

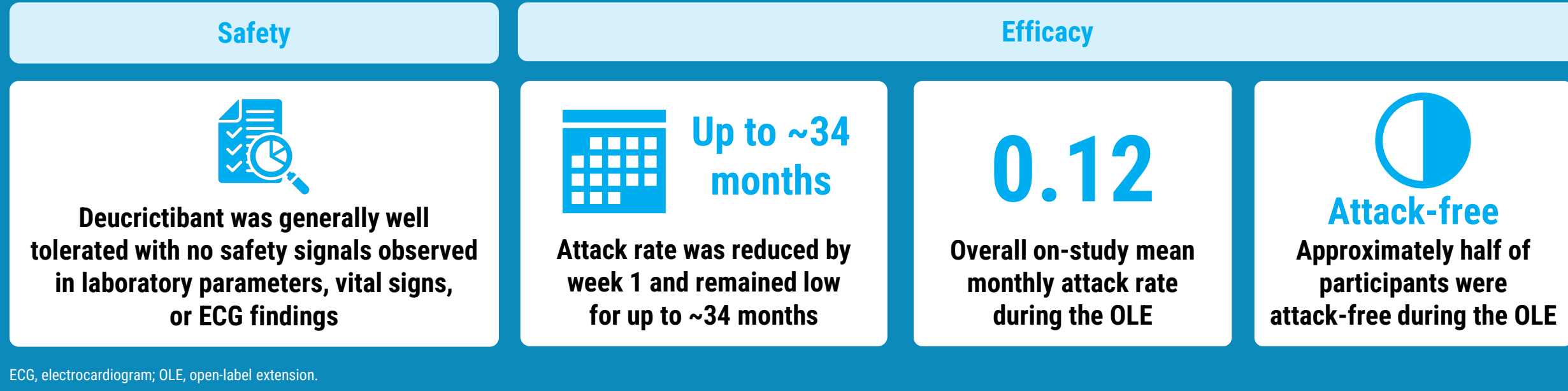
Long-Term Safety and Efficacy of Oral Deucricitbant for Prophylaxis in Hereditary Angioedema: Final Results of the Phase 2 CHAPTER-1 Open-Label Extension Study

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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.



ECG, electrocardiogram; OLE, open-label extension.

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 bradykinin B2 receptor antagonist under development for prophylaxis and on-demand treatment of bradykinin-mediated attacks.⁶⁻¹⁴

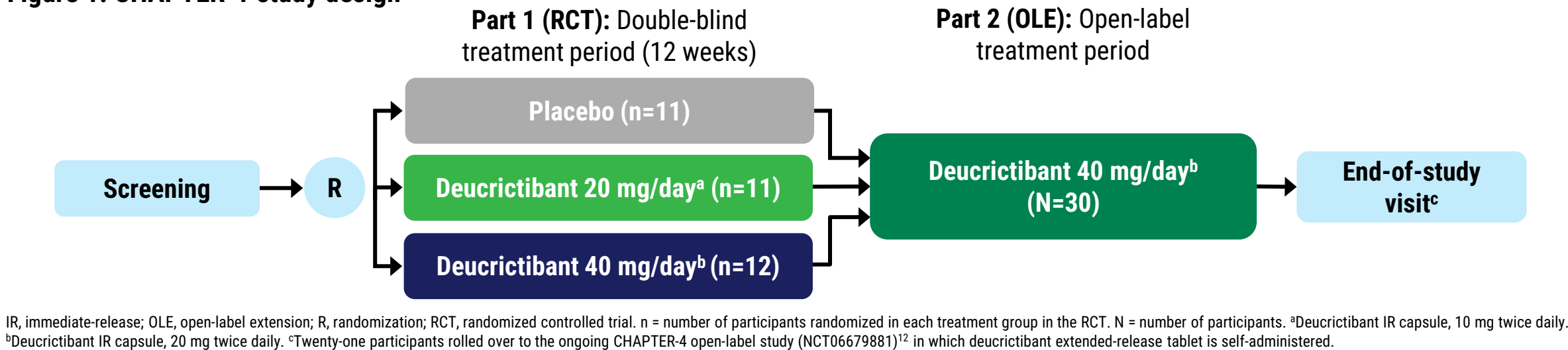
Objective

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.¹³

Methods

- CHAPTER-1 (NCT05047185)*:** a two-part, Phase 2 study.¹³
 - 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



