

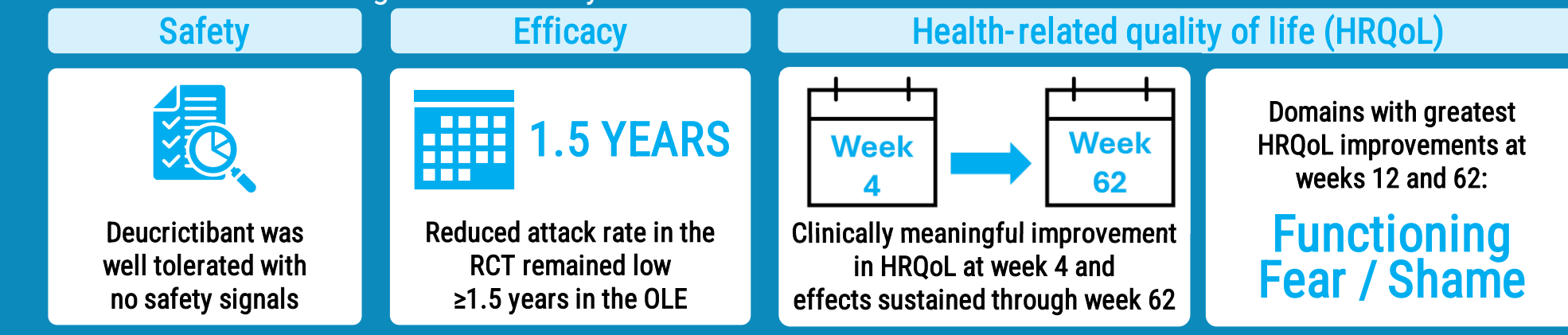
# Long-Term Safety, Efficacy and Health-Related Quality of Life of Oral Deucricitbant for Prophylaxis in Hereditary Angioedema: Results of the CHAPTER-1 Open-Label Extension Study

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## Key takeaways

- The ongoing Phase 2 CHAPTER-1 open-label extension (OLE) study provides evidence on the long-term safety and efficacy of oral deucricitbant for prevention of hereditary angioedema (HAE) attacks.
- Consistent with clinical outcomes, clinically meaningful improvement in health-related quality of life (HRQoL) was maintained through more than 1 year of deucricitbant treatment.



## Background

- Hereditary angioedema (HAE):** a rare genetic condition caused by excess bradykinin production and characterized by painful, often debilitating, swelling attacks affecting multiple locations in the body<sup>1-3</sup>
- Health-related quality of life (HRQoL):** HAE can negatively impact HRQoL and people with HAE may experience high burden of illness and healthcare resource utilization.<sup>4,5</sup>
- Unmet need:** additional prophylactic treatments combining injectable-like efficacy, a well-tolerated profile, and ease of administration.<sup>6-9</sup>
- Oral deucricitbant:** a selective, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.<sup>10-20</sup>

