Long-Term Safety and Efficacy of Oral Deucrictibant for Prophylaxis in Hereditary Angioedema: Data Snapshot Results of the CHAPTER-1 Open-Label Extension Study

E. Aygören-Pürsün, J. Anderson, F. Arcoleo, M. Cancian, H. Chapdelaine, N. Conlon, E. Eren, M. Gompels, S. Grigoriadou, M.D. Guarino, P. Gurugama, S. Kiani-Alikhan, T. Kinaciyan, M. Magerl, M.E. Manning, M. Stobiecki, M.D. Tarzi, A. Valerieva, H.J. Wedner, W.H. Yang, A. Zanichelli, R. Crabbé, S. Mulders, J. Levy, U. Freudensprung, U. Katbeh, J. Knolle, A. Lesage, P. Lu, M.A. Riedl

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

Conflicts of interest disclosure

E.A-P.: Astria, BioCryst, CSL Behring, Kalvista, Intellia, Otsuka, Pharvaris, Takeda; **J.A.:** BioCryst, BioMarin, CSL Behring, Cycle Pharma, KalVista, Pharming, Pharvaris, Takeda; **F.A.:** CSL Behring, Takeda; **M.C.:** BioCryst, CSL Behring, KalVista, Menarini, MSD, Novartis, Otsuka, Pharming, Pharvaris, Sobi, Takeda, UCB; **H.C.:** AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobi, Takeda; **N.C.:** Novartis, Takeda; **E.E.:** BioCryst, Dr Falk Pharma, Novartis, Pharming, Pharvaris; **M.G.:** BioCryst, CSL Behring, KalVista, Novartis, Otsuka, member of the immunology clinical reference group; **S.G.:** Baxter, CSL Behring, Dyax, Grifols, Pharming/Swedish Orphan, Takeda, ViroPharma; **M.D.G.:** CSL Behring; **P.G.:** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **S.K-A.:** BioCryst, Biotest, CSL Behring, Ionis, KalVista, Pharvaris, Takeda, X4 Pharmaceuticals; **T.K.:** BioCryst, CSL Behring, KalVista, Novartis, Sanofi/Regeneron, Pharvaris, Takeda; **M.M.:** Astria, BioCryst, CSL Behring, Intellia, KalVista, Novartis, Octapharma, Otsuka, Pharvaris, Takeda; **M.E.M.:** Allakos, Amgen, AstraZeneca, BioCryst, Blueprint, CSL Behring, Cycle Pharma, Genentech, GSK, KalVista, Merck, Novartis, Pharming, Pharvaris, Sanofi/Regeneron, Takeda; **M.S.:** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **M.D.T.:** no conflicts of interests to disclose relative to this work; **A.V.:** AstraZeneca, Berlin-Chemie/Menarini Group, CSL Behring, KalVista, Novartis, Pharming, Pharvaris, Sobi, Takeda; **H.J.W.:** BioCryst, BioMarin, CSL Behring, Genentech, GSK, Takeda; **W.H.Y.:** Aimmune Therapeutics, ALK Abello, AnaptysBio, Areteia, Aslan, AstraZeneca, Astria, BioCryst, BluePrint, Bristol Myers, Celgene, Celldex, CSL Behring, DBV Technologies, Dermira, Eli Lilly, Escient, Galderma, Genentech, GSK, Glenmark, Haleon, Incyte, Intellia, Ionis, Merck, Moderna, Novartis, Novavax, Pharming, Pharvaris, Providence, RAPT Therapeutics, Regeneron, Roche Sanofi, Stallergenes, Takeda, Upstream Bio, VBI; **A.Z.:** BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda; **R.C.:** employee of RC Consultancy and consultant to Pharvaris, holds stocks in Pharvaris; **S.M.:** employee of Mulders Clinical Consulting and consultant to Pharvaris, holds stocks in Pharvaris; **J.L., U.F., U.K.:** employees of Pharvaris, holds stocks in Pharvaris; **J.K.:** employee of JCK Consult and consultant to Pharvaris, holds stocks/stock options in Pharvaris; **A.L.:** employee of GrayMatters Consulting and consultant to Pharvaris, holds stocks/stock options in Pharvaris; advisor to Kosa Pharma; **P.L.:** employee of Pharvaris, holds stocks/stock options in Pharvaris; **M.A.R.:** Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, Takeda.

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CHAPTER-1 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185

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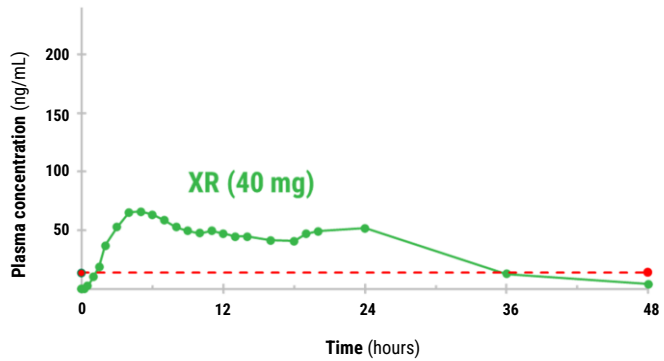
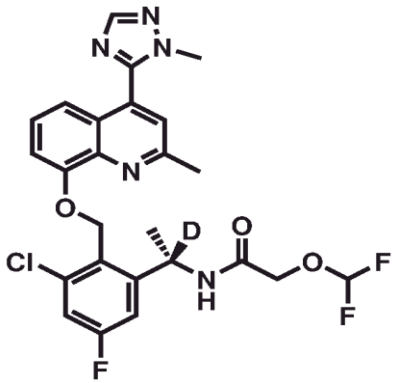
Deucrictibant is an investigational oral therapy for both the prophylactic and on-demand treatment of HAE attacks

DEUCRICTIBANT extended-release (XR) tablet

sustained absorption[1]



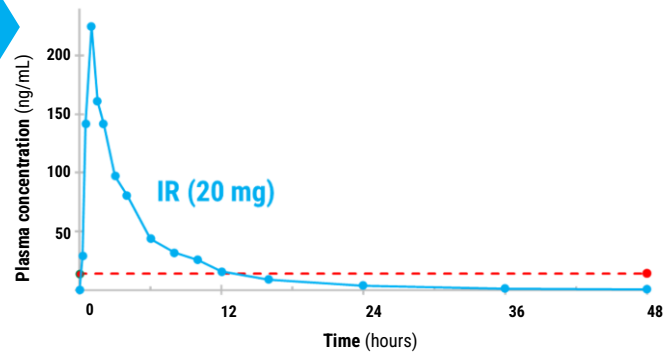
In studies, deucrictibant maintained sustained therapeutic exposure over 24 hours[1] from day one, allowing for once-daily oral prevention HAE attacks[2]



deucrictibant

DEUCRICTIBANT immediate-release (IR) capsule

rapid absorption[3]



