

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

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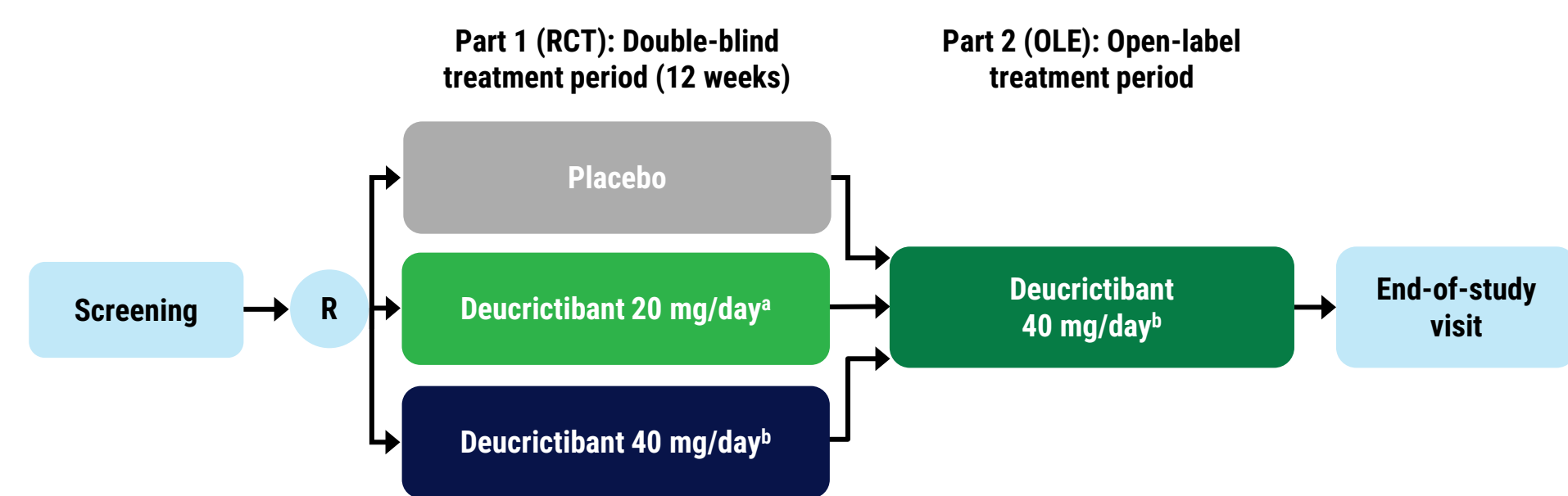
## Introduction

- Excess bradykinin is the main mediator of the clinical manifestations of bradykinin-mediated angioedema, including hereditary angioedema (HAE), attacks.<sup>1</sup>
- Despite the availability of approved therapies, an unmet need remains for additional prophylactic treatments combining injectable-like efficacy, a well-tolerated profile, and ease of administration.<sup>2-5</sup>
- Deucricitbant is a selective, orally administered bradykinin B2 receptor antagonist under development for prophylactic and on-demand treatment of HAE attacks.<sup>3,6-14</sup>
- CHAPTER-1 (NCT05047185)\* is a two-part Phase 2 study evaluating the efficacy and safety of deucricitbant for long-term prophylaxis of HAE attacks.<sup>12,15</sup>
- In the double-blind, placebo-controlled, randomized controlled trial period (RCT; Part 1), deucricitbant demonstrated<sup>15</sup>:
  - Reduction in attack rate
  - Reduction in occurrence of moderate and severe attacks, and attacks treated with on-demand medication
  - Well-tolerated safety profile at both studied doses

## Methods

- In the ongoing, open-label extension period (OLE; Part 2), participants receive open-label treatment with deucricitbant 40 mg/day to evaluate long-term safety and efficacy of deucricitbant administered for prophylaxis against HAE attacks (Figure 1).

Figure 1. Study design



IR, immediate-release; OLE, open-label extension; R, randomization; RCT, randomized controlled trial. \*Deucricitbant IR capsule, 10 mg twice daily. †Deucricitbant IR capsule, 20 mg twice daily.

