EAACI Congress 2024

Valencia, Spain

31 May - 3 June

EAACI 2024 HYBRID VALENCIA

Revolutionising Patient Care
Through the Power of Data Science

EAACI
EUROPEAN ACADEMY OF ALLERGY AND CLINICAL IMMUNOLOGY

#EAACIcongress

www.eaaci.org

Prophylactic Treatment with Oral Deucrictibant Improves Health-Related Quality of Life of Patients With Hereditary Angioedema

A. Valerieva, J. Anderson, F. Arcoleo, M. Cancian, H. Chapdelaine, N. Conlon, E. Eren, M. Gompels, S. Grigoriadou, M.D. Guarino, P. Gurugama, T. Kinaciyan, M. Magerl, M.E. Manning, M.A. Riedl, M. Stobiecki, M.D. Tarzi, H.J. Wedner, W.H. Yang, A. Zanichelli, R. Crabbé, S. Mulders, J. Levy, L. Zhu, J. Knolle, A. Lesage, P. Lu, E. Aygören-Pürsün

Saturday, 1 June 2024

Conflicts of interest disclosure

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

A.V.: AstraZeneca, Berlin-Chemie/Menarini Group, CSL Behring, Novartis, Pharming, Pharvaris, Shire/Takeda, Sobi, Teva; **J.A.**: BioCryst, BioMarin, CSL Behring, Cycle Pharmaceuticals, KalVista, Pharming, Pharvaris, Takeda; **F.A.**: CSL Behring, Takeda; **M.C.**: BioCryst, CSL Behring, KalVista, Menarini, MSD, Novartis, Pharming, Pharvaris, Shire/Takeda, Sobi, UCB; **H.C.**: AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobi, Takeda; **N.C.**: Novartis, Takeda; **E.E.**: none; **M.G.**: BioCryst, CSL Behring, Novartis; **S.G.**: Baxter, CSL Behring, Dyax, Grifols, Jerini/Shire, Pharming/Swedish Orphan, Viropharma; **S.G.**: Baxter, CSL Behring, Dyax, Grifols, Jerini/Shire, Pharming/Swedish Orphan, Viropharma; **M.D.G.**: CSL Behring; **P.G.**: BioCryst, CSL Behring, KalVista, Pharming, Shire, Takeda; **T.K.**: BioCryst, CSL Behring, KalVista, Novartis, Sanofi-Regeneron, Pharvaris, Shire/Takeda; **M.M.**: BioCryst, CSL Behring, Intellia, KalVista, Novartis, Octapharma, Pharming, Pharvaris, Shire/Takeda; **M.E.M.**: Allakos, Amgen, AstraZeneca, BioCryst, Blueprint, CSL Behring, Cycle, Genentech, GSK, KalVista, Merck, Novartis, Pharming, Pharvaris, Sanofi/Regeneron, Takeda; **M.A.R.**: Astria, BioCryst, BioMarin, CSL Behring, Cycle Pharma, Fresenius-Kabi, Grifols, Ionis, Ipsen, KalVista, Ono Pharma, Pfizer, Pharming, Pharvaris, RegenxBio, Sanofi-Regeneron, Takeda; **M.S.**: BioCryst, CSL Behring, KalVista, Pharming, Shire/Takeda; **M.D.T.**: none**; H.J.W.**: BioCryst, BioMarin, CSL Behring, Genentech, GSK, Takeda; **W.H.Y.**: Aimmune, ALK, Amgen, AnaptysBio, Aslan Therapeutics, AstraZeneca, BioCryst, Celgene, CSL Behring, DBV Technologies, Dermira, Eli Lilly, Galderma, Genentech/Roche, Glenmark, GSK, Haleon, Incyte Biosciences, Ionis, Merck, Novartis, Novavax, Pharming, Pharvaris, Providence, Regeneron, Sanofi Genzyme, Shire/Takeda, VBI; **A.Z.**: BioCryst, CSL Behring, KalVista, Pharming, Takeda; **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**, **L.Z.**: employees of Pharvaris, hold stock/stock options 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 stock/stock options in Pharvaris; **E.A-P.**: Astria, BioCryst, BioMarin, Centogene, CSL Behring, Intellia, KalVista, Pharming, Pharvaris, Shire/Takeda.