In studies, deucrictibant rapidly reached therapeutic exposure within 15-30 minutes[3], supporting on-demand oral treatment of HAE attacks[4]

HAE, hereditary angioedema; IR, immediate-release; XR, extended-release. **1.** Lesage A, et al. Presented at IDDST; May 22-24, 2024. **2.** CHAPTER-3. ClinicalTrials.gov identifier: NCT06669754. Accessed May 13, 2025. https://clinicaltrials.gov/study/NCT06669754. **3.** Maurer M, et al. Presented at AAAAI; Feb 24-27, 2023; San Antonio, TX, USA. **4.** RAPIDe-3. ClinicalTrials.gov identifier: NCT06343779. Accessed May 13, 2025. https://www.clinicaltrials.gov/study/NCT06343779.

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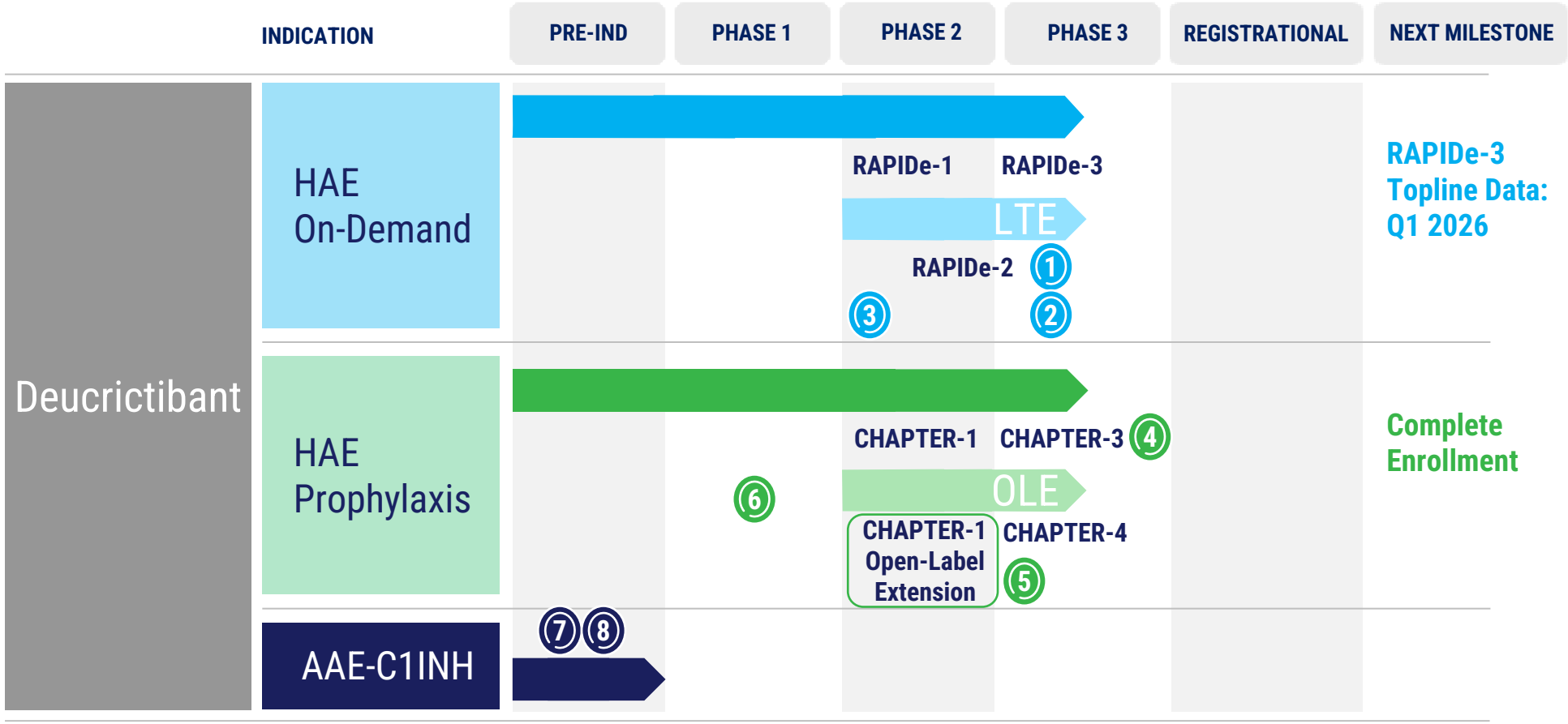
Deucrictibant development program in bradykinin-mediated angioedema



Other oral presentations

1. Riedl MA, et al. RAPIDe-2 May 31, 15:45-16:00

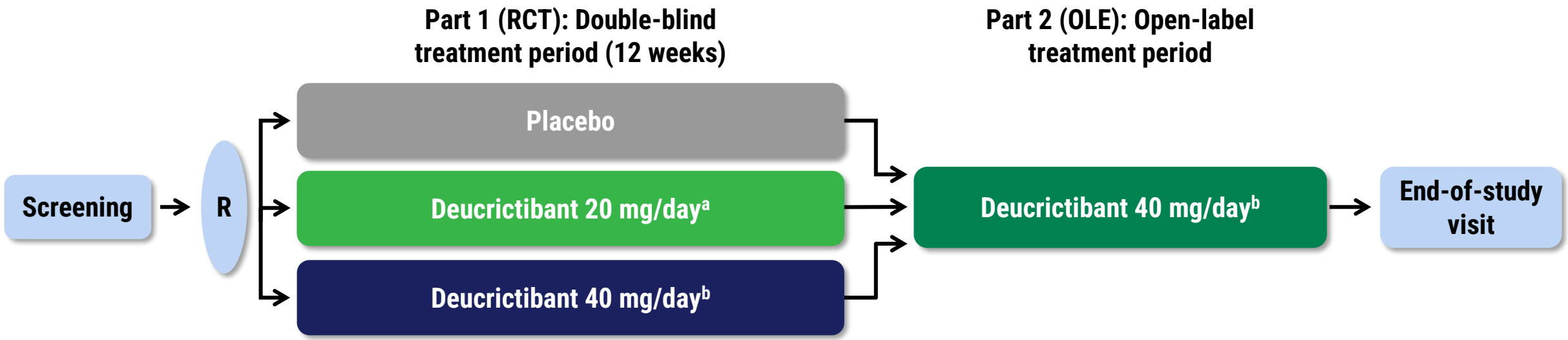
Poster presentations at C1-Inhibitor Workshop

