

# Long-term Safety and Efficacy of Navenibart in Participants with Hereditary Angioedema (HAE): Initial Combined Results from ALPHA-STAR and ALPHA-SOLAR

D1.390

W. YANG<sup>1\*</sup>; M. RIEDL<sup>2</sup>; T. CRAIG<sup>3</sup>; J. JACOBS<sup>4</sup>; A. ADATIA<sup>5</sup>; R. TACHDJIAN<sup>6</sup>; W. LUMRY<sup>7</sup>; K. SITZ<sup>8</sup>; H. LI<sup>9</sup>; W. SOONG<sup>10</sup>; M. MANNING<sup>11</sup>; J. WEDNER<sup>12</sup>; C. MORABITO<sup>13</sup>; T. COHEN<sup>13</sup>; K. BERNARD<sup>13</sup>; C. VANEENWYK<sup>13</sup>; J. BEST<sup>13</sup>; A. BANERJI<sup>14</sup>

\*Presenting Author

## OBJECTIVE

- To evaluate the long-term safety and effectiveness of navenibart as prophylaxis in patients with hereditary angioedema (HAE).

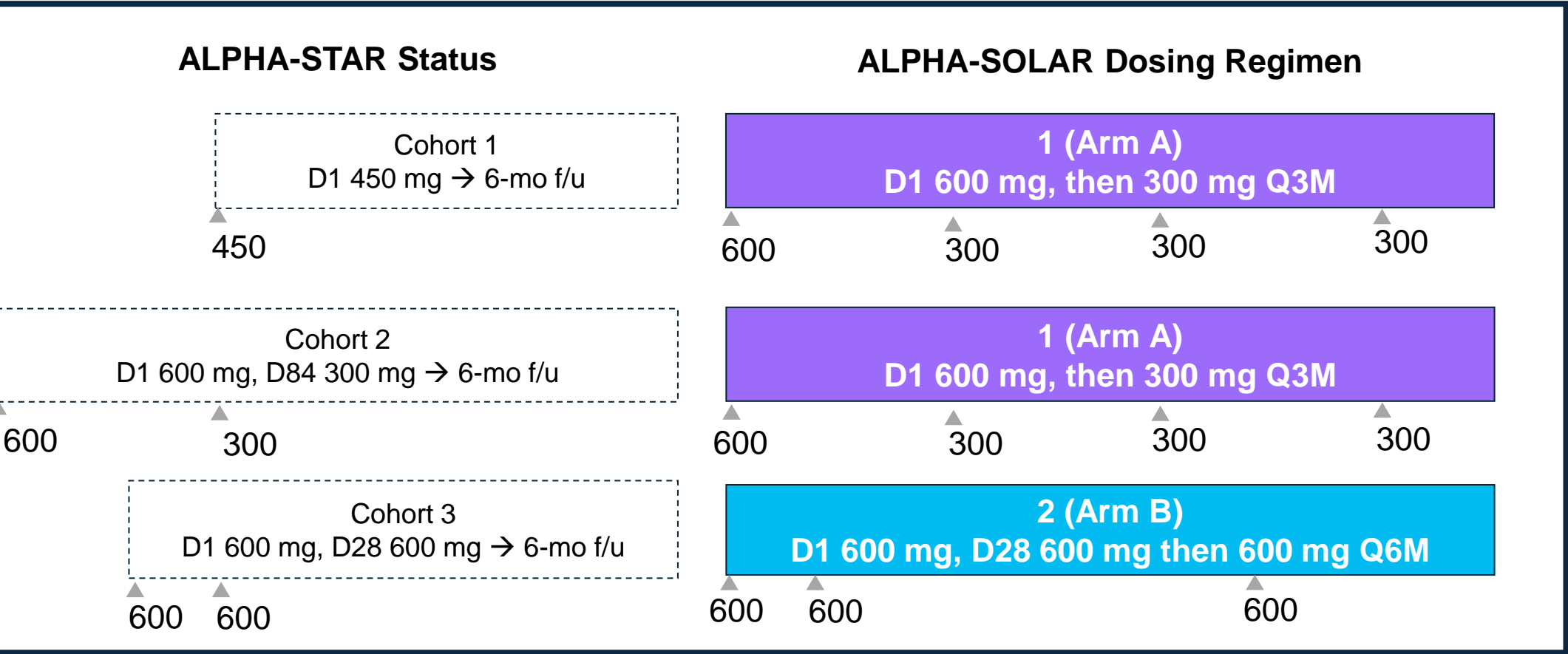
## INTRODUCTION

- HAE is a rare, autosomal dominant disease associated with dysregulation of the kallikrein-kinin system.
- Navenibart is a novel investigational therapeutic monoclonal antibody inhibitor of plasma kallikrein with extended half-life.
- Here, we report the initial results from ALPHA-SOLAR, a Phase 2 long-term open-label trial (NCT06007677), combined with ALPHA-STAR, a Phase 1b/2 trial (NCT05695248), with navenibart in participants with HAE.