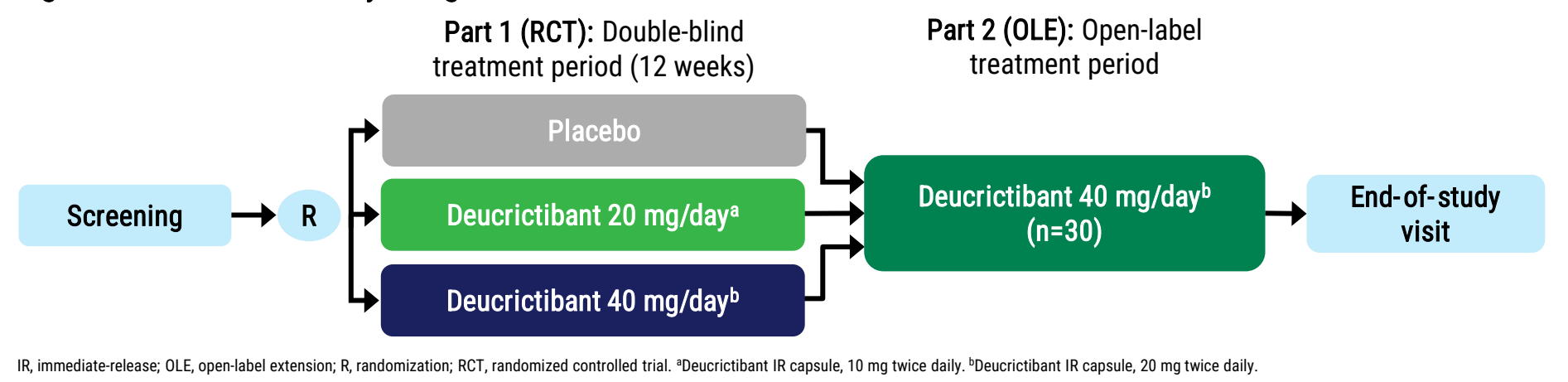
## Objective

Evaluate the safety and efficacy of deucricitbant for long-term prophylaxis of HAE attacks and impact on HRQoL through 62 weeks in adults in the CHAPTER-1 OLE study.<sup>16</sup>

## Methods

- CHAPTER-1 (NCT05047185)\*:** two-part, Phase 2 study.<sup>16</sup>
  - Part 1 randomized placebo-controlled trial (RCT) is complete. Part 2 OLE is ongoing.
- Eligible participants:** adults diagnosed with HAE-1/2, not receiving other prophylactic treatments at screening, and with a pre-specified minimum number of attacks.

Figure 1. CHAPTER-1 study design



- Angioedema Quality of Life Questionnaire (AE-QoL)<sup>21-23</sup>:** patient-reported outcome measure validated for HAE to measure HRQoL. Total score (0–100) is calculated from responses on a five-point scale (never, rarely, sometimes, often, very often) to 17 questions on HRQoL across four domains (functioning, fatigue/mood, fear/shame, nutrition)

## Results

### Participants in the OLE

- All 30 participants who completed Part 1 RCT enrolled in Part 2 OLE.
- At data cutoff (10 June 2024): 5 participants had discontinued. 25 were ongoing, of which 14 had reached the week 62 visit.
- Mean (SD) exposure to deucricitbant 40 mg/day for 30 participants in the OLE: 12.8 (5.0) months
- Maximum exposure to deucricitbant: 20.8 months in the OLE. 23.7 months in the entire study.

### Safety analysis

- Deucricitbant was generally well tolerated.
- One treatment-related treatment-emergent adverse event (TEAE) of tooth discoloration was reported.

