Quality of life (QoL) improvements in patients with hereditary angioedema (HAE); interim results from the phase 1b/2 ALPHA-STAR clinical trial

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SUMMARY

Navenibart exhibited an immediate and sustained impact on normalizing the lives of patients with HAE during the first 84 days, by:

1 **Reducing median HAE attack rate from baseline by >90%**

2 **Rapidly improving and maintaining improved QoL (80% of participants had clinically significant improvements)**

3 **Demonstrating a favorable safety profile**

OBJECTIVES

- To assess the treatment effects of navenibart (STAR-0215), including safety, prevention of HAE attacks, and impact on quality of life (QoL), over the first 3-month period (84 days) in the ALPHA-STAR clinical trial.
- ALPHA-STAR (NCT05695248) is an ongoing Phase 1b/2 clinical trial in patients with HAE that evaluates single and multiple doses of navenibart with six months of follow-up after the last dose.

INTRODUCTION

- HAE is a rare, autosomal dominant disease associated with heterogeneous, recurrent and unpredictable clinical manifestations of angioedema with variable severity.
- HAE attacks can incur substantial morbidity, diminished quality of life, high economic burden, and increased mortality.
- Navenibart (STAR-0215) is an investigational monoclonal antibody inhibitor of plasma kallikrein with long-lasting activity enabled by a YTE-modified Fc domain, that has demonstrated proof-of-concept in the ALPHA-STAR clinical trial, with favorable safety and >90% reduction of HAE attacks that was maintained up to 6 months after navenibart administration.[1]

METHODS

- Adults with HAE-C1INH-Types 1 and 2 were recruited into three dose cohorts. Cohort 1: 450 mg (day 1); Cohort 2: 600 mg (day 1), 300 mg (day 84); Cohort 3: 600 mg (day 1 and day 28), all subcutaneously.
- Quality of life was assessed at baseline and monthly thereafter using the Angioedema Quality of Life (AE-QoL) questionnaire, which has a minimal clinically important difference (MCID) of –6 points.

RESULTS

DEMOGRAPHICS AND BASELINE CHARACTERISTICS

- At the time of analysis, 16 participants had received navenibart treatment.
- **Table 1** presents the baseline characteristics of enrolled participants as of the data cutoff (March 13, 2024).
- This analysis uses data accrued during the first 84 days of the treatment period, including 4 participants who received 450 mg SC (Cohort 1), 6 participants who received 600 mg SC on day 1, and 300 mg on day 84 (Cohort 2) and 6 participants who received 600 mg on day 1 and another 600 mg dose on day 28 (Cohort 3).

Table 1. ALPHA-STAR Participant's Demographic and Baseline Characteristics

Demographic	Navenibart 450 mg SC (N = 4)	Navenibart 600/300 mg SC (N = 6)	Navenibart 600/600 mg SC (N = 6)	Navenibart All Cohorts (N = 16)
Age, years; mean (SD)	51 (21)	39 (15)	49 (24)	46 (20)
Sex, Female; %	75	67	33	56
Race, white, %	100	83	83	88
BMI, kg/m; mean (SD)	29 (8)	30 (2)	32 (6)	30 (5)
HAE-C1INH, Type 1, %	100	83	83	88
Age at onset of the first HAE symptoms, years; mean (SD)	11 (11)	14 (8)	12 (6)	13 (8)
Number of HAE attacks in the previous 12 months; mean (SD)	18 (23)	34 (29)	11 (9)	22 (23)
Run-in HAE attack rate:				
Monthly, mean (SD)	3 (1)	2 (2)	2 (1)	2 (1)
Monthly, median	3	2	2	2

SAFETY

- The most common treatment emergent adverse events (TEAEs), occurring in 2 or more participants who received navenibart included nasopharyngitis, contusion, and headache, none of which were considered related to the treatment.
- No serious or severe TEAEs and no treatment discontinuations were reported.