- Eligible participants were aged  $\geq 18$  and  $\leq 75$  years, diagnosed with HAE-1/2, not receiving other prophylactic treatments at screening, and experienced  $\geq 3$  attacks within 3 months prior to screening or  $\geq 2$  attacks during screening (up to 8 weeks).
- Deucricitbant immediate-release (IR) capsule was dosed twice per day as a proof-of-concept for the once-daily deucricitbant extended-release (XR) tablet, which is the intended formulation of deucricitbant for prophylactic treatment against HAE attacks.<sup>16,17</sup>
  - Efficacy and safety of deucricitbant XR tablet for prophylaxis in HAE will be investigated in the Phase 3 CHAPTER-3 RCT (NCT06669754) and CHAPTER-4 OLE (NCT06679881).<sup>13,14</sup>
- All 30 participants who completed the double-blind, placebo-controlled RCT after randomizing into treatment groups with deucricitbant 20 mg/day (N=11) or 40 mg/day (N=10) or with placebo (N=9) enrolled into the ongoing OLE.

## Results

- This Part 2 data snapshot (cutoff: 10 June 2024) included 30 participants in the OLE who received deucricitbant 40 mg/day with a mean (SD) treatment duration of 12.83 (5.03) months in the OLE.
- Mean age (SD) was 39.1 years (14.5) at CHAPTER-1 Part 1 baseline and 60.0% were female.
- Deucricitbant was well tolerated, with one treatment-related treatment-emergent adverse event (TEAE) of tooth discoloration (Table 1).
- No treatment-related serious or severe TEAEs, no treatment-related TEAEs in laboratory parameters, vital signs, or electrocardiogram findings, and no TEAEs leading to treatment discontinuation, study withdrawal, or death were reported (Table 1).