CHAPTER-1 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185.

Acknowledgments: Medical writing services were provided by Holly Richendrfer, PhD, and Cara Bertozzi, PhD, of Two Labs Pharma Services.

Unmet need for additional HAE therapies with demonstrated efficacy in improving HRQoL

- Hereditary angioedema (HAE) negatively impacts functional and psychological domains of health-related quality of life (HRQoL)[1-5]
- Patients with HAE desire new oral therapies that may improve HRQoL[6,7]
- Currently, there is an unmet need for oral prophylactic therapies demonstrating statistically significant and clinically meaningful improvement of HRQoL in Phase 3 randomized placebo-controlled trials[8,9]

1. Bork K, et al. *Allergy Asthma Clin Immunol.* 2021;17:40. **2**. Bygum A, et al. *Front Med*. 2017;4:212. **3**. Mendivil J, et al. *Orphanet J Rare Dis*. 2021;16:94. **4**. Chong-Neto HJ. *World Allergy Organ J*. 2023;16:100758. **5**. Lumry WR, et al. *Allergy Asthma Proc*. 2010;31(5):407-14. **6**. Radojicic C, et al. *Allergy Asthma Proc.* 2021;42:S4-S10. **7**. Geba D, et al. *J Drug Assessment*. 2021;10(1):51-6. **8**. Zuraw B, et al. *J Allergy Clin Immunol*. 2021;148(1):164-72.e9. **9.** Berotralstat (Orladeyo) [Summary of Product Characteristics]. https://www.ema.europa.eu/en/documents/product-information/orladeyo-epar-product-information_en.pdf. Accessed May 23, 2024. *This presentation includes data for an investigational product not yet approved by regulatory authorities.*

HRQoL and treatment satisfaction outcomes in Phase 3 HAE long-term prophylaxis randomized placebo-controlled trials

Oral

Berotralstat[1,2]

AE-QoL Total Score: Mean difference from baseline at 24 weeks

Berotralstat 150 mg: 14.6 (NS)

TSQM version 1.4: Mean difference from placebo at 24 weeks

Berotralstat 150mg

- Effectiveness: 18.7 (*P*=0.013)
- Side effects: NS
- Convenience: NS
- Global satisfaction: 18.9 (*P*=0.010)

SC injection

Garadacimab[3]*

AE-QoL Total Score: Mean difference from baseline at 26 weeks

Garadacimab 200 mg: 26.5 (*P* value not reported)

Lanadelumab[4,5]

AE-QoL Total Score: Mean difference from baseline at 26 weeks

Lanadelumab 300mg q2wk: 21.3 (*P*=0.003 vs placebo)

Lanadelumab 300mg q4wk: 17.4 (*P*=0.03 vs placebo)

Plasma derived C1-Inhibitor SC[6,7]

TSQM†: Mean difference from placebo at 14 weeks

C1-Inhibitor SC 60 IU/kg:

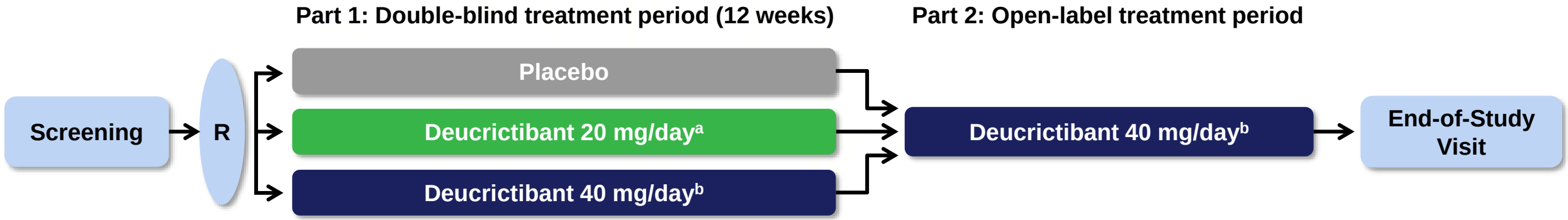
- Effectiveness: 30.0 (*P*<0.05)
- Side effects: –50.0 (NS, small n)
- Convenience: 7.6 (NS)
- Global satisfaction: 31.6 (*P*<0.05)

*NOTE: No direct comparison between trials – data not adjusted for baseline characteristics/other covariables. This summary is based on results that are publicly available as of 23 May 2024. *Garadacimab is an investigational product not yest approved by regulatory authorities.*

AE-QoL, Angioedema QoL Questionnaire; NS, not significant; SC, subcutaneous; TSQM, Treatment Satisfaction Questionnaire for Medication. †Version not reported.