2. Lleonart R, et al. RAPIDe-2 upper airway attack outcomes
3. Valerieva A, et al. RAPIDe-1/2 durability of treatment response
4. Zanichelli A, et al. CHAPTER-3 study design
5. Magerl M, et al. CHAPTER-1 OLE patient-reported outcomes
6. Zhang Z-Y, et al. Once-daily XR tablet for prophylaxis
7. Aygören-Pürsün E, et al. Epidemiology in European population
8. Zanichelli A, et al. Qualitative interviews

AAE-C1INH, acquired angioedema due to C1-inhibitor deficiency; HAE, hereditary angioedema; LTE, long-term extension; OLE, open-label extension; XR, extended-release. Study, ClinicalTrials.gov identifier: RAPIDe-1, NCT05396105; RAPIDe-3, NCT06343779; CHAPTER-1, NCT05047185; CHAPTER-3, NCT06669754; CHAPTER-4, NCT06679881.

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

CHAPTER-1: Two-part, Phase 2 study of deucrictibant for long-term prophylaxis of HAE attacks



Part 1 - RCT: Key findings

- Efficacy:
  - Primary endpoint: Monthly attack rate significantly reduced vs placebo
  - Reduction in occurrence of 'moderate and severe' attacks and attacks treated with on-demand medication.
- Safety:
  - Deucrictibant was generally well tolerated with no safety signals.
- All 30 participants who completed the RCT enrolled in the OLE.

Part 2 - OLE: Key objectives

- Evaluate safety (primary objective) and efficacy of deucrictibant administered for long-term prophylaxis against HAE attacks.

HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; R, randomization; RCT, randomized controlled trial. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.
CHAPTER-1 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185. Accessed May 12, 2025. https://www.clinicaltrials.gov/study/NCT05047185.

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

Deucrictibant was well tolerated with no safety signals in the OLE

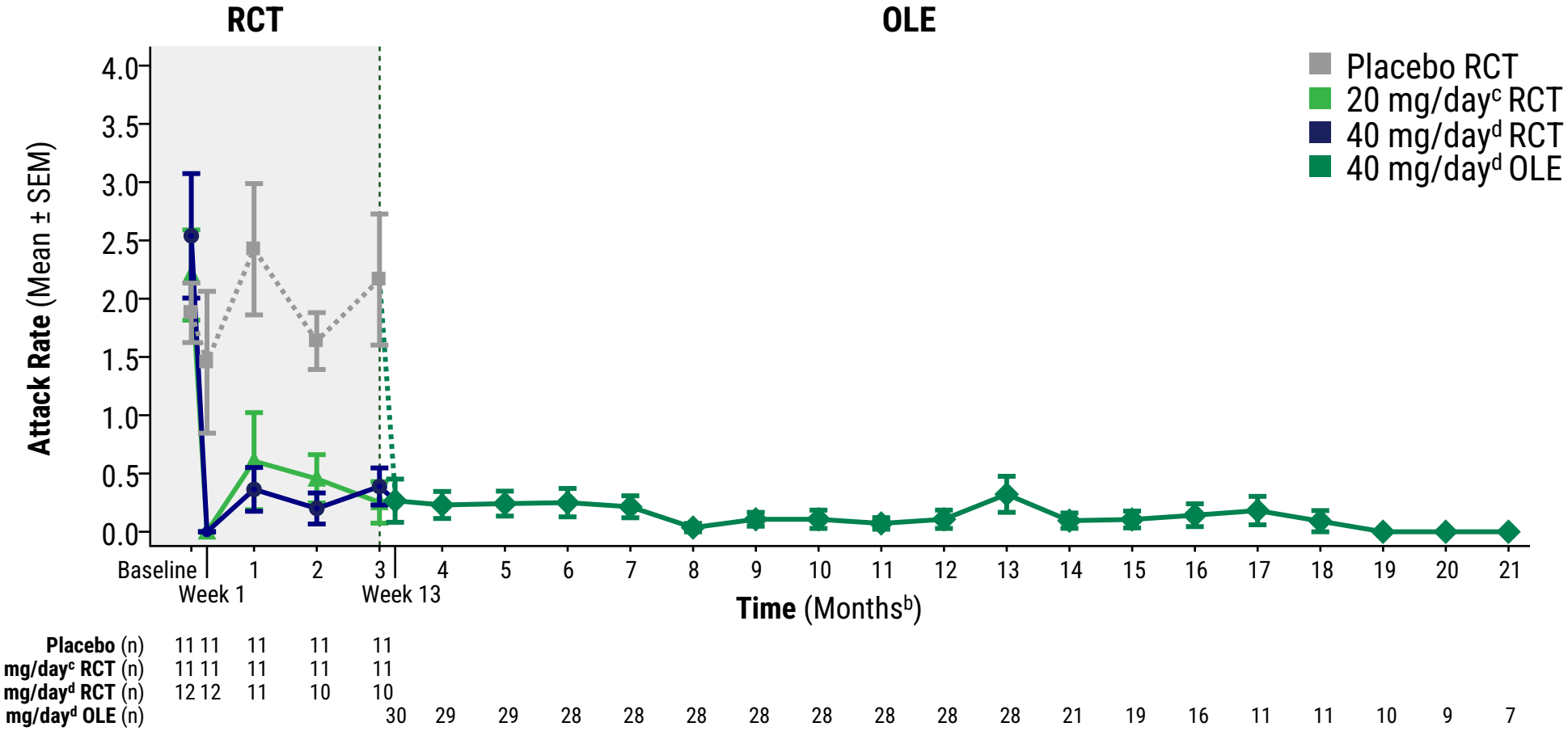
- Deucrictibant was generally well tolerated with one treatment-related TEAE of tooth discoloration.
  - No treatment-related serious or severe TEAEs.
  - No treatment-related TEAEs in laboratory parameters, vital signs (including blood pressure), or electrocardiogram findings, and no TEAEs leading to treatment discontinuation, study withdrawal, or death were reported.
- Mean (SD) exposure to deucrictibant 40 mg/day for 30 participants in the OLE: 12.8 (5.0) months.
  - Maximum exposure to deucrictibant: 20.8 months in the OLE; 23.7 months in the entire study.