Table 1. Adverse events in the OLE

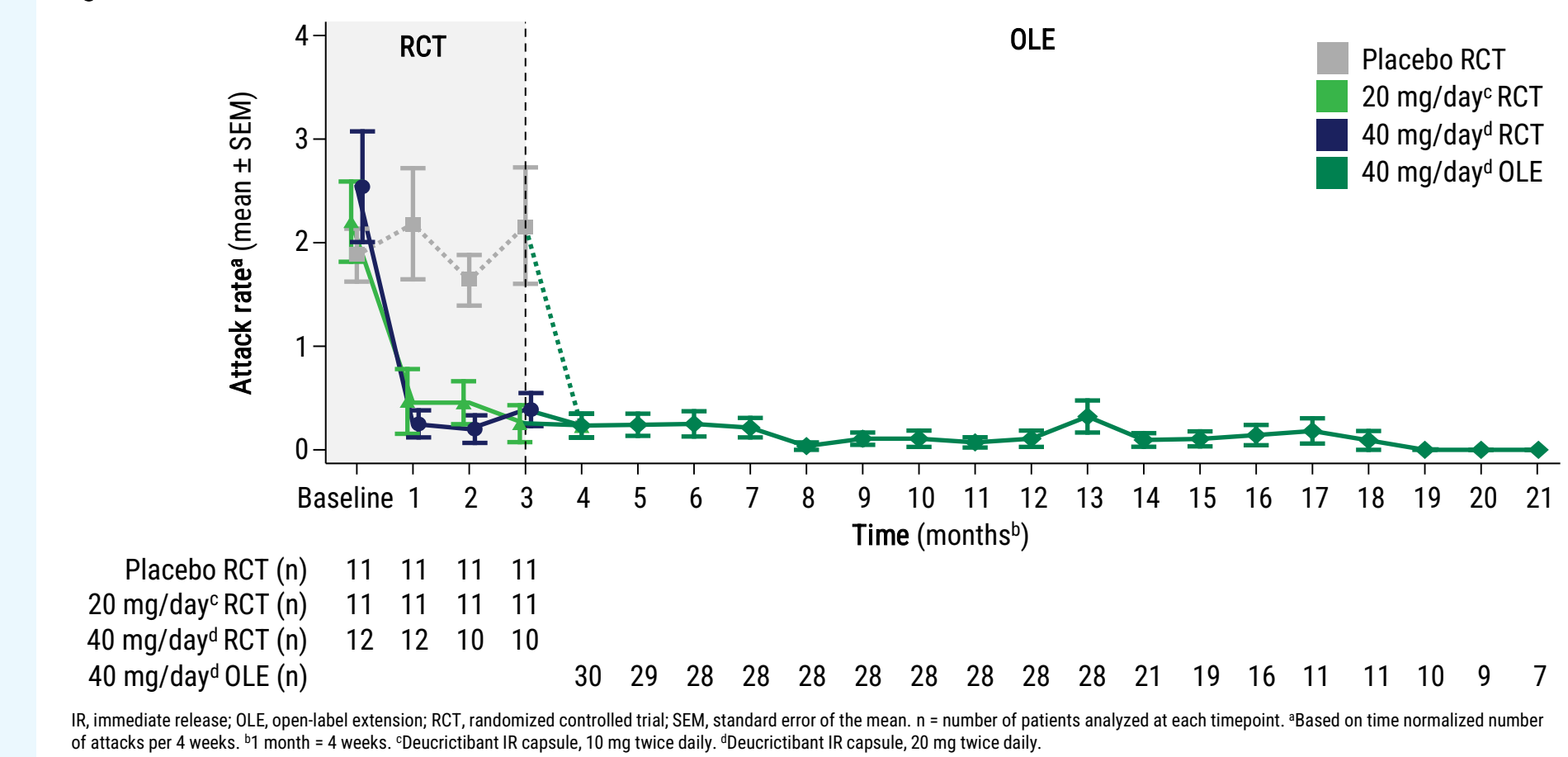
	Placebo to 40 mg/day <sup>a</sup> (N=9)		20 mg/day <sup>a</sup> to 40 mg/day <sup>a</sup> (N=11)		40 mg/day <sup>a</sup> to 40 mg/day <sup>a</sup> (N=10)		Total (N=30)	
	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n
TEAEs	5 (55.6)	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

IR, immediate release; OLE, open-label extension; TEAE, treatment-emergent adverse event. TEAE defined as adverse event occurring during time window from first study drug administration. N = number of participants who received ≥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.

### Efficacy analysis

- RCT: Deucricitbant reduced the attack rate, with effects observed within the first month.
- OLE: Low attack rate maintained through ≥1.5 years.

