

Navenibart Demonstrates Durable Efficacy and Tolerability Across Biological Sexes: Subgroup Analysis from the ALPHA-STAR Trial



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SUMMARY

NAVENIBART IS AN INVESTIGATIONAL, LONG-ACTING ANTI-PLASMA KALLIKREIN MONOCLONAL ANTIBODY EVALUATED IN THE PHASE 1B/2 ALPHA-STAR TRIAL. THIS POST-HOC SUBGROUP ANALYSIS ASSESSED SAFETY, TOLERABILITY, AND CLINICAL ACTIVITY ACROSS BIOLOGICAL SEXES, INCLUDING PARTICIPANTS OF CHILDBEARING POTENTIAL, WITH THE FOLLOWING FINDINGS:

- 1 Navenibart was well tolerated, with no new or unexpected safety signals.
- 2 The incidence and pattern of treatment-emergent adverse events were generally consistent across biological sexes.
- 3 Among participants of childbearing potential, tolerability findings were consistent with the overall safety profile.
- 4 These results support continued clinical evaluation of navenibart across diverse patient subgroups with HAE-C1INH.

INTRODUCTION

- HAE-C1INH is a rare, lifelong disease with recurrent swelling attacks that can be severe and unpredictable.
- HAE disease burden and triggers, particularly hormonal influences, differ by biological sex. Assessing navenibart across these subgroups is essential to confirm consistent safety and dosing across the diverse real-world patient population..
- Prior HAE prophylaxis programs (including plasma kallikrein pathway therapies and other targeted biologics) have reported overall safety, but detailed sex-specific tolerability and sub-analyses for participants of childbearing-potential are not always highlighted, particularly in smaller early-phase studies.
- ALPHA-STAR achieved balanced representation of both male and female participants, providing a robust dataset to characterize the safety and clinical activity of navenibart across biological sexes.
- This ALPHA-STAR subgroup analysis summarizes treatment-emergent adverse events by biological sex and among participants of childbearing potential to inform ongoing development.

METHODS

- Participants who had completed required washout from long-term prophylaxis (LTP), if applicable, entered an 8-week run-in period (baseline) during which they had ≥2 attacks.
- Twenty-nine participants were enrolled into one of three treatment cohorts (Figure 1).
- Findings from this post-hoc analysis are descriptive.

RESULTS

Figure 3. Efficacy was generally consistent across biological sex and childbearing potential

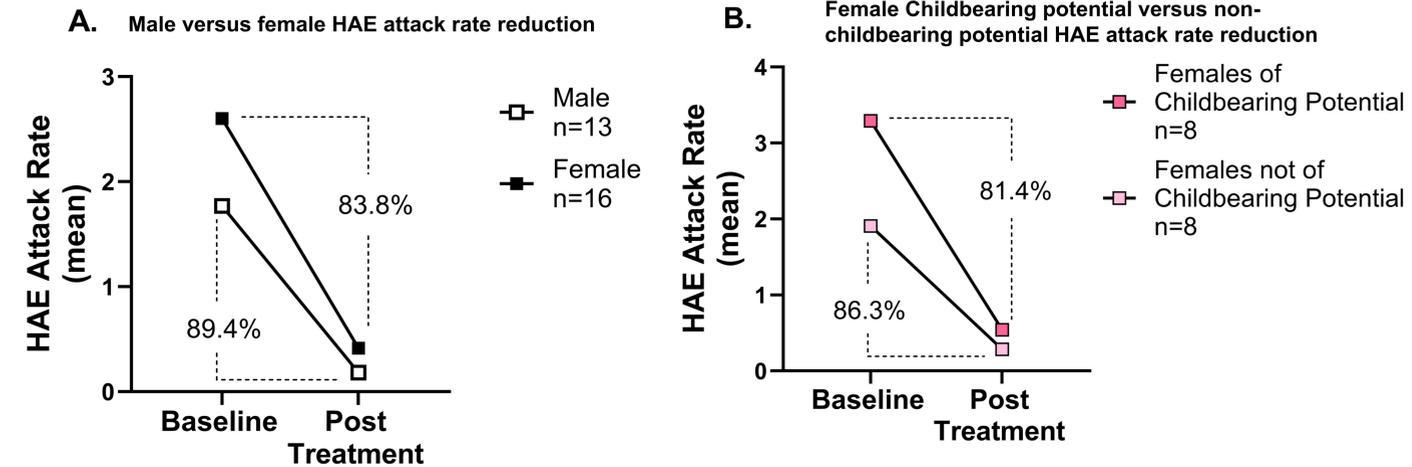


FIGURE 3. Efficacy was generally consistent across biological sex.

(A) At baseline, females had a higher mean monthly HAE attack rate than males (2.6 vs 1.8). Both sexes experienced substantial reductions over the treatment period; percentage reductions were greater in males with a mean (SEM) of 89.4% (4.6%) compared to females who had a mean (SEM) of 83.8% (4.3%). Post-treatment mean monthly attack rates were similar for both subgroups.

(B) Reductions were observed regardless of childbearing potential. For females of childbearing potential, the mean (SEM) percentage reduction was 81% (6.28%) while for those without childbearing potential the mean (SEM) percent reduction was 86.3% (6.21%). Post-treatment mean monthly attack rates were similar across both subgroups.

