



Correlation between Subjective and Objective Disease Control in Hereditary Angioedema: Association between the Angioedema Control Test and Attack Rate

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BACKGROUND

- Hereditary angioedema (HAE) is a rare disorder characterized by disabling episodes of local skin swellings, painful abdominal attacks, and laryngeal attacks that can be life-threatening¹
- Substantial burden of disease remains among patients with HAE and their caregivers, particularly for those with breakthrough attacks on prophylaxis or poor disease control^{2–5}
- The Angioedema Control Test (AECT) is a validated, 4-item, patient-reported instrument capturing subjective control of angioedema (AE) attacks in patients with recurrent AE, including HAE⁶
- There is no existing research examining the correlation between subjective disease control, as assessed by AECT, and frequency or number of HAE attacks

OBJECTIVE

- To evaluate association between subjective disease control, as measured by AECT scores, and objective disease control, as measured by time-normalized attack rate, in patients with HAE participating in OASIS-HAE, a phase 3, double-blind, placebo-controlled study (NCT05139810)

METHODS

- In OASIS-HAE, patients with HAE received donidalorsen 80 mg every 4 weeks or every 8 weeks or matching placebo subcutaneously over 24 weeks
- Analyses included all dosed patients (N = 90), pooled across treatment arms
- All *p*-values are nominal and were not corrected for multiplicity of testing
- AECT, scored from 0 to 16 points, was administered at Baseline (Week 0) and every 4 weeks through Week 24
 - AECT scores of 16 points indicate perceived complete disease control, scores ≥10 points indicate well-controlled disease, and scores <10 points indicate poorly-controlled disease⁷
- Time-normalized, investigator-confirmed HAE attack rate captured from Baseline through Week 24
 - Patients instructed to report HAE attacks within 72 hours of onset and prompted to report during weekly study contacts
 - Investigator-confirmed number of HAE attacks (i.e., HAE attack): Events, separated by 24-hour symptom-free intervals, characterized by signs or symptoms consistent with an attack in ≥1 pre-specified bodily locations
 - HAE attack rate calculated as number of attacks occurring during each 28-day interval, starting on study Day 1
- To measure association between AECT scores and HAE attack rates over previous 4 weeks, examined Spearman correlation coefficients at Baseline, at Week 24, and change from Baseline to Week 24
- HAE attack rates for patients with AECT scores <10 or ≥10 at Week 24 were evaluated using summary statistics, independent samples *t*-tests, and Cohen's *d* effect sizes (ES) at Baseline and at Week 24
 - |ES| ≤0.2: negligible effect
 - ≥0.2 to <0.5: small effect
 - ≥0.5 to <0.8: medium effect
 - ≥0.8: large effect
- HAE attack rates for patients with AECT scores of 16 or <16 at Week 24, and AECT scores for patients with HAE attack rates of 0 or >0 at Week 24, were evaluated using summary statistics, independent samples *t*-tests, and Cohen's *d* ES at Baseline and at Week 24

RESULTS

Figure 2. Mean HAE Attack Rates* between Subgroups with AECT Scores <10 (Poorly-Controlled Disease) and AECT Scores ≥10 (Well-Controlled Disease) at Week 24

