Durability of response to a single dose of oral deucrictibant for on-demand treatment of hereditary angioedema attacks

Markus Magerl[1,2*], John Anderson[3], Emel Aygören-Pürsün[4], Maria Luisa Baeza[5], Laurence Bouillet[6], Hugo Chapdelaine[7], Danny M. Cohn[8], Aurélie Du-Thanh[9], Olivier Fain[10], Henriette Farkas[11], Delphine Gobert[12] Jens Greve[13], Mar Guilarte[14], David Hagin[15], Roman Hakl[16], Joshua S. Jacobs[17], Aharon Kessel[18], Sorena Kiani-Alikhan[19], Pavlína Kralickova[20], H. Henry Li[21], Ramon Lleonart[22], Michael E. Manning[23], Avner Reshef[24], Bruce Ritchie[25], Giuseppe Spadaro[26], Maria Staevska[27], Petra Staubach[28], Marcin Stobiecki[29], Gordon L. Sussman[30], Michael D. Tarzi[31], Anna Valerieva[27], William H. Yang[32], Yumeng Li[33], Li Zhu[33], Ming Yu[33], Peng Lu[33], Umar Katbeh[34], Giorgio Giannattasio[34], Marc A. Riedl[35]

[1]Institute of Allergology, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Germany; [2]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany; [3]AllerVie Health, Clinical Research Center of Alabama, Birmingham, AL, USA; [4]Goethe University Frankfurt, Department of Pediatrics, Frankfurt am Main, Germany; [5]Allergy Department, Hospital General Universitario Gregorio Marañón, Biomedical Research Network on Rare Diseases–U761, Institute for Health Research, Gregorio Marañón, Spain; [6]Grenoble Alpes University, Laboratoire T-RAIG, UMR 5525 TIMC-IMAG (UGA-CNRS), National Reference Center for Angioedema (CREAK), Department of Internal Medicine, Grenoble, France; [7]CHU de Montréal, Université de Montréal, Montréal, QC, Canada; [8]Amsterdam UMC, University of Amsterdam, Department of Vascular Medicine, Amsterdam, The Netherlands; [9]Department of Dermatology, University Montpellier, Montpellier, France; [10]Department of Internal Medicine, Sorbonne University, AP-HP, Saint Antoine Hospital, Paris, France; [11]Hungarian Angioedema Center of Reference and Excellence, Department of Internal Medicine and Haematology, Semmelweis University, Budapest, Hungary; [12]Sorbonne Université, Médecine Interne, AP-HP, Centre de référence des angiœdèmes à kinines, Hôpital Saint-Antoine, Paris, France; [13]Department of Otorhinolaryngology, Head and Neck Surgery, Ulm University Medical Center, Ulm, Germany; [14]Department of Allergy, Hospital Universitari Vall d'Hebron, Vall d'Hebron Research Unit (VHIR), Barcelona, Spain; [15]Allergy and Clinical Immunology Unit, Department of Medicine, Tel Aviv, Israel; [16]Department of Clinical Immunology and Allergology, St. Anne´s University Hospital in Brno, Faculty of Medicine, Masaryk University, Brno, Czech Republic; [17]Allergy and Asthma Clinical Research, Walnut Creek, CA, USA; [18]Bnai Zion Medical Center, Technion-Israel Institute of Technology, Haifa, Israel; [19]Department of Immunology, Royal Free London NHS Foundation Trust, London, UK; [20]Institute of Clinical Immunology and Allergy, University Hospital Hradec Kralove, Charles University, Faculty of Medicine in Hradec Kralove, Hradec Kralove, Czech Republic; [21]Institute for Asthma and Allergy, Chevy Chase, MD, USA; [22]Allergology Department, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Spain; [23]Allergy, Asthma and Immunology Associates, Ltd., Scottsdale, AZ, USA; [24]Barzilai University Hospital, Allergy, Immunology and Angioedema Center, Ashkelon, Israel; [25]Division of Hematology, Department of Medicine, University of Alberta, Edmonton, AB, Canada; [26]University of Naples Federico II, Department of Translational Medical Sciences and Center for Basic and Clinical Immunology Research (CISI), Napoli, Italy; [27]Medical University of Sofia, Department of Allergology, Sofia, Bulgaria; [28]Department of Dermatology, University Medicine Mainz, Mainz, Germany; [29]Department of Clinical and Environmental Allergology, Jagiellonian University Medical College, Krakow, Poland; [30]Division of Clinical Immunology and Allergy, Gordon Sussman Clinical Research, University of Toronto, Toronto, ON, Canada; [31]Department of Respiratory Medicine, University Hospitals Sussex NHS Foundation Trust, Brighton, UK; [32]Ottawa Allergy Research Corporation, Department of Medicine, University of Ottowa, Ottawa, ON, Canada; [33]Pharvaris Inc., Lexington, MA, United States of America; [34]Pharvaris GmbH, Zug, Switzerland; [35]Division of Clinical Immunology and Allergy, University of California San Diego, La Jolla, CA, United States of America

