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12-15 DECEMBER 2024 I KUALA LUMPUR, MALAYSIA

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RAPIDe-2 Study: Long-term Efficacy and Safety of Oral Deucrictibant for Treatment of Hereditary Angioedema Attacks

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***Our distinguished colleague and friend, Prof. Marcus Maurer, sadly passed away during the finalization of this slide presentation.**

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

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Conflicts of interest disclosure

Grants/research support, honoraria or consultation fees, sponsored speaker bureau

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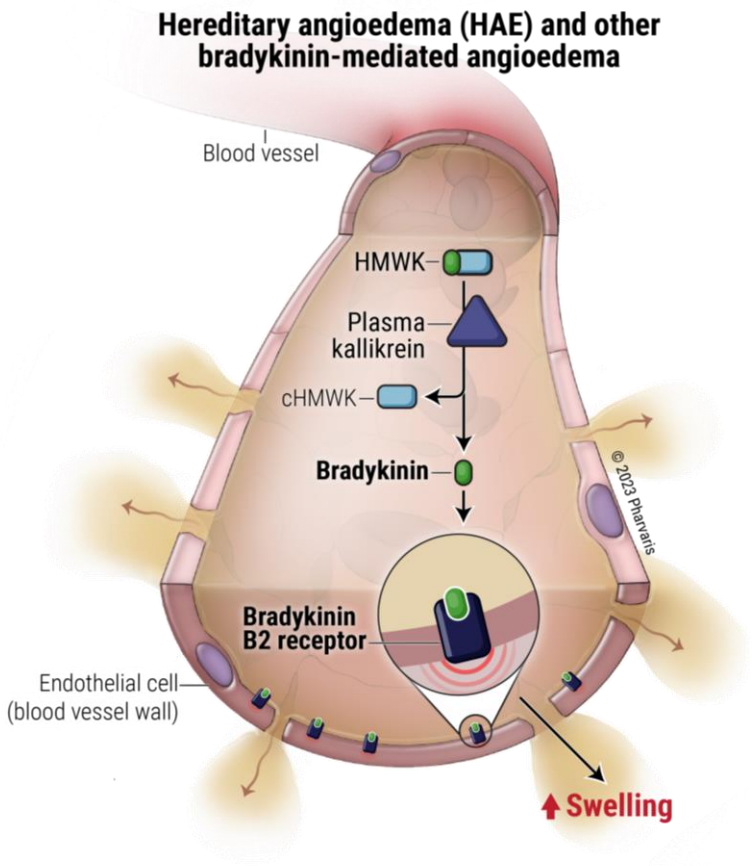
Hereditary angioedema (HAE) is a bradykinin-mediated condition with unmet medical needs



- International guidelines recommend that HAE attacks are **treated as early as possible**.[1-3]
- Burden associated with **parenteral administration** of currently approved on-demand medications[4-8] leads to treatment of a number of HAE attacks being **delayed or forgone**.[9-13]
- An unmet need exists for **on-demand oral** therapies that are effective and well tolerated and may reduce the treatment burden thus enabling prompt administration.[13]

cHMWK, cleaved HMWK; HMWK, high-molecular-weight kininogen. **1**. Betschel S, et al. *Allergy Asthma Clin Immunol.* 2019;15:72. **2**. Busse PJ, et al. *J Allergy Clin Immunol Pract.* 2021;9:132-50. **3**. Maurer M. et al. *Allergy.* 2022;77:1961-90. **4**. Berinert®. Package insert. Accessed November 12, 2024. https://labeling.cslbehring.com/pi/us/berinert/en/berinert-prescribing-information.pdf; **5**. Cinryze®. Summary of product characteristics. Accessed November 12. https://www.ema.europa.eu/en/documents/product-information/cinryze-epar-product-information_en.pdf; **6**. Firazyr®. Package insert. Accessed November 12, 2024. https://www.shirecontent.com/PI/PDFs/Firazyr_USA_ENG.pdf; **7**. Kalbitor®. Package insert. Accessed November 12, 2024. https://www.shirecontent.com/PI/PDFs/Kalbitor_USA_ENG.pdf; **8**. Ruconest®. Package insert. Accessed November 12, 2024. https://www.ruconest.com/wp-content/uploads/Ruconest_PI_Apr2020.pdf; **9**. Burnette A, et al. Presented at: AAAAI; February 24–27, 2023; San Antonio, TX, USA. **10**. Tuong LA, et al. *Allergy Asthma Proc* 2014;35:250-4. **11.** Center for Biologics Evaluation and Research. The voice of the patient–Hereditary angioedema. US Food and Drug Administration. Accessed November 12, 2024. https://www.fda.gov/media/113509/download; **12**. Radojicic C, et al. Presented at: AAAAI; February 24–27, 2023; San Antonio, TX, USA. **13**. Mendivil J, et al. Presented at: ACAAI; November 9–13, 2023; Anaheim, CA, USA.

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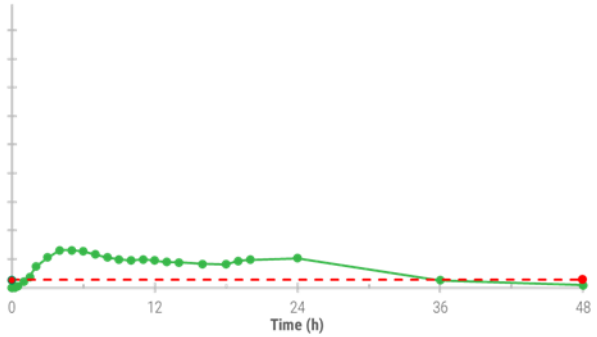
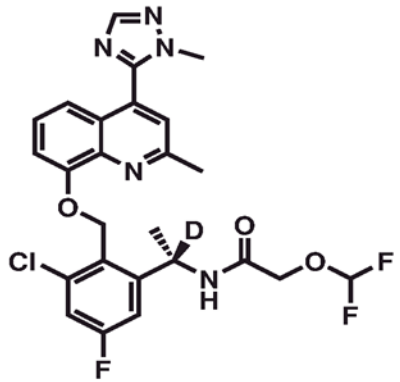
Deucrictibant under development for the prophylactic and on-demand treatment of HAE attacks

DEUCRICTIBANT extended-release (XR) tablet

sustained absorption[1]