1. Zuraw B, et al. *J Allergy Clin Immunol*. 2021;148:164-72.e9. **2.** Berotralstat (Orladeyo) [Summary of Product Characteristics]. https://www.ema.europa.eu/en/documents/product-information/orladeyo-epar-product-information_en.pdf. Accessed May 23, 2024. **3.** Craig TJ, et al. *Lancet*. 2023;401:1079-1090. **4.** Banerji A, et al. *JAMA*. 2018;320:2108-2121. **5.** Takhzyro (lanadelumab) [Summary of Product Characteristics]. https://www.ema.europa.eu/en/documents/product-information/takhzyro-epar-product-information_en.pdf. Accessed May 23, 2024. **6.** Lumry WR, et al. *J Allergy Clin Immunol Pract*. 2018;6:1733-41.e3. **7.** Berinert 2000-3000 (pdC1-INH SC) [Summary of Product Characteristics]. https://labeling.cslbehring.com/SMPC/EU/Berinert/EN/Berinert-2000-3000-SPC.pdf. Accessed May 23, 2024. *This presentation includes data for an investigational product not yet approved by regulatory authorities.*

CHAPTER-1: Two-part, Phase 2 study of deucrictibant for long-term prophylaxis of HAE attacks



Primary and secondary efficacy and safety outcomes:

- Time-normalized number of investigator-confirmed HAE attacks
- Time-normalized number of moderate and severe HAE attacks and HAE attacks treated with on-demand medication
- Treatment-emergent adverse events

HRQoL and treatment satisfaction were assessed using pre-defined endpoints:

- Patient Global Assessment of Change (PGA-Change)
- Angioedema QoL Questionnaire (AE-QoL)[1,2]
- Treatment Satisfaction Questionnaire for Medication (TSQM) Version II[3]

HRQoL, health-related quality of life; IR, immediate-release; R, randomization. CHAPTER-1 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185. https://www.clinicaltrials.gov/study/NCT05047185. Accessed March 26, 2024. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

1. Weller K, et al. *Allergy*. 2012;67:1289-98. **2**. Weller K, et al. *Allergy*. 2016;71:1203-9. **3**. Atkinson MJ, et al. *Value Health*. 2005;8(s1):S9-24. *This presentation includes data for an investigational product not yet approved by regulatory authorities.*

Measuring HRQoL in CHAPTER-1

- **Patient Global Assessment of Change** (PGA-Change)[1]: Overall change from pre-treatment in how the patient's HRQoL has been impacted by their HAE since starting study treatment with a five-point Likert response scale

- **Angioedema QoL Questionnaire** (AE-QoL)[2,3,4]: A tool validated for HAE and comprising a 17-item questionnaire across four domains, 'functioning', 'fatigue/mood', 'fear/shame', and 'nutrition,' on a five-point response scale

HAE, hereditary angioedema; HRQoL, health-related quality of life.

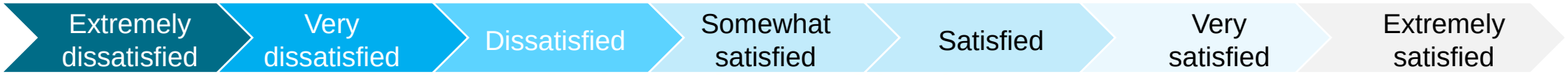
1. Guy W (ed). ECDEU Assessment Manual for Psychopharmacology. Rockville, MD: US Department of Heath, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, 1976. **2.** Weller K, et al. *Allergy*. 2012;67:1289-98. **3**. Weller K, et al. *Allergy*. 2016;71:1203-9. **4.** Vanya M, et al. J Patient Rep Outcomes. 2023; 7:33.