- 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.
 - For the 14 participants that were attack-free during the OLE, the mean (SD) duration on treatment was 22.4 (7.6) months.
- Twenty-one participants were on study at the time of CHAPTER-1 study end and all continued into the ongoing CHAPTER-4 open-label study (NCT06679881)¹² in which deucricitbant extended-release (XR) tablet, 40 mg, is self-administered. None of the nine 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: isolated, mild, asymptomatic increased gamma-glutamyltransferase (<2 upper limit of normal).
- No clinically significant abnormalities in laboratory parameters, vital signs, or electrocardiogram findings.
 - Blood pressure remained stable during the OLE.
- No treatment-related severe or serious TEAEs were reported.
- No TEAEs leading to study drug discontinuation, study withdrawal, or death.

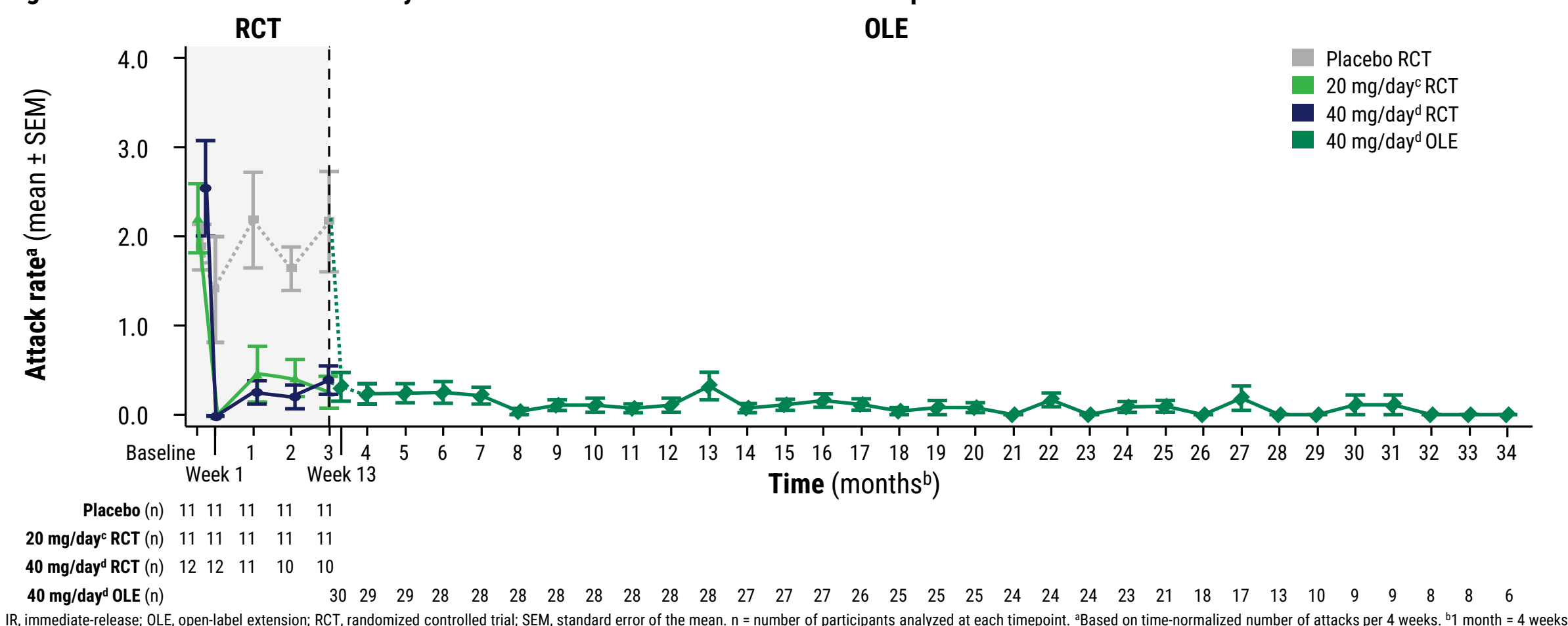
Table 1. Adverse events in the OLE