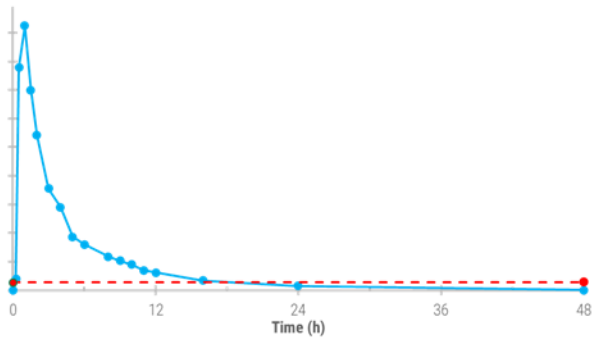
Maintains sustained therapeutic exposure over 24 hours[2] from day one, allowing for once-daily oral treatment to prevent HAE attacks[a]



deucrictibant

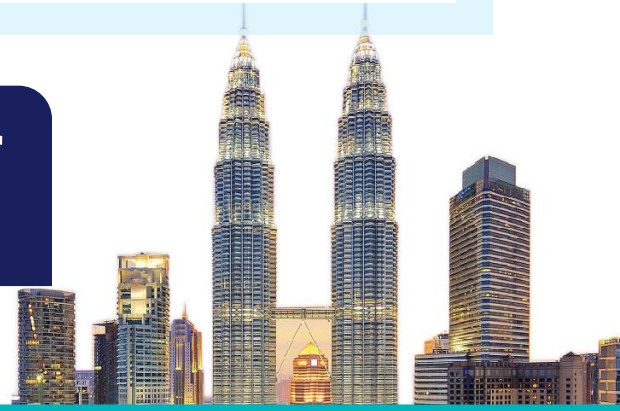
DEUCRICTIBANT immediate-release (IR) capsule

rapid absorption[3]



Rapidly reaches therapeutic exposure within 15-30 minutes[4], making it suitable for on-demand oral treatment of HAE attacks[a]

Two oral products with the same active ingredient for the prevention and treatment of HAE attacks



HAE, hereditary angioedema. [a]Aspirational; to be confirmed with clinical data from Phase 3 studies. **1.** Company data: single-dose cross-over PK study in healthy volunteers (n=14) under fasting conditions. **2.** Lesage A, et al. Presented at IDDST; May 22-24, 2024. **3.** Crabbé R, et al. Presented at AAAAI; Feb 26-Mar 1, 2021. **4.** Maurer M, et al. Presented at AAAAI; Feb 24-27, 2023; San Antonio, TX, USA.

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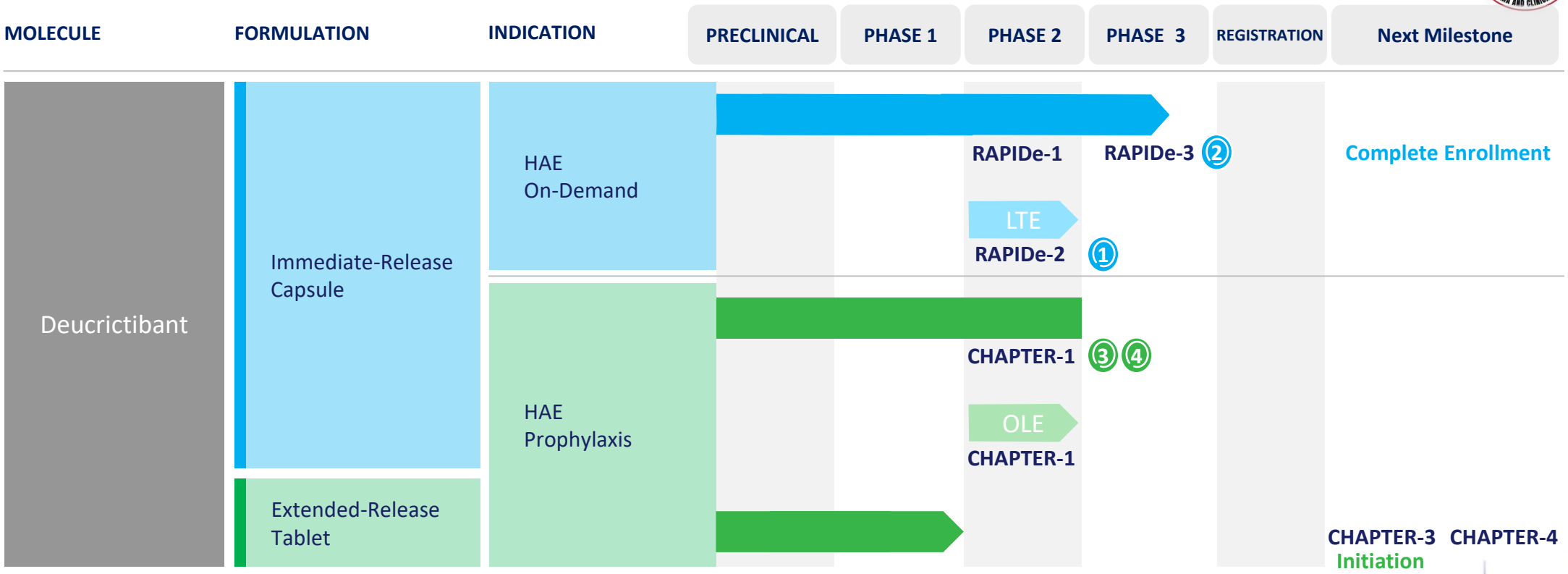
Deucrictibant development program in HAE



Presentations at APAAACI 2024 poster session

① Li et al. Propensity score matching: RAPIDe-2 vs. mixed methods
December 15, 8.00 AM – 6.00 PM

② Li et al. RAPIDe-3 study design
December 15, 8.00 AM – 6.00 PM

Additional oral clinical presentations at APAAACI 2024

③ Magerl et al. CHAPTER-1 RCT clinical and quality-of-life outcomes:
December 14, 2.00-2.10PM

④ Magerl et al. CHAPTER-1 Open-label extension results:
December 15, 3.20-3.30PM

HAE, hereditary angioedema; LTE, long-term extension; OLE, open-label extension; RCT, randomized controlled trial. RAPIDe-1. ClinicalTrials.gov identifier: NCT04618211. Accessed November 11, 2024. https://www.clinicaltrials.gov/study/NCT04618211. RAPIDe-2. ClinicalTrials.gov identifier: NCT05396105. Accessed November 11, 2024. https://www.clinicaltrials.gov/study/NCT05396105. RAPIDe-3. ClinicalTrials.gov identifier: NCT06343779. Accessed November 11, 2024. https://www.clinicaltrials.gov/study/NCT06343779. CHAPTER-1. ClinicalTrials.gov identifier: NCT05047185. Accessed November 11, 2024. https://www.clinicaltrials.gov/study/NCT05047185. CHAPTER-3. ClinicalTrials.gov identifier: NCT06669754. Accessed November 11, 2024. https://clinicaltrials.gov/study/NCT06669754. CHAPTER-4. ClinicalTrials.gov identifier: NCT06679881. Accessed November 11, 2024. https://clinicaltrials.gov/study/NCT06679881.

