Treatment with Navenibart (STAR-0215) Reduces Attack Severity and Use of Rescue Medication in Patients with Hereditary Angioedema (HAE): Interim Results from the ALPHA-STAR Trial

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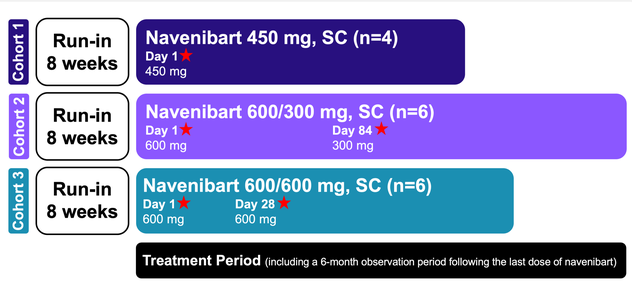
OBJECTIVE

- Discuss final results from target enrollment (n=16) in the ALPHA-STAR (NCT05695248) clinical trial assessing HAE attack severity (mild/moderate/severe) and the number of HAE attacks requiring on-demand therapy after navenibart (STAR-0215) subcutaneous (SC) administration.

Figure 1. ALPHA-STAR (NCT05695248) clinical trial design



INTRODUCTION

- Hereditary angioedema is a rare, autosomal dominant disease associated with a high disease and treatment burden.
- Navenibart is the first investigational monoclonal antibody with an extended half-life exhibiting rapid and sustained inhibition of plasma kallikrein.

METHODS

- After wash-out from long-term preventative therapies (LTPs), if applicable, participants entered a run-in period of 2 months (Baseline), during which they had to have ≥2 attacks.
- Participants were enrolled sequentially into 1 of 3 treatment cohorts (**Figure 1**).
- HAE attacks were assessed throughout the study to evaluate the efficacy of navenibart. Assessment of HAE attacks included attack location, severity, timing, and treatment.

SUMMARY

1. THERE WERE NO SEVERE ATTACKS DURING THE 6-MONTH OBSERVATION PERIOD FOLLOWING EITHER 1 OR 2 DOSES OF NAVENIBART.
2. THE NEED FOR ACUTE TREATMENT FOR ATTACKS WAS GREATLY REDUCED COMPARED TO THE BASELINE PERIOD.
3. MONTHLY ATTACK RATE, COMPARED TO THE RUN-IN BASELINE, WAS REDUCED BY 91-95% DURING THE 6 MONTHS FOLLOWING THE FIRST DOSE.
4. NAVENIBART WAS WELL-TOLERATED; THERE WERE NO SEVERE OR SERIOUS TREATMENT EMERGENT ADVERSE EVENTS (TEAES) AND NO DISCONTINUATIONS DUE TO TEAES.

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RESULTS

DEMOGRAPHICS, BASELINE CHARACTERISTICS AND SAFETY

- The mean age was 46 years, and 9 (56%) of 16 participants were female. 88% of participants had HAE-C1INH Type 1.
- All TEAEs were mild to moderate in severity, and most TEAEs were assessed as not related to navenibart (**Table 1**).
- No severe, serious, or fatal TEAEs were reported, and no participant discontinued navenibart or the trial because of a TEAE.

Table 1. Cumulative safety in ALPHA-STAR participants

	Navenibart 450 mg (N = 4)	Navenibart 600/300 mg (N = 6)	Navenibart 600/600 mg (N = 6)	Navenibart Total (N = 16)
At least 1 TEAE, n (%)	4 (100)	5 (83)	6 (100)	15 (94)
TEAEs occurring in ≥2 participants				
Nasopharyngitis	1 (25)	1 (17)	2 (33)	4 (25)
Sinusitis	-	1 (17)	1 (17)	2 (13)
Headache	2 (50)	-	-	2 (13)
Participants with ≥1 navenibart-related TEAE[1], n (%)	-	-	2 (33)	3 (19)
Injection site erythema	-	-	1 (17)	1 (6)
Injection site pruritus	-	-	1 (17)	1 (6)
Injection site rash	-	-	1 (17)	1 (6)
Dizziness	-	1 (17)	-	1 (6)
At least 1 Serious TEAE, n (%)	-	-	-	-
TEAE leading to trial discontinuation, n (%)	-	-	-	-
TEAE leading to death, n (%)	-	-	-	-

Data cutoff date: 04 Sep 2024; TEAE = treatment emergent adverse event; [1]If a participant experienced > 1 event in a given category, that participant is counted only once in that category.
One participant experienced mild dizziness occurring 6 days after the first dose in Cohort 2 and lasting < 1 day. One participant experienced 2 injection site reactions: injection site erythema and injection site pruritus occurring 1 day after the second dose in Cohort 3 and lasting < 1 day. One participant experienced injection site rash occurring 5 days after the second dose in Cohort 3 and lasting < 1 day.

Figure 2. Mean Time-Normalized Moderate or Severe Attacks

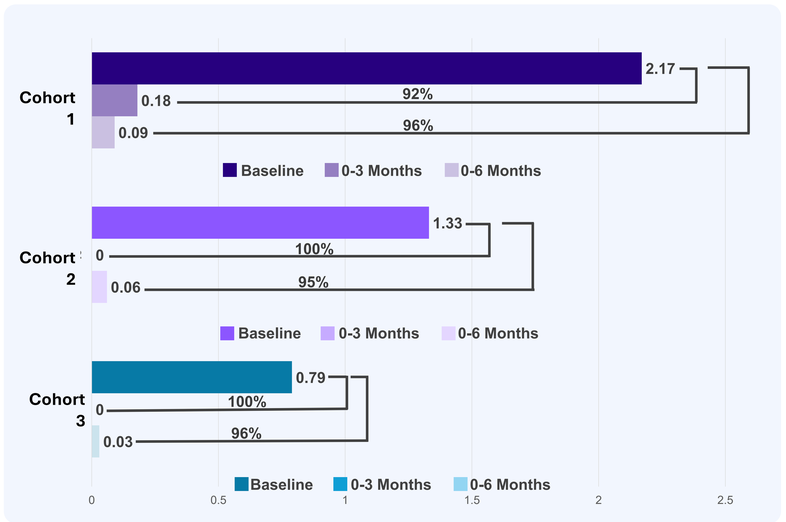
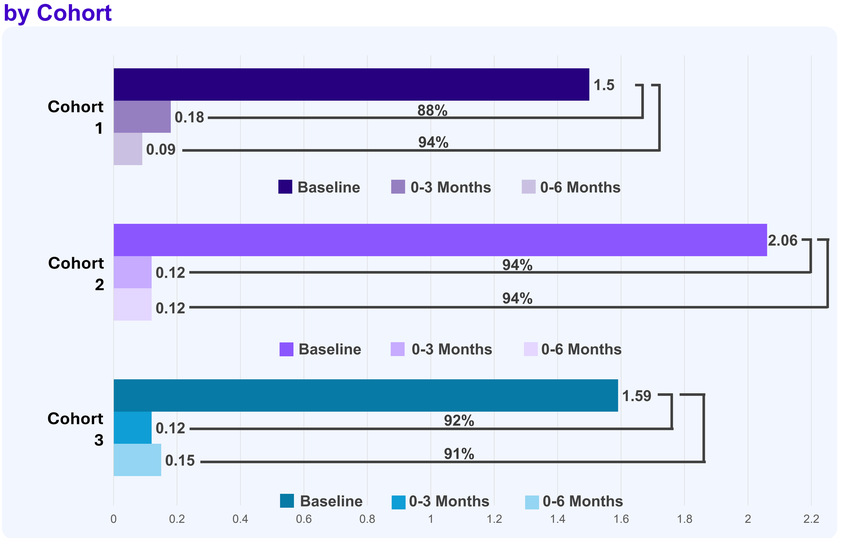


Figure 3. Changes in Time-Normalized Attacks Requiring Rescue Medication by Cohort



REDUCTION IN HAE ATTACK SEVERITY AND RESCUE MEDICATION USE

- Rates of moderate and severe attacks (**Figure 2**) and attacks requiring rescue medication (**Figure 3**) significantly decreased in each cohort.
- Before the treatment period commenced, 4 (100%) of 4 participants in Cohort 1, 5 (83%) of 6 in Cohort 2, and 6 (100%) of 6 in Cohort 3 required rescue medication for at least one attack during the 56-day run-in period.
- Throughout the treatment and follow-up periods, 2 (50%) of 4 participants in Cohort 1, 3 (50%) of 6 in Cohort 2, and 2 (33%) of 6 in Cohort 3 utilized rescue medication.

CONCLUSIONS

- Navenibart was well-tolerated and, compared to baseline, significantly reduced the number, severity, and acute treatment of HAE attacks following navenibart's single- or multiple-dose administration.
- These data suggest that navenibart may be a valuable prophylactic treatment option for patients with HAE and warrants further evaluation in the ongoing phase 3 global pivotal trial, ALPHA-ORBIT (NCT06842823).