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

Measuring treatment satisfaction in CHAPTER-1

- **Treatment Satisfaction Questionnaire for Medication (TSQM) Version II**[1]: An 11-item questionnaire to gauge patients' satisfaction with 'effectiveness', 'side effects', 'convenience', and 'global satisfaction' of a medication

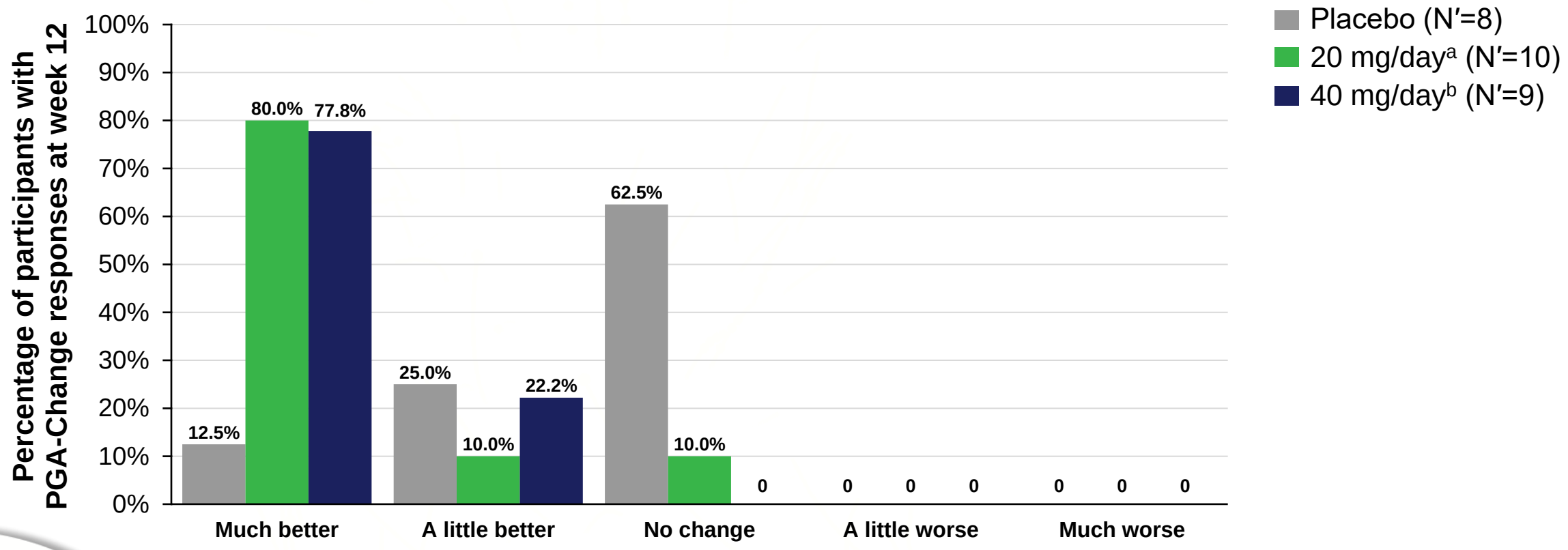
TSQM Version II questions
1. How satisfied or dissatisfied are you with the ability of the medication to prevent or treat your condition?
2. How satisfied or dissatisfied are you with the way the medication relieves your symptoms?
3. As a result of taking this medication, do you currently experience any side effects at all (Yes/No)?
4. How dissatisfied are you by side effects that interfere with your physical health and ability to function (e.g., strength, energy levels)?
5. How dissatisfied are you by side effects that interfere with your mental function (e.g., ability to think clearly, stay awake)?
6. How dissatisfied are you by side effects that interfere with your mood or emotions (e.g., anxiety/fear, sadness, irritation/anger)?
7. How satisfied or dissatisfied are you with how easy the medication is to use?
8. How satisfied or dissatisfied are you with how easy it is to plan when you will use the medication each time?
9. How satisfied or dissatisfied are you by how often you are expected to use/take the medication?
10. How satisfied are you that the good things about this medication outweigh the bad things?
11. Taking all things into account, how satisfied or dissatisfied are you with this medication?