## METHODS

- ALPHA-SOLAR is a long-term open-label extension trial for participants who completed the ALPHA-STAR Phase 1b/2 trial (**Figure 1**).
- Participants entering ALPHA-SOLAR were assigned to one of two Arms:
  - Arm A (Cohort 1 and Cohort 2 of ALPHA-STAR): 600 mg and then 300 mg navenibart every 3 months.
  - Arm B (Cohort 3 of ALPHA-STAR): 600 mg and then 600 mg navenibart on Day 28 followed by 600 mg navenibart every 6 months.
- The primary endpoint was the incidence of treatment-emergent adverse events (TEAEs)
- Secondary endpoints included efficacy assessments, including attack frequency, severity, and use of rescue medication.
- This initial analysis was performed once participants had achieved approximately 12-18 months of follow-up since the start of ALPHA-STAR and 6-12 months since the start of ALPHA-SOLAR. Participation may continue for up to 4 years.

Figure 1. ALPHA-SOLAR Clinical Trial Design



## SUMMARY

- WITH >17 MONTHS (MEAN) FOLLOW-UP, NAVENIBART WAS WELL TOLERATED AND THE SAFETY PROFILE WAS FAVORABLE.
- IN ALPHA-SOLAR, NAVENIBART SHOWED AN OVERALL MONTHLY REDUCTION OF 92% IN MEAN HAE ATTACK RATES AFTER A MEAN FOLLOW-UP OF 10.1 MONTHS.
- A SIMILAR REDUCTION IN RATES OF MODERATE AND SEVERE HAE ATTACKS AND ATTACKS REQUIRING RESCUE MEDICATION WERE OBSERVED (95% AND 92%, RESPECTIVELY).
- NAVENIBART CONTINUES TO DEMONSTRATE FAVORABLE SAFETY AND ROBUST EFFICACY FOR HAE. Q3M AND Q6M REGIMENS ARE BEING EVALUATED IN AN ONGOING PIVOTAL PHASE 3 TRIAL, ALPHA-ORBIT (NCT06842823).

ACKNOWLEDGMENT: Authors acknowledge Jan Markind, PharmD, for medical writing and data visualization



Presented at European Academy of Allergy and Clinical Immunology  
June 13-June 16, 2025 • Glasgow, UK

## RESULTS

### DEMOGRAPHICS AND BASELINE CHARACTERISTICS

- All 16 participants in the initial cohort completed ALPHA-STAR and enrolled in ALPHA-SOLAR.
- The overall mean (SD) age was 46 (20) years, and 9 (56%) were female (**Table 1**).
- The mean (median) duration of follow-up is 17.4 (17.1) months across ALPHA-STAR and ALPHA-SOLAR, and 10.1 (9.1) months on ALPHA-SOLAR alone.

Table 1. ALPHA-STAR and ALPHA-SOLAR Baseline Demographics and Disease Characteristics

	Arm A (600/300 Q3M) (n=10)	Arm B (600/600/600 Q6M) (n=6)	Total (n=16)
Age (Years), Mean (SD)	44 (17)	49 (24)	46 (20)
Sex, n (%)			
Female	7 (70)	2 (33)	9 (56)
Race, n (%)			
White	9 (90)	5 (83)	14 (88)
Black or African-American	2 (20)	1 (17)	3 (19)
Multiracial	2 (20)	-	2 (13)
American Indian or Alaska-native	1 (10)	-	1 (6)
HAE-C1INH type, n (%)			
Type 1	9 (90)	5 (83)	14 (88)
Type 2	1 (10)	1 (17)	2 (13)
Age at the onset of first HAE symptoms (years), Mean (SD)	13 (9)	12 (6)	13 (8)
Baseline (run-in) monthly attack rate, Mean (SD)	2.5 (1.4)	1.8 (0.6)	2.2 (1.2)

Abbreviations: n, total number of participants; Q3M, every 3 months; Q6M, every 6 months; SD, standard deviation.