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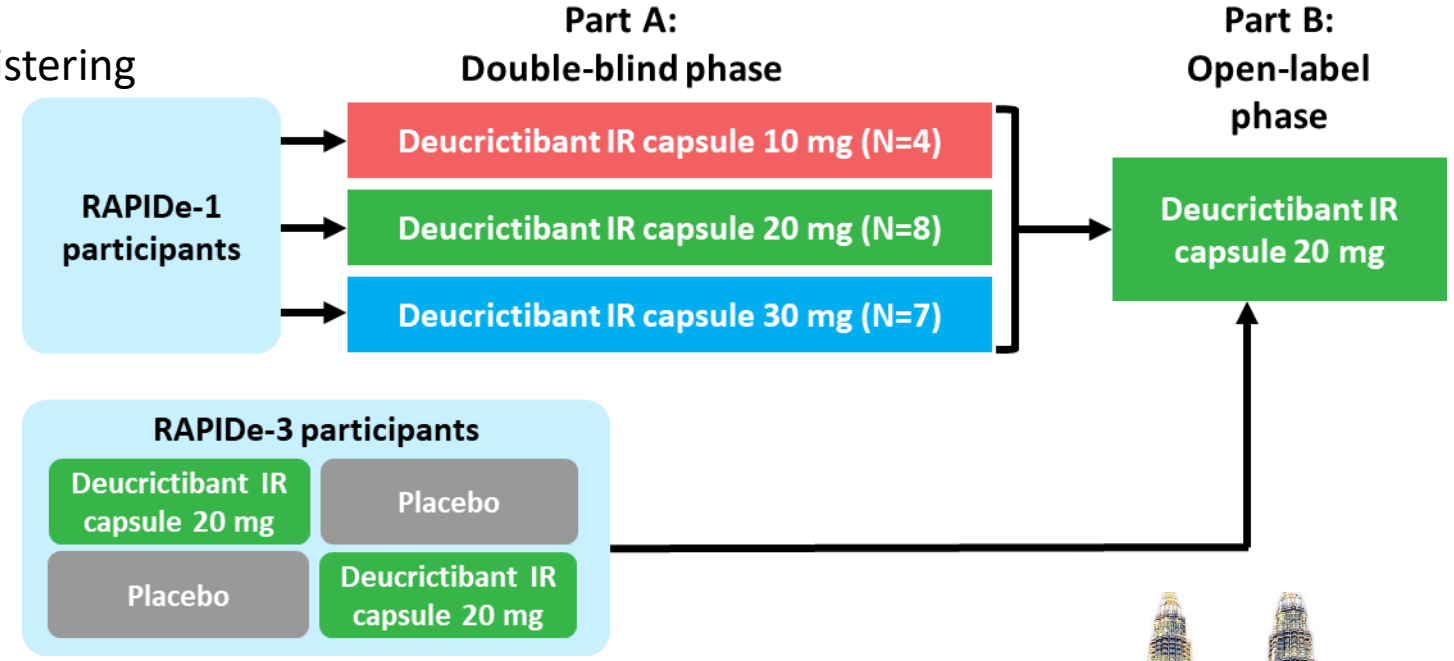
RAPIDe-2 objectives and study design

- RAPIDe-2[1] is an ongoing, two-part, Phase 2/3 extension study evaluating long-term safety and efficacy of orally administered deucrictibant IR capsule for the treatment of HAE attacks.
  - Part A enrolls adult (≥18 years) participants who completed RAPIDe-1[2].
  - In Part A, participants continue self-administering the same double-blinded dose of deucrictibant IR capsule (10 mg, 20 mg, or 30 mg) received in RAPIDe-1 to treat qualifying non-laryngeal attacks (≥1 symptom with Visual Analogue Scale score ≥30), and laryngeal attacks presenting without breathing difficulties.
  - This presentation reports the data from the RAPIDe-2 Part A combined-dose group at the date of cutoff.



HAE, hereditary angioedema; IR, immediate-release. **1.** RAPIDe-2. ClinicalTrial.org identifier NCT05396105. Accessed November 18, 2024. https://clinicaltrials.gov/study/NCT05396105. **2.** RAPIDe-1. ClinicalTrials.gov identifier: NCT04618211. Accessed November 18, 2024. https://www.clinicaltrials.gov/study/NCT04618211.

Study endpoints

- **Primary endpoint:** Safety, including TEAEs, clinical laboratory tests, vital signs, and ECG findings.
- **Efficacy:** Assessed using PRO tools.
- **Secondary efficacy endpoints**:
  - **Time to onset of symptom relief**:
    PGI-C rating of at least "a little better" for
    2 consecutive timepoints by 12 hours post-treatment
  - **Time to reduction in attack severity**:
    ≥1-level reduction in PGI-S from pre-treatment for
    2 consecutive timepoints by 12 hours post-treatment
  - **Time to substantial symptom relief:**
    PGI-C rating of at least "better" for
    2 consecutive timepoints by 12 hours post-treatment
  - **Proportion of attacks achieving complete attack resolution**:
    PGI-S rating of "none" at 24 hours post-treatment

Patient Global Impression of Change[1]

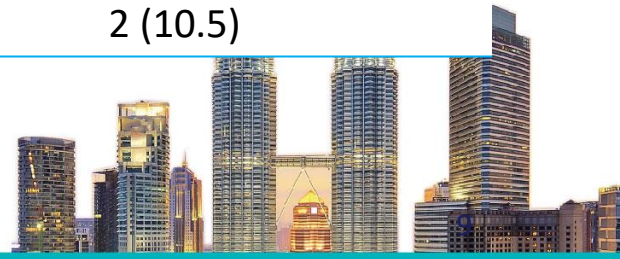
Patient Global Impression of Severity[1]

ECG, electrocardiogram; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity; PRO, patient-reported outcome; TEAE, treatment-emergent adverse event (defined as adverse event occurring during time window from first study drug administration). **1.** Cohn DM, et al. *Clin Transl Allergy*. 2023;e12288.