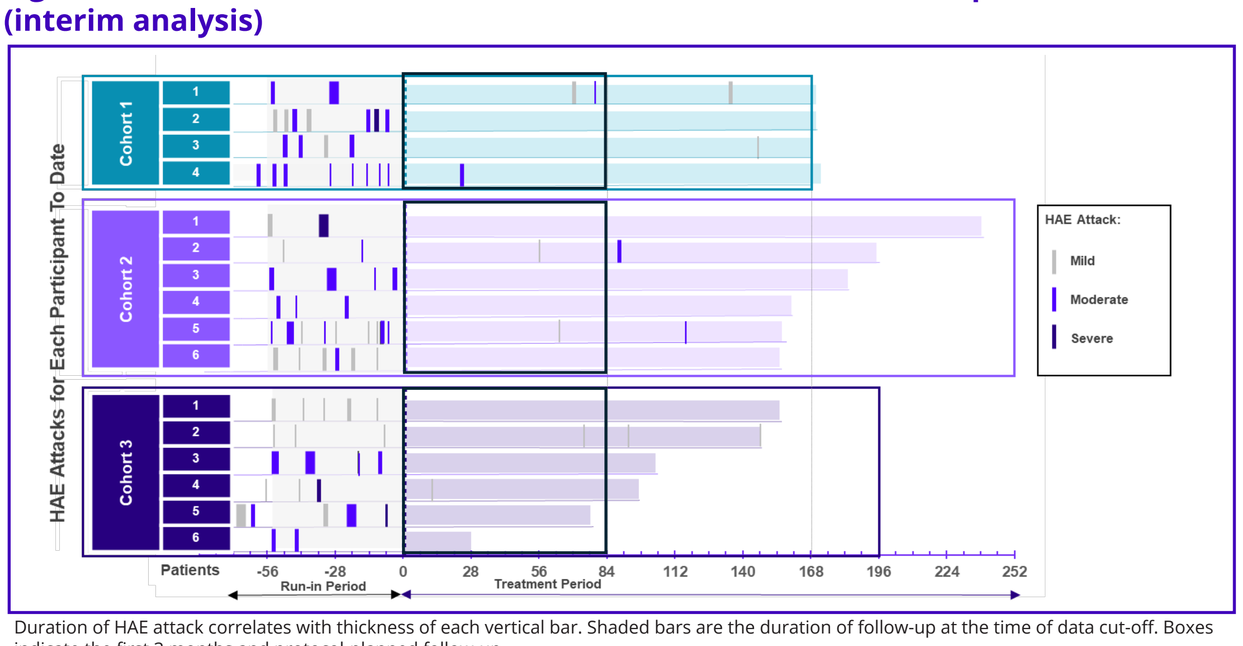
REDUCTIONS IN HAE ATTACKS

- At the cut-off date, ALPHA-STAR participants accrued 6.5 years of exposure to navenibart.
- For the first three months (**Boxes in Figure 1.**), 50%, 67%, and 50% of participants with available follow-up were HAE attack-free in Cohorts 1-3, respectively.