### SAFETY

- Navenibart was well tolerated in ALPHA-STAR and ALPHA-SOLAR, with a combined mean (median) follow-up of 17.4 (17.1) months (**Table 2**).
- No treatment-related serious adverse events or discontinuations were reported.
- The most common treatment-emergent adverse events related to navenibart were injection site reactions, occurring in 3 participants.
- No navenibart-related, clinically significant changes in safety labs (including aPTT), vital signs, or ECGs were reported.
- No safety signals for navenibart have been observed across ALPHA-STAR and ALPHA-SOLAR.

Table 2. Safety in Combined ALPHA-STAR and ALPHA-SOLAR

	Arm A (600/300 Q3M) (n=10)	Arm B (600/600/ 600 Q6M) (n=6)	Total* (n=16)
Participants with at least 1 Treatment-Emergent Adverse Event (TEAE)	10	6	16
TEAEs occurring in ≥2 participants			
Nasopharyngitis	3	2	5
Sinusitis	2	1	3
Urinary tract infection	2	1	3
Skin Laceration	2	1	3
Nasal congestion	1	1	2
Headache	2	-	2
Participants with ≥1 related TEAE	1	3	4
Injection site reaction <sup>1</sup>	-	1	1
Injection site erythema <sup>2</sup>	-	1	1
Injection site pruritus <sup>2</sup>	-	1	1
Injection site rash <sup>3</sup>	-	1	1
Dizziness <sup>4</sup>	1	-	1

1. One participant experienced 2 injection site reactions starting 0-1 day after the first and second doses in STAR-0215-202 Arm B (tenderness and pruritus lasting <1 day; erythema and pruritus lasting 5 days).  
2. One participant experienced 2 injection site reactions: injection site erythema and injection site pruritus occurring 1 day after the second dose in STAR-0215-201 Cohort 3 and lasting <1 day.  
3. One participant experienced injection site rash occurring 5 days after the second dose in STAR-0215-201 Cohort 3 and lasting <1 day.  
4. One participant experienced mild dizziness occurring 6 days after the first dose in STAR-0215-201 Cohort 2 and lasting <1 day.  
\*Mean (Median) follow-up: 17.4 (17.1) months  
Abbreviations: n, number of participants; Q3M, every 3 months; Q6M, every 6 months; SD, standard deviations.

<sup>1</sup>OTTAWA ALLERGY RESEARCH CORPORATION, OTTAWA, CANADA; <sup>2</sup>UNIVERSITY OF CALIFORNIA SAN DIEGO, SAN DIEGO, UNITED STATES OF AMERICA; <sup>3</sup>PENN STATE HEALTH ALLERGY, ASTHMA AND IMMUNOLOGY, HERSHEY, UNITED STATES OF AMERICA; <sup>4</sup>ALLERGY & ASTHMA MEDICAL GROUP OF THE BAY AREA, WALNUT CREEK, UNITED STATES OF AMERICA; <sup>5</sup>UNIVERSITY OF ALBERTA, EDMONTON, CANADA; <sup>6</sup>UC LA SANTA MONICA MEDICAL CENTER, SANTA MONICA, UNITED STATES OF AMERICA; <sup>7</sup>MEDICAL CITY CHILDREN'S HOSPITAL, DALLAS, UNITED STATES OF AMERICA; <sup>8</sup>LITTLE ROCK ALLERGY & ASTHMA CLINIC, LITTLE ROCK, UNITED STATES OF AMERICA; <sup>9</sup>INSTITUTE FOR ASTHMA & ALLERGY, CHEVY CHASE, UNITED STATES OF AMERICA; <sup>10</sup>ALLERVIE HEALTH - HOMEWOOD, BIRMINGHAM, UNITED STATES OF AMERICA; <sup>11</sup>THE UNIVERSITY OF ARIZONA COLLEGE OF MEDICINE, PHOENIX, UNITED STATES OF AMERICA; <sup>12</sup>WASHINGTON UNIVERSITY PHYSICIANS, CREVE COEUR, UNITED STATES OF AMERICA; <sup>13</sup>ASTRIA THERAPEUTICS, BOSTON, UNITED STATES OF AMERICA; <sup>14</sup>MASSACHUSETTS GENERAL HOSPITAL, BOSTON, UNITED STATES OF AMERICA

