Relationship Between Time to On-demand Treatment and Quality of Life During Hereditary Angioedema Attacks

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CoI Disclosures

- Sandra Christiansen reports advisory boards: KalVista, BioCryst, US HAEA Medical Advisory Board
- Timothy Craig reports research support and consultancy: CSL Behring, Ionis, Takeda, BioCryst, BioMarin, KalVista, Pharvaris, Intellia, Astria; speaker fees: CSL Behring and Takeda; travel support: CSL Behring, Takeda, BioCryst
- Maeve O'Connor reports speaker/consultant/advisor or research: KalVista, Pharming, CSL, GSK, Blueprint, TEVA, AZ, Sanofi, Grifols, Abbvie. She is the Chief Medical Officer of the CIIC
- Cristine Radojicic reports honorarium from the following participation: Medical Advisory Board- KalVista, BioCryst, CSL Behring, Astria, Safety Monitoring Board- Astria, Speakers Bureau- CSL Behring
- Julie Ulloa and Sherry Danese have received consulting fees from KalVista
- Vibha Desai and Paul Audhya are employees of KalVista Pharmaceuticals
- Paula Busse reports consulting fees: Takeda, KalVista, CVS Specialty, BioCryst, CSL, Behring, ADArx, Astria, Pharvaris. Cristine Radojicic reports honorarium from the following participation: Medical Advisory Board- KalVista, BioCryst, CSL Behring, Astria, Safety Monitoring Board- Astria, Speakers Bureau- CSL Behring

Background

- Hereditary angioedema (HAE) treatment guidelines recommend[1-3]
  - All attacks are eligible for treatment, irrespective of the location or severity
  - All patients should have access to at least 2 standard doses of a Food and Drug Administration (FDA)-approved on-demand medication for treatment of HAE attacks
  - Treating attacks as soon as clearly recognized to reduce morbidity and prevent mortality
  - Self-administering on-demand treatment when feasible, with the exception of ecallantide
    - Approved on-demand treatment options all require injection, either IV or SQ, which pose potential challenges including ease of administration, portability/access, and injection site reactions
- The purpose of our investigation was to explore the relationship between the time to administration of on-demand treatment and the impact on quality of life (QoL) experienced by participants during an attack

1. Betschel S, Badiou J, Binkley K, et al. The International/Canadian Hereditary Angioedema Guideline. *Allergy, Asthma & Clinical Immunology.* 2019/11/25 2019;15(1):72. doi:10.1186/s13223-019-0376-8. **2.** Maurer M, Magerl M, Betschel S, et al. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2021 revision and update. *Allergy.* 2022;77(7):1961-1990. doi:10.1111/all.15214. **3.** Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. *J Allergy Clin Immunol Pract.* 2021;9(1):132-150.e3. doi:10.1016/j.jaip.2020.08.046.

Methods

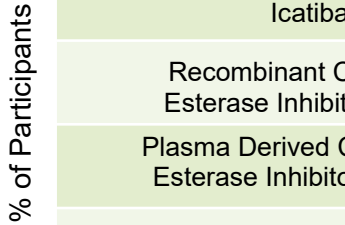
- Participants ≥12 years diagnosed with Type 1 or 2 HAE were recruited by the US Hereditary Angioedema Association between April and June 2023
  - Enrollment was stratified to include approximately 50% of participants taking on-demand only and 50% receiving long-term prophylaxis (LTP) plus on-demand therapy
- Participants completed a 20-minute, self-reported, online survey interrogating their last treated HAE attack
- Participants were required to have treated at least 1 HAE attack within the 3 months prior to the study using an approved on-demand therapy

US Participant Demographics

	Total (n=94)	Adults (85%, n=80)	Adolescents (15%,n=14)
Current mean age, (SD)	39.4 (17.4)	43.8 (15.0)	14.4 (1.5)
Mean age at diagnosis, years (SD)	18 (12.6)	20 (12.5)	6 (4.1)
HAE Type			
Type 1	81%	81%	79%
Type 2	19%	19%	21%
Gender			
Female	72%	79%	36%
Race / Ethnicity			
White	87%	89%	79%
Hispanic or Latino	9%	8%	14%
Black / African American	3%	3%	7%
American Indian/Alaskan Native	2%	–	14%
Asian	3%	4%	–
Other	1%	1%	–