Baseline characteristics[a]

- 265 attacks from 17 participants included in the mITT efficacy analysis set (data cutoff: 01 March 2024).[b]
- 337 attacks from 19 participants included in the safety analysis set (data cutoff: 10 June 2024).[c]
  - 7 of 337 attacks were laryngeal.
- Baseline characteristics were similar to those of the RAPIDe-1 Phase 2 trial population.

	Deucrictibant IR capsule (combined dose group)
Number of attacks treated[d]	337
Number of participants[d]	19
Age in years, mean (SD)	42.7 (17.6)
Sex: Male/female, n (%)	7 (36.8) / 12 (63.2)
Race: White/other, n	18 / 1
BMI, mean (SD)	27.0 (3.8)
Years since HAE diagnosis, mean (SD)	21.7 (15.2)
HAE type, n (%)	
HAE-1	17 (89.5)
HAE-2	2 (10.5)



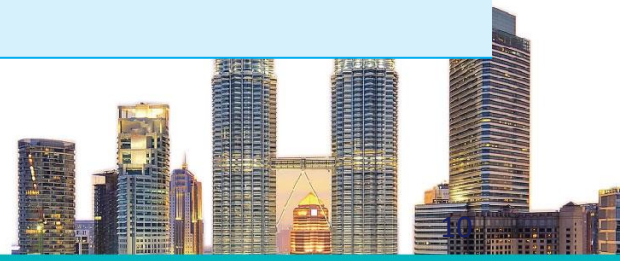
BMI, body mass index; HAE, hereditary angioedema; IR, immediate-release; mITT, modified intention-to-treat; PGI-C, Patient Global Impression of Change; SD, standard deviation. [a]The baseline characteristics of RAPIDe-2 participants at RAPIDe-1 initiation are shown. [b]All participants who had ≥1 attack treated with deucrictibant and non-missing PGI-C results from ≥1 post-treatment timepoint. [c]All participants who received any dose of deucrictibant in the study. [d]Number by the cutoff date of 10 June 2024.

Deucrictibant was well tolerated across all doses

- No treatment-related TEAEs.
- No treatment-related serious or severe TEAEs, no treatment-related TEAEs in laboratory parameters, vital signs, or ECG findings.
- No TEAEs leading to treatment discontinuation, study withdrawal, or death.

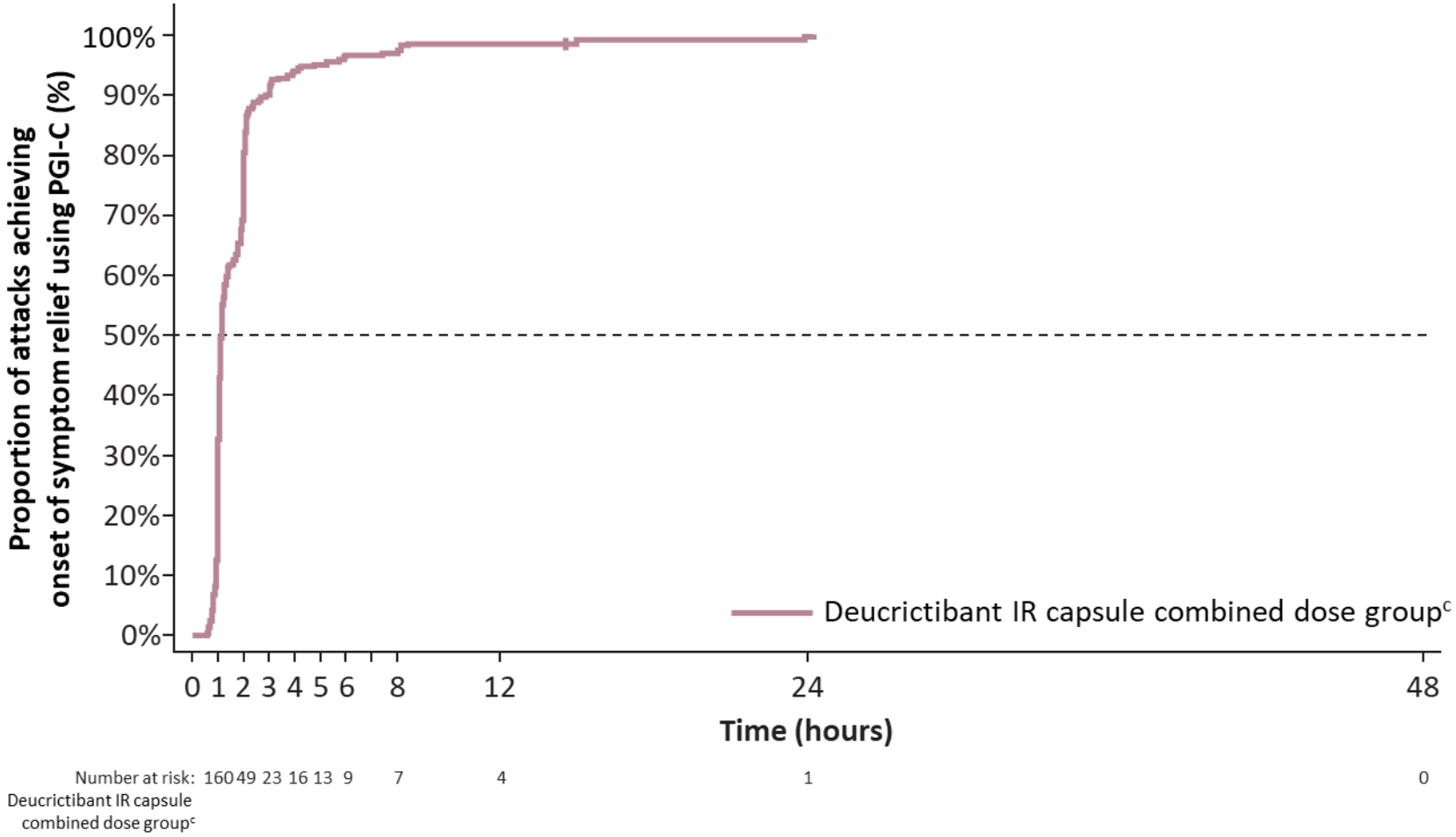
TEAEs within 5 days after administration of study drug