OBJECTIVES

- ALPHA-STAR (NCT05695248) was a global, dose-ranging, proof-of-concept Phase 1b/2 trial designed to evaluate the safety, tolerability, and clinical activity of subcutaneous (SC) navenibart (STAR-0215) in adults with Type 1 or Type 2 hereditary angioedema (HAE-C1INH).
- The goal of this post-hoc analysis was to assess safety of navenibart by biological sex and participants of childbearing potential. Reductions in HAE attack rates between sexes were also assessed.

Figure 2. Baseline Characteristics of Trial Participants

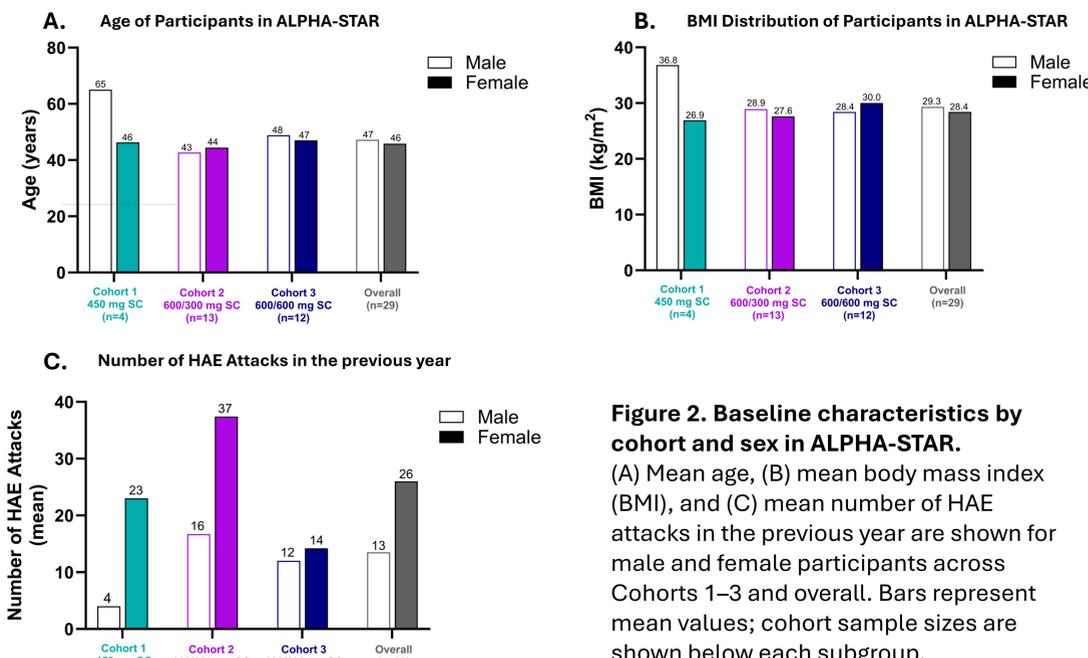


Figure 2. Baseline characteristics by cohort and sex in ALPHA-STAR. (A) Mean age, (B) mean body mass index (BMI), and (C) mean number of HAE attacks in the previous year are shown for male and female participants across Cohorts 1–3 and overall. Bars represent mean values; each sample size are shown below each subgroup.

Table 1. Participant Incidence of Treatment-Emergent Adverse Events

	Male (N = 13)	Female CBP: Yes (N=8)	Female CBP: No (N=8)	Overall Total (N = 29)
Participants with at least 1 Treatment-Emergent Adverse Event (TEAE) n (%)	11 (84.6)	7 (87.5)	7 (87.5)	
Participants with ≥ 1 moderate TEAE n (%)	6 (46.2)	4 (50.0)	5 (62.5)	
TEAEs occurring in ≥2 participants, n (%)				
Headache	4 (30.8)	-	2 (25.0)	
Nasopharyngitis	3 (23.1)	3 (37.5)	-	
Skin laceration	2 (15.4)	-	-	
Nasal congestion	-	2 (25.0)	-	
Sinusitis	-	-	-	
Urinary tract Infection	1 (7.7)	-	-	
Breast pain	-	-	1 (12.5)	
Treatment-related TEAEs (≥ 1 participant, n (%))				
Injection site erythema	1 (7.7)	-	-	
Injection site pruritus	1 (7.7)	-	-	
Injection site rash	-	-	1 (12.5)	
Injection site swelling	-	1 (12.5)	-	
Dizziness	-	-	-	

No serious or severe TEAEs occurred, and no TEAE led to trial discontinuation or resulted in death | CBP, childbearing potential

CONCLUSION

- **Safety and Tolerability:** Treatment was well-tolerated in both sexes, with no serious or severe adverse events and no discontinuations due to safety concerns. The incidence of treatment-emergent adverse events (TEAEs) was similar between the subgroups, occurring in 84.6% of males and 87.5% of females.
- **Consistent Efficacy Across Sexes:** Navenibart demonstrated robust reductions in HAE attack rates regardless of biological sex. By the end of the treatment period, mean monthly attack rates decreased by 84.6% in females and 88.9% in males.
- **Impact on Participants of Childbearing Potential:** Within the female subgroup, 50% (8/16) were of childbearing potential. This subgroup showed a favorable safety profile consistent with the other subgroups, supporting the potential use of navenibart in this clinically relevant population.
- **Support for Long-Term Prevention:** Durable efficacy and favorable safety of 3- or 6-month dosing schedules in both sexes, including participants of childbearing potential, support the evaluation of these schedules in the Phase 3 ALPHA-ORBIT trial.

Acknowledgement

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References

Lumry WR. Am J Manag Care. Sinnathamby ES et al. Adv Ther. 2023; Busse P et al. J Allergy Clin Immunol Pract. 2022