract*. 2023;11:2315-25. 6. Lesage A, et al. *Front Pharmacol*. 2020;11:516. 7. Lesage A, et al. *Int Immunopharmacol*. 2022;105:108523. 8. RAPiDe-3. <https://clinicaltrials.gov/study/NCT04618211>. Accessed February 4, 2026. 9. RAPiDe-2. <https://www.clinicaltrials.gov/study/NCT05396105>. Accessed February 4, 2026. 10. RAPiDe-3. <https://clinicaltrials.gov/study/NCT06343779>. Accessed February 4, 2026. 11. Maurer M, et al. *Lancet Haem*. 2026; In press. 12. CHAPTER-1. <https://www.clinicaltrials.gov/study/NCT05047185>. Accessed February 4, 2026. 13. CHAPTER-3. <https://clinicaltrials.gov/study/NCT06669754>. Accessed February 4, 2026. 14. CHAPTER-4. <https://clinicaltrials.gov/study/NCT06679881>. Accessed February 4, 2026. 15. Ayygören-Pürsün E, et al. *Lancet Haem*. 2026; In press. 16. CREAATE. <https://clinicaltrials.gov/study/NCT07266805>. Accessed February 4, 2026.