### EFFICACY

- In ALPHA-SOLAR, monthly HAE attack rate decreased after treatment and remained low throughout a mean (median) follow-up of 10.1 (9.1) months (**Figure 2**).
- Overall, there was a 92% (97%) reduction in mean (median) rate of time-normalized monthly HAE attacks, from 2.22 (2.02) at baseline (from ALPHA-STAR) to 0.17 (0.06) during the ALPHA-SOLAR treatment period.
- The reduction from baseline in Arm A / Arm B was 95% (99%) / 86% (90%) mean (median).

- Moderate-severe attacks (**Figure 3**) and attacks requiring rescue medication (**Figure 4**) were markedly reduced in alignment with overall attack rate reduction. Findings were consistent across treatment groups.

- There was a 95% (100%) reduction in mean (median) rate of time-normalized monthly moderate-severe attack rate, from 1.34 (1.2) at baseline (from ALPHA-STAR) to 0.07 (0.0) during the ALPHA-SOLAR treatment period.
- Overall proportion of moderate-severe attacks compared to mild attacks was lower post-treatment.
- There was a 92% (98%) reduction in mean (median) monthly rate of attacks requiring on-demand treatment (rescue medication), from baseline of 1.74 (1.55) (ALPHA-STAR) to 0.14 (0.03) during the ALPHA-SOLAR treatment period.

Figure 2. Changes in Mean and Median Monthly Time-Normalized HAE Attack Rates in ALPHA-SOLAR.