- At the time of their most recent treated attack, 46% were using on-demand treatment only, while 54% of participants were on prophylaxis and on-demand therapy

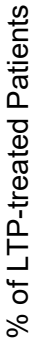
On-Demand Therapy Used for Last Treated Attack



On-Demand Therapy	On-Demand Only Treatment (n=43)	On-Demand Treatment + LTP (n=51)	Adults (n=80)	Adolescents (n=14)
Icatibant	63%	66%	77%	NA*
Recombinant C1 Esterase Inhibitor	21%	16%	13%	50%
Plasma Derived C1 Esterase Inhibitor	14%	16%	9%	50%
Ecallantide	2%	2%	3%	0%

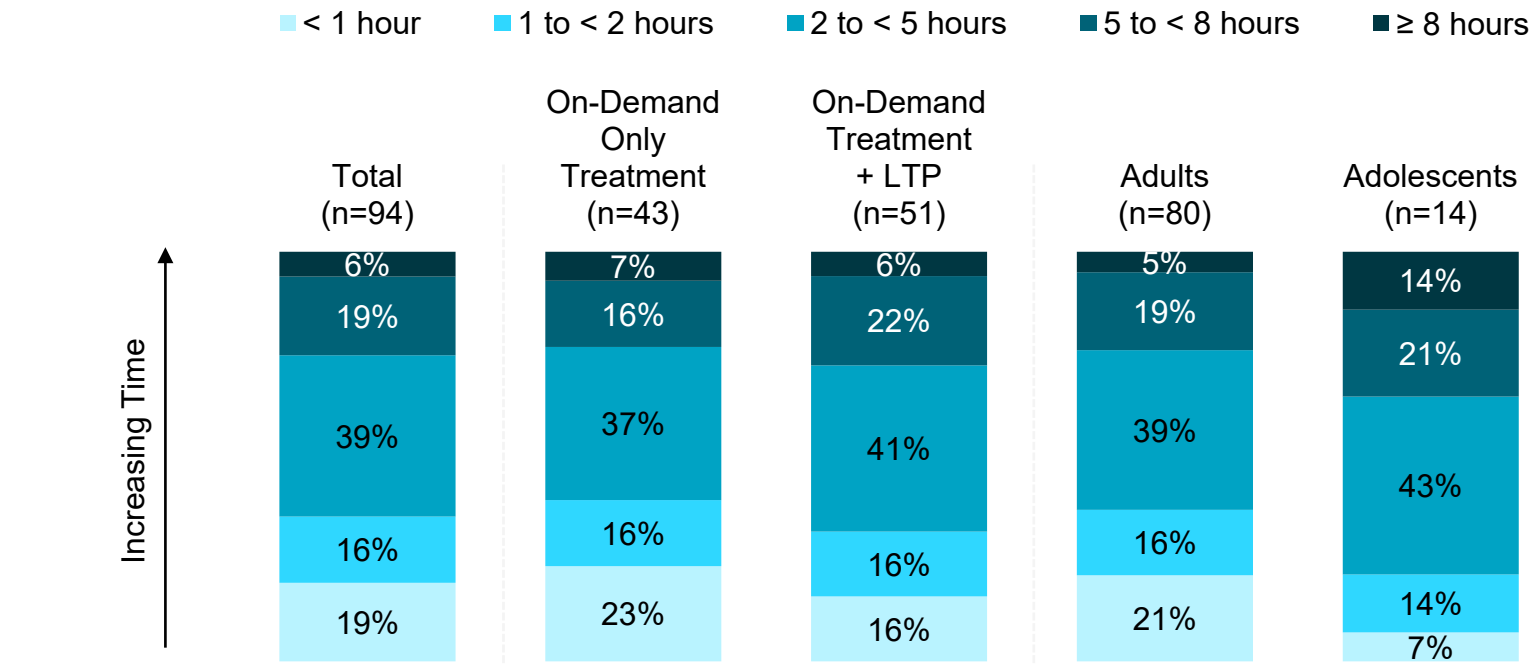
*Not approved for patients under 18 years old.