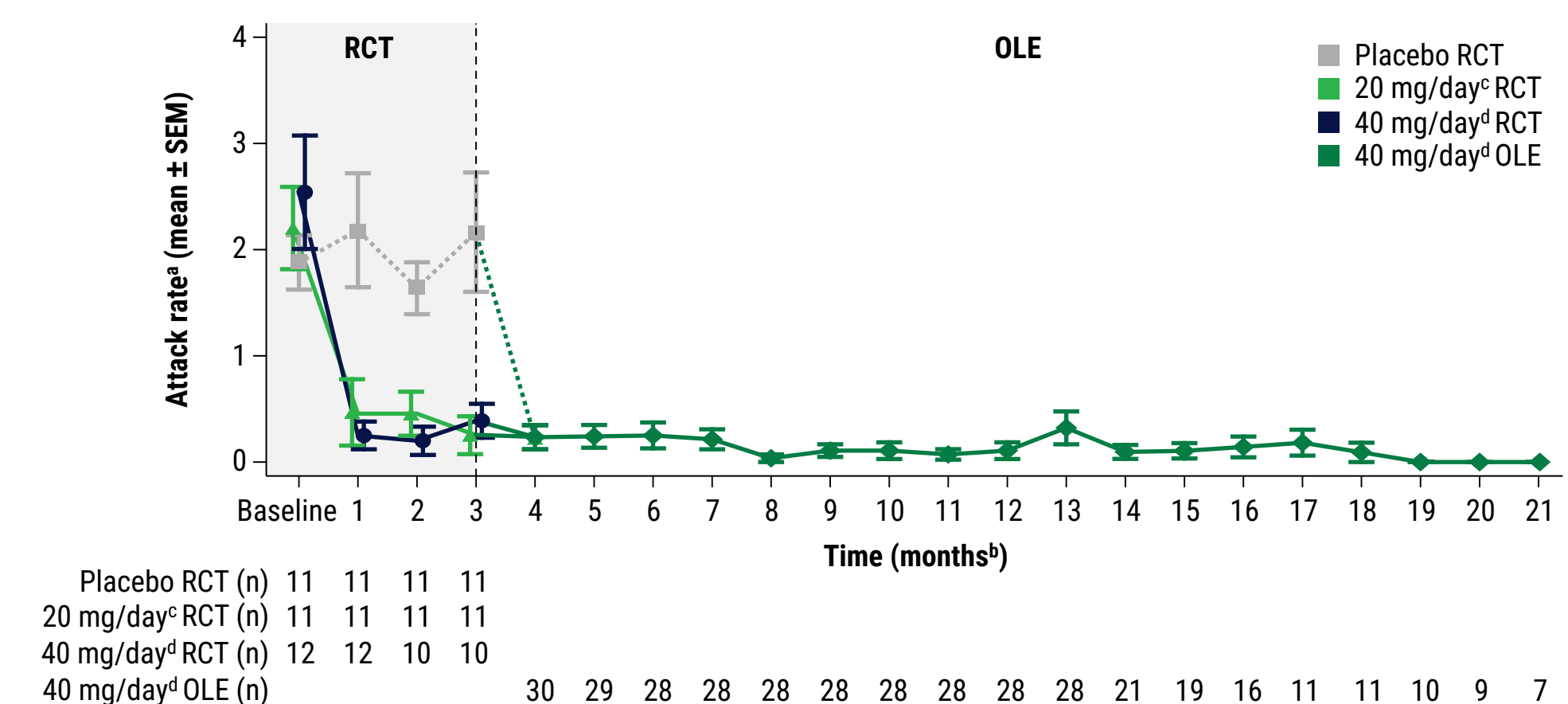
Table 1. Adverse events in the OLE

Adverse events	Placebo to 40 mg/day <sup>a</sup> (N=9)		20 mg/day <sup>b</sup> to 40 mg/day <sup>a</sup> (N=11)		40 mg/day <sup>a</sup> to 40 mg/day <sup>a</sup> (N=10)		Total (N=30)	
	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n
<b>TEAEs</b>	<b>5 (55.6)</b>	<b>25</b>	<b>7 (63.6)</b>	<b>31</b>	<b>6 (60.0)</b>	<b>16</b>	<b>18 (60.0)</b>	<b>72</b>
<b>Treatment-related TEAEs</b>	<b>1 (11.1)</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>1 (3.3)</b>	<b>1</b>
Tooth discoloration	1 (11.1)	1	0	0	0	0	1 (3.3)	1
<b>Serious TEAEs</b>	<b>0</b>	<b>0</b>	<b>1 (9.1)</b>	<b>1</b>	<b>1 (10.0)</b>	<b>1</b>	<b>2 (6.7)</b>	<b>2</b>
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
<b>Treatment-related serious TEAEs</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
<b>TEAEs leading to study drug discontinuation, study withdrawal, or death</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>

IR, immediate release; OLE, open-label extension; TEAE, treatment-emergent adverse event defined as adverse event occurring during time window from first study drug administration. N = number of participants who received  $\geq 1$  dose of study treatment in the OLE by the cutoff date of 10 June 2024. <sup>a</sup>Deucricitbant IR capsule, 20 mg twice daily. <sup>b</sup>Deucricitbant IR capsule, 10 mg twice daily.

- Following early-onset reduction in attack rate with deucricitbant in the first month of the RCT, attack rate remained low during long-term (up to >1.5 years) deucricitbant 40 mg/day treatment in the OLE (Figure 2).