Key takeaways

In a post-hoc analysis of two phase 2 studies, the response to a single dose of deucrictibant immediate-release (IR) capsule was durable and the majority of hereditary angioedema (HAE) attacks achieving symptom relief and resolution maintained a durable response without reoccurrence of symptoms.

Efficacy

~85%
of attacks were treated with a single dose of deucrictibant IR capsule in RAPIDe-2

Durable response

95-100%
of attacks that achieved symptom relief and resolution had a durable response without symptom reoccurrence in RAPIDe-1

98-100%
of attacks that achieved symptom relief and resolution had a durable response without symptom reoccurrence in RAPIDe-2

IR, immediate-release.

Background

- **Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.[1]
- **Unmet need:** guidelines recommend HAE attacks are treated as early as possible.[2-4] Parenteral administration often leads to on-demand treatment of HAE attacks being delayed or forgone.[5-9]
- **Treatment response:** a rapid and durable response to on-demand treatment through to complete resolution is paramount to abate the physical, functional, and emotional burdens associated with symptoms and to enable the prompt restart of daily activities.[6,10]
- **Deucrictibant:** a selective, investigational, orally administered, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.[11-18]

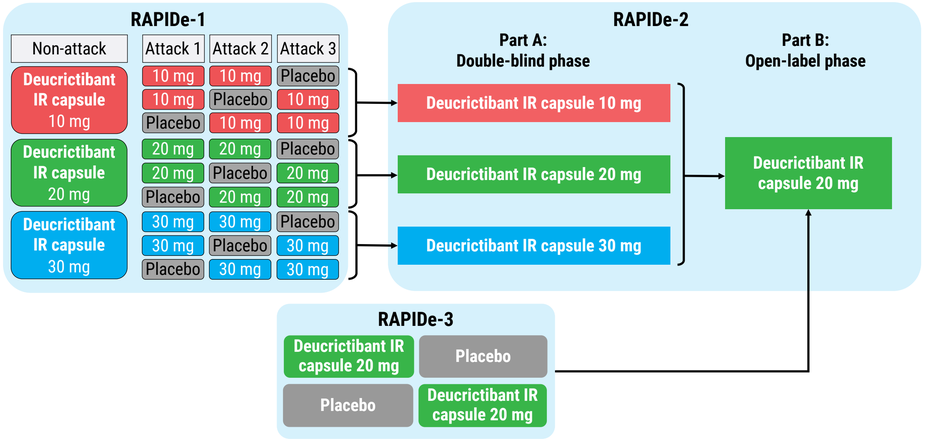
Objective

To assess the durability of effects following a single dose of deucrictibant IR capsule for treatment of HAE attacks in the placebo-controlled RAPIDe-1 trial (NCT04618211)* and in the RAPIDe-2 open-label long-term extension study (NCT05396105)*.

