Durability of Response to a Single Dose of Oral Deucrictibant for On-Demand Treatment of Hereditary Angioedema Attacks

Joshua S. Jacobs[1], John Anderson[2], Emel Aygören-Pürsün[3], Maria L. Baeza[4], Laurence Bouillet[5], Hugo Chapdelaine[6], Danny M. Cohn[7], Aurélie Du-Thanh[8], Olivier Fain[9], Henriette Farkas[10], Delphine Gobert[11], Jens Greve[12], Mar Guilarte[13], David Hagin[14], Roman Hakl[15], Aharon Kessel[16], Sorena Kiani-Alikhan[17], Pavlína Králíčková[18], H. Henry Li[19], Ramón Lleonart[20], Markus Magerl[21,22], 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]Allergy and Asthma Clinical Research, Walnut Creek, CA, USA; [2]AllerVie Health, Clinical Research Center of Alabama, Birmingham, AL, USA; [3]University Hospital Frankfurt, Goethe University Frankfurt, Frankfurt, Germany; [4]Hospital General Universitario Gregorio Marañón, Biomedical Research Network on Rare Diseases–U761, Institute for Health Research, Gregorio Marañón, Spain; [5]Grenoble Alpes University, Laboratoire T-RAIG, UMR 5525 TIMC-IMAG (UGA-CNRS), National Reference Center for Angioedema (CREAK), Grenoble, France; [6]CHU de Montréal, Université de Montréal, Montréal, QC, Canada; [7]Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands; [8]University Montpellier, Montpellier, France; [9]Sorbonne University, AP-HP, Saint Antoine Hospital, Paris, France; [10]Hungarian Angioedema Center of Reference and Excellence, Semmelweis University, Budapest, Hungary; [11]Sorbonne Université, Médecine Interne, AP-HP, Centre de référence des angiœdèmes à kinines, Hôpital Saint-Antoine, Paris, France; [12]Ulm University Medical Center, Ulm, Germany; [13]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [14]University of Tel Aviv, Tel Aviv Sourasky Medical Center and Sackler Faculty of Medicine, Tel Aviv, Israel; [15]St. Anne's University Hospital in Brno and Faculty of Medicine, Masaryk University, Brno, Czech Republic; [16]Bnai Zion Medical Center, Technion-Israel Institute of Technology, Haifa, Israel; [17]Royal Free London NHS Foundation Trust, London, UK; [18]University Hospital Hradec Kralove, Charles University, Faculty of Medicine in Hradec Kralove, Hradec Kralove, Czech Republic; [19]Institute for Asthma and Allergy, Chevy Chase, MD, USA; [20]Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Spain; [21]Charité-Universitätsmedizin Berlin, Institute of Allergology, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin; [22]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany; [23]Allergy, Asthma and Immunology Associates, Ltd., Scottsdale, AZ, USA; [24]Barzilai University Hospital, Allergy, Immunology and Angioedema Center, Ashkelon, Israel; [25]University of Alberta, Edmonton, AB, Canada; [26]University of Naples Federico, Napoli, Italy; [27]Medical University of Sofia, Sofia, Bulgaria; [28]University Medicine Mainz, Mainz, Germany; [29]Jagiellonian University Medical College, Krakow, Poland; [30]Gordon Sussman Clinical Research, University of Toronto, Toronto, ON, Canada; [31]University Hospitals Sussex NHS Foundation Trust, Brighton, UK; [32]Ottawa Allergy Research Corporation, University of Ottowa, Ottawa, ON, Canada; [33]Pharvaris Inc., Lexington, MA, USA; [34]Pharvaris GmbH, Zug, Switzerland; [35]University of California San Diego, Division of Allergy and Immunology, La Jolla, CA, USA

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 that achieved symptom relief and resolution maintained a durable response without reoccurrence of symptoms.

Efficacy

~85%
of attacks 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]
- **Current landscape:** 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 burden associated with symptoms and to enable the prompt restart of daily activities.[6,10]
- **Deucrictibant:** a selective, orally bioavailable, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.[11-18]