Long-Term Prophylaxis at Time of Last Treated Attack

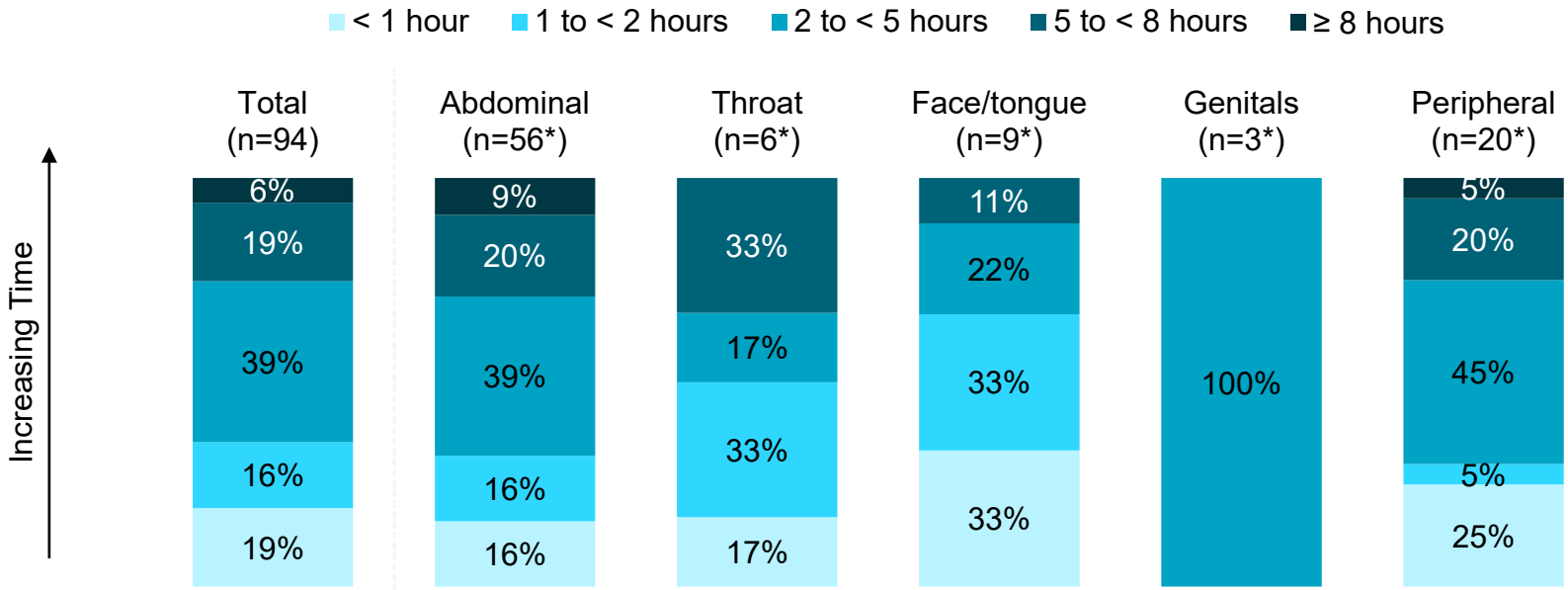


Long-term prophylaxis (n=51)	Adults (n=43)	Adolescents (n=8)
Lanadelumab 57%	63%	25%
Subcutaneous Human C1 Esterase Inhibitor 24%	26%	13%
Berotralstat 14%	9%	38%
Intravenous Human C1 Esterase Inhibitor 6%	2%	25%

Time to Treatment with On-Demand Therapy: Subgroups



Time to Treatment with On-Demand Therapy: Location



	Total (n=94)	Abdominal (n=56*)	Throat (n=6*)	Face/tongue (n=9*)	Genitals (n=3*)	Peripheral (n=20*)
≥ 8 hours	6%	9%	33%	11%	100%	5%
5 to < 8 hours	19%	20%	17%	22%		20%
2 to < 5 hours	39%	39%	33%	33%		45%
1 to < 2 hours	16%	16%	17%	33%		5%
< 1 hour	19%	16%				25%
Mean (SD) hours	3.8 (6.3)	4.7 (7.9)	2.5 (2.4)	1.4 (1.6)	2.3 (0.6)	3.1 (2.8)
Median (IQR Q1, Q3) hours	2 (1,5)	3 (1,5)	2 (1,5)	1 (0,2)	2 (2,3)	3 (1,5)