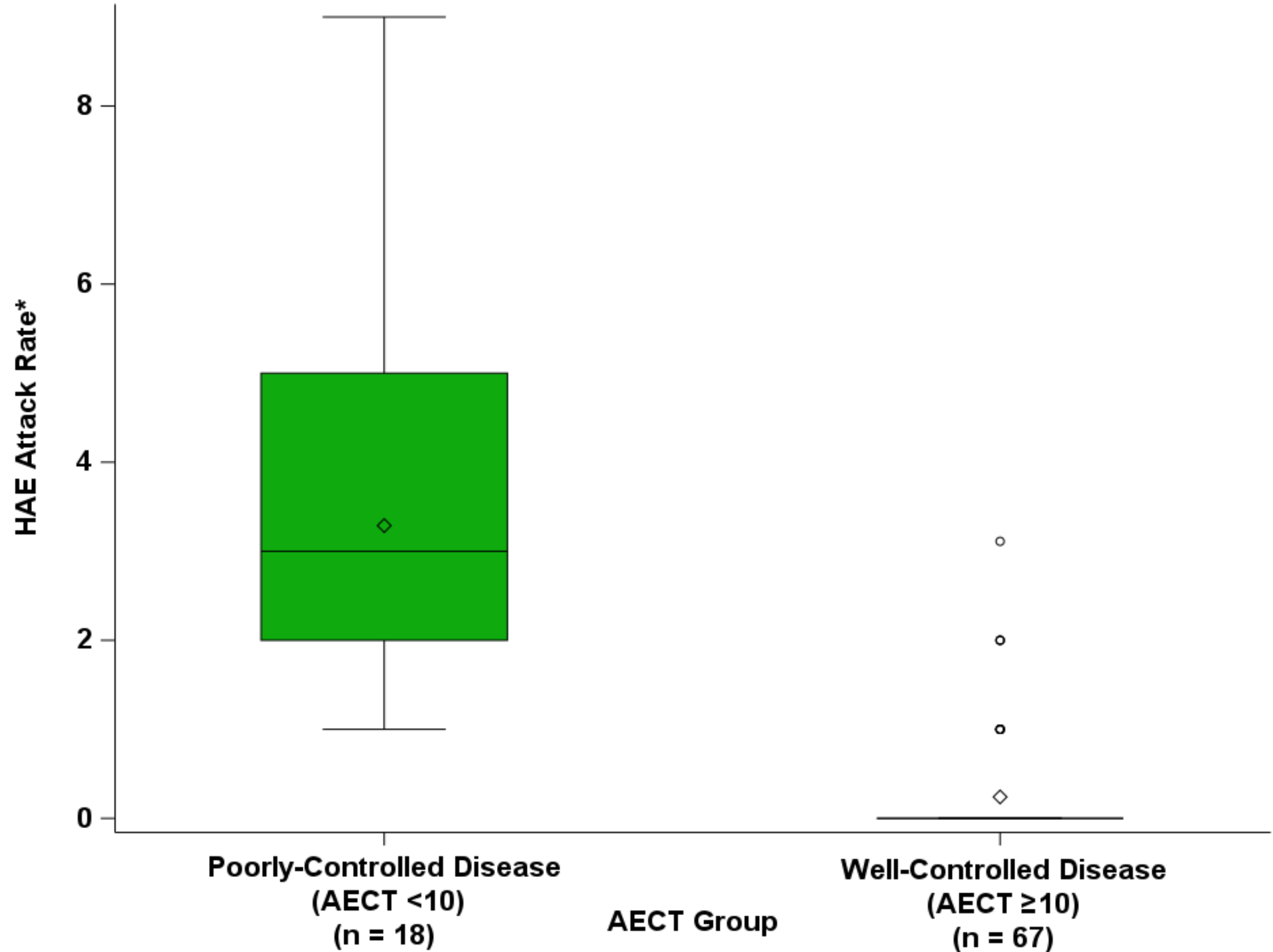