	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	**5 (55.6)**	**25**	**7 (63.6)**	**31**	**6 (60.0)**	**16**	**18 (60.0)**	**72**
Treatment-related TEAEs	**1 (11.1)**	**1**	**0**	**0**	**0**	**0**	**1 (3.3)**	**1**
Tooth discoloration	1 (11.1)	1	0	0	0	0	1 (3.3)	1
Serious TEAEs	**0**	**0**	**1 (9.1)**	**1**	**1 (10.0)**	**1**	**2 (6.7)**	**2**
Tendon injury	0	0	0	0	1 (10.0)	1	1 (3.3)	1
Hip arthroplasty (arthritis)	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**

OLE, open-label extension; SD, standard deviation; TEAE, treatment-emergent adverse event defined as adverse events that start or pre-existing adverse events that have worsened during the period between first study dose in OLE and 4 weeks after last dose in OLE or the End of Study Visit, whichever is later. N = number of participants who received ≥1 dose of study treatment in the OLE by the cutoff date (10 June 2024). [a]Deucrictibant IR capsule, 20 mg twice daily. [b]Deucrictibant IR capsule, 10 mg twice daily.

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

Attack rate reduced by week 1 in the RCT and remained low through ≥1.5 years in the OLE



IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial; SEM, standard error of the mean. [a]Based on time normalized number of attacks per 4 weeks. [b]1 month = 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

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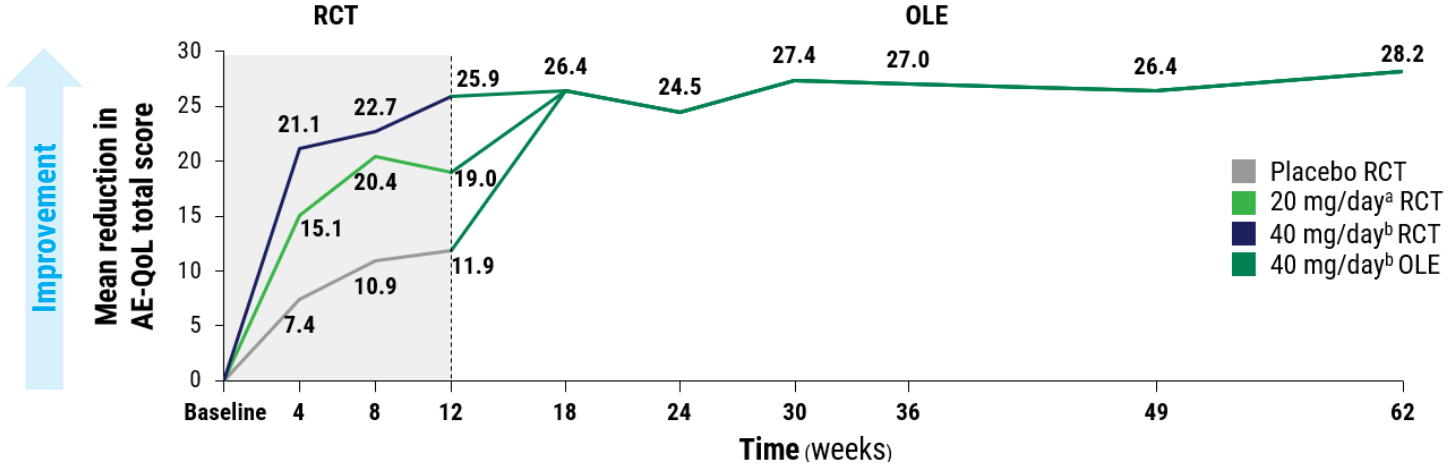
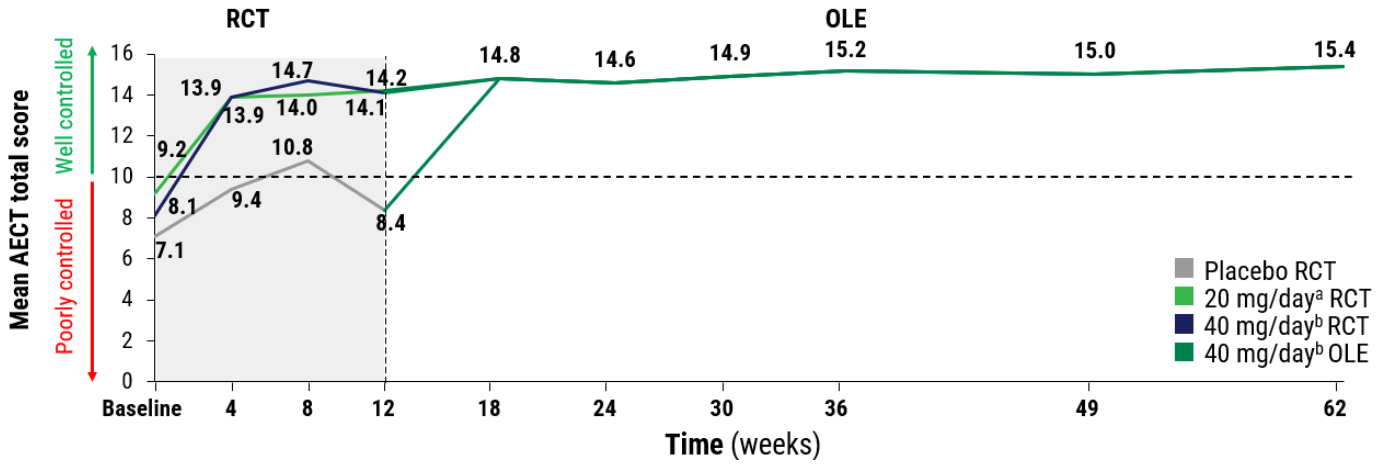
Improvements in patient-reported outcomes reflect reduction in attack rate





Health-related quality of life (HRQoL)

As measured using the Angioedema Quality of Life Questionnaire (AE-QoL), treatment with deucrictibant resulted in:

- improved HRQoL by week 4 in the RCT
- sustained effects through week 62 in the OLE

Disease control

As measured using the Angioedema Control Test (AECT), treatment with deucrictibant resulted in

- improved disease control by week 4 in the RCT
- sustained effects through week 62 in the OLE

For more details, please see
Magerl M, et al. Poster Session I, P19

IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. n = number of participants with AE-QoL or AECT data at the given week. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