	Placebo to 40 mg/day* (N=9)		20 mg/day* to 40 mg/day* (N=11)		40 mg/day* to 40 mg/day* (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 events 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. *Deucricitbant IR capsule, 20 mg twice daily. †Deucricitbant IR capsule, 10 mg twice daily. ‡Started during the RCT, resolved while continuing deucricitbant treatment during the OLE, and reoccurred by end of the OLE; alanine aminotransferase, aspartate aminotransferase, bilirubin, and alkaline phosphatase levels were normal. †Three serious TEAEs required reconstruction surgery, hip replacement, or knee replacement. These were not considered treatment-related.

Efficacy analysis

Figure 2. Attack rate was reduced by week 1 and week 13 and remained low for up to ~34 months



Results

Efficacy analysis

Figure 3. Average of 92.4% attack reduction from study baseline^a

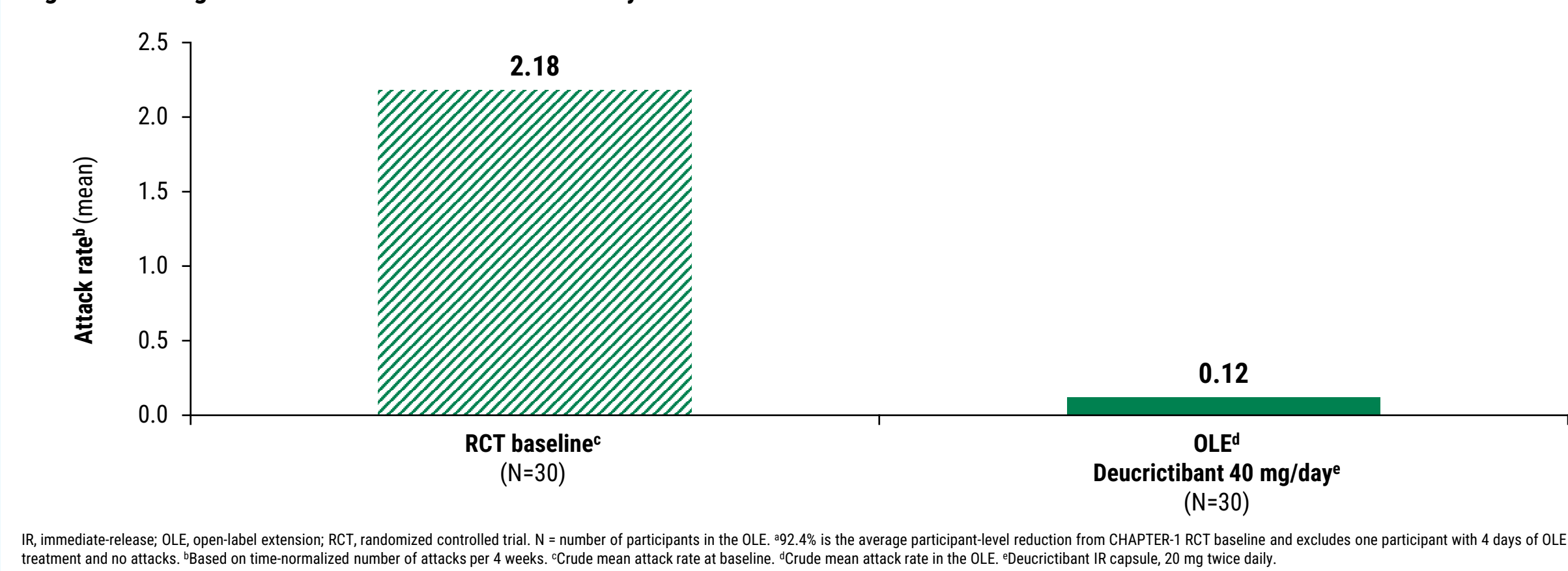


Figure 4. Moderate-to-severe attack rate was reduced in the RCT and remained low in the OLE