Figure 2. Reduced attack rate in the RCT remained low in the OLE

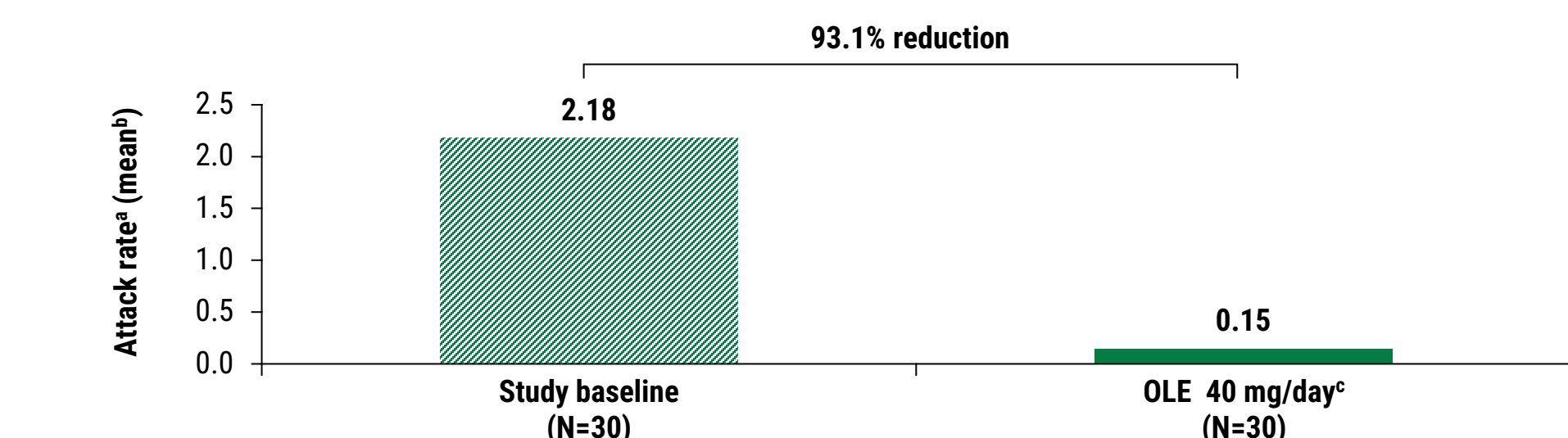


IR, immediate release; OLE, open-label extension; RCT, randomized controlled trial; SEM, standard error of the mean. n = number of patients analyzed at each timepoint. <sup>a</sup>Based on time normalized number of attacks per 4 weeks. <sup>b</sup>1 month = 4 weeks. <sup>c</sup>Deucricitbant IR capsule, 10 mg twice daily. <sup>d</sup>Deucricitbant IR capsule, 20 mg twice daily.

## Results

- Deucricitbant 40 mg/day reduced the attack rate in the OLE by 93.1% compared to CHAPTER-1 RCT study baseline (Figure 3).

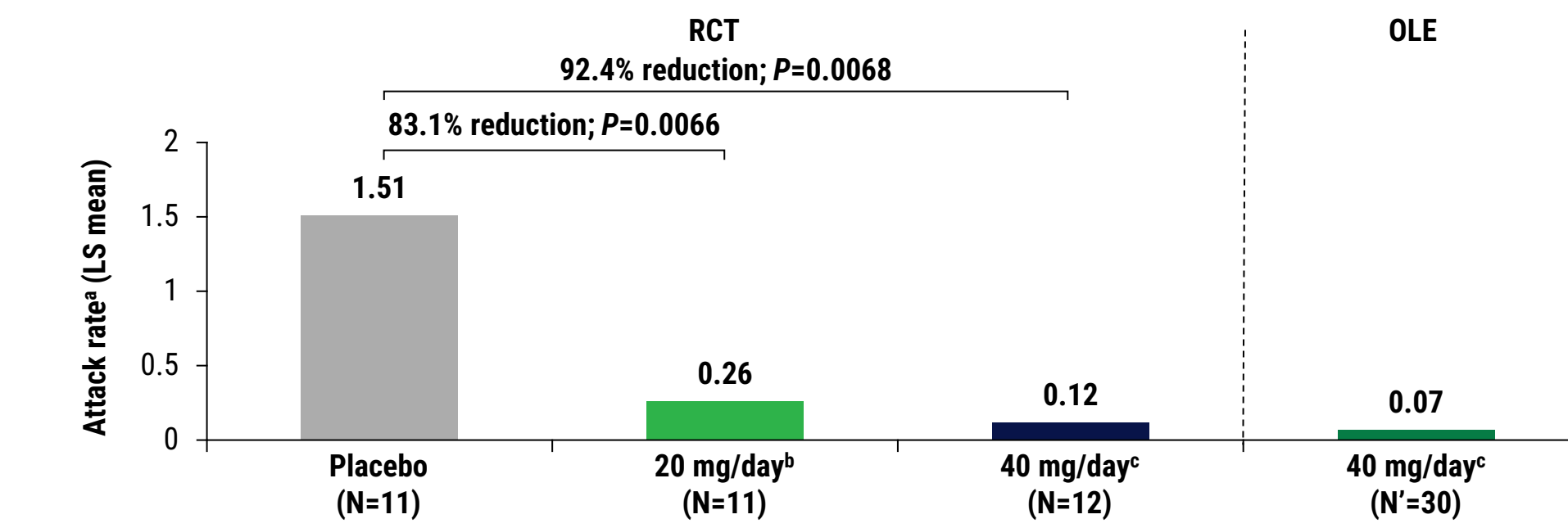
Figure 3. Attack rate reduction in the OLE