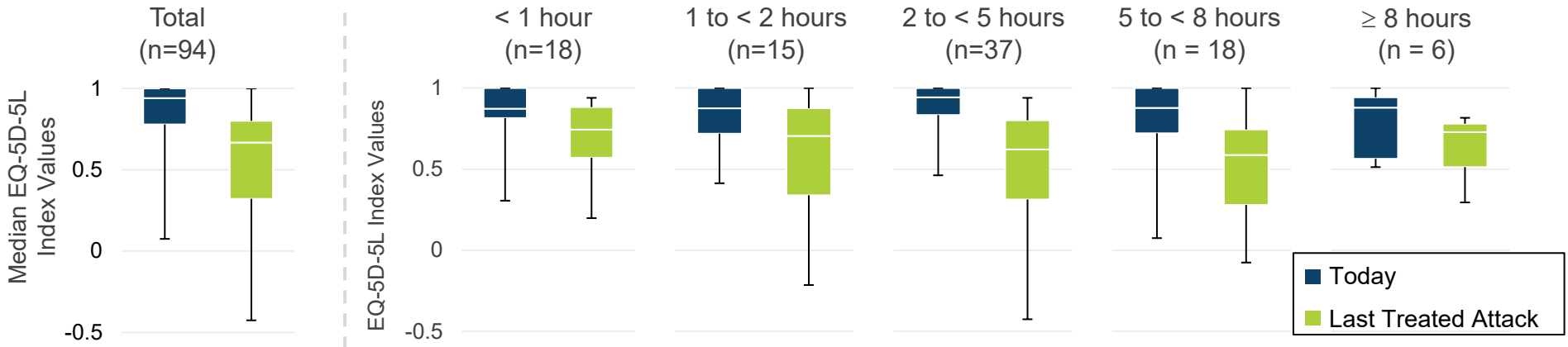
* Adults and adolescents.

- Time to treatment was fastest for attacks affecting the face/tongue, throat, and genitals

Participant Quality of Life Assessments

- EuroQol Five-Dimensions Five-Levels (EQ-5D-5L), a self-report survey, was used to assess quality of life (QoL) "today" (i.e., current QoL) and at the time of the last treated attack
  - EQ-5D-5L Index Score = QoL composite of items across 5 domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression
    - Range from −0.59 (lowest possible health state) to 1 (best possible health state)
  - Visual Analogue Score (VAS) = is a single item assessing self-rated overall health status
    - Range from 0 (“worst imaginable health state”) to 100 (“best imaginable health state”)