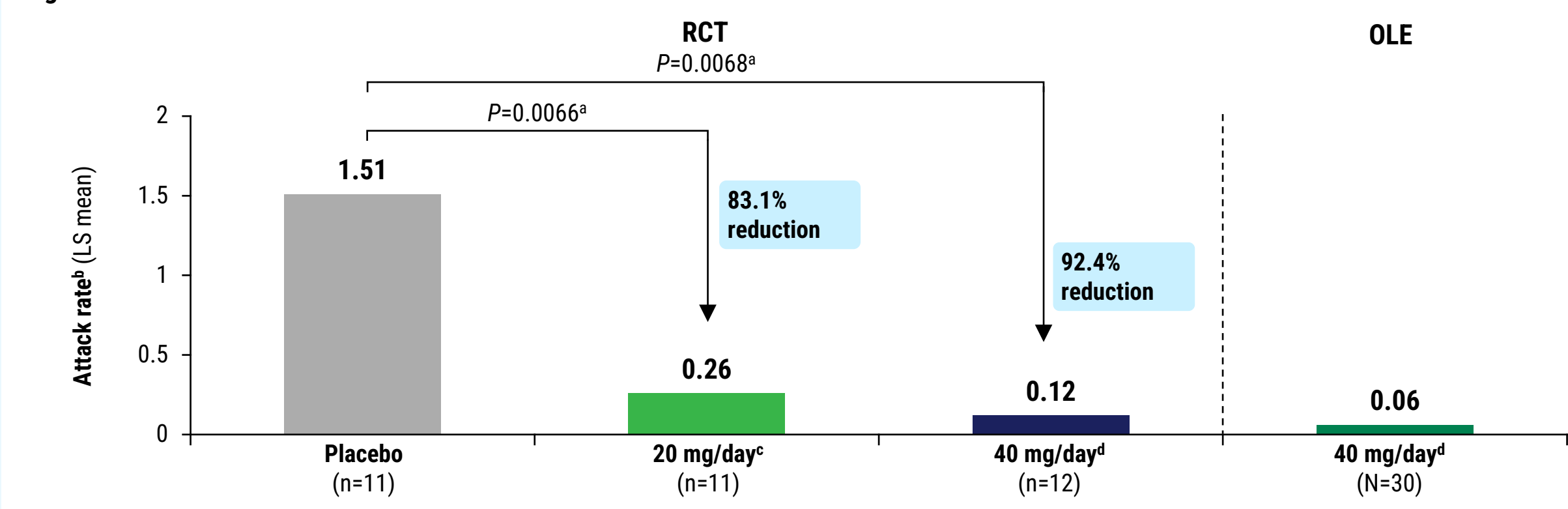


Figure 5. On-demand treated attack rate was reduced in the RCT and remained low in the OLE