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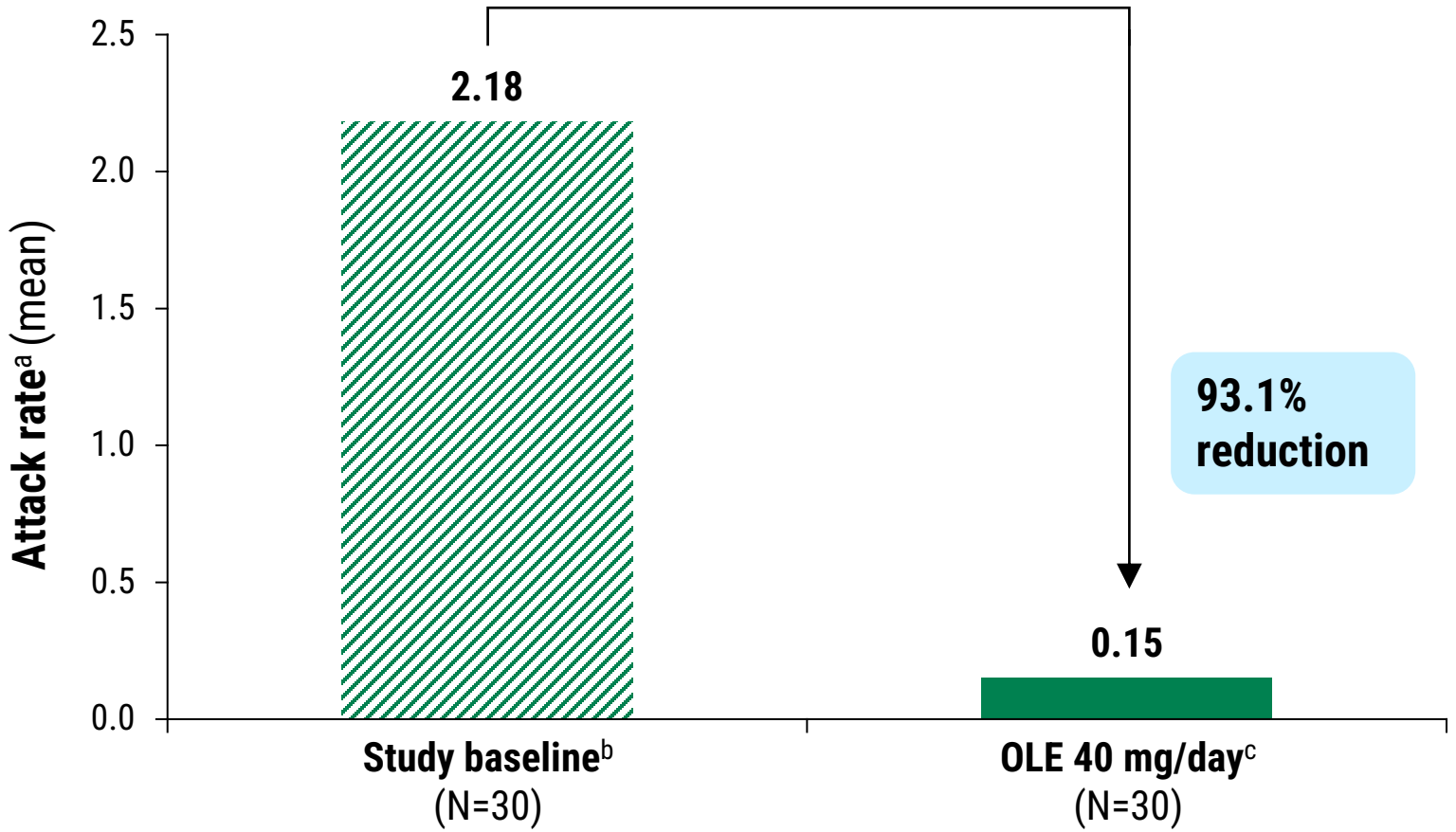
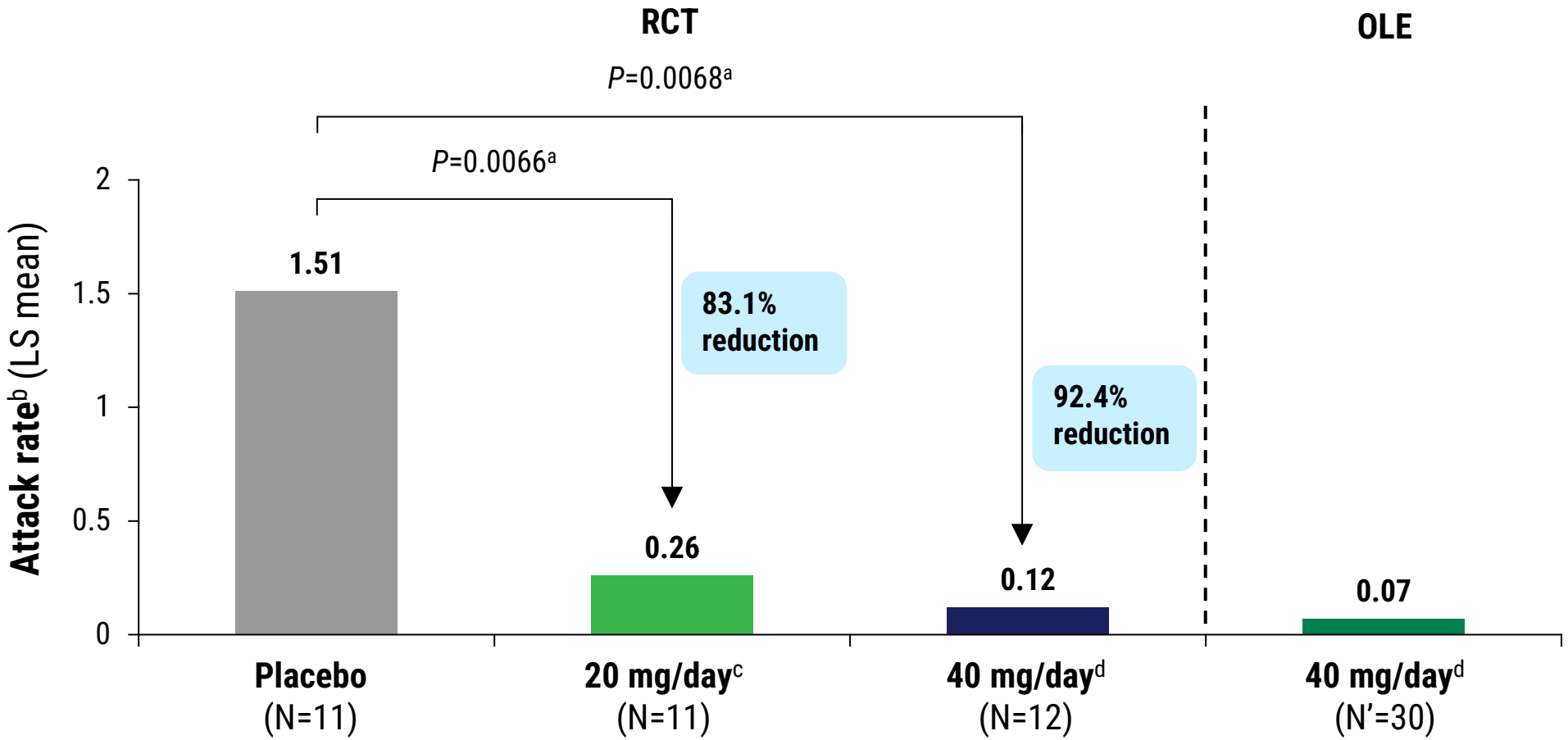
Attack rate reduced in the OLE compared to study baseline



