Poster Number 248

Long-Term Safety and Efficacy of Oral Deucrictibant for Prophylaxis in Hereditary Angioedema: Data Snapshot Results of the CHAPTER-1 Open-Label Extension Study

Andrea Zanichelli[1,2], John Anderson[3], Francesco Arcoleo[4], Emel Aygören-Pürsün[5], Mauro Cancian[6], Hugo Chapdelaine[7], Niall Conlon[8], Efrem Eren[9], Mark Gompels[10], Sofia Grigoriadou[11], Maria D. Guarino[12], Padmalal Gurugama[13], Sorena Kiani-Alikhan[14], Tamar Kinaciyan[15], Markus Magerl[16,17], Michael E. Manning[18], Marcin Stobiecki[19], Michael D. Tarzi[20], Anna Valerieva[21], H. James Wedner[22], William H. Yang[23], Rafael Crabbé[24], Susan Mulders[25], Jonathan Levy[26], Ulrich Freudensprung[27], Umar Katbeh[27], Jochen Knolle[28], Anne Lesage[29], Peng Lu[26], Marc A. Riedl[30]

[1]Universita degli Studi di Milano, Dipartimento di Scienze Biomediche per la Salute, Milan, Italy; [2]I.R.C.C.S., Policlinico San Donato, Centro Angioedema, UO Medicina, Milan, Italy; [3]AllerVie Health, Clinical Research Center of Alabama, Birmingham, AL, USA; [4]AOR Villa Sofia-Cervello, UOC di Patologia Clinica e Immunologia, Palermo, Italy; [5]Goethe University Frankfurt, Department of Pediatrics, Frankfurt am Main, Germany; [6]Azienda Ospedale Università di Padova, Padua, Italy; [7]Université de Montréal, CHU de Montréal, Montréal, QC, Canada; [8]St. James's Hospital and Trinity College, Wellcome Trust CRF, Dublin, Ireland; [9]University Hospital Southampton NHS Foundation Trust, Southampton, UK; [10]North Bristol NHS Trust, Bristol, UK; [11]Barts Health NHS Trust, Department of Immunology, London, UK; [12]Ospedale di Civitanova Marche, Civitanova Marche, Italy; [13]Cambridge University Hospitals NHS Foundation Trust, Department of Clinical Immunology, Cambridge, UK; [14]Royal Free London NHS Foundation Trust, London, UK; [15]Medical University of Vienna, Department of Dermatology, Vienna, Austria; [16]Charité – Universitätsmedizin Berlin, Institute of Allergology, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; [17]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany; [18]Allergy, Asthma and Immunology Associates, Ltd., Scottsdale, AZ, USA; [19]Jagiellonian University Medical College, Department of Clinical and Environmental Allergology, Krakow, Poland; [20]University Hospitals Sussex NHS Foundation Trust, Department of Respiratory Medicine, Brighton, UK; [21]Medical University of Sofia, Department of Allergology, Sofia, Bulgaria; [22]Washington University School of Medicine, Division of Allergy and Immunology, Department of Medicine, St Louis, MO, USA; [23]Ottawa Allergy Research Corporation, Department of Medicine, University of Ottawa, Ottawa, ON, Canada; [24]RC Consultancy, Bassins, Switzerland; [25]Mulders Clinical Consulting, Groesbeek, The Netherlands; [26]Pharvaris Inc., Lexington, MA, USA; [27]Pharvaris GmbH, Zug, Switzerland; [28]JCK Consult, Frankfurt, Germany; [29]GrayMatters Consulting, Schilde, Belgium; [30]University of California San Diego, Division of Allergy and Immunology, La Jolla, CA, USA

Key takeaways

The Phase 2 CHAPTER-1 open-label extension (OLE) study provides further evidence on the long-term safety and efficacy of deucrictibant for the prevention of hereditary angioedema (HAE) attacks.

Safety

Deucrictibant was generally well tolerated with one treatment-related TEAE

Efficacy

1.5 YEARS

Attack rate reduced by week 1 (RCT) and remained low ≥1.5 years (OLE)

93.1%

Reduction in attack rate in the OLE relative to baseline

Attack rate during OLE remained consistent across groups with different

Baseline attack rates

OLE, open-label extension; RCT, randomized controlled trial; TEAE, treatment-emergent adverse event.

