Long-term Safety, Efficacy, and Quality of Life with Navenibart in Hereditary Angioedema: ALPHA-SOLAR Interim Results

Aleena Banerji,[1] Adil Adatia,[2] Joshua S. Jacobs,[3] H. Henry Li,[4] William Lumry,[5] Raffi Tachdjian,[6] Daniel Long,[7] Lori Mixson,[7] Daniel Petroni,[7] Marc Riedl[8]

[1]Massachusetts General Hospital, Boston, MA, USA; [2]Division of Pulmonary Medicine, Department of Medicine, University of Alberta, Edmonton, AB, Canada; [3]Allergy & Asthma Medical Group of the Bay Area, Inc, Walnut Creek, CA, USA; [4]Institute For Asthma and Allergy, Chevy Chase, MD, USA; [5]AARA Research Center, Dallas, TX, USA; [6]Division of Allergy, Immunology and Rheumatology, UCLA School of Medicine, Los Angeles, CA, USA; [7]BioCryst Pharmaceuticals, Inc, Durham, NC, USA; [8]University of California – San Diego, La Jolla, CA, USA

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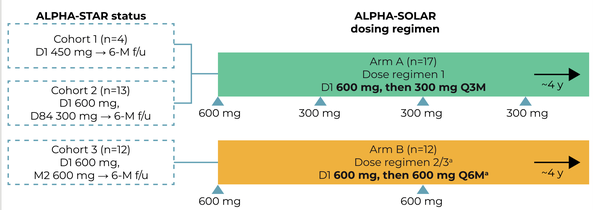
INTRODUCTION

- Hereditary angioedema (HAE) is a rare, autosomal dominant disorder associated with dysregulation of the kallikrein-kinin system, resulting in recurrent swelling attacks.
- Navenibart is the first investigational long-acting highly selective inhibitor of plasma kallikrein, being evaluated for dosing every 3 months (Q3M) or every 6 months (Q6M).[1]
- Here, we present the interim results from ALPHA-SOLAR (NCT06007677), an ongoing Phase 2, open-label extension trial of navenibart in participants with HAE due to C1-inhibitor deficiency, for 29 patients who previously completed ALPHA-STAR (NCT05695248).[1]

METHODS

- ALPHA-SOLAR is a long-term, open-label extension trial that includes 29 participants who completed the Phase 1b/2 ALPHA-STAR trial, presented herein (**Figure 1**).
- Baseline was defined as monthly HAE attack rates reported during the 8-week ALPHA-STAR run-in period.
- Participants entering ALPHA-SOLAR were assigned to one of three Arms:
  - Arm A: 600 mg and then 300 mg navenibart Q3M
  - Arm B: 600 mg and then 600 mg navenibart Q6M
    - B1 (n=5): The first 5 participants in Arm B received 600 mg on Day 1, then 600 mg on Day 28 and then 600 mg Q6M
    - B2 (n=7): 600 mg Q6M
    - Participant data for Arms B1 and B2 are pooled in the present analysis
- The primary endpoint was treatment-emergent adverse events (TEAEs).
- Secondary endpoints included efficacy assessments of attack frequency, severity, use of on-demand medication, and quality of life as measured by the Angioedema Quality of Life Questionnaire (AE-QoL).
- This interim analysis was conducted when the first participant enrolled had completed 2 years of treatment.

Figure 1. ALPHA-SOLAR Clinical Trial Design



Data cut-off on 10-Oct-2025.
D, day; f/u, follow-up; M, month; Q3M, every 3 months; Q6M, every 6 months; y, years.
[a]The first 5 participants in Arm B received 600 mg on Days 1 and 28, then 600 mg Q6M.