IR, immediate-release; LS, least squares; OLE, open-label extension. N = number of participants in the OLE. [a]Based on time-normalized number of attacks per 4 weeks. [b]Baseline attack rate is raw (unadjusted) mean; OLE attack rate is LS mean; No multiplicity adjustment was applied. [c]Deucrictibant IR capsule, 20 mg twice daily.

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

“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. [a]The *P*-values in this figure are nominal. [b]Based on time-normalized number of attacks per 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

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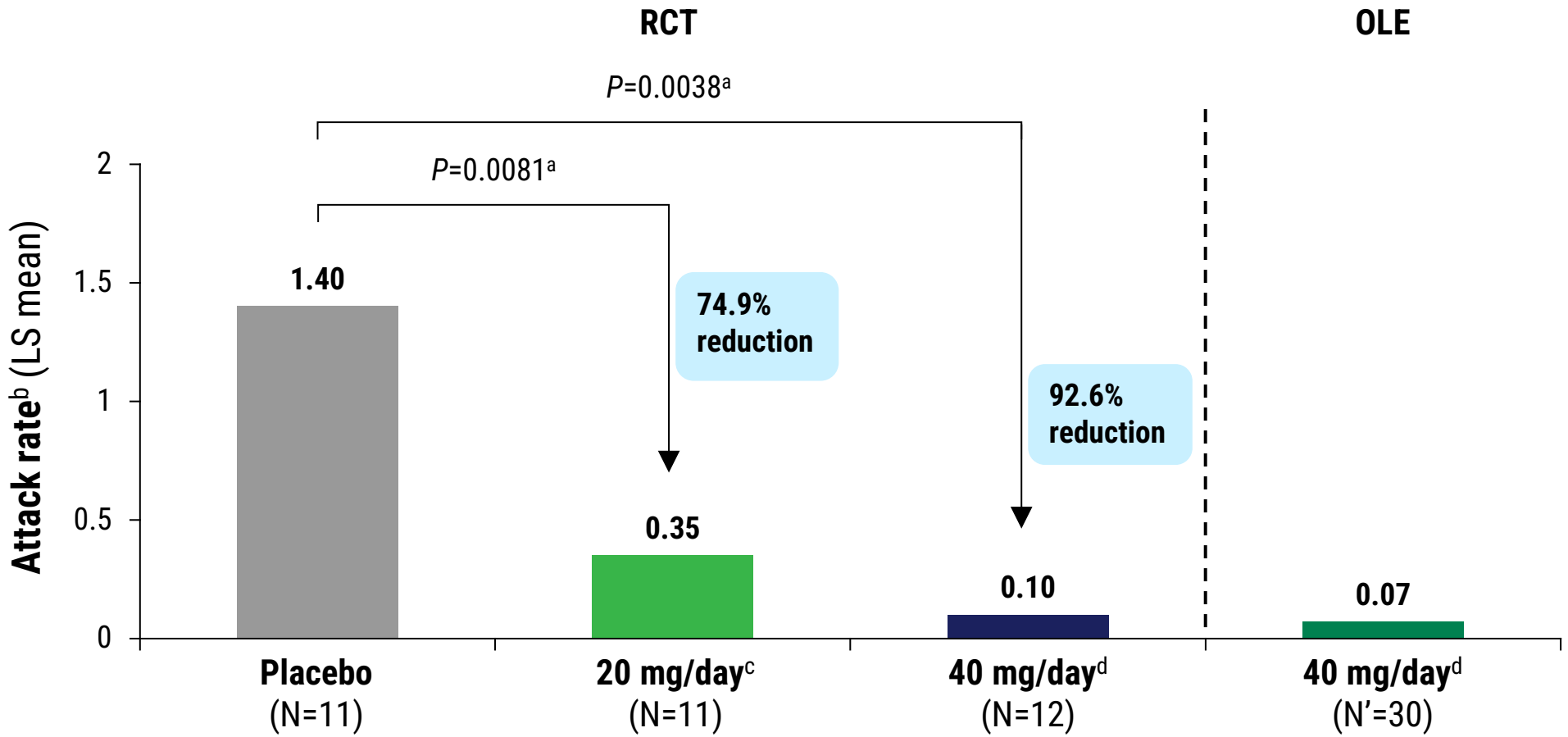
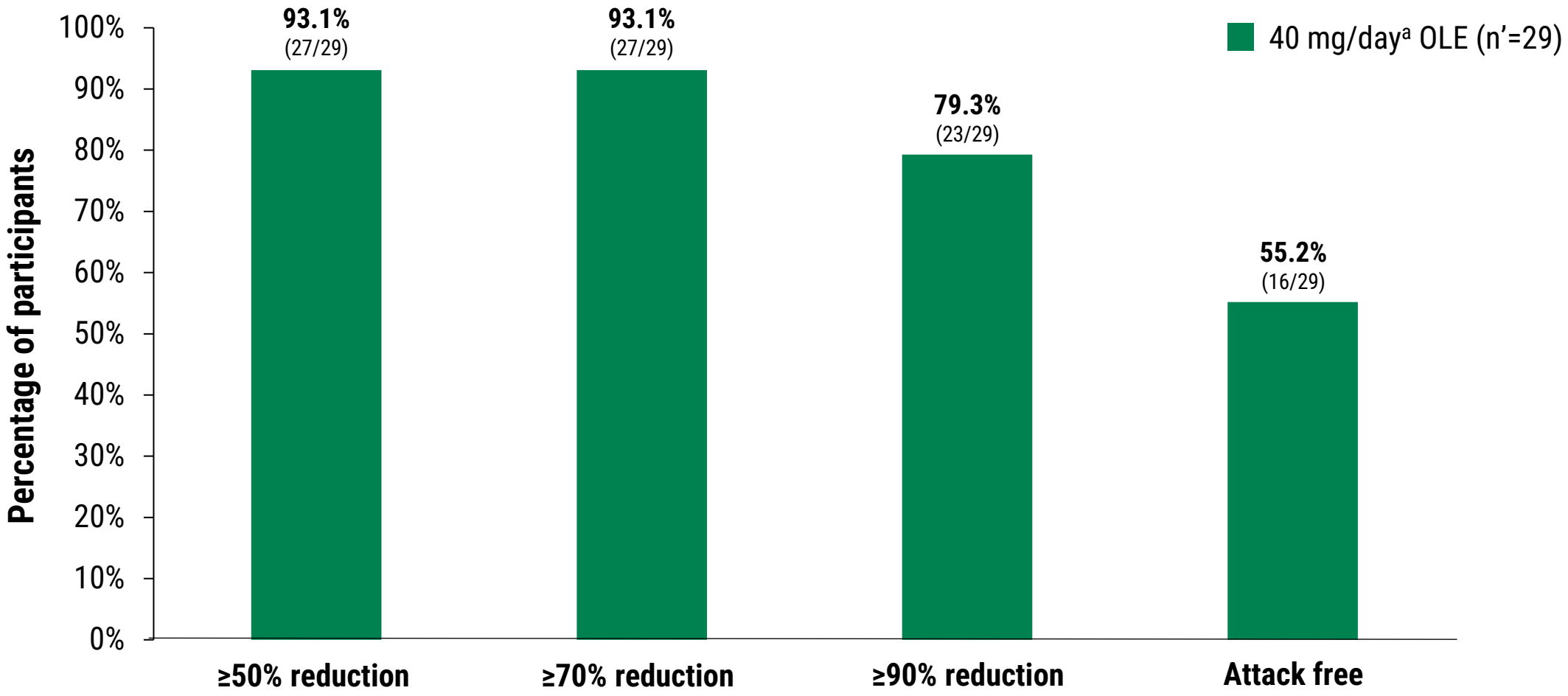
On-demand treated attack rate reduced in the RCT and remained low in the OLE