Background

- **Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks.[1]
- **Unmet need:** additional prophylactic treatments offering injectable-like efficacy that are well tolerated and easy to administer.[2-5]
- **Deucrictibant:** a selective, investigational, orally administered bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.[5-15]

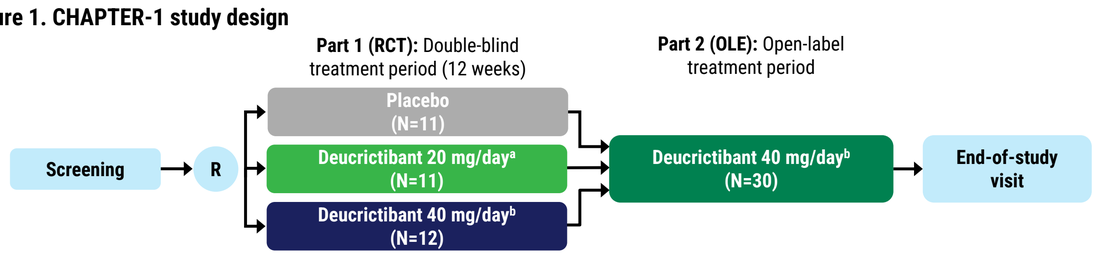
Objective

To evaluate the safety and efficacy of deucrictibant for long-term prophylaxis of HAE attacks in adults in the CHAPTER-1 open-label extension (OLE) study.[12]

Methods

- **CHAPTER-1 (NCT05047185)*:** a two-part, Phase 2 study.[12]
- **Eligible participants:** adults diagnosed with HAE-1/2, not receiving other prophylactic treatments, and with a pre-specified minimum number of attacks.

Figure 1. CHAPTER-1 study design



IR, immediate-release; OLE, open-label extension; R, randomization; RCT, randomized controlled trial. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

- All 30 participants who completed the RCT enrolled into the OLE.
  - In the RCT, participants were randomized to deucrictibant 20 mg/day (N=11), deucrictibant 40 mg/day (N=12), or placebo (N=11).

Results

Participants in the OLE

- At data cutoff (10 June 2024), 30 participants had received deucrictibant 40 mg/day for a mean (SD) treatment duration of 12.8 (5.0) months.
  - Maximum exposure to deucrictibant (months): 20.8 (OLE); 23.7 (entire study).

Safety analysis

- Deucrictibant was generally well tolerated.

Table 1. Adverse events in the OLE

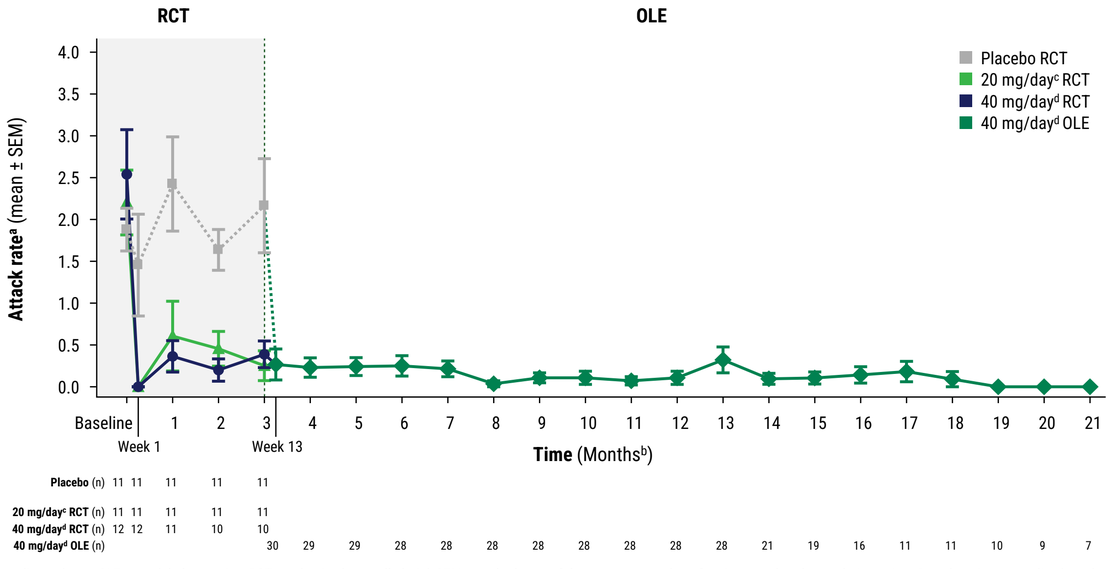
	Placebo to 40 mg/day[a] (N=9)		20 mg/day[b] to 40 mg/day[a] (N=11)		40 mg/day[a] to 40 mg/day[a] (N=10)		Total (N=30)	
	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n
TEAEs	**5 (55.6)**	**25**	**7 (63.6)**	**31**	**6 (60.0)**	**16**	**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 events that started or pre-existing adverse events that ~~have~~ 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 is later. N = number of participants who received ≥1 dose of study treatment in the OLE by the cutoff date of 10 June 2024. [a]Deucrictibant IR capsule, 20 mg twice daily. [b]Deucrictibant IR capsule, 10 mg twice daily.

Efficacy analysis

- RCT: Reduced attack rate by week 1.
- OLE: Low attack rate sustained through ≥1.5 years.