RESULTS

- All 29 participants who completed ALPHA-STAR enrolled in ALPHA-SOLAR.
- Baseline demographic and disease characteristics are reported in **Table 1**.
  - Mean (standard deviation [SD]) age was 46 (16.6) years
  - 16/29 participants (55.2%) were female
  - Mean (SD) treatment duration was 12.5 (4.8) months
  - Median (range) treatment duration was 12.3 (6–24) months

Table 1. Baseline Demographic and Disease Characteristics

	Arm A (600/300 Q3M) (n=17)	Arm B (600 Q6M) (n=12)	Total (n=29)
Age (years), mean (SD)	45 (16.2)	48 (17.8)	46 (16.6)
Sex at birth, n (%), female	10 (58.8)	6 (50.0)	16 (55.2)
Race, n (%)			
White	13 (76.5)	10 (83.3)	23 (79.3)
Black or African-American	3 (17.6)	1 (8.3)	4 (13.8)
Multiracial	2 (11.8)	–	2 (6.9)
American Indian or Alaska Native	1 (5.9)	–	1 (3.4)
HAE-C1INH type, n (%), Type 1	14 (82.4)	11 (91.7)	25 (86.2)
Weight (kg), mean (SD)	79.8 (20.1)	84.8 (22.1)	81.9 (20.7)
Number of attacks in the prior 12 months, mean (SD)[a]	25.6 (23.3)	13.1 (13.3)	20.4 (20.5)
Baseline (run-in) time-normalized monthly HAE attack rate, mean (SD)[a]	2.3 (1.3)	2.1 (1.7)	2.2 (1.5)
Treatment duration, mean (SD)	12.9 (5.8)	11.9 (2.9)	12.5 (4.8)

Data cut-off on 10-Oct-2025.
HAE, hereditary angioedema; HAE-C1INH, hereditary angioedema due to C1-inhibitor deficiency; n, total number of participants; Q3M, every 3 months; Q6M, every 6 months; SD, standard deviation.
[a]Baseline from ALPHA-STAR.

Safety

- The most common adverse event related to study treatment (10.3%) was injection site reaction (**Table 2**).
- No serious adverse events or adverse events leading to discontinuation related to study treatment were reported.
- One unrelated serious adverse event of invasive ductal breast carcinoma led to navenibart discontinuation.

Table 2. TEAEs Observed in ALPHA-SOLAR

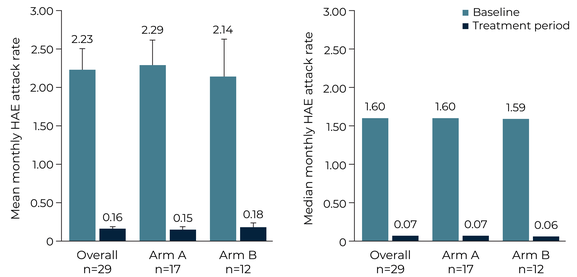
	Arm A (600/300 Q3M) (n=17)	Arm B (600 Q6M) (n=12)	Total (n=29)
Participants with ≥1 TEAE, n (%)	12 (70.6)	8 (66.7)	20 (69.0)
TEAEs occurring in ≥2 participants, n (%)			
Nasopharyngitis	2 (11.8)	1 (8.3)	3 (10.3)
Urinary tract infection	2 (11.8)	1 (8.3)	3 (10.3)
Headache	3 (17.6)	–	3 (10.3)
Injection site reaction	1 (5.9)	2 (16.7)	3 (10.3)
Myalgia	2 (11.8)	1 (8.3)	3 (10.3)
Skin laceration	1 (5.9)	2 (16.7)	3 (10.3)
Nasal congestion	1 (5.9)	1 (8.3)	2 (6.9)
Arthralgia	1 (5.9)	1 (8.3)	2 (6.9)
Participants with ≥1 navenibart-related TEAE, n (%)	2 (11.8)	3 (25.0)	5 (17.2)
Injection site reaction	1 (5.9)	2 (16.7)	3 (10.3)
Myalgia	–	1 (8.3)	1 (3.4)
Dizziness	1 (5.9)	–	1 (3.4)
Participants with ≥1 serious TEAE, n (%)	1 (5.9)	–	1 (3.4)
Invasive ductal breast carcinoma	1 (5.9)	–	1 (3.4)
Participants with TEAE leading to navenibart discontinuation,[a] n (%)	1 (5.9)	–	1 (3.4)
Participants with TEAE leading to death, n (%)	–	–	–

n, total number of participants; Q3M, every 3 months; Q6M, every 6 months; TEAE, treatment-emergent adverse event.
[a]Navenibart discontinuation owing to serious TEAE of invasive ductal breast carcinoma.