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. [a]The *P*-values in this figure are nominal. [b]Based on time-normalized number of attacks per 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

Attack rate reduced relative to CHAPTER-1 RCT study baseline with over half of participants attack free during the OLE



IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. n' = participants with ≥4 weeks of treatment in the OLE. [a]Deucrictibant IR capsule, 20 mg twice daily.

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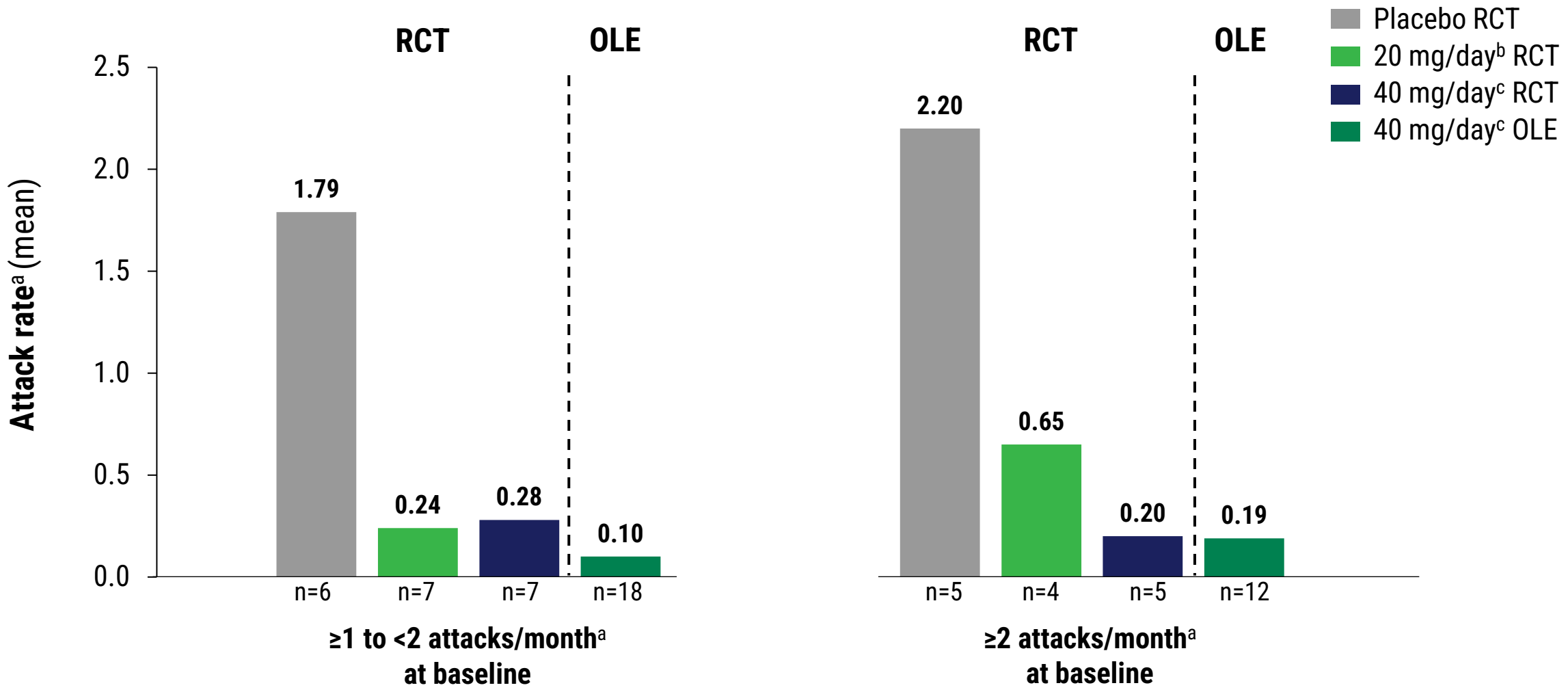
Attack rate decreased in the RCT and remained low in the OLE regardless of baseline attack rate



IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. n = number of participants in each treatment group. [a]Attack rate is raw unadjusted mean number of attacks per 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.