Figure 2. Attack rate reduced in the RCT remained low in the OLE



## Results

Figure 3. Attack rate reduced in the OLE compared to study baseline

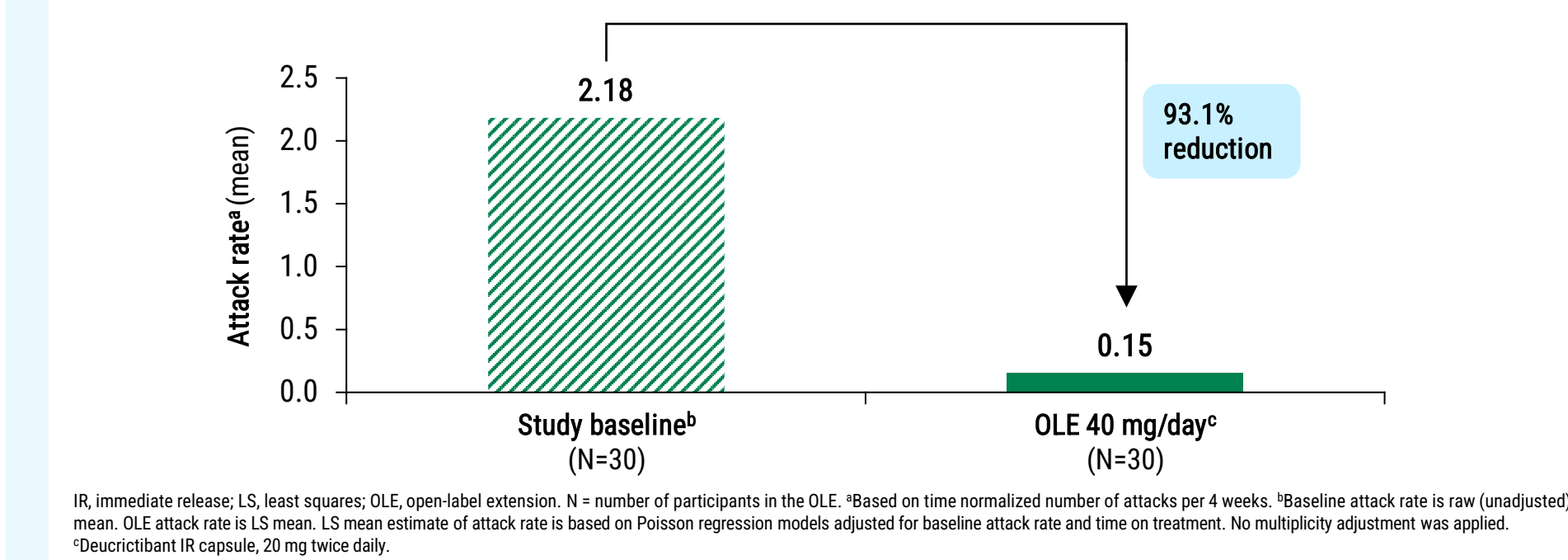


Figure 4. "Moderate and severe" attack rate reduced in the RCT and remained low in the OLE