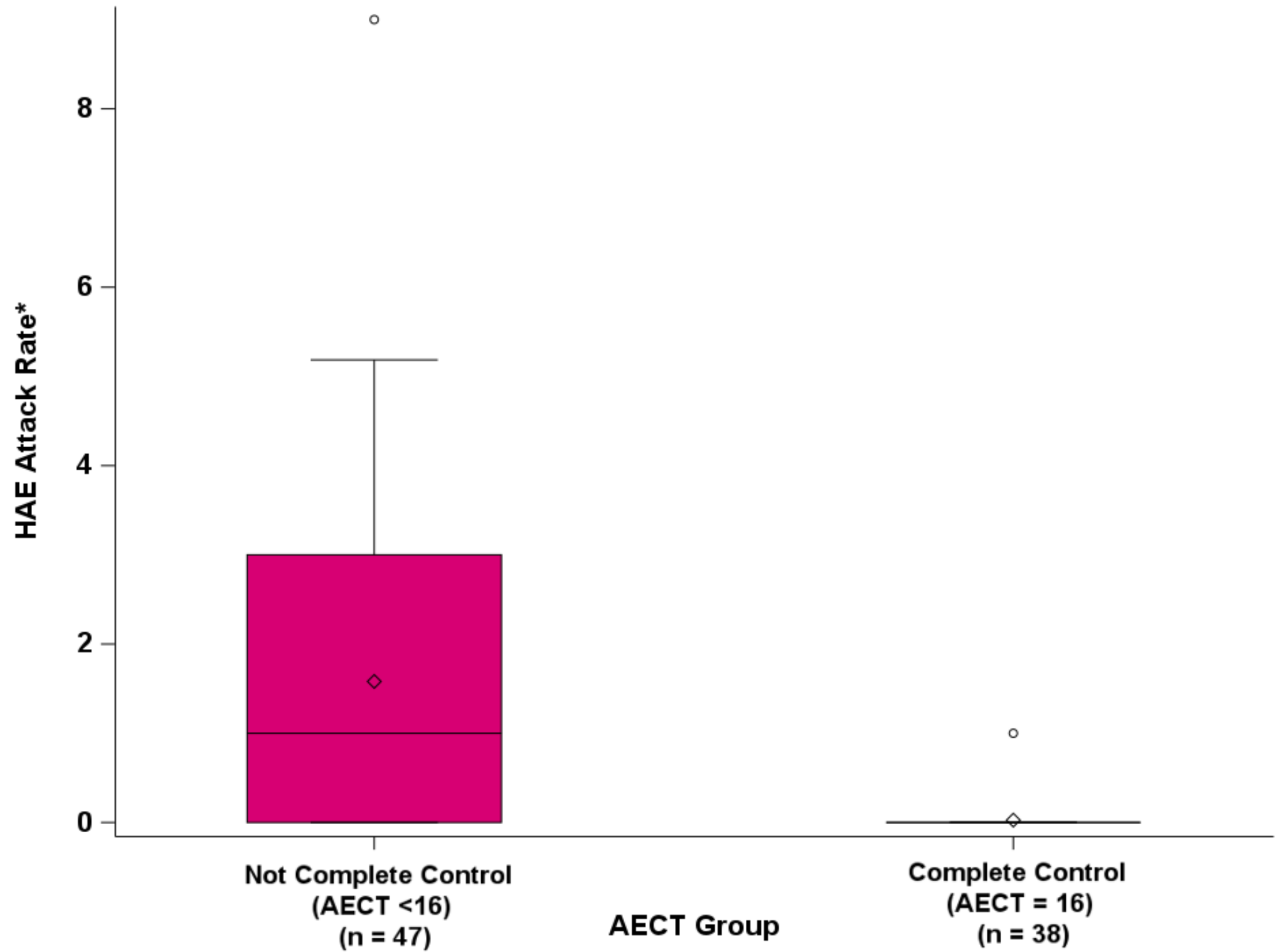