1. Atkinson MJ, et al. *Value Health.* 2005;8(s1):S9–24.

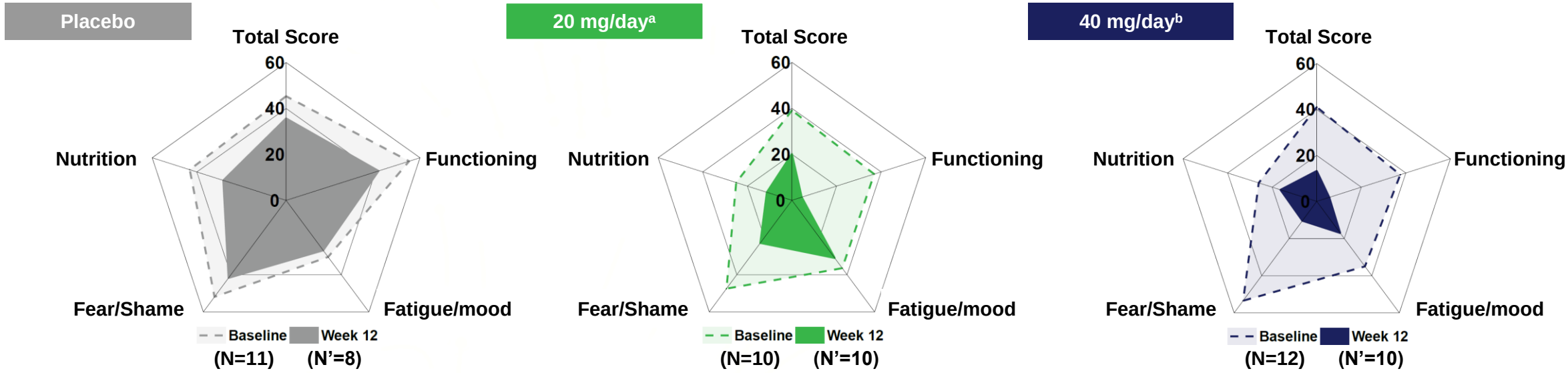
This presentation includes data for an investigational product not yet approved by regulatory authorities

All participants in the deucrictibant 40 mg/day group reported an improvement in PGA-Change



IR, immediate-release; PGA-Change, Patient Global Assessment of Change questionnaire. N′ = number of participants with PGA-Change results at week 12.
[a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. *This presentation includes data for an investigational product not yet approved by regulatory authorities.*