Methods

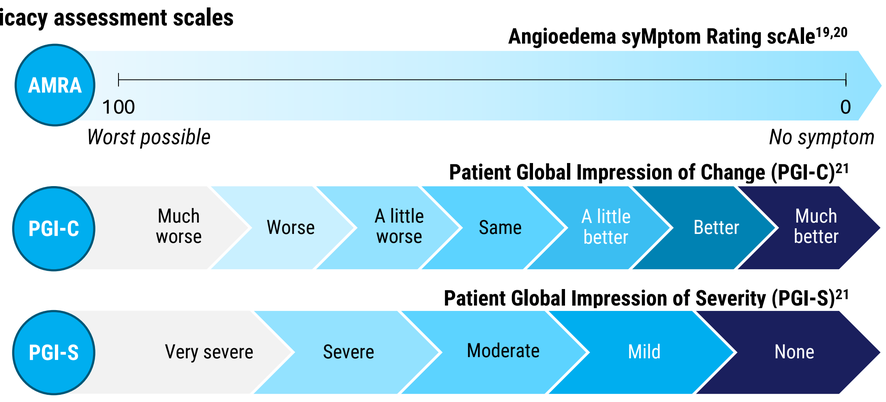
- **RAPIDe-1:** a phase 2, double-blind, placebo-controlled, randomized, crossover, dose-ranging study of deucrictibant IR capsule for on-demand treatment of angioedema attacks.
- **Eligible participants:** adults with HAE type 1 or type 2 (HAE-1/2); ≥3 attacks in the last 4 months or ≥2 attacks in the last 2 months prior to screening; access to and experience with use of on-demand medications.
- **RAPIDe-2:** a two-part, phase 2/3 long-term extension study. Participants in Part A were adults who completed RAPIDe-1.

Figure 1. Study design



IR, immediate-release.

Figure 2. Efficacy assessment scales



Post-hoc analysis of both studies

- **Durability of response:** the achievement and maintenance of serial milestones of symptom relief and resolution without reoccurrence of symptoms following a single-dose of deucrictibant only.
  - **Symptom reoccurrence:** following the achievement of each pre-specified efficacy milestone and defined as any instance of the milestone no longer being met within 24 hours post-treatment.

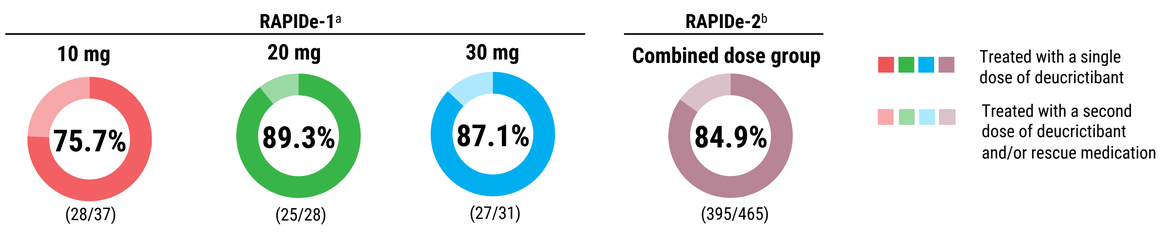
Results

Data

- These final RAPIDe-1 results included 96 HAE attacks treated with deucrictibant among 57 participants.
- These final RAPIDe-2 Part A results included 465 HAE attacks treated with deucrictibant by 19 participants.

Efficacy

Figure 3. Majority of attacks were treated with a single dose of deucrictibant IR capsule within 24 hours



IR, immediate-release. [a]In RAPIDe-1, a second dose was not permitted; in case of inadequate response ≥4 hours after first dose, rescue medication was permitted. In RAPIDe-2, a second dose was permitted ≥4 hours after first dose if symptoms persisted or progressed. If symptoms still persisted or progressed after the second dose, rescue medication was permitted. For upper airway attacks with inadequate response or symptom recurrence ≥4 hours after first dose, only rescue medication was permitted.