EQ-5D-5L Index Scores for Current and Last Treated Attack* by Treatment Delay

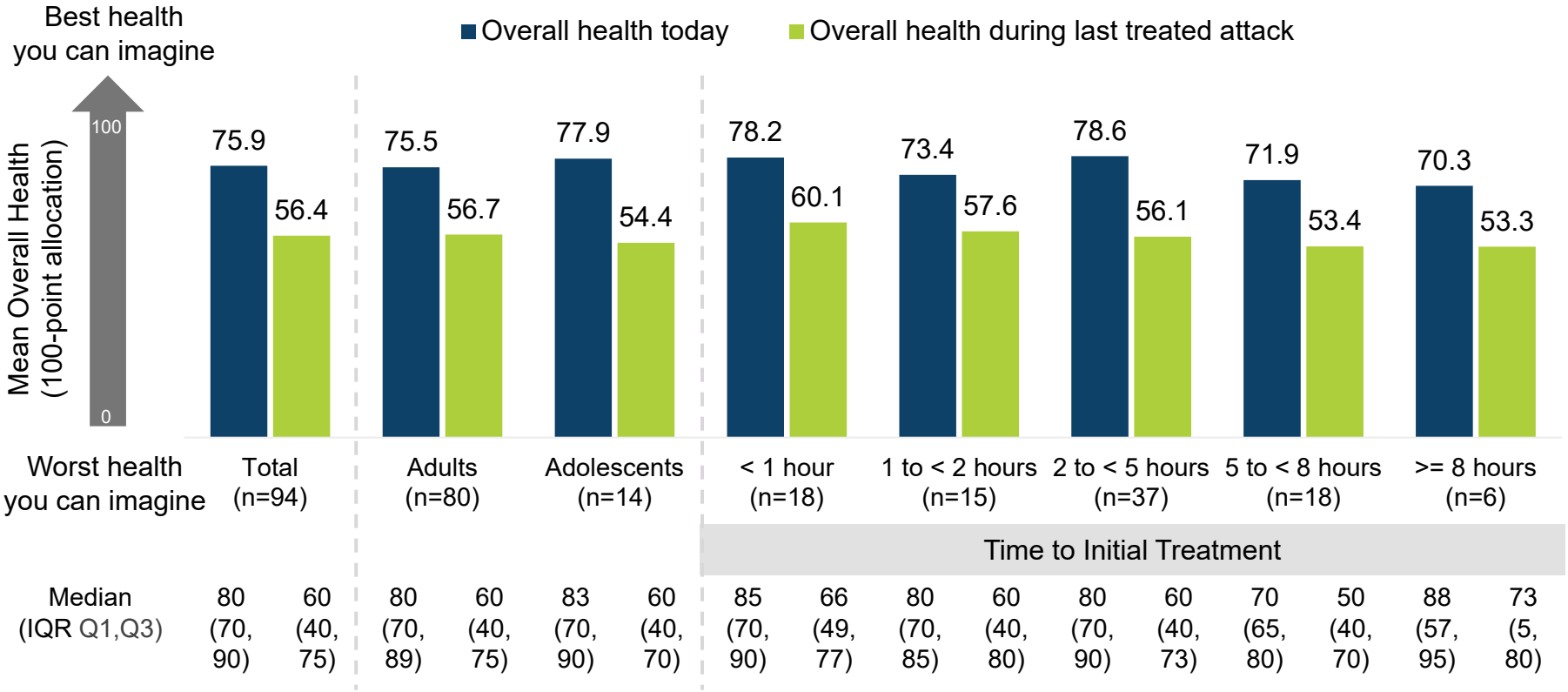


	Total (n=94)		< 1 hour (n=18)		1 to < 2 hours (n=15)		2 to < 5 hours (n=37)		5 to < 8 hours (n = 18)		≥ 8 hours (n = 6)	
Median (IQR Q1, Q3)	0.94 (0.78, 1.0)	0.67 (0.32, 0.80)	0.87 (0.82, 1.0)	0.74 (0.57, 0.88)	0.88 (0.72, 1.0)	0.71 (0.34, 0.88)	0.94 (0.83, 1.0)	0.62 (0.31, 0.80)	0.88 (0.72, 1.0)	0.59 (0.28, 0.75)	0.88 (0.56, 0.94)	0.73 (0.51, 0.78)
Mean (SD)	0.85 (0.2)	0.57 (0.30)	0.82 (0.2)	0.67 (0.30)	0.84 (0.2)	0.59 (0.40)	0.89 (0.1)	0.53 (0.40)	0.82 (0.2)	0.50 (0.30)	0.80 (0.2)	0.64 (0.20)

- QoL index scores generally worsened with increasing treatment delay

*29% of participants had attack in the past 7 days; median (IQR) time since last treated attack 14 (7, 28) days.

EQ-5D-5L VAS (General Health) Scores for Current and Last Treated Attack by Treatment Delay



- General health scores generally worsened with increasing treatment delay

Conclusions

- Our findings demonstrate that the majority of participants do not treat their attacks early despite guideline recommendations. Overall, an average delay of nearly 4-hours was recorded
- The data suggest that treatment delays are associated with a lower QoL and reduction in general health during an HAE attack
- These results emphasize the need for an improved awareness of the HAE guideline recommendations for on-demand attack treatment
- It is anticipated that a reduction in treatment delay may translate into improved QoL and general health status associated with attacks for individuals with HAE