Improved AE-QoL score across all domains

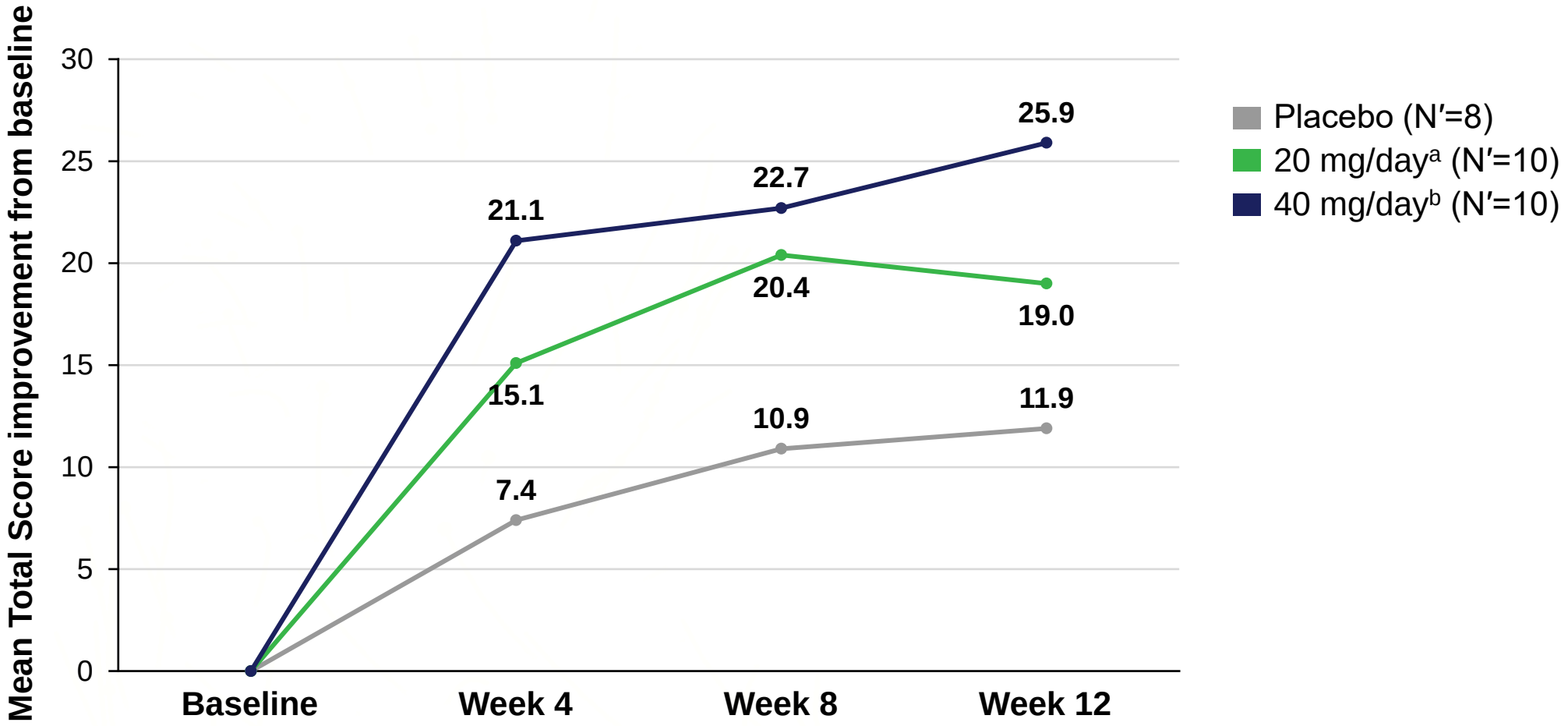


AE-QoL Total Score	Placebo	Deucrictibant 20 mg/day[a]	Deucrictibant 40 mg/day[b]
Baseline	**N=11**	**N=10**	**N=12**
Mean (SD)	45.3 (18.5)	39.1 (22.0)	41.1 (15.5)
Median (Q1, Q3)	42.6 (29.4, 57.4)	37.5 (16.2, 55.9)	40.4 (31.6, 49.3)
Week 12	**N′=8**	**N′=10**	**N′=10**
Mean (SD)	35.7 (19.6)	20.2 (15.6)	13.2 (6.9)
Median (Q1, Q3)	37.5 (19.1, 49.3)	18.4 (7.4, 33.8)	12.5 (10.3, 17.7)

AE-QoL, Angioedema Quality of Life Questionnaire; IR, immediate-release. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. N = number of randomized participants with AE-QoL data at baseline. N′ = number of participants with AE-QoL data at week 12.