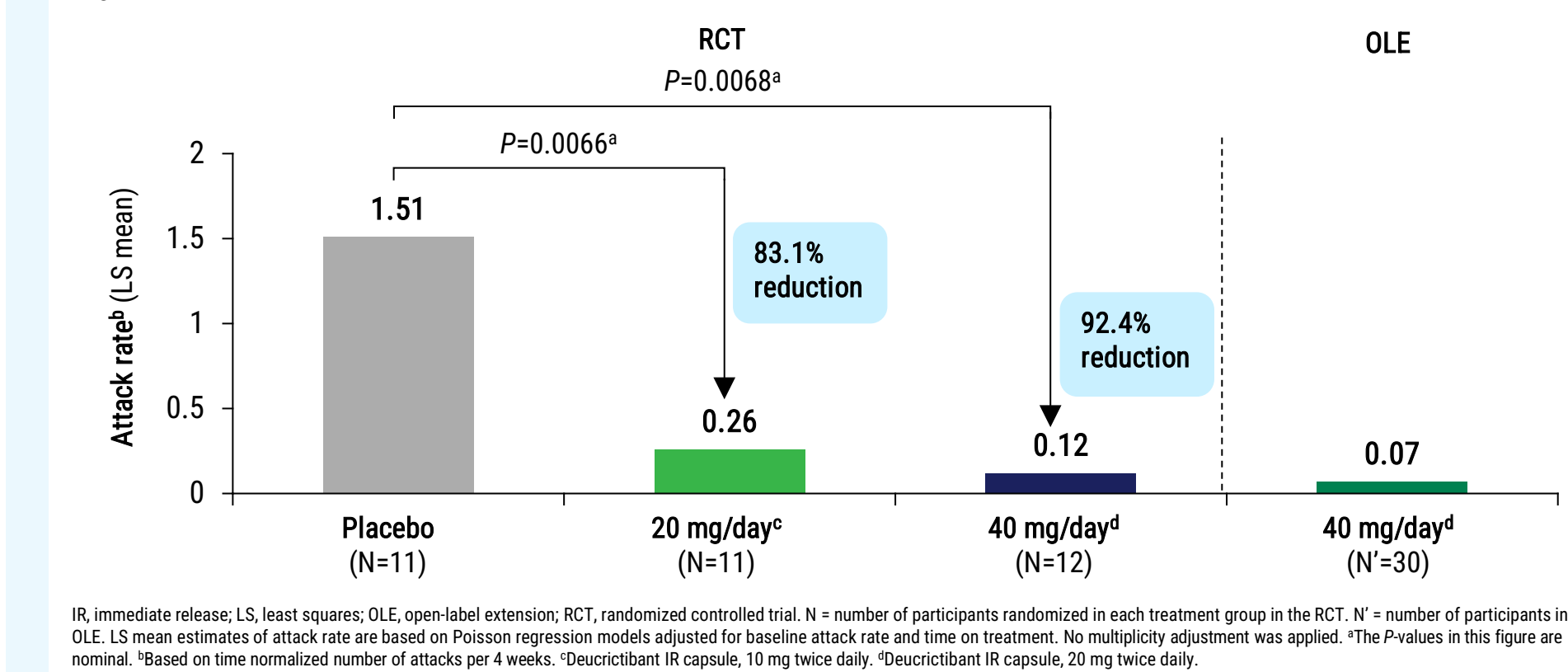
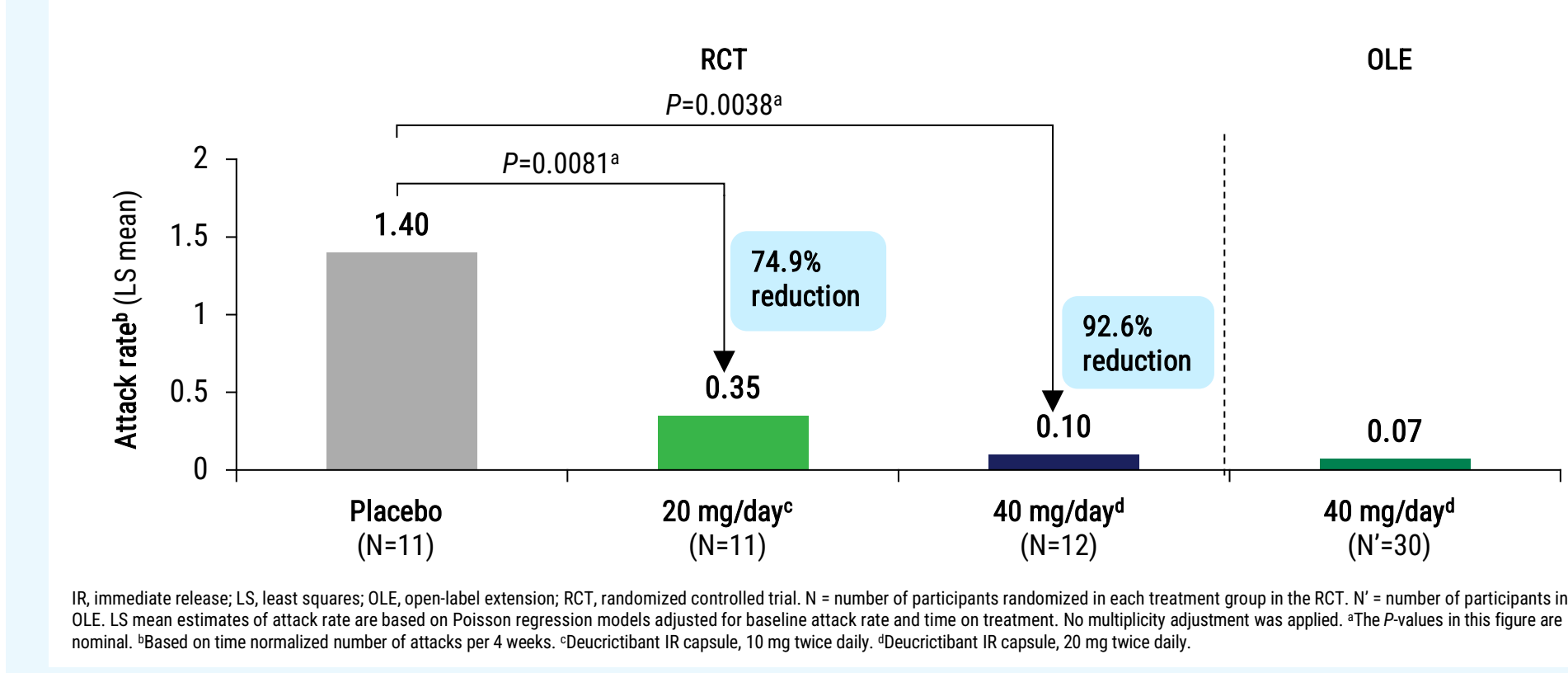