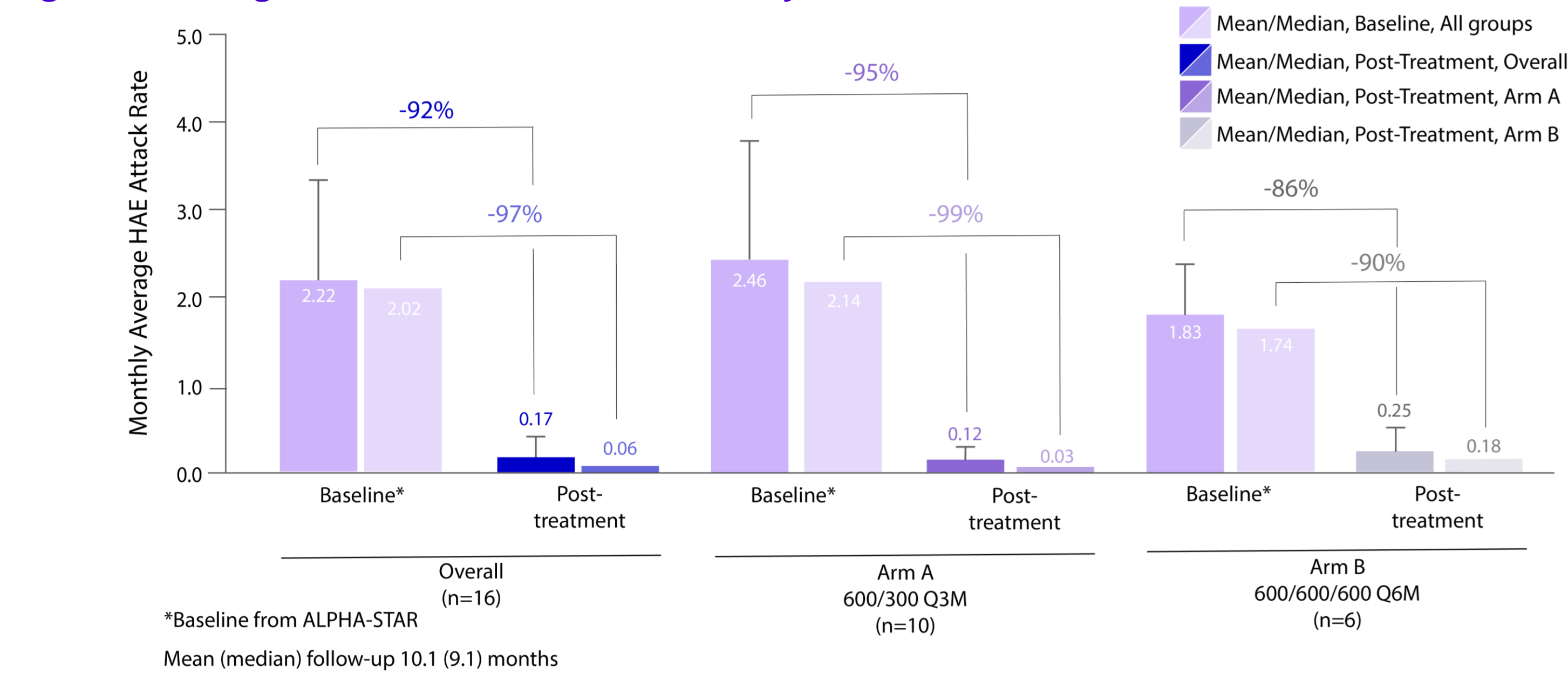


Figure 3. Changes in Mean and Median Moderate or Severe Monthly Time-Normalized HAE Attack Rates in ALPHA-SOLAR.