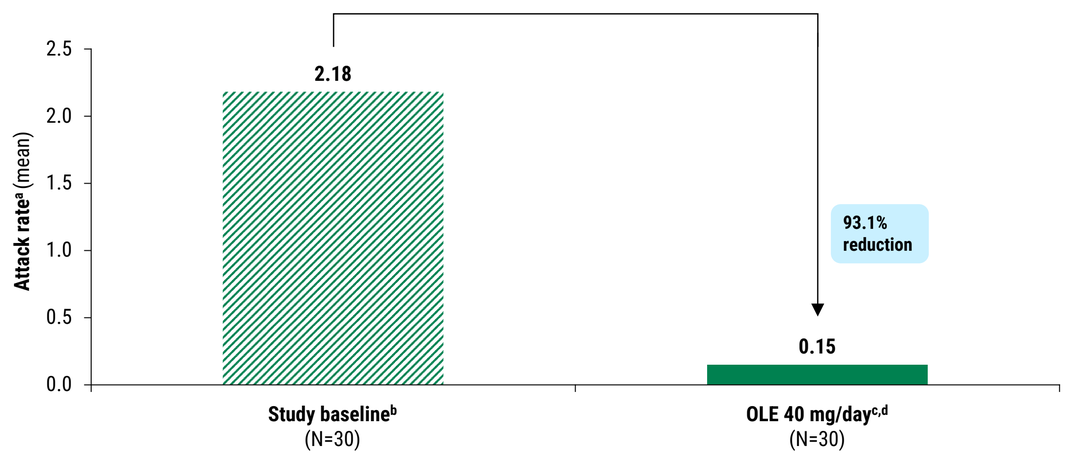
Figure 2. Attack rate remained low through ≥1.5 years in the OLE



IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial; SEM, standard error of the mean. n = number of patients analyzed at each timepoint. [a]Based on time normalized number of attacks per 4 weeks. [b]1 month = 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

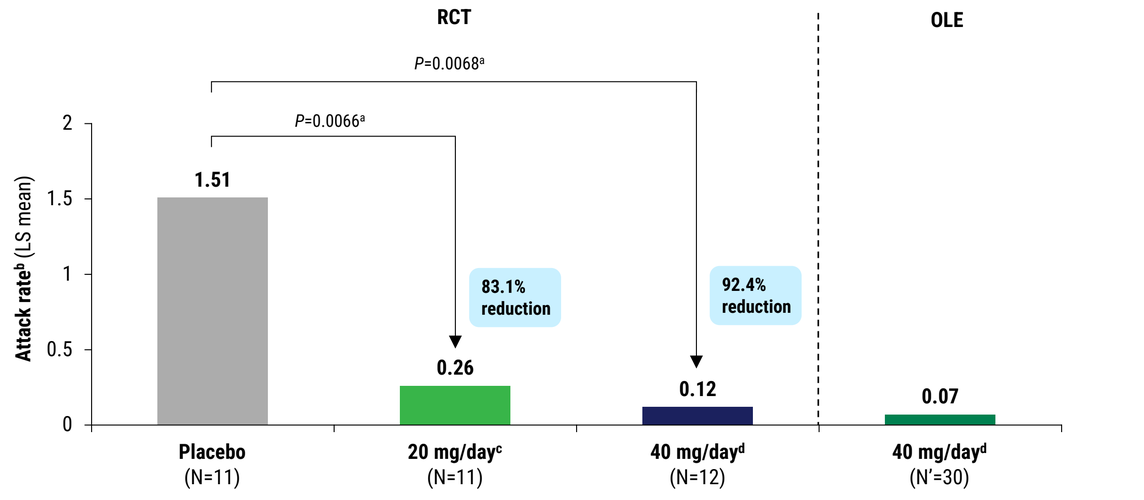
Results

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



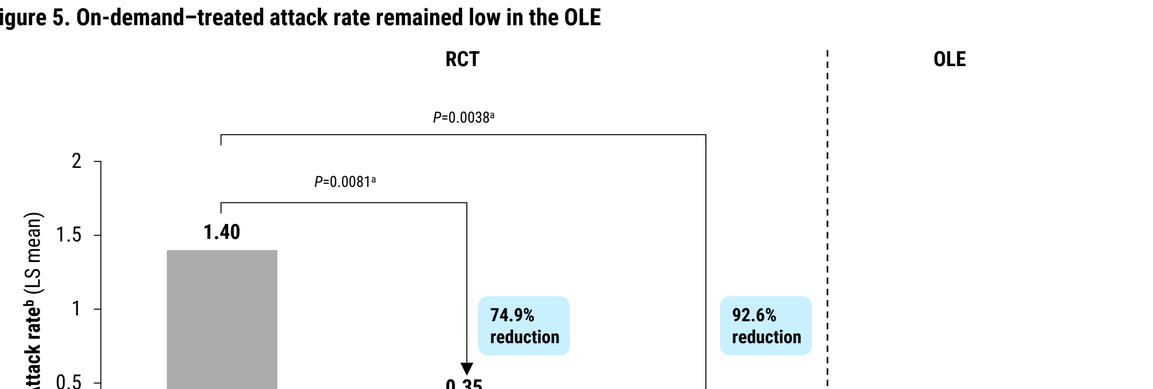
IR, immediate-release; LS, least squares; OLE, open-label extension. N = number of participants in the OLE. [a]Based on time normalized number of attacks per 4 weeks. [b]Baseline attack rate is raw (unadjusted) mean. [c]OLE attack rate is LS mean. No multiplicity adjustment was applied. [d]Deucrictibant IR capsule, 20 mg twice daily.