Figure 5. On-demand-treated attack rate reduced in the RCT and remained low in the OLE



## Results

### Participants at week 62

- At data cutoff: 14 participants had reached at least the week 62 visit.
- Mean (SD) exposure to deucricitbant 40 mg/day in the OLE: 16.9 (3.0) months.

Figure 6. AE-QoL: Improvement in HRQoL by week 4 and effects sustained through week 62

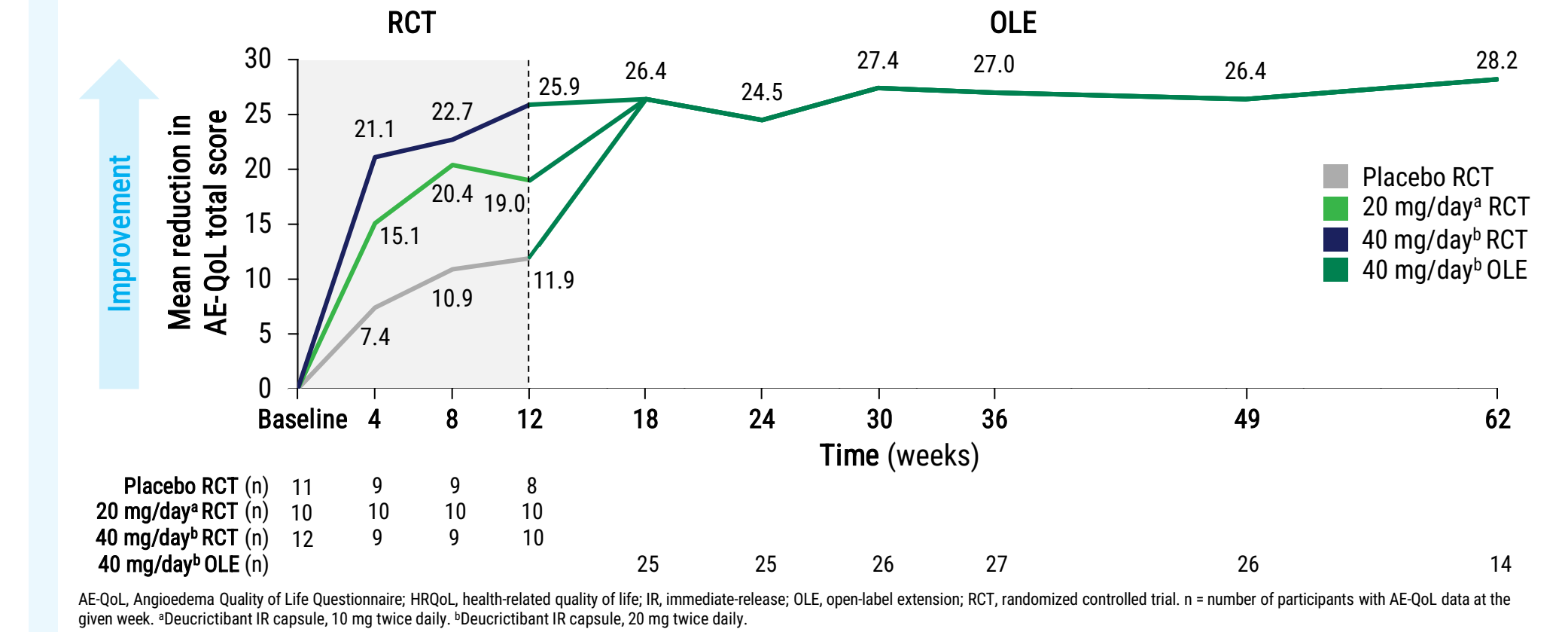
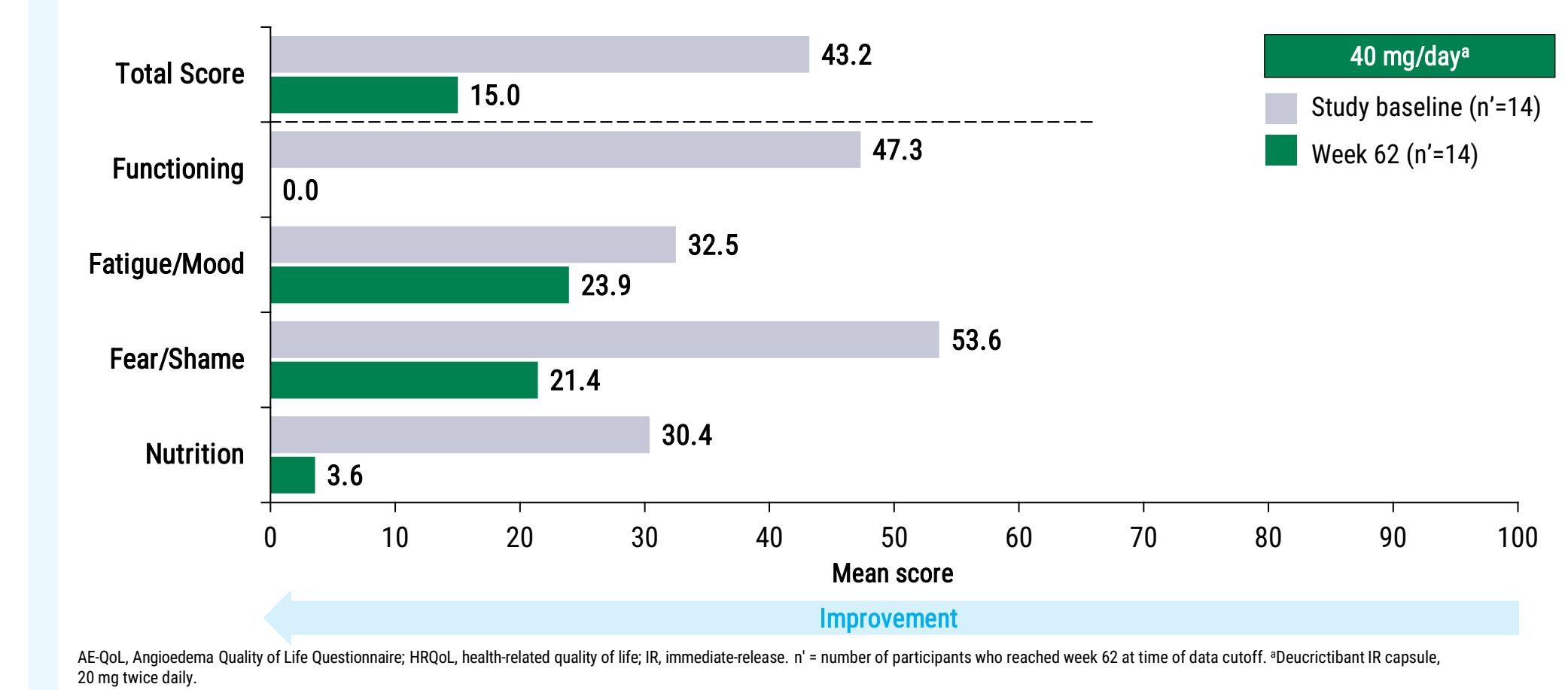


Figure 7. AE-QoL: Reduction in total score and in all HRQoL domain scores from study baseline at week 62



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