Adverse events	Deucrictibant IR capsule (combined dose group)
Number of attacks treated[a]	337
Number of participants[a]	19
Attacks with any TEAE, n (%)	13 (3.9)
Treatment-related TEAEs, n	0
Serious TEAEs, n	1[b]
Treatment-related serious TEAEs, n	0
TEAEs leading to study drug discontinuation, study withdrawal, or death, n	0

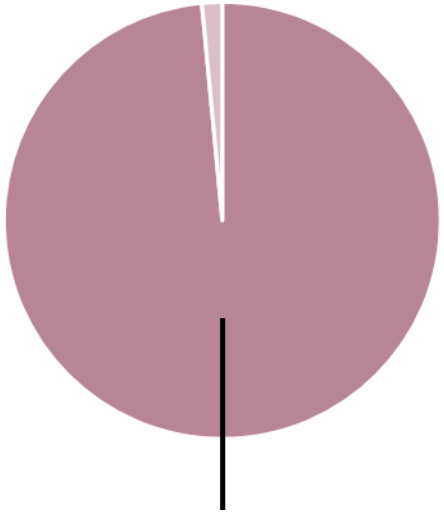


ECG, electrocardiogram; IR, immediate-release; TEAE, treatment-emergent adverse event (defined as adverse event occurring during time window from first study drug administration).
[a]Number in the safety analysis set (data cutoff: 10 June 2024). [b]Tooth caries unrelated to treatment.

1.1 hours median time to onset of symptom relief[a,b]



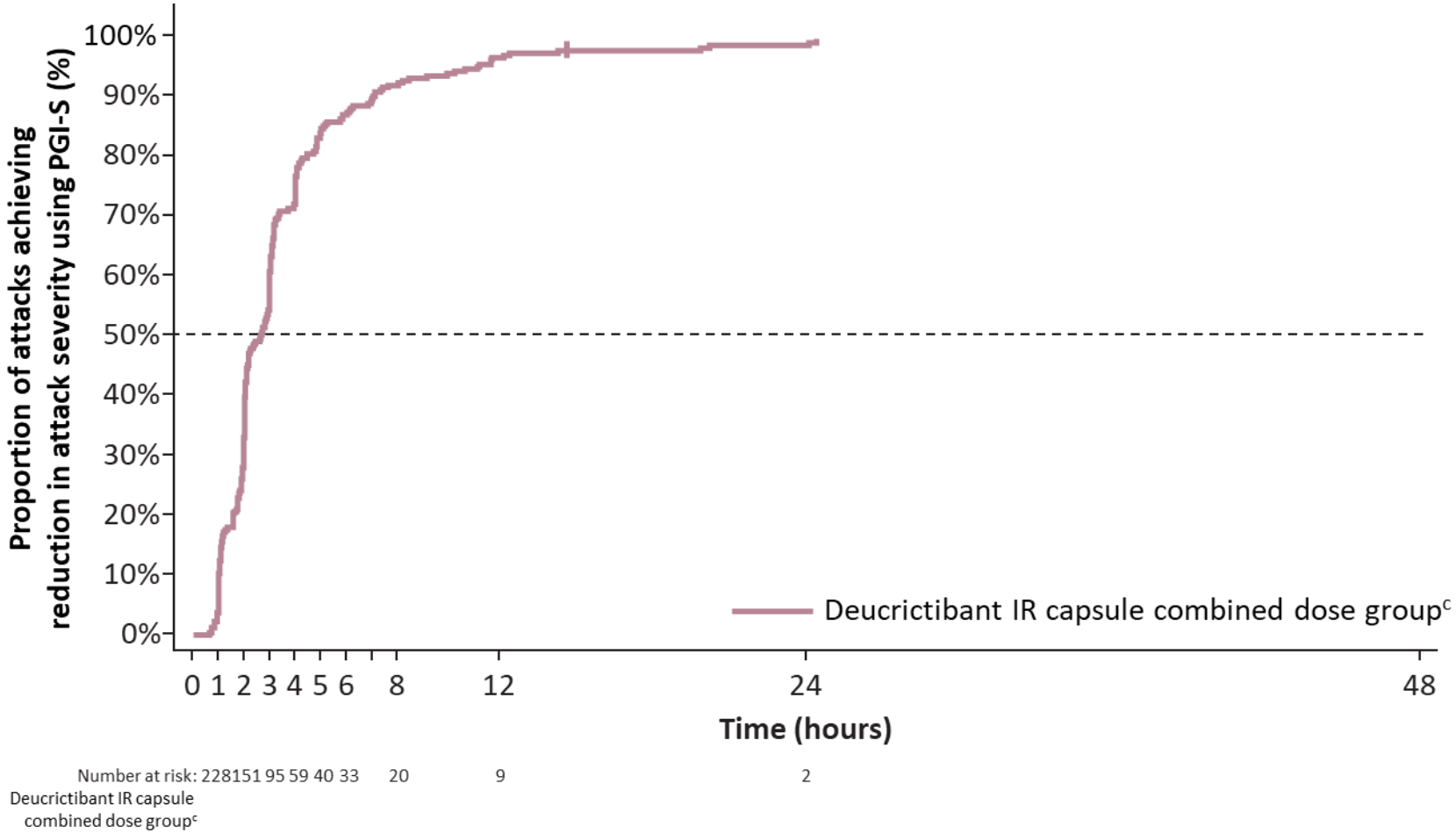
1.1 hours (95% CI, 1.0, 1.2)
median time to onset of symptom relief using PGI-C[a,b]



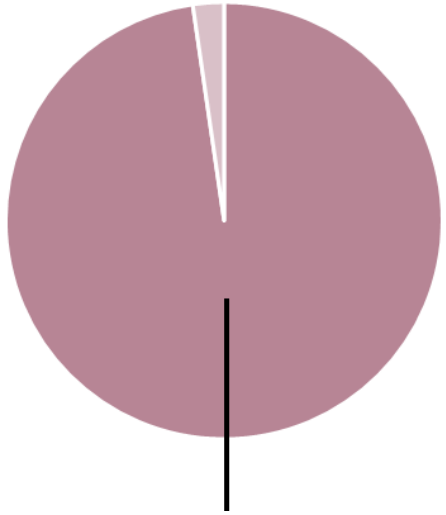
98.5%
(261/265) of attacks achieved onset of symptom relief by 12 hours[a]

IR, immediate-release; PGI-C, Patient Global Impression of Change. [a]PGI-C rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment. [b]Within-participant correlation was not accounted for in all Kaplan-Meier estimates. [c]Includes 10 mg, 20 mg, and 30 mg dose groups.