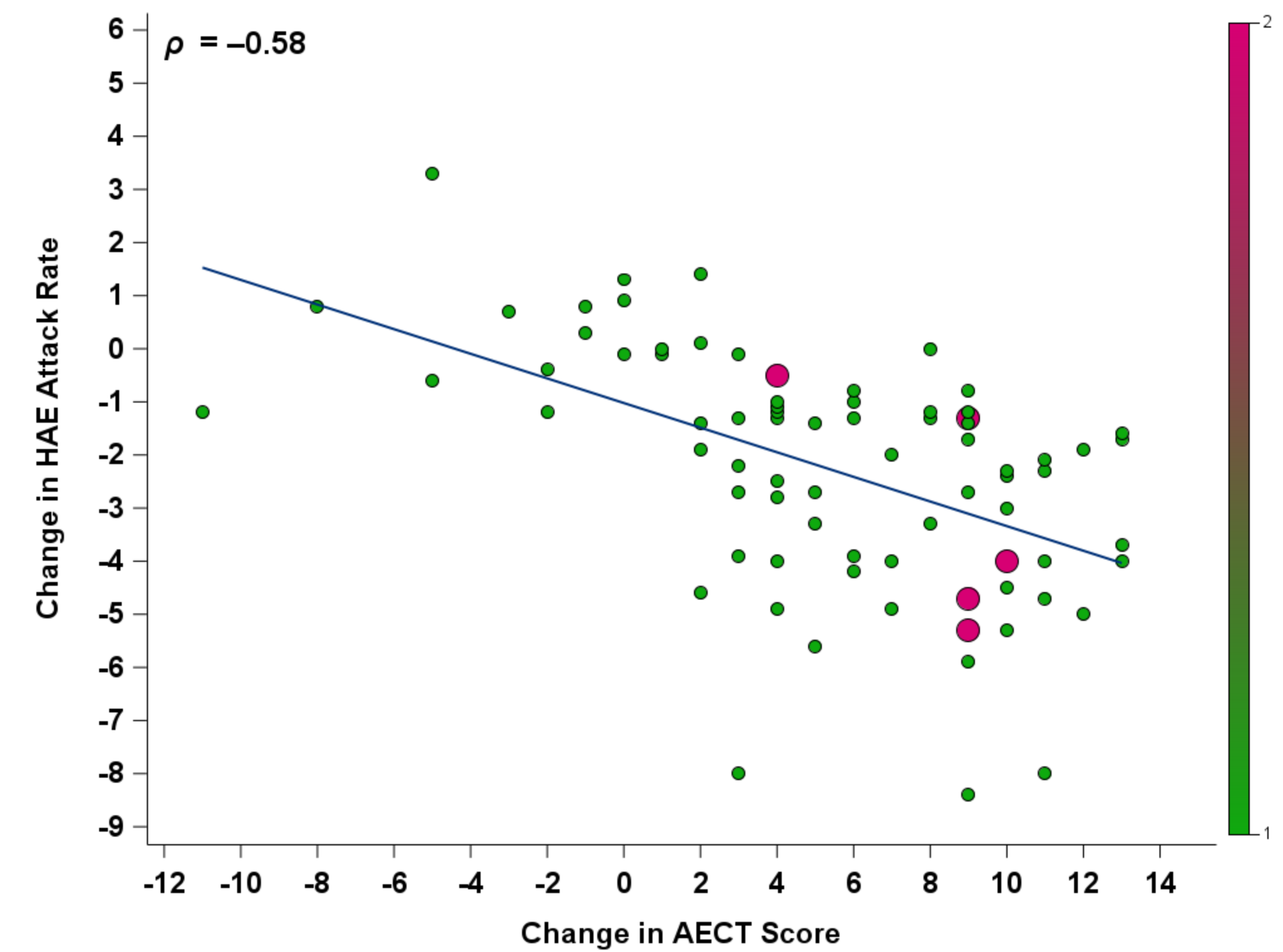
Figure 3. Mean HAE Attack Rates* between Subgroups of Patients with AECT Scores <16 and Patients with AECT Scores = 16 at Week 24