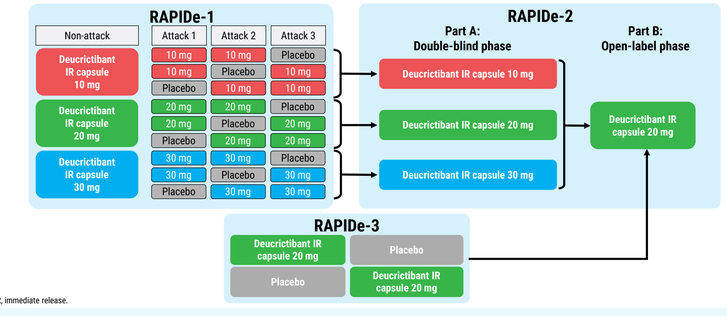
Objective

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

Methods

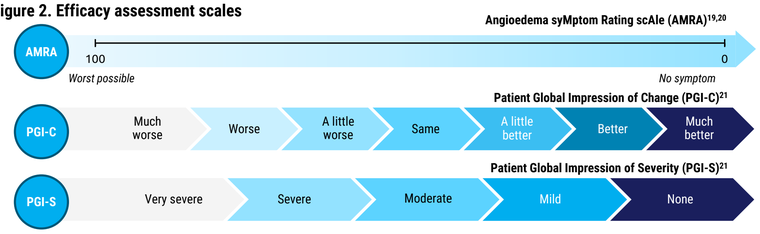
- **RAPIDe-1:** a Phase 2, double-blind, placebo-controlled, randomized, crossover, dose-ranging trial of deucrictibant IR capsule for on-demand treatment of angioedema attacks.
- **Eligible participants:** adults with HAE type 1 or type 2 (HAE-1/2); ≥3 attacks in the last 4 months or ≥2 attacks in the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

Figure 1. RAPIDe-1 and RAPIDe-2 study design



Methods

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, symptom reoccurrence was defined as any instance of the milestone no longer being met within 24 hours post-treatment.

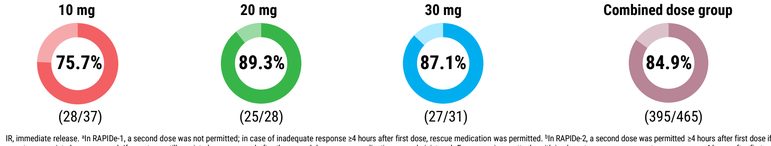
Results

Data

- These final RAPIDe-1 results included 96 HAE attacks treated with deucrictibant by 57 participants.
- These final RAPIDe-2 Part A results included 465 HAE attacks treated with deucrictibant by 19 participants.
- Combined dose group data are shown.

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. [b]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 administered. For upper airway attacks with inadequate response or symptom recurrence ≥4 hours after first dose, only rescue medication was permitted.

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

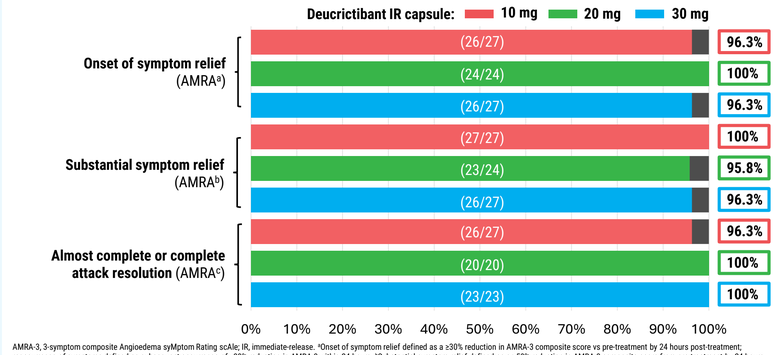
Attack milestone	Pre-specified efficacy milestone	RAPIDe-1			RAPIDe-2
		10 mg	20 mg	30 mg	Combined
Onset of symptom relief	**AMRA:** ≥30% reduction in AMRA-3 from pre-treatment[a]	**96.4%** (27/28)	**96.0%** (24/25)	**100%** (27/27)	**95.2%** (376/395)
	PGI-C: PGI-C rating of at least "a little better" 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.

Results

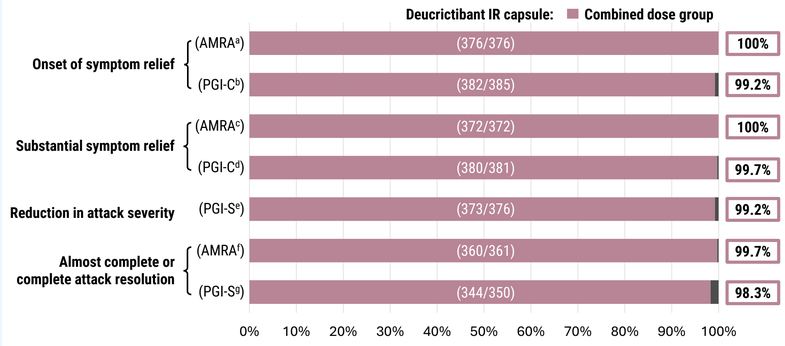
Durability of response

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 <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 <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 <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 <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 <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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