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



IR, immediate-release; LS, least squares; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants randomized in each treatment group in the RCT. N' = number of participants in the OLE. LS mean estimates of attack rate are based on Poisson regression models adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. [a]The *P*-values in this figure are nominal. [b]Based on time normalized number of attacks per 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

Figure 5. On-demand–treated attack rate remained low in the OLE



IR, immediate-release; LS, least squares; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants randomized in each treatment group in the RCT. N' = number of participants in the OLE. LS mean estimates of attack rate are based on Poisson regression models adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. [a]The *P*-values in this figure are nominal. [b]Based on time normalized number of attacks per 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

Figure 6. Attack rate remained low in the OLE regardless of baseline attack rate

IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. n = number of participants in each treatment group. [a]Attack rate is raw unadjusted mean number of attacks per 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.

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

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COI: A.Z.: BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda; **J.A.:** Astria, BioCryst, CSL Behring, Ionis, KalVista, Pharming, Pharvaris, Takeda; **F.A.:** CSL Behring, Takeda; **E.A-P.:** Astria, BioCryst, BioMarin, CSL Behring, Intellia, Kalvista, Otsuka, Pharming, Pharvaris, Takeda; **M.C.:** BioCryst, CSL Behring, KalVista, Menarini, MSD, Novartis, Otsuka, Pharming, Pharvaris, Sobi, Takeda, UCB; **H.C.:** AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobi, Takeda; **N.C.:** BioCryst, CSL Vifor, GSK, Novartis, Pharvaris, Pharming, Takeda; **E.E.:** BioCryst, Dr Falk Pharma, Novartis, Pharming; **M.G.:** BioCryst, CSL Behring, Novartis, member of the immunology clinical reference group; **S.G.:** Baxter, CSL Behring, Dyax, Grifols, Pharming/Swedish Orphan, Takeda, ViroPharma; **M.D.G.:** BioCryst, CSL Behring, Takeda; **P.G.:** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **S.K-A.:** BioCryst, Biotest, CSL Behring, Ionis, KalVista, Otsuka, Pharvaris, Takeda; **T.K.:** BioCryst, CSL Behring, KalVista, Otsuka, Pharvaris, Sanofi/Regeneron, Takeda; **M.M.:** Astria, BioCryst, CSL Behring, Intellia, KalVista, Novartis, Octapharma, Otsuka, Pharvaris, Takeda; **M.E.M.:** Astria, AstraZeneca, BioCryst, Blueprint, CSL Behring, Celldex, Cogent, GSK, Ionis, Intellia, KalVista, Merck, Novartis, Pharming, Pharvaris, Regeneron, Takeda, Teva; **M.S.:** BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda; **M.D.T.:** none; **A.V.:** AstraZeneca, Berlin-Chemie/Menarini Group, CSL Behring, KalVista, Novartis, Pharming, Pharvaris, Sobi, Takeda; **H.J.W.:** BioCryst, BioMarin, CSL Behring, Genentech, GSK, Takeda; **W.H.Y.:** Aimmune Therapeutics, ALK Abello, AnaptysBio, Areteia, Aslan, AstraZeneca, Astria, BioCryst, Blueprint, Bristol Myers, Celgene, Celldex, CSL Behring, DBV Technologies, Dermira, Eli Lilly, Escient, Galderma, Genentech, GSK, Glenmark, Haleon, Incyte, Intellia, Ionis, Merck, Moderna, Novartis, Novavax, Pharming, Pharvaris, Providence, RAPT Therapeutics, Regeneron, Roche, Sanofi, Stallergenes, Takeda, Upstream Bio, VBI, medical advisor (volunteer) for Hereditary Angioedema Canada, a patient organization; member of Angioedema Centers of Reference and Excellence; **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.:** 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 and consultant to Pharvaris, holds stocks/stock options in Pharvaris, advisor to Kosa Pharma; **P.L.:** employee of Pharvaris, holds stocks in Pharvaris; **M.A.R.:** Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, Takeda.

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