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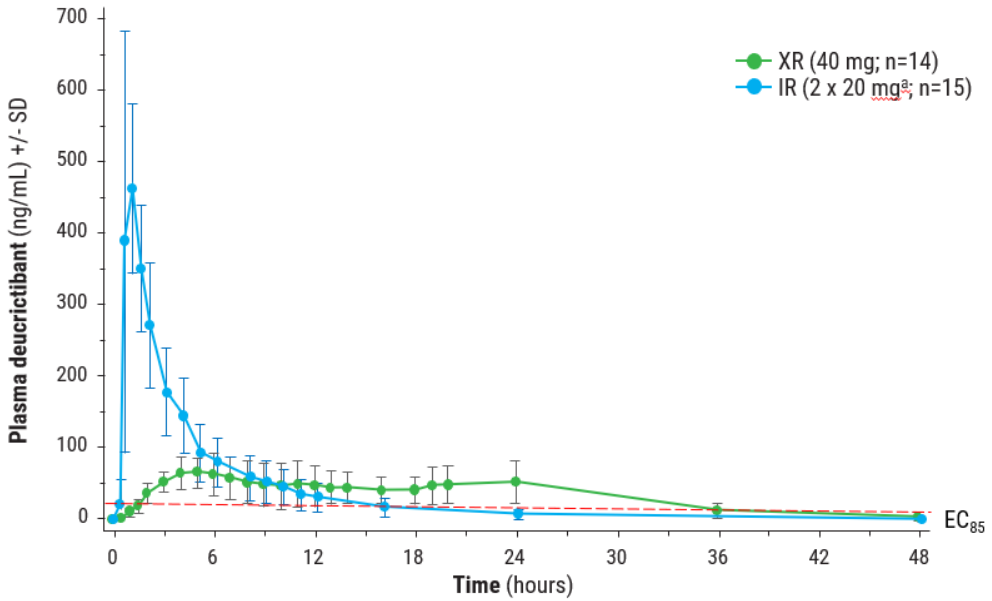
Post-hoc analysis: Use of bradykinin B2 receptor antagonism for both LTP and ODT did not alter ODT response

- Duration of attacks was not a pre-specified CHAPTER-1 measure and was calculated post-hoc based on onset and resolution of attacks that used icatibant once only as on-demand treatment (ODT).

	Icatibant as ODT in placebo group (RCT)		Icatibant as ODT in deucrictibant group (RCT & OLE)	
Attack Severity	Number of participants (n) and attacks (a)	Mean (SD) duration[a] of attack, days	Number of participants (n) and attacks (a)	Mean (SD) duration[a] of attack, days
Mild	n=3, a=4	**2.11** (1.32)	n=1, a=2	**2.58** (2.00)
Moderate	n=4, a=13	**1.03** (1.15)	n=6, a=11	**1.03** (0.79)
Severe	n=4, a=8	**0.76** (0.32)	n=2, a=7	**0.64** (0.54)
Total	n=5, a=25	**1.12** (1.06)	n=8, a=20	**1.05** (0.98)

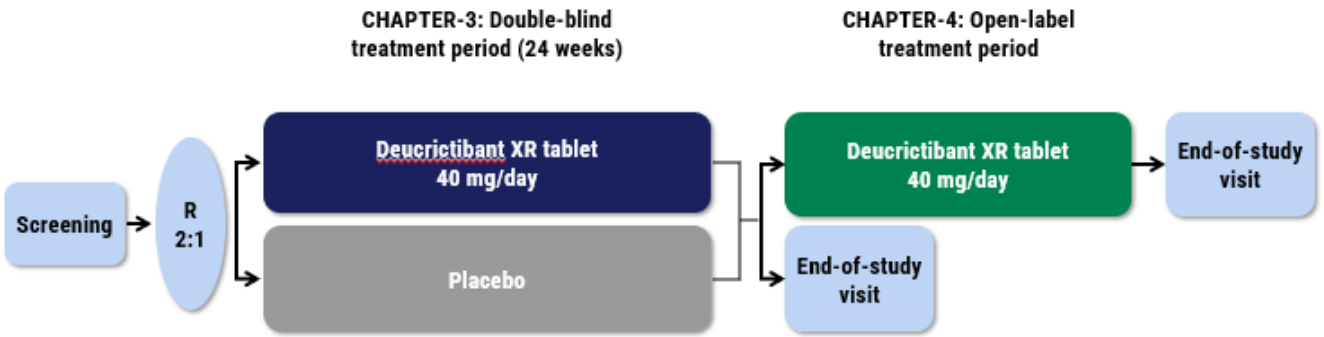
OLE open-label extension; RCT, randomized controlled trial; SD, standard deviation. [a]Duration of attack calculated as the time between the reported time of onset of attack symptoms and the reported time of resolution of attack symptoms.

Once-daily oral deucrictibant extended-release (XR) tablet investigated for prophylaxis of HAE attacks in Phase 3 trial



In a Phase 1 study, deucrictibant XR tablet showed sustained exposure through ≥24-hours post-dose, thus supporting once-daily dosing for HAE attack prevention.

For more details, please see
Zhang Z-Y, et al. Poster Session I, P20



CHAPTER-3 is an ongoing, global, Phase 3 trial designed to evaluate the efficacy and safety of once daily, oral deucrictibant XR tablet for prophylaxis of attacks in adolescents and adults with HAE.

For more details, please see
Zanichelli A, et al. Poster Session II, P42

EC_{85}, effective concentration estimated to provide 85% maximal response (13.8 ng/mL); HAE, hereditary angioedema; IR, immediate-release; R, randomization; XR, extended-release. [a]Single oral dose of 2 x 20 mg deucrictibant IR capsules.

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

CHAPTER-1 OLE: Conclusions

The ongoing Phase 2 CHAPTER-1 OLE study provides further evidence on the long-term safety and efficacy of oral deucrictibant for prevention of HAE attacks.

Deucrictibant was generally well tolerated with one treatment related TEAE of tooth discoloration

1.5 years

Attack rate reduced by week 1 in the RCT and remained low ≥1.5 years in the OLE

Attack rate in OLE remained consistent across groups with different Baseline attack rates

~80% of participants achieved ≥90% reduction in attack rate in the OLE

0.07 **"Moderate and severe" monthly attack rate in the OLE**

Use of bradykinin B2 receptor antagonism for both LTP and ODT did not alter ODT response

The Authors and the Sponsor would like to thank all the people with HAE as well as all study site staff who have been participating in the CHAPTER-1 trial.

HAE, hereditary angioedema; LTP, long-term prophylaxis; ODT, on-demand treatment; OLE, open-label extension; RCT, randomized controlled trial; TEAE, treatment-emergent adverse event.