IR, immediate release; LS, least squares; OLE, open-label extension. N = number of participants in the OLE. <sup>a</sup>Based on time normalized number of attacks per 4 weeks. <sup>b</sup>Baseline attack rate is raw (unadjusted) mean. OLE attack rate is LS mean. LS mean estimate of attack rate is based on Poisson regression models adjusted for baseline attack rate with offset of the log of time on treatment. No multiplicity adjustment was applied. <sup>c</sup>Deucricitbant IR capsule, 20 mg twice daily.

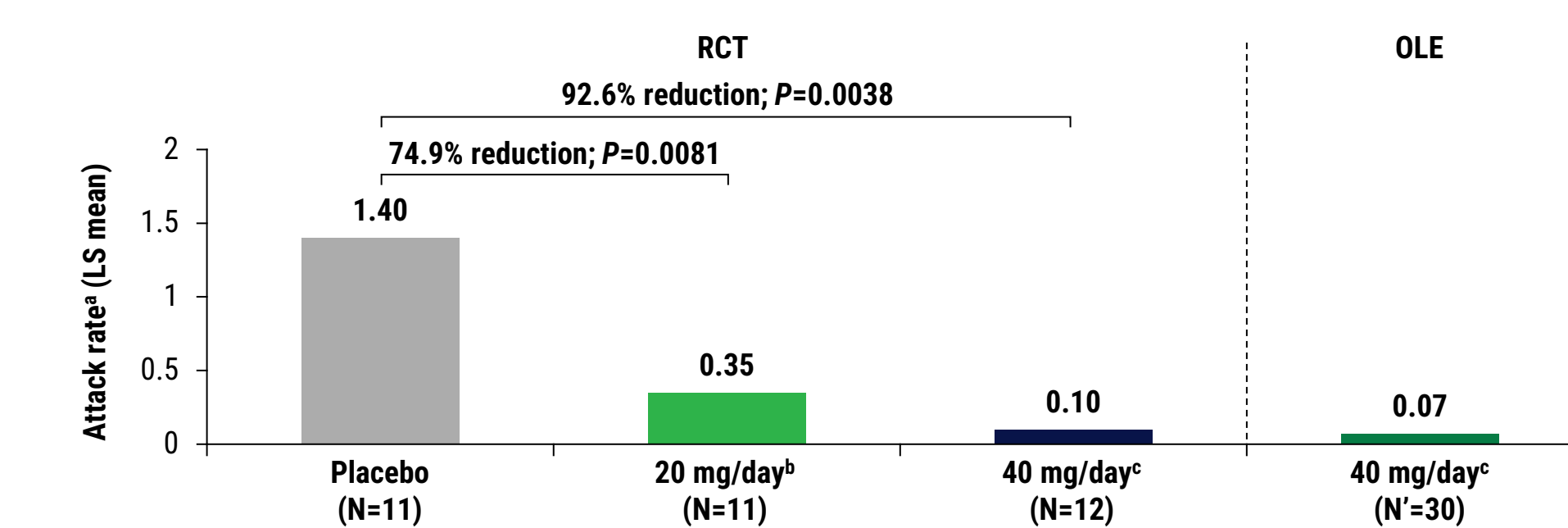
- Rates of "moderate and severe" attacks (Figure 4) and attacks treated with on-demand medication (Figure 5) were reduced during the RCT and remained low in the OLE.