Results

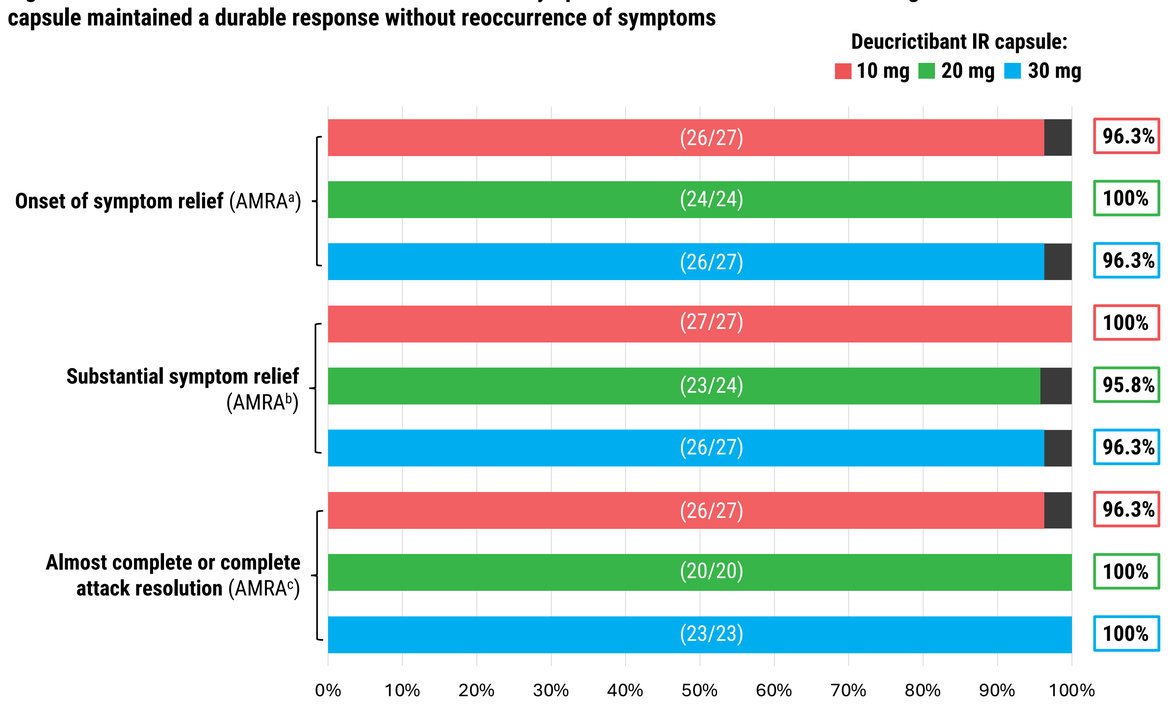
Table 1. Majority of attacks treated with a single dose of deucrictibant IR capsule achieved key efficacy endpoints

Attack milestone	Pre-specified efficacy milestone	RAPIDe-1 10 mg	RAPIDe-1 20 mg	RAPIDe-1 30 mg	RAPIDe-2 Combined
Onset of symptom relief	**AMRA:** ≥30% reduction in AMRA-3 from pre-treatment[a]	**96.4%** (27/28)	**96.0%** (24/25)	**100%** (27/27)	**95.2%** (376/395)
	PGI-C: PGI-C rating of at least "a little better" for 2 consecutive timepoints[b]				**97.5%** (385/395)
Substantial symptom relief	**AMRA:** ≥50% reduction in AMRA-3 from pre-treatment[a]	**96.4%** (27/28)	**96.0%** (24/25)	**100%** (27/27)	**94.2%** (372/395)
	PGI-C: PGI-C rating of at least "better" for 2 consecutive timepoints[b]				**96.5%** (381/395)
Reduction in attack severity	**PGI-S:** ≥1 point reduction in PGI-S score[b]				**95.2%** (376/395)
Almost complete or complete attack resolution	**AMRA:** All 3 AMRA item scores (skin pain, skin swelling, and abdominal pain) ≤10 for 2 consecutive timepoints[c]	**96.4%** (27/28)	**80.0%** (20/25)	**85.2%** (23/27)	**91.4%** (361/395)
	PGI-S: PGI-S rating "none"[c]				**88.6%** (350/395)

AMRA, Angioedema syMptom Rating scAle (skin pain, skin swelling, and abdominal pain); IR, immediate-release; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]Achieved by 24 hours post-treatment in RAPIDe-1 and by 12 hours post-treatment in RAPIDe-2. [b]Achieved by 12 hours post-treatment. [c]Achieved by 24 hours post-treatment.