IMPROVEMENTS IN AE-QOL

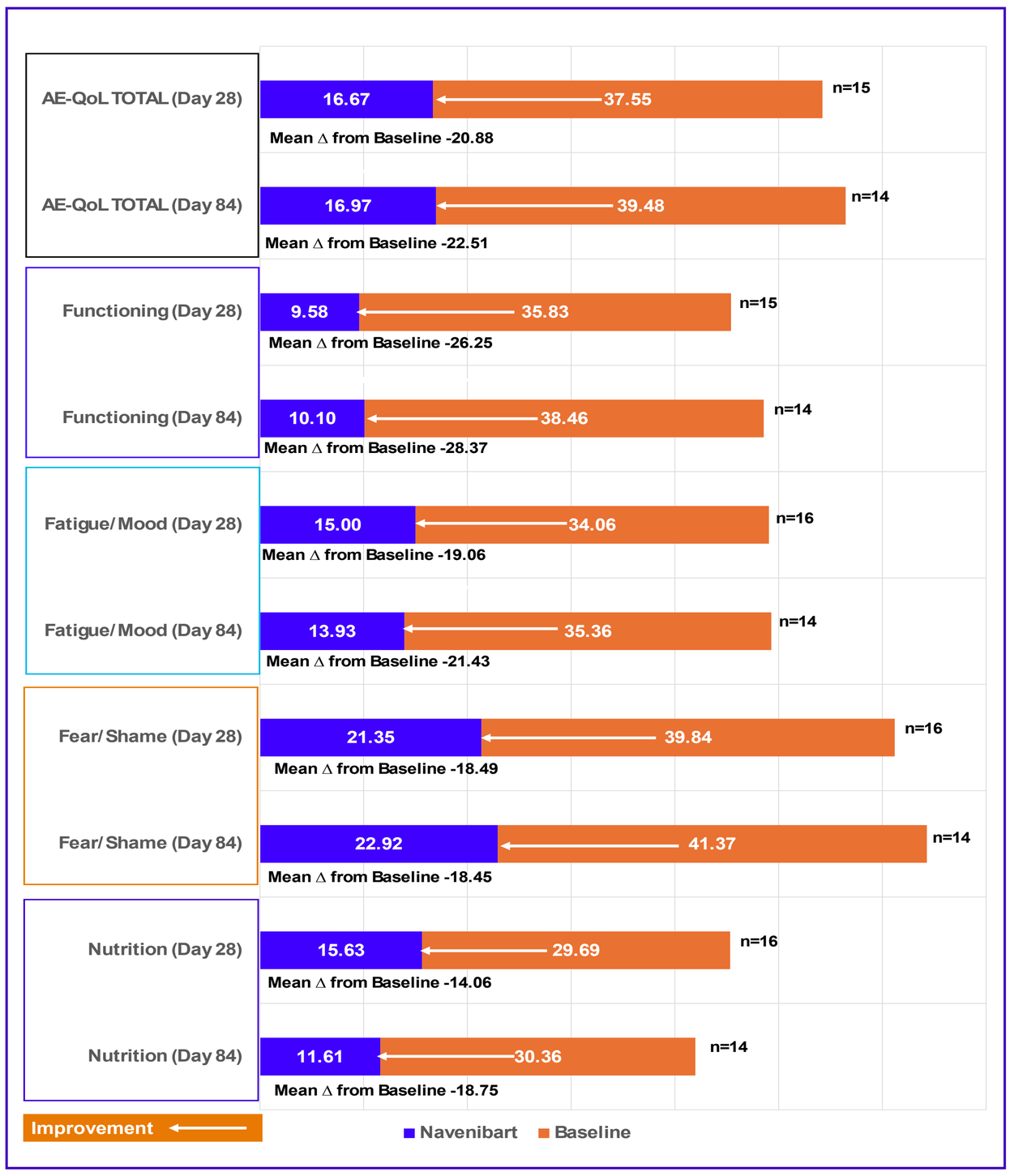
- Navenibart treatment resulted in early and sustained clinically meaningful improvements in quality of life (MCID=-6 points) in 80% of participants.
- Figure 2 shows improvements from baseline at day 28 (Month 1) and day 84 (Month 3) for Total AE-QoL score and all four domains (Functioning, Fatigue/Mood, Fear/Shame and Nutrition).

Figure 1. HAE Attack Occurrence in Individual ALPHA-STAR Participants (interim analysis)



Duration of HAE attack correlates with thickness of each vertical bar. Shaded bars are the duration of follow-up at the time of data cut-off. Boxes indicate the first 3 months and protocol-planned follow-up.

Figure 2. . Improvement in AE-QoL in the First Three Months (Day 28 and Day 84) after Navenibart in ALPHA-SOLAR (interim analysis)



CONCLUSIONS

- These interim results provide proof of concept for navenibart treatment in participants with HAE, evidenced by reductions in HAE attacks and a favorable safety profile.
- The majority of participants in the ALPHA-STAR trial experienced early and consistent improvements in their quality of life in all four domains of AE-QoL, with the most significant improvement seen in the functioning domain.
- These findings support that navenibart may be an important preventive treatment option for patients with HAE.

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REFERENCES: 1. Maurer et al. (2024), ALPHA-STAR, a Phase 1b/2 Clinical Trial of Single and Multiple Doses of Navenibart (STAR-0215) in Patients with Hereditary Angioedema: Interim Safety and Efficacy Outcomes, EADV 2024, Amsterdam.

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