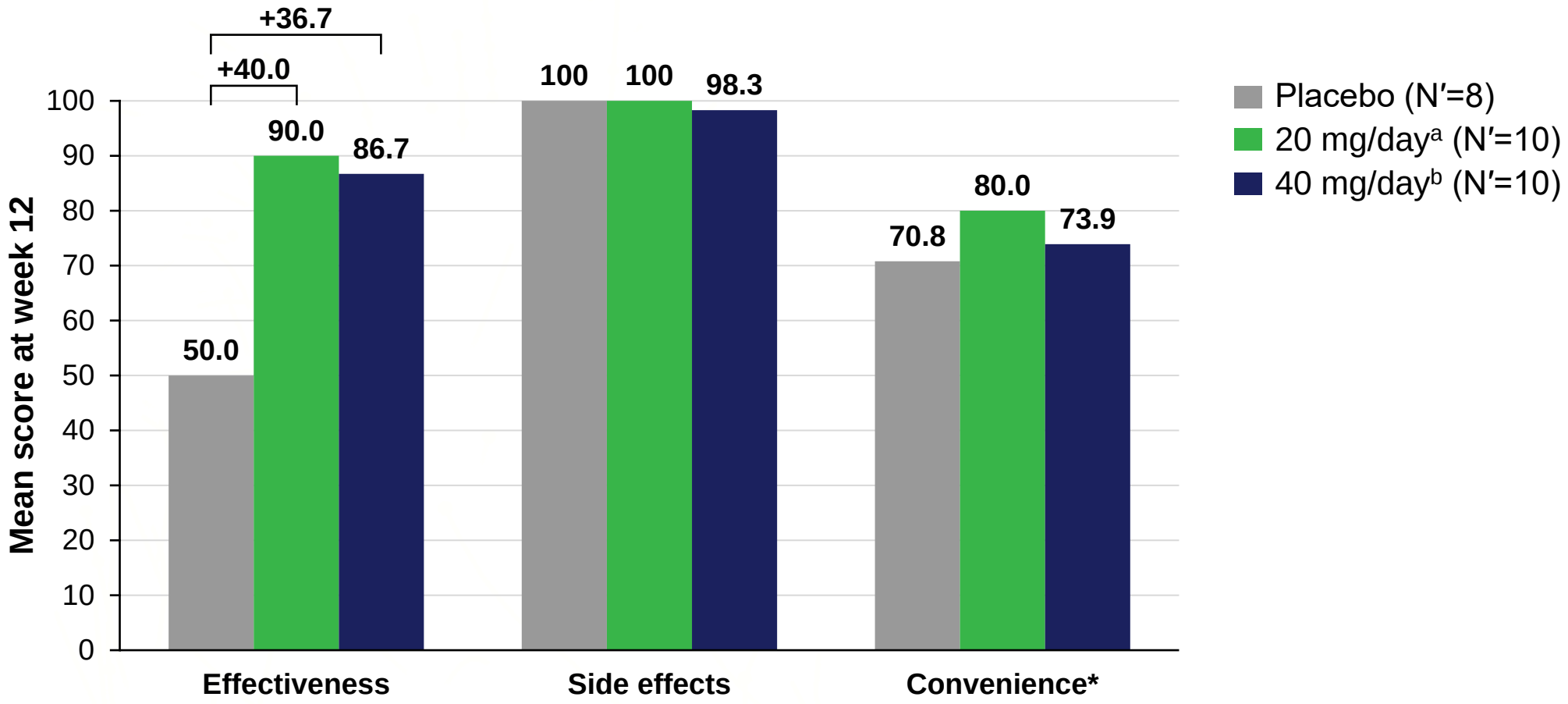
This presentation includes data for an investigational product not yet approved by regulatory authorities.