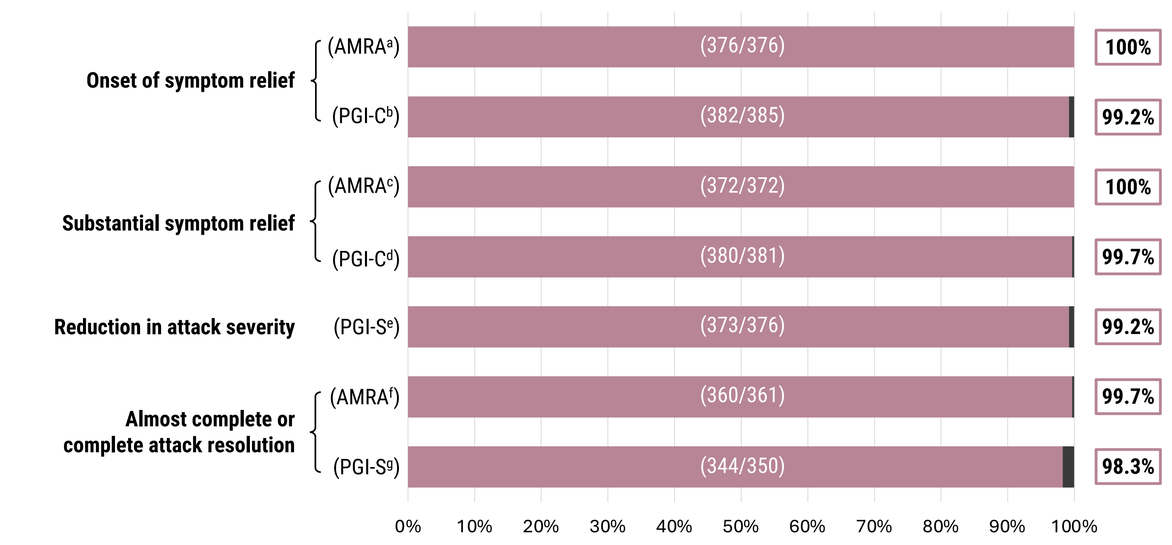
Durability of response

Figure 4. RAPIDe-1: 95-100% of attacks that achieved symptom relief and resolution with a single dose of deucrictibant IR capsule maintained a durable response without reoccurrence of symptoms



AMRA-3, 3-symptom composite Angioedema syMptom Rating scAle; IR, immediate-release. [a]Onset of symptom relief defined as a ≥30% reduction in AMRA-3 composite score vs. pre-treatment by 24 hours post-treatment; reoccurrence of symptoms defined as subsequent occurrence of less than 30% reduction in AMRA-3 within 24 hours. [b]Substantial symptom relief defined as a ≥50% reduction in AMRA-3 composite score from pre-treatment by 24 hours post-treatment; reoccurrence of symptoms defined as subsequent occurrence of less than 50% reduction in AMRA-3 within 24 hours. [c]Almost complete or complete attack resolution defined as time when all 3 AMRA scores have values ≤10 for ≥2 consecutive timepoints by 24 hours post-treatment; reoccurrence of symptoms defined as subsequent occurrence of >10 for any individual AMRA score within 24 hours.

Figure 5. RAPIDe-2: 98-100% of attacks that achieved symptom relief and resolution with a single dose of deucrictibant IR capsule maintained a durable response without reoccurrence of symptoms



AMRA-3, 3-symptom composite Angioedema syMptom Rating scAle; IR, immediate-release; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]Onset of symptom relief defined as a ≥30% reduction in AMRA-3 composite score from pre-treatment by 12 hours; reoccurrence of symptoms defined as subsequent occurrence of less than 30% reduction in AMRA-3 within 24 hours. [b]Onset of symptom relief defined as PGI-C rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment; reoccurrence of symptoms defined as subsequent rating of "same" or lower within 24 hours. [c]Substantial symptom relief defined as a ≥50% reduction in AMRA-3 composite score from pre-treatment by 12 hours post-treatment; reoccurrence of symptoms defined as subsequent occurrence of less than 50% reduction in AMRA-3 within 24 hours. [d]Substantial symptom relief defined as PGI-C rating of "better" for 2 consecutive timepoints by 12 hours post-treatment; reoccurrence of symptoms defined as subsequent rating of "a little better" or lower within 24 hours. [e]Reduction in attack severity defined as PGI-S ≥1 point reduction from pre-treatment by 12 hours post-treatment; reoccurrence of symptoms defined as subsequent occurrence of less than 1 point reduction within 24 hours. [f]Almost complete or complete attack resolution defined as time when all 3 AMRA scores have values ≤10 for ≥2 consecutive timepoints by 24 hours post-treatment; reoccurrence of symptoms defined as subsequent occurrence of >10 for any individual AMRA score within 24 hours. [g]Complete attack resolution defined as PGI-S rating of "none" at 24 hours post-treatment; reoccurrence of symptoms defined as subsequent occurrence of rating above "none" within 24 hours. Data for combined dose group shown (deucrictibant 10 mg, 20 mg, and 30 mg).

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

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