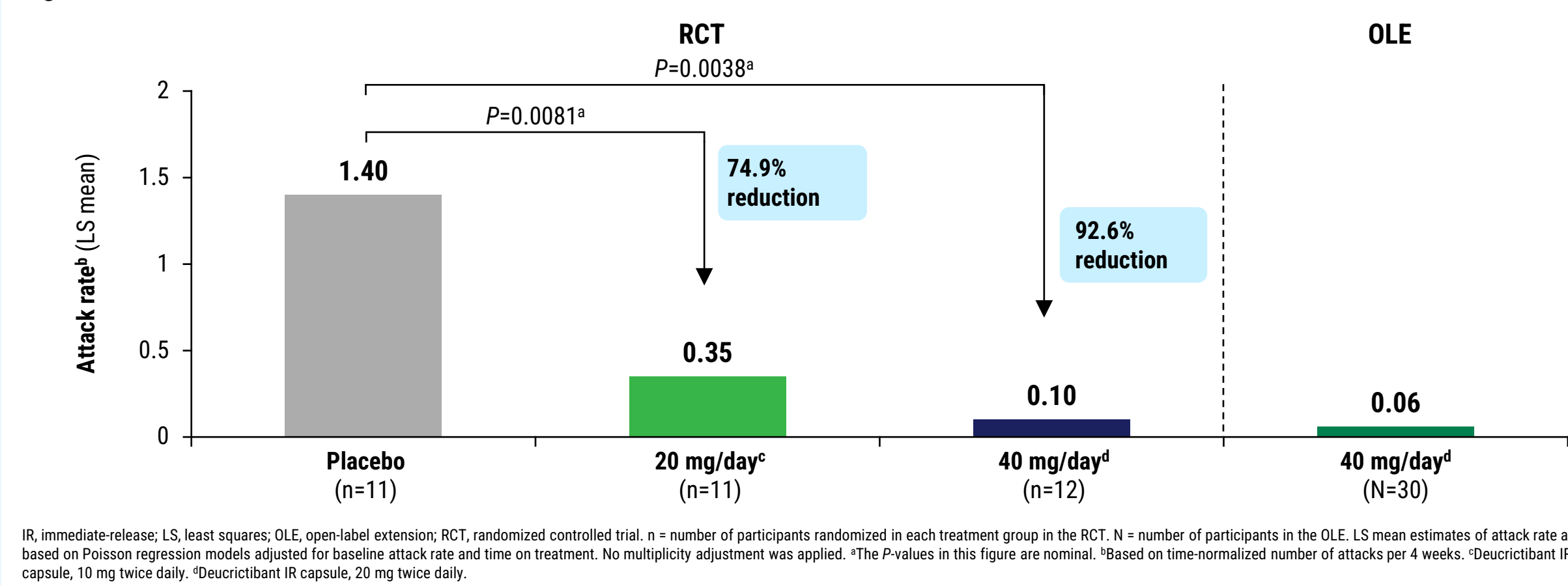


Figure 6. Attack rate reduced relative to RCT study baseline with approximately half of participants attack-free during the OLE