Efficacy

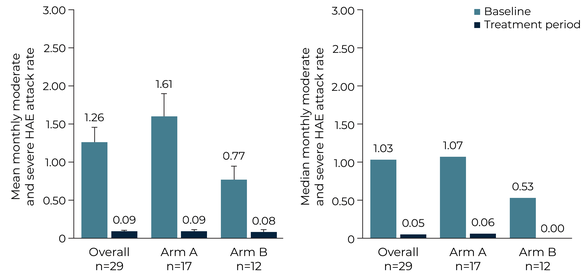
- Navenibart reduced monthly HAE attack rates from baseline across both treatment arms, with mean (SD) attack rates decreasing from 2.29 (1.34) to 0.15 (0.18) in Arm A and from 2.14 (1.68) to 0.18 (0.25) in Arm B, and median (range) attack rates decreasing from 1.60 (0.95–4.81) to 0.07 (0.00–0.72) and from 1.59 (0.86–7.13) to 0.06 (0.00–0.67), respectively (**Figure 2**).
- Monthly moderate and severe HAE attack rates were also reduced, with mean (SD) attack rates decreasing from 1.61 (1.22) to 0.09 (0.12) in Arm A and from 0.77 (0.66) to 0.08 (0.15) in Arm B, and median (range) attack rates decreasing from 1.07 (0.48–4.81) to 0.06 (0.00–0.45) and from 0.53 (0.00–1.90) to 0.00 (0.00–0.47), respectively (**Figure 3**).
- These reductions were sustained over the observed follow-up period (mean 12.5 months).

Figure 2. Mean and Median HAE Attack Rate in ALPHA-SOLAR



Baseline from ALPHA-STAR. Error bars show standard error of the mean. HAE, hereditary angioedema.

Figure 3. Mean and Median Moderate and Severe HAE Attack Rates in ALPHA-SOLAR

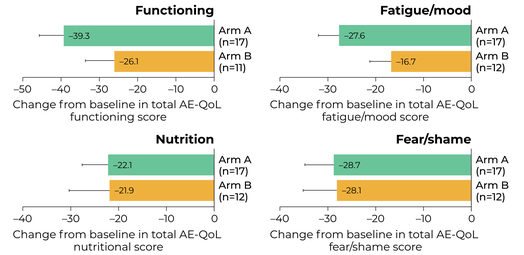


Baseline from ALPHA-STAR. Error bars show standard error of the mean. HAE, hereditary angioedema.

Quality of Life

- Mean (SD) AE-QoL total scores improved (decreased) from baseline across dosing arms over 6 months of treatment with navenibart (Arm A: −30.1 [18.2] points; Arm B: −24.7 [17.2] points), exceeding the 6-point minimum clinically important difference threshold.
- Improvements from baseline were observed across all AE-QoL domains (**Figure 4**).

Figure 4. Change from Baseline in AE-QoL Domain Scores at 6 Months



Data shown represent change from baseline at 6 months after the loading dose in ALPHA-SOLAR. A reduction in score indicates improvements in the AE-QoL domain. Error bars show standard error of the mean.
AE-QoL, Angioedema Quality of Life Questionnaire.

Limitations

- Limitations include the open-label design, small sample size, descriptive analyses, differing Arm B loading schedules, and variable duration of treatment at the interim data cutoff.

CONCLUSIONS

1. Navenibart was generally well tolerated, with no serious adverse events or adverse events leading to discontinuation related to study treatment over a mean duration of 12.5 months.
2. Monthly HAE attack rates during ALPHA-SOLAR decreased from baseline for up to 2 years.
3. AE-QoL scores demonstrated consistent improvement across all domains relative to baseline following 6 months of treatment.

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REFERENCE

1. Banerji et al. *J Allergy Clin Immunol*. 2026;157:1127-1135.e6.

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