2.6 hours median time to reduction in attack severity[a,b]



2.6 hours (95% CI, 2.0, 2.9)
median time to reduction in attack severity using PGI-S[a,b]



97.7%
(255/261[d]) of attacks achieved reduction in attack severity by 12 hours

IR, immediate-release; PGI-S, Patient Global Impression of Severity. [a]≥1 point reduction in PGI-S from pre-treatment for 2 consecutive timepoints by 12 hours post-treatment. [b]Within-participant correlation was not accounted for in all Kaplan-Meier estimates. [c]Includes 10 mg, 20 mg, and 30 mg dose groups. [d]261 attacks have non-missing pre-treatment PGI-S.

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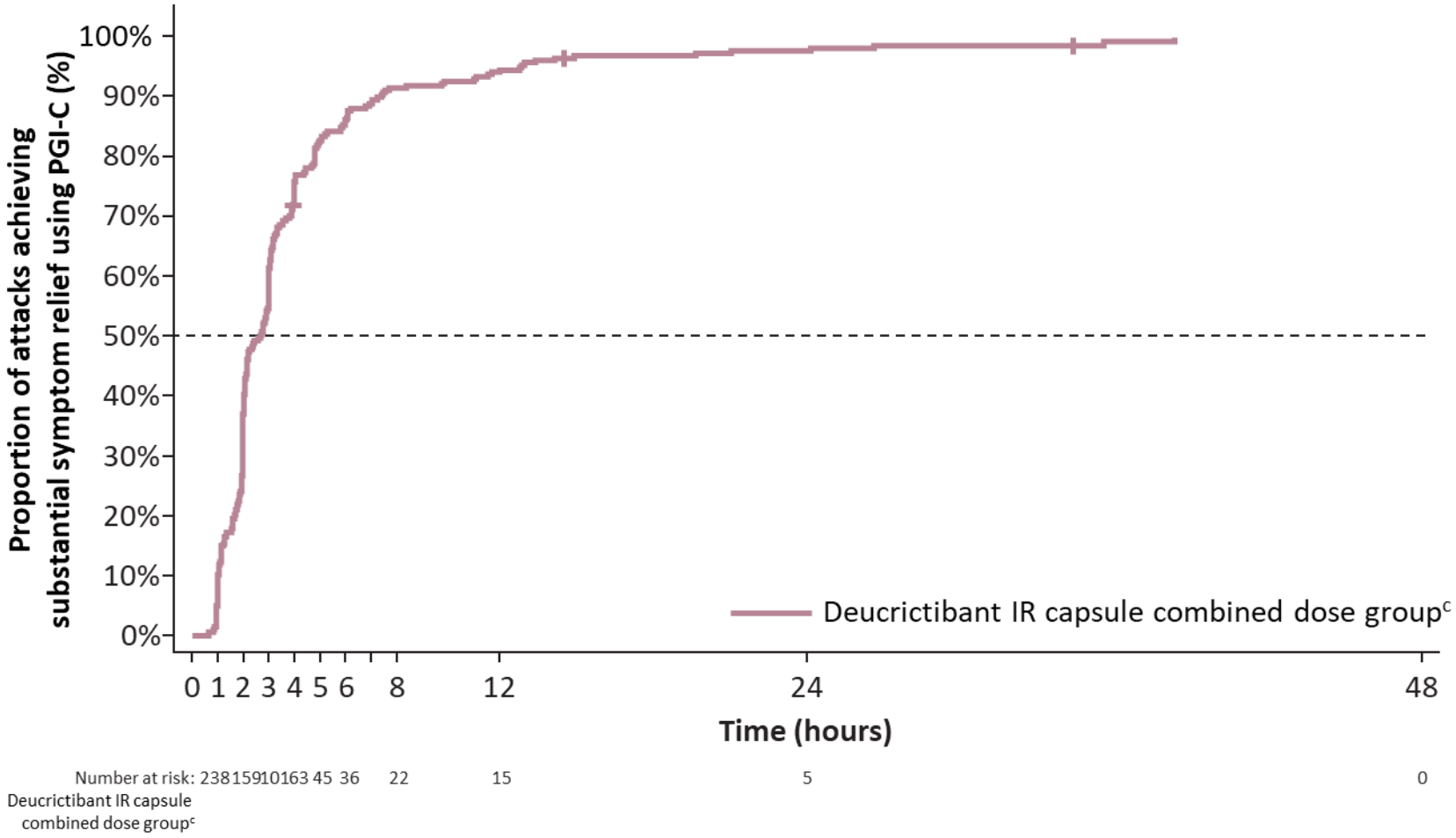
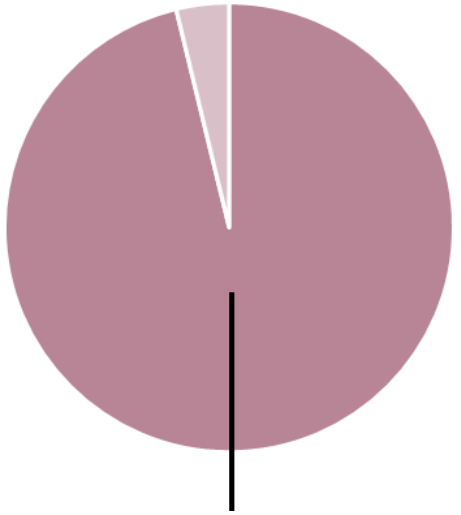
2.7 hours median time to substantial symptom relief[a,b]



2.7 hours (95% CI, 2.1, 2.9)
median time to substantial symptom relief using PGI-C[a,b]



96.2%
(255/265) of attacks achieved substantial symptom relief by 12 hours[a]

IR, immediate-release; PGI-C, Patient Global Impression of Change. [a]PGI-C rating of at least "better" for 2 consecutive timepoints by 12 hours post-treatment. [b]Within-participant correlation was not accounted for in all Kaplan-Meier estimates. [c]Includes 10 mg, 20 mg, and 30 mg dose groups.