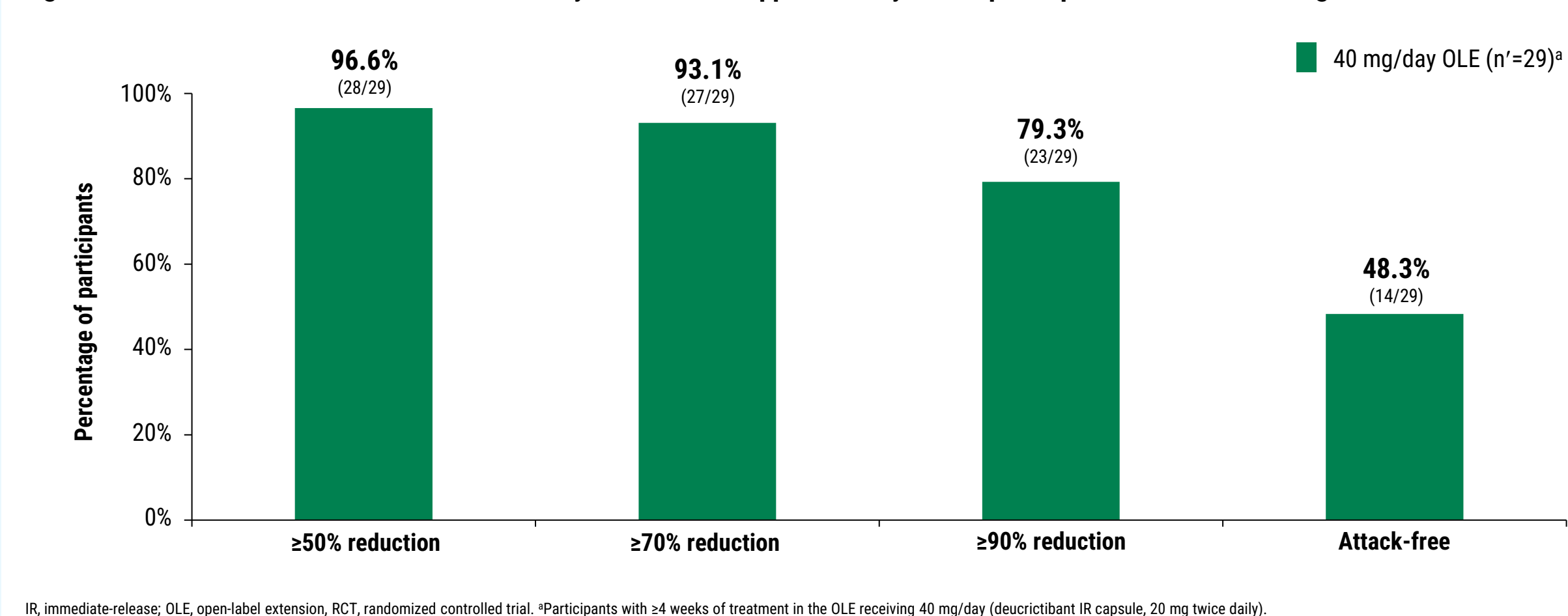
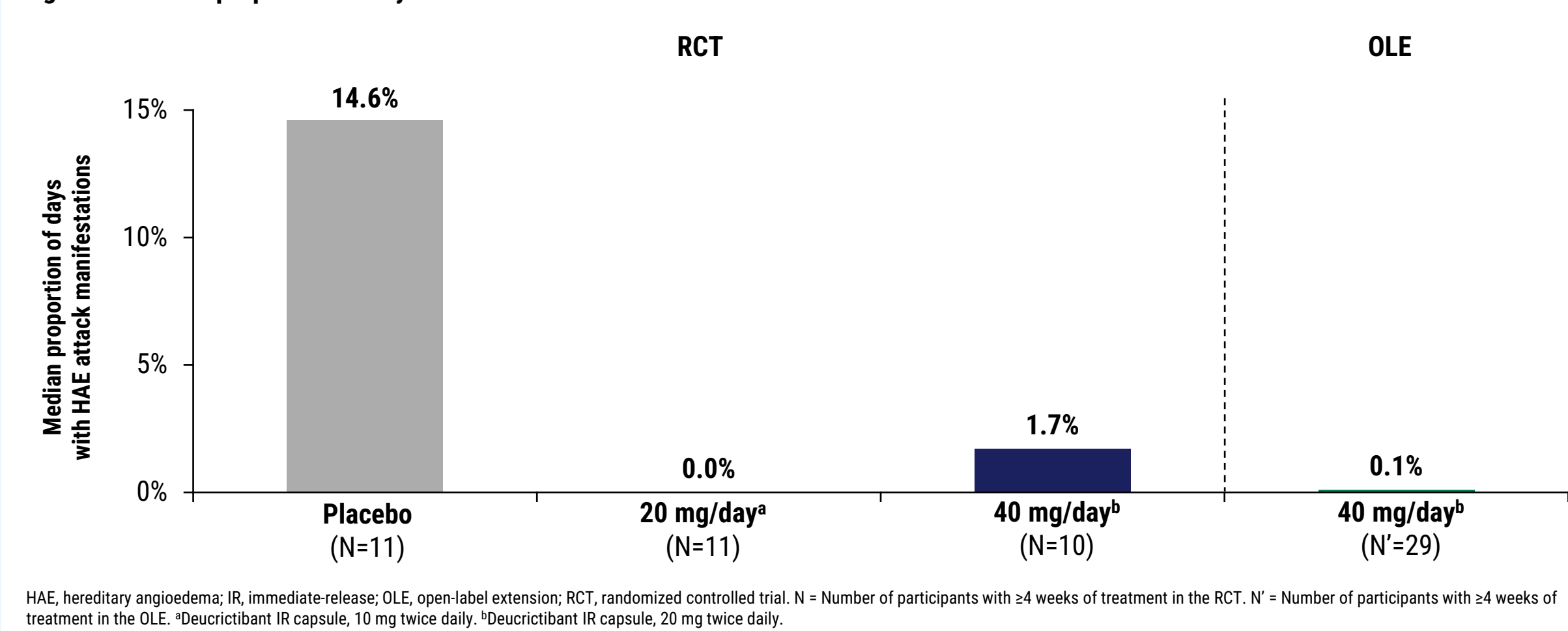