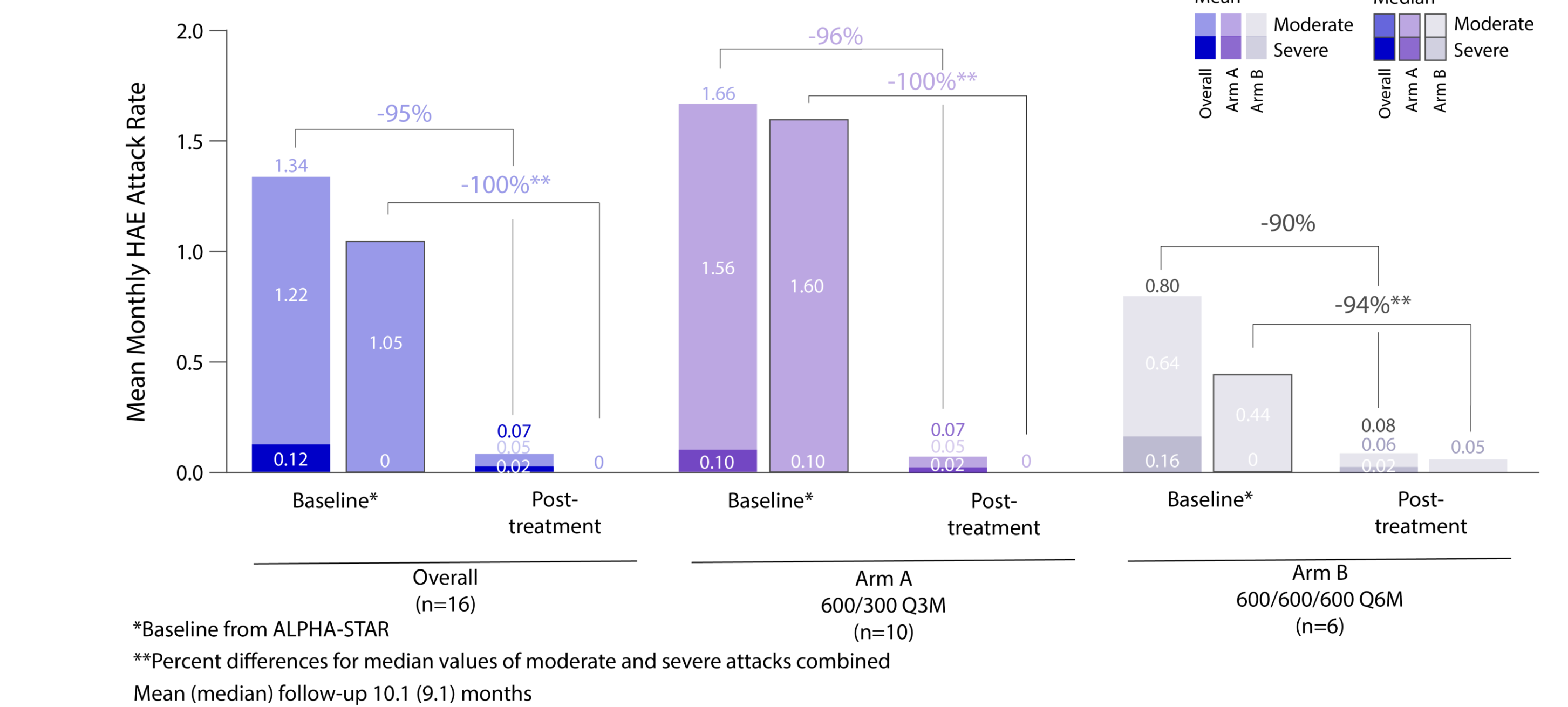
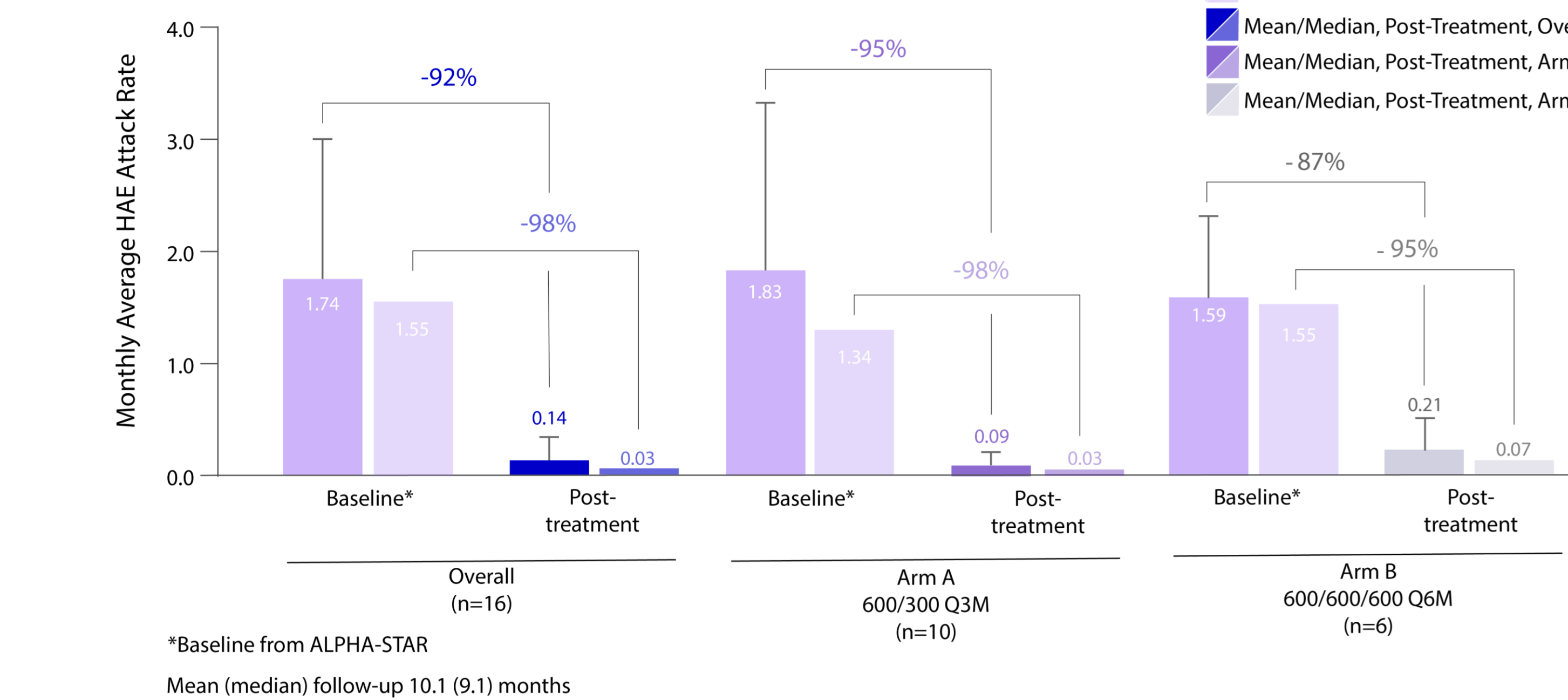


Figure 4. Changes in Mean and Median Monthly Time-Normalized Rates of HAE Attacks Requiring Rescue Medication in ALPHA-SOLAR.



## CONCLUSIONS

- These initial results demonstrate navenibart's favorable safety profile and robust, durable efficacy for the treatment of HAE attacks and potential as a long-acting first choice prophylaxis in HAE.
- The ongoing phase 3 global pivotal trial, ALPHA-ORBIT (NCT06842823), is investigating the efficacy and safety of navenibart when administered Q3M and Q6M to adults and adolescents with HAE.