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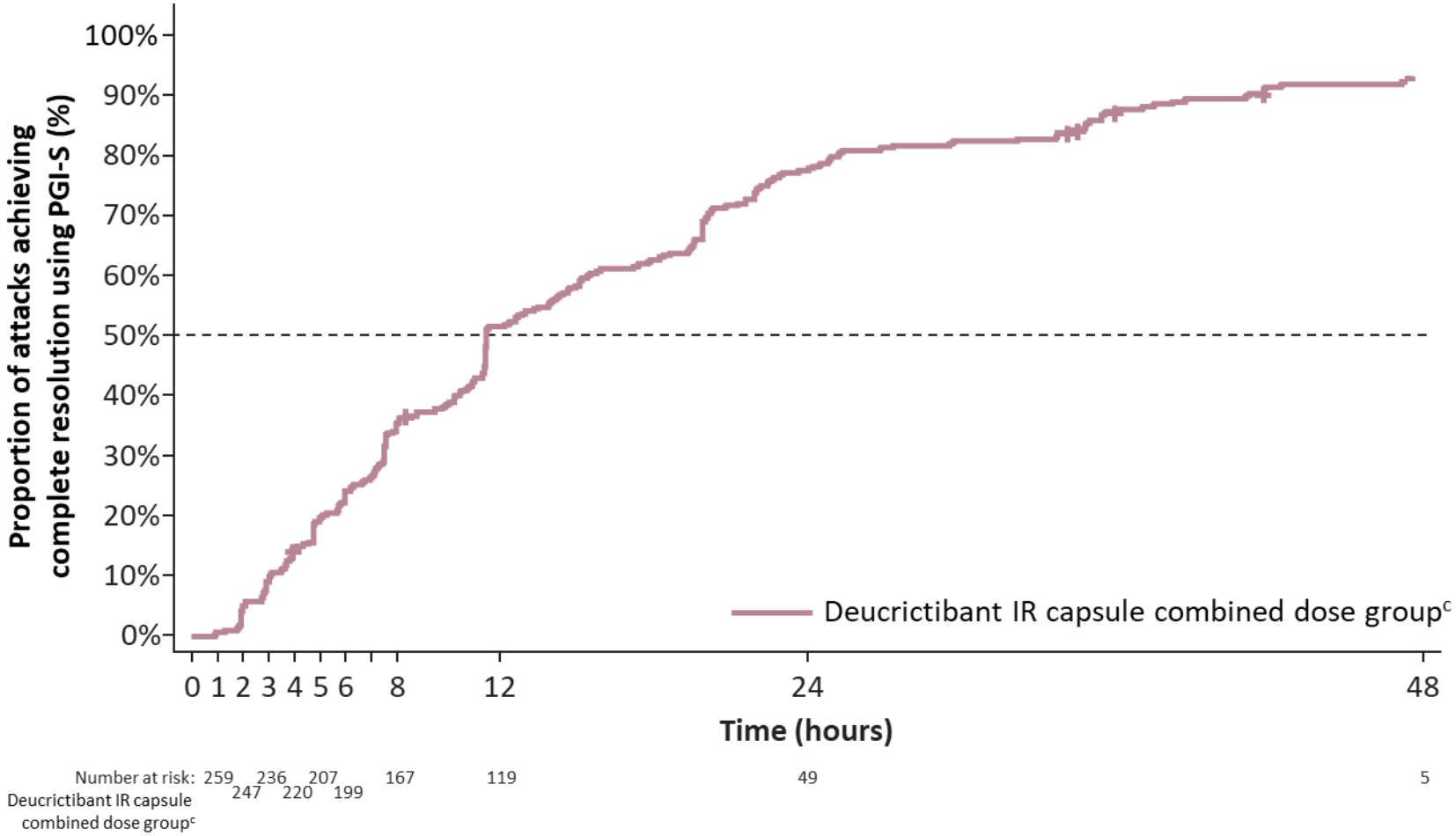
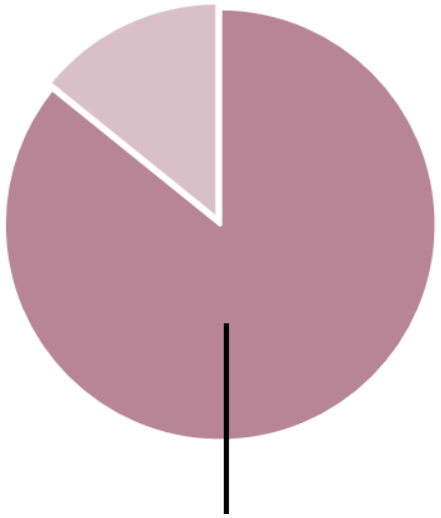
11.5 hours median time to complete attack resolution[a,b]



11.5 hours (95% CI, 11.0, 13.0)
median time to complete attack resolution using PGI-S[a,b]



85.8%
(224/261[d]) of attacks achieved complete resolution[a] by 12 hours

IR, immediate-release; PGI-S, Patient Global Impression of Severity. [a]PGI-S rating of "none" at 24 hours post-treatment. [b]Within-participant correlation was not accounted for in all Kaplan-Meier estimates. [c]Includes 10 mg, 20 mg, and 30 mg dose groups. [d]261 attacks have non-missing pre-treatment PGI-S.