Figure 7. Median proportion of days with HAE attack manifestations was reduced in the RCT and remained low in the OLE



- Attack rate decreased during the RCT and remained low through the OLE regardless of baseline attack rate:
 - For participants with ≥1 to <2 attacks per month at baseline, mean attack rate per 4 weeks in the RCT was 1.79, 0.24, and 0.28 for participants in the placebo, deucricitbant 20 mg/day, and deucricitbant 40 mg/day groups, respectively, and 0.09 for participants in the OLE.
 - For participants with ≥2 attacks per month at baseline, mean attack rate per 4 weeks in the RCT was 2.20, 0.65, and 0.20 for participants in the placebo, deucricitbant 20 mg/day, and deucricitbant 40 mg/day groups, respectively, and 0.16 for participants in the OLE.

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COI: E.A.P.: Astra, BioCryst, BioMarin, CSL Behring, Intellia, KalVista, Otsuka, Pharming, Pharvaris, Takeda; J.A.: Astra Therapeutics, BioCryst, CSL Behring, Intellia Therapeutics, Ionis, KalVista, Pharming, Pharvaris, Takeda; F.A.: BioCryst, CSL Behring, KalVista, Otsuka, Pharming, Pharvaris, Sobli, Takeda, UCB, H.C.: AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobli, Takeda; N.C.: ALK, BioCryst, CSL Vifor, HSE Dublin and Midlands, Laboratory Reform, Novartis, Pharming, Pharvaris, Takeda; E.E.: BioCryst, Dr. Falk Pharma, Novartis, Pharming, Pharvaris; M.G.: None to disclose; S.G.: BioCryst, BioCryst/Neopharm Gentili, CSL Behring, KalVista, Otsuka, Pharming, Pharvaris, Takeda; M.D.G.: BioCryst, CSL Behring, Takeda; P.G.: BioCryst, CSL Behring, KalVista, Pharming, Takeda; S.K.A.: BioCryst, Biotech, CSL Behring, Ionis, KalVista, Otsuka, Pharvaris, Takeda; T.K.: ADARx, Astra, BioCryst, CSL Behring, KalVista, Otsuka, Pharvaris, Sanofi, Takeda; M.M.: Argo, Astra, BioCryst, CSL Behring, Intellia, KalVista, Octapharma, Otsuka, Pharvaris, Takeda; M.E.M.: AstraZeneca, Astra, BioCryst, Blueprint, Bristol Myers, Celgene, CSL Behring, DBV Technologies, Dermira, Eli Lilly, Escent, Galderma, Genentech, GSK, Glenmark, Halozon, Hereditary Angioedema Canada, Incyte, Intellia, Ionis, Merck, Moderna, Novartis, Novartis, Pharming, Pharvaris, Providence, RAPID Therapeutics, Regeneron, Roche, Sanofi, Stallergenes, Takeda, Upstream Bio, VBI; A.Z.: Astra, BioCryst, CSL Behring, Intellia, KalVista, Otsuka, 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., P.L.: employees of Pharvaris, hold 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; consultant to Pharvaris, holds stocks/stock options in Pharvaris; advisor to Kosa Pharma; M.A.R.: ADARx, Astra, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Enliva, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, Takeda, US Hereditary Angioedema Association.

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