*HAE attack rate is defined as the number of investigator-confirmed HAE attacks per 4 weeks. Abbreviations: AECT, Angioedema Control Test; HAE, hereditary angioedema

- At Baseline and at Week 24, moderate-to-large Spearman correlations ($\rho = -0.40$ and -0.78 , respectively) were observed between AECT scores and HAE attack rates
- A large Spearman correlation ($\rho = -0.58$) was observed for changes in AECT scores and HAE attack rate from Baseline to Week 24 (Figure 1)

Figure 1. Bubble Plot of Change in AECT Score and Change in HAE Attack Rate, from Baseline to Week 24

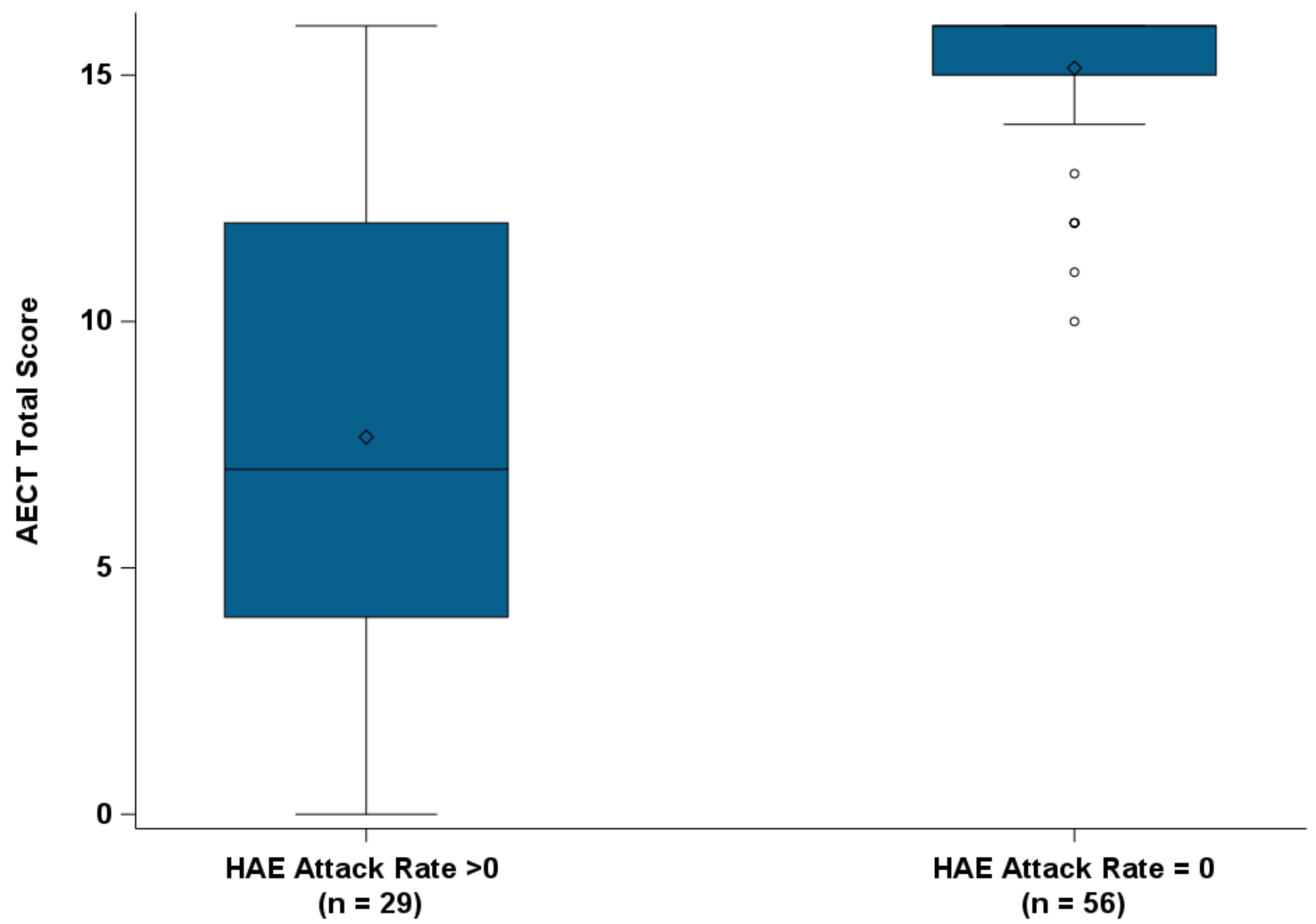


*HAE attack rate is defined as the number of investigator-confirmed HAE attacks per 4 weeks. Abbreviations: AECT, Angioedema Control Test; HAE, hereditary angioedema

- At Week 24, mean HAE attack rates differed substantially between poorly-controlled (AECT <10) and well-controlled (AECT ≥10) disease subgroups (3.29 versus 0.24, $p < 0.001$, Cohen's $d = 2.03$) (Figure 2)
- At Week 24, mean HAE attack rates differed substantially between not completely controlled (AECT <16) and completely controlled (AECT = 16) disease subgroups (1.58 versus 0.03, $p < 0.001$, Cohen's $d = 1.12$) (Figure 3)
 - 97.4% of patients reporting complete control (AECT = 16) had a monthly attack rate of 0, while the remaining patient had an attack rate of 1

- At Week 24, patients with an HAE attack rate of 0 had a mean AECT score of 15.1 points, while patients with an HAE attack rate greater than 0 had a mean AECT score of 7.7 points ($p < 0.001$, Cohen's $d = 2.14$) (Figure 4)
 - Of those patients with an attack rate of 0, 66.1% had an AECT score of 16, while none of these patients had an AECT score <10

Figure 4. Mean AECT Scores Between Patients with HAE Attack Rate >0 and Patients with HAE Attack Rate = 0 at Week 24



*HAE attack rate is defined as the number of investigator-confirmed HAE attacks per 4 weeks. Abbreviations: AECT, Angioedema Control Test; HAE, hereditary angioedema

CONCLUSIONS

- Results support strong correlation between subjective (AECT) and objective (attack rate) disease control in patients with HAE
 - Generally, there were strong associations between continuous AECT scores and HAE attack rates and between change in AECT scores and change in HAE attack rates
 - Mean attack rates differed significantly between well-controlled and poorly-controlled disease subgroups as defined by dichotomized AECT scores
 - Additionally, of 38 patients reporting complete control (AECT = 16) at Week 24, all but 1 had a monthly attack rate of 0, and the remaining patient had an attack rate of 1
 - Findings indicate that AECT scores are strongly associated with HAE attack rates

REFERENCES AND DISCLOSURES

This research was funded by Ionis. Please visit the QR code at the top of this poster to view additional disclosure and reference information.