AE-QoL: Total Score improved from baseline by Week 4



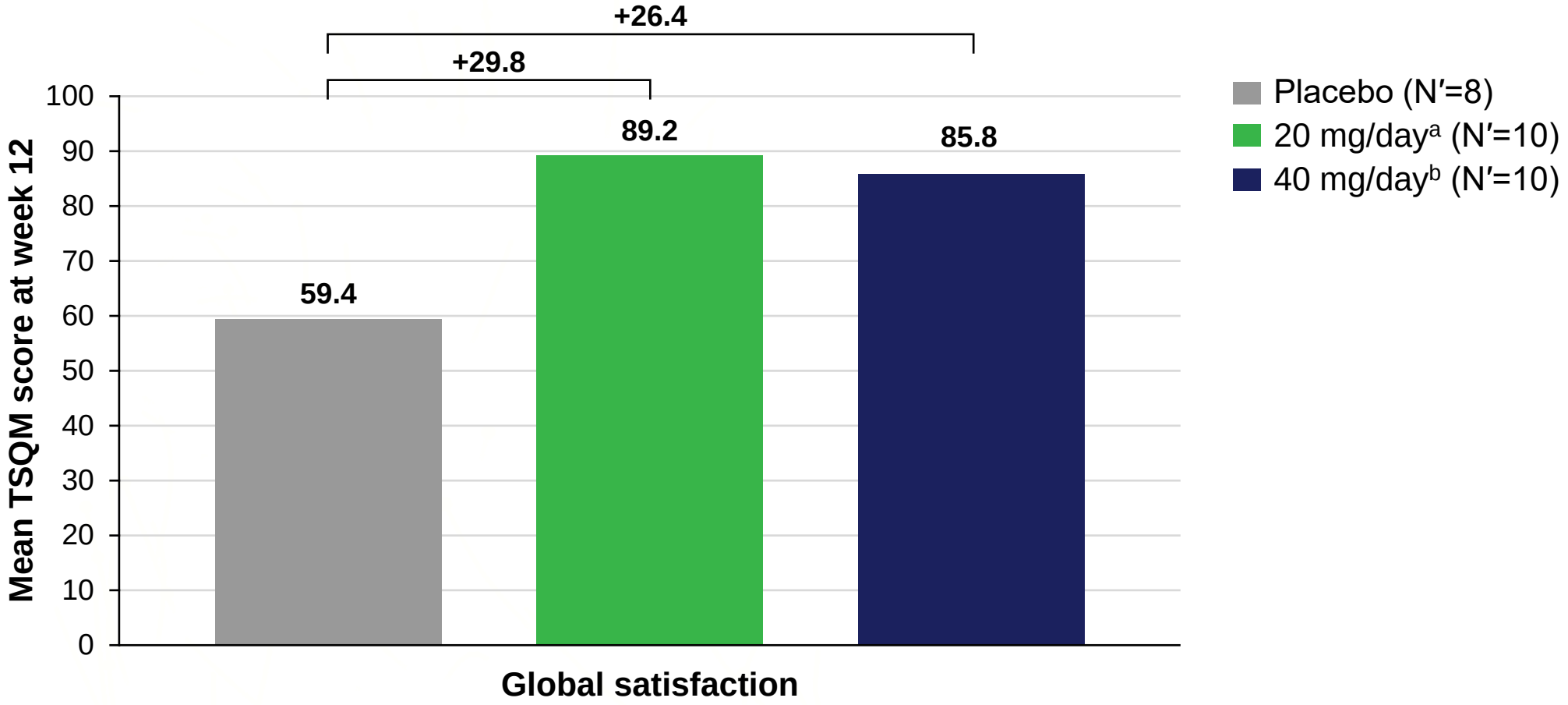
AE-QoL, Angioedema Quality of Life Questionnaire; BL, baseline; IR, immediate-release. N′ = number of participants with AE-QoL data at week 12.
[a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. *This presentation includes data for an investigational product not yet approved by regulatory authorities.*

TSQM: Greater patient satisfaction with effectiveness vs placebo



*Dose frequency was twice daily using IR capsule. Once daily tablet is intended formulation for Phase 3 trial.
IR, immediate-release; TSQM, Treatment Satisfaction Questionnaire for Medication. N′ = number of participants with TSQM results at week 12.
[a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.*This presentation includes data for an investigational product not yet approved by regulatory authorities.*

TSQM: Greater overall patient satisfaction vs placebo



IR, immediate-release; TSQM, Treatment Satisfaction Questionnaire for Medication. N′ = number of participants with TSQM results at week 12.
[a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.*This presentation includes data for an investigational product not yet approved by regulatory authorities.*

Conclusions

- Analyses of CHAPTER-1 Phase 2 trial data provide encouraging results on the effects of prophylactic treatment with oral deucrictibant for 12 weeks on HRQoL in people living with HAE
  - All (100%) participants on deucrictibant 40mg/day showed improvement on PGA-Change
  - Treatment with deucrictibant improved AE-QoL Questionnaire scores, particularly in ‘functioning’ and ‘fear/shame’ domains
  - Participants reported high levels of satisfaction with treatment
- If these data are confirmed in the planned Phase 3 Study, deucrictibant may be the first oral prophylactic option demonstrating statistically significant and clinically meaningful HRQoL improvement vs control in a Phase 3 randomized placebo-controlled trial

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 CHAPTER-1 trial.

AE-QoL, Angioedema Quality of Life Questionnaire; HAE, hereditary angioedema; HRQoL, health-related quality of life; PGA-Change, Patient Global Assessment of Change.

EAACI Congress 2024

Valencia, Spain

31 May - 3 June

EAACI 2024 HYBRID VALENCIA

Revolutionising Patient Care
Through the Power of Data Science

EAACI
EUROPEAN ACADEMY OF ALLERGY AND CLINICAL IMMUNOLOGY

#EAACIcongress

www.eaaci.org