Figure 4. Reduced rate of "moderate and severe" attacks in the RCT 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 estimate of attack rate is based on Poisson regression models adjusted for baseline attack rate with offset of the log of time on treatment. No multiplicity adjustment was applied. The P-values in this figure are nominal. <sup>a</sup>Based on time normalized number of attacks per 4 weeks. <sup>b</sup>Deucricitbant IR capsule, 10 mg twice daily. <sup>c</sup>Deucricitbant IR capsule, 20 mg twice daily.

Figure 5. Reduced rate of on-demand-treated attacks in the RCT remained low in the OLE

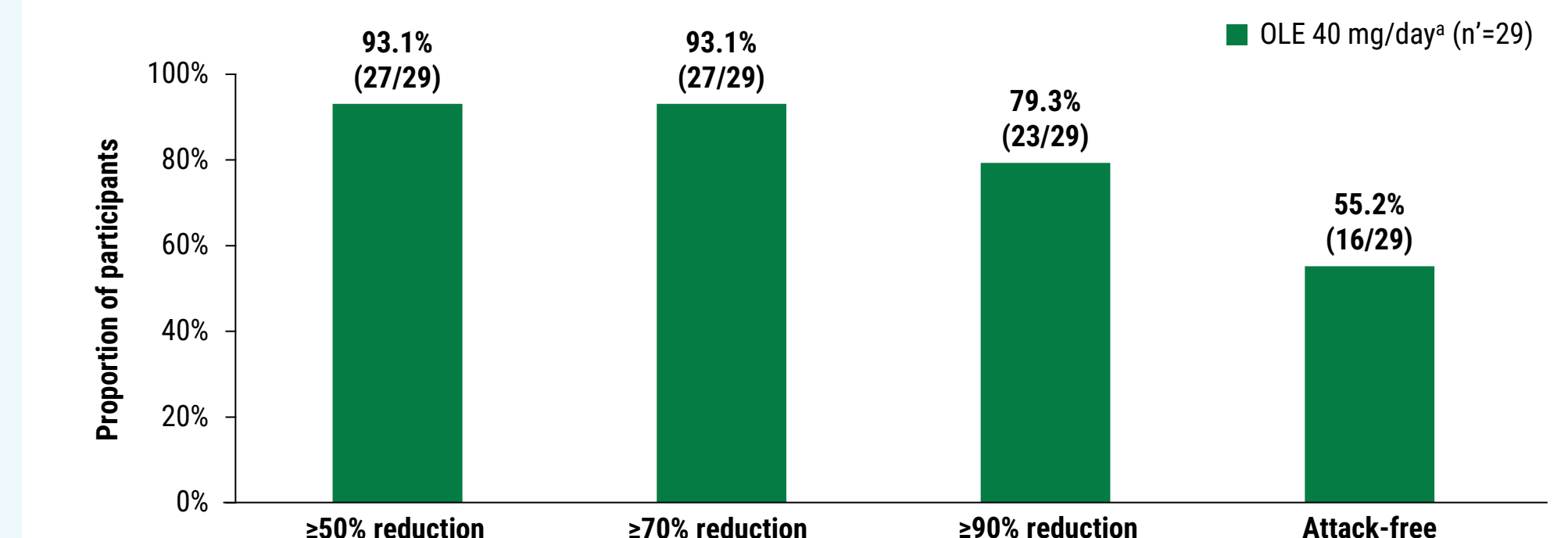


IR, immediate release; LS, least squares; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants randomized in each treatment group in the RCT. N = number of participants in the OLE. LS mean estimate of attack rate is based on Poisson regression models adjusted for baseline attack rate with offset of the log of time on treatment. No multiplicity adjustment was applied. The P-values in this figure are nominal. <sup>a</sup>Based on time normalized number of attacks per 4 weeks. <sup>b</sup>Deucricitbant IR capsule, 10 mg twice daily. <sup>c</sup>Deucricitbant IR capsule, 20 mg twice daily.