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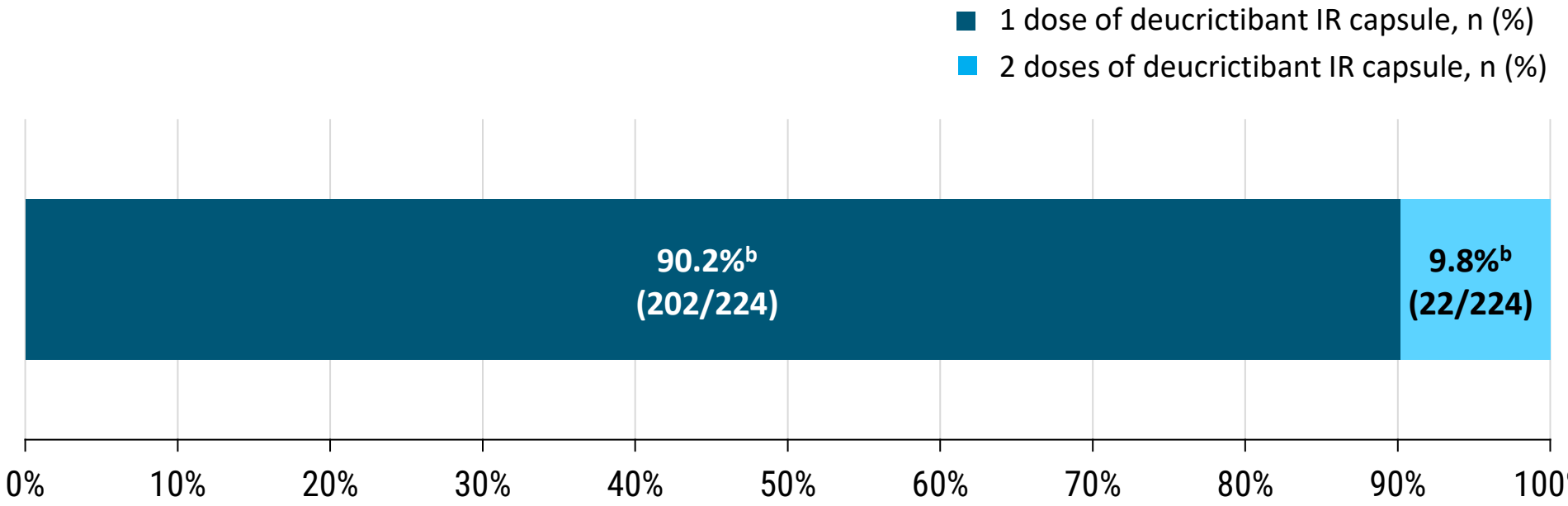
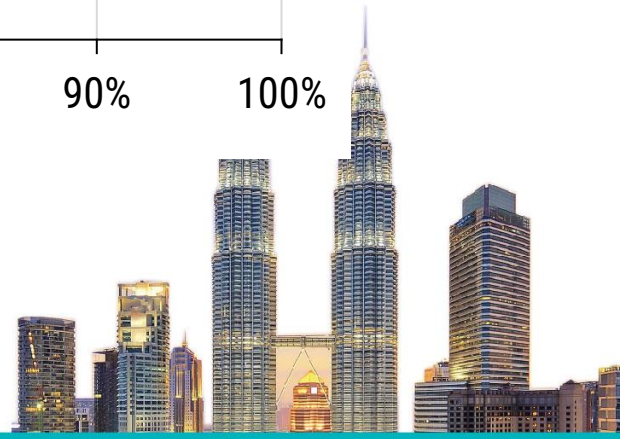
90.2% of attacks achieved complete resolution[a] by 24 hours with a single dose of deucrictibant

Attacks treated with 1 or 2 doses of deucrictibant IR capsule prior to achieving complete attack resolution[a]





IR, immediate-release; PGI-S, Patient Global Impression of Severity. [a]PGI-S rating of "none" at 24 hours post-treatment. [b]Proportion of 224 attacks achieving complete attack resolution using PGI-S by 24 hours.

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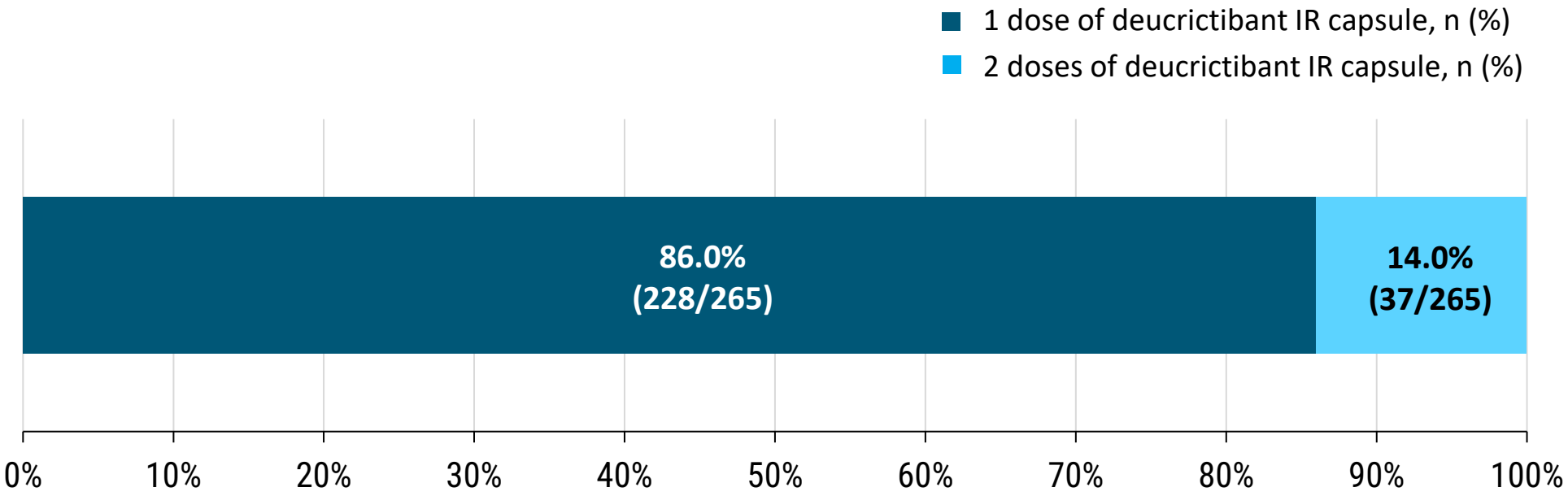
Overall, 86.0% of attacks were treated with a single dose of deucrictibant

Attacks treated with 1 or 2 doses of deucrictibant



IR, immediate-release.

Conclusions

- In the current analysis of the ongoing RAPIDe-2 Phase 2/3 extension study, deucrictibant IR capsule was well tolerated for all studied doses with no safety signals observed.
- Efficacy analysis showed:
  - 1.1 hours median time to onset of symptom relief using PGI-C – 98.5% of attacks by 12 hours.
  - 2.6 hours median time to reduction in attack severity using PGI-S – 97.7% of attacks by 12 hours.
  - 2.7 hours median time to substantial symptom relief using PGI-C –96.2% of attacks by 12 hours.
  - 11.5 hours median time to complete attack resolution using PGI-S – 85.8% of attacks by 24 hours.
  - 86.0% of attacks were treated with a single dose of deucrictibant IR capsule.
- Results from the ongoing RAPIDe-2 extension are consistent with the Phase 2 RAPIDe-1 study and provide evidence on the long-term safety and efficacy of deucrictibant IR capsule for repeat treatment of HAE attacks.

The Authors and the Sponsor would like to thank all the people with HAE as well as all study site staff who participated in the RAPIDe-2 trial.

HAE, hereditary angioedema; IR, immediate-release; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity.