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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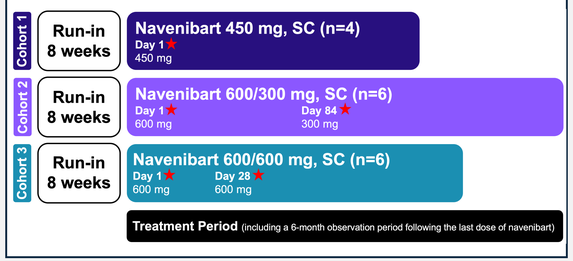
OBJECTIVE

- 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



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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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.

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.

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.

Figure 2. Mean Time-Normalized Moderate or Severe Attacks

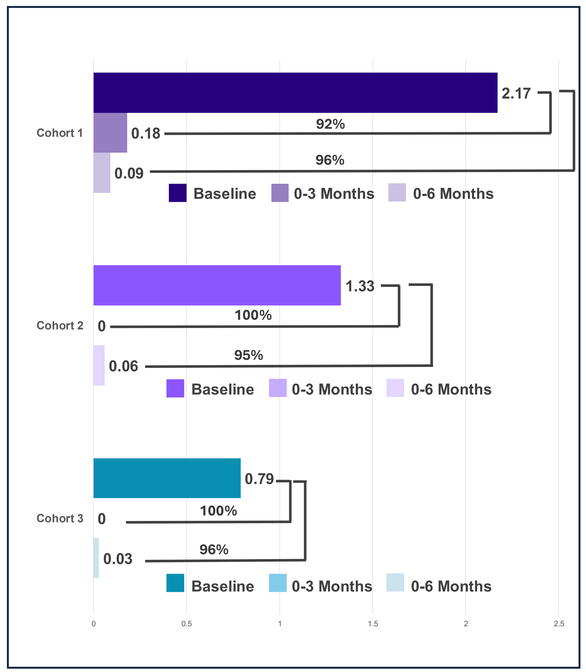
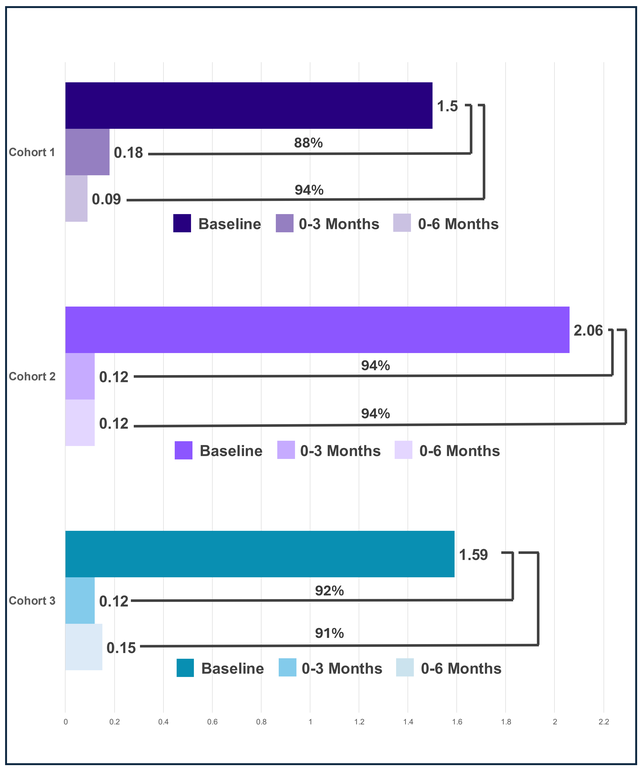


Figure 3. Changes in Time-Normalized Attacks Requiring Rescue Medication by Cohort



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-CINH Type 1 or 2 and warrants further evaluation in a phase 3 trial.