## Results

- At data cutoff in the OLE, 93.1%, 93.1%, and 79.3% of participants had achieved  $\geq 50\%$ ,  $\geq 70\%$ , and  $\geq 90\%$  attack rate reduction relative to CHAPTER-1 RCT study baseline, respectively (Figure 6).
- 55.2% of participants were attack-free in the OLE.

Figure 6. Attack rate reduction relative to RCT study baseline and proportion of attack-free participants during the OLE



IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. n = participants with  $\geq 4$  weeks of treatment in the OLE. <sup>a</sup>Deucricitbant IR capsule, 20 mg twice daily.

## Conclusions

- In the current analysis of the ongoing Phase 2 CHAPTER-1 open-label extension study, deucricitbant 40 mg/day was well tolerated, with no safety signals observed.
- Results of this analysis provide evidence that during treatment with deucricitbant 40mg/day:
  - Following early-onset reduction, attack rate remained low through >1.5 years.
  - An early-onset reduction of attack rate was observed in participants switching from placebo to deucricitbant 40 mg/day in the OLE that was comparable to that observed in participants initiating deucricitbant in the RCT.
  - Rates of "moderate and severe" attacks and attacks treated with on-demand medication were reduced during the RCT and remained low in the OLE.
  - Approximately 80% of participants achieved  $\geq 90\%$  reduction in attack rate relative to RCT study baseline and 55% were attack-free in the OLE.
- Results of the ongoing CHAPTER-1 open-label extension study provide further evidence on the long-term safety and efficacy of deucricitbant for prevention of HAE attacks and support further development of deucricitbant as a potential prophylactic therapy for HAE.

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

COI: Grants/research support, honoraria or consultation fees, sponsored speaker bureau – M.A.R.: Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, 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, Pharming, Pharvaris, Sobri, Takeda, UCB; H.C.: AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobri, Takeda; N.C.: Novartis, Takeda; E.E.: Biocryl, Dr. Falk Pharma, Novartis, Pharming, Pharvaris; M.G.: BioCryst, CSL Behring, Novartis; 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; T.K.: BioCryst, CSL Behring, KalVista, Novartis, Pharming, Pharvaris, Sanofi/Regeneron, Takeda; M.M.: BioCryst, CSL Behring, Intellia, KalVista, Novartis, Octapharma, Pharming, Pharvaris, Takeda; M.D.T.: none; A.V.: AstraZeneca, Berlin-Chemie/Menarini Group, CSL Behring, KalVista, Novartis, Pharming, Pharvaris, Sobri, Takeda; H.J.W.: BioCryst, BioMarin, CSL Behring, Genentech, GSK, Takeda; W.H.Y.: Aimimmune, ALK, Amgen, AnaptysBio, Aslan Therapeutics, AstraZeneca, BioCryst, Celgene, CSL Behring, DBV Technologies, Dermira, Eli Lilly, Galderma, Genentech/Roche, Glenmark, GSK, Haleon, Incyte Biosciences, Ionis, Merck, Novartis, Novavax, Pharming, Pharvaris, Providence, Regeneron, Sanofi Genzyme, Takeda, VBI; medical advisor (volunteer) for Hereditary Angioedema Canada, a patient organization; member of Angioedema Centers of Reference and Excellence; A.Z.: BioCryst, CSL Behring, KalVista, Pharming, 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.: Employee of Pharvaris, holds stocks in Pharvaris; U.F.: Employee of Pharvaris, holds stocks in Pharvaris; U.K.: Employee of Pharvaris, holds stocks in Pharvaris; J.K.: Employee of JCK Consult and consultant to Pharvaris, holds stocks/stock options in 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; Takeda, Intellia, Otsuka, Pharvaris, Takeda. **\*CHAPTER-1 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185.**

Acknowledgments: Medical writing services were provided by Holly Richendfer, PhD, of Two Labs Pharma Services.