



# THE RELATIONSHIP BETWEEN OBJECTIVE DISEASE CONTROL AT BASELINE AND CHANGE IN SUBJECTIVE DISEASE CONTROL AND QUALITY OF LIFE IN PATIENTS WITH HEREDITARY ANGIOEDEMA RECEIVING DONIDALORSEN

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## BACKGROUND

- Hereditary angioedema (HAE) is a rare form of angioedema (AE), characterized by potentially life-threatening attacks of localized severe swelling in the body<sup>1</sup>
- Patients with HAE experience impacts across multiple dimensions of quality of life (QoL), including mental and physical wellbeing<sup>2</sup>
- Donidalorsen, a novel prekallikrein-directed antisense oligonucleotide, is an FDA-approved, effective treatment for HAE that delivers significant and sustained reductions in HAE attacks<sup>1</sup>

## OBJECTIVE

- To evaluate whether change in subjective disease control and QoL varied by baseline objective disease control in 2 cohorts of HAE patients treated with donidalorsen

## METHODS

### Data Source

- Post-hoc analyses of 2 donidalorsen study cohorts:
  - 24-week, phase 3 study (**OASIS-HAE**, NCT05139810, N=90)
  - 52-week, open-label extension study (**OASISplus**, NCT05392114, N=72)

### Measures

- Objective disease control: Time-normalized, investigator-confirmed HAE attack rate, defined as number of HAE attacks during a 28-day (4-week) run-in period
  - Baseline HAE attack rate was used to define subgroups as “low” (2 or less), “moderate” (> 2 to 5), and “high” (> 5)
- Subjective disease control: Angioedema Control Test (AECT) total score
  - 4-item measure of AE symptom frequency/severity in the past month<sup>3</sup>
  - Total score ranges from 0-16; **higher scores indicate greater disease control**
  - Administered at Baseline (Week 0) and follow-up (OASIS-HAE: Week 24; OASISplus: Week 52)
- QoL: Angioedema Quality of Life Questionnaire (AE-QoL) total and domain scores
  - 17-item, symptom-specific measure of the global impact of HAE on functioning and wellbeing over a 4-week period<sup>4</sup>
  - Total and domain scores (functioning, fatigue/mood, fears/shame, nutrition) range from 0-100; **lower scores indicate better QoL**
  - Administered at Baseline (Week 0) and follow-up (OASIS-HAE: Week 24; OASISplus: Week 52)

### Statistical Analyses

- Analysis of variance (ANOVA) evaluated statistically significant differences in mean change in AECT and AE-QoL scores across baseline HAE attack rate subgroups ( $\alpha=0.05$ )
  - Bonferroni correction used to adjust for multiplicity for pairwise comparisons

## RESULTS

Similar, substantial improvements in AECT and AE-QoL scores were observed across all subgroups and study cohorts

### OASIS-HAE Cohort

- The magnitude of change in AECT total and AE-QoL total scores was similar across attack rate subgroups (**Table 1, Figure 1, Figure 2**)
- No significant differences were observed in mean change for any measure across subgroups (**Table 1**)

### OASISplus Cohort

- Improvements observed in AE-QoL total and domain scores were similar to the OASIS-HAE cohort (**Table 2, Figure 1, Figure 2**)
- At Week 52, statistically significant differences were observed for mean change in AECT total score across attack rate subgroups ( $p=0.049$ ; **Table 2**)
  - Pairwise comparisons between attack rate subgroups were not statistically significant

**Table 1. Change from Baseline to Week 24 in AECT Total and AE-QoL Total and Domain Scores by Baseline HAE Attack Rate Subgroups Among the OASIS-HAE Cohort**

	Baseline HAE Attack Rate Subgroups									p-value*
	Low			Moderate			High			
	n	Mean	SD	n	Mean	SD	n	Mean	SD	
<b>AECT Total Score</b>	26	5.6	4.2	47	5.1	5.6	14	4.9	4.5	0.908
<b>AE-QoL Score</b>										
<b>Total</b>	26	-19.7	21.0	44	-20.1	18.8	12	-21.1	19.0	0.979
<b>Functioning</b>	26	-29.9	27.2	44	-28.2	27.1	12	-34.1	31.6	0.805
<b>Fatigue/Mood</b>	26	-10.2	23.8	44	-6.5	18.2	12	-16.2	29.0	0.377
<b>Fears/Shame</b>	26	-23.7	28.0	44	-26.0	25.2	12	-18.1	17.1	0.631
<b>Nutrition</b>	26	-11.0	20.7	44	-20.7	23.5	12	-16.4	22.1	0.221

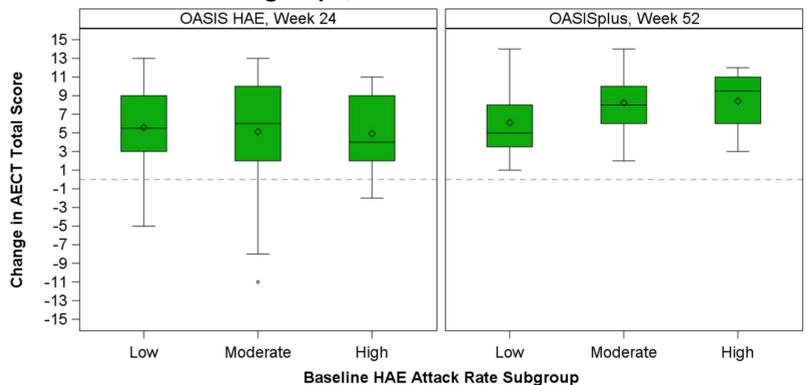
\* Based on omnibus ANOVA model. Abbreviations: AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; ANOVA, analysis of variance; HAE, hereditary angioedema; SD, standard deviation. Note(s): Baseline 4-week HAE attack rate subgroups are defined as: low (2 or less), moderate (> 2 to 5), and high (> 5).

**Table 2. Change from Baseline to Week 52 in AECT Total and AE-QoL Total and Domain Scores by Baseline HAE Attack Rate Subgroups Among the OASISplus Cohort**

	Baseline HAE Attack Rate Subgroups									p-value*
	Low			Moderate			High			
	n	Mean	SD	n	Mean	SD	n	Mean	SD	
<b>AECT Total Score</b>	20	6.1	3.4	38	8.2	2.9	12	8.4	3.2	<b>0.049</b>
<b>AE-QoL Score</b>										
<b>Total</b>	21	-26.1	19.8	39	-27.8	14.6	12	-30.7	14.4	0.744
<b>Functioning</b>	21	-33.8	21.3	39	-39.8	20.6	12	-41.4	25.5	0.511
<b>Fatigue/Mood</b>	21	-12.8	22.8	39	-8.7	17.5	12	-20.0	19.1	0.213
<b>Fears/Shame</b>	21	-34.9	27.0	39	-35.7	22.9	12	-34.4	15.7	0.983
<b>Nutrition</b>	21	-17.7	18.6	39	-27.8	20.5	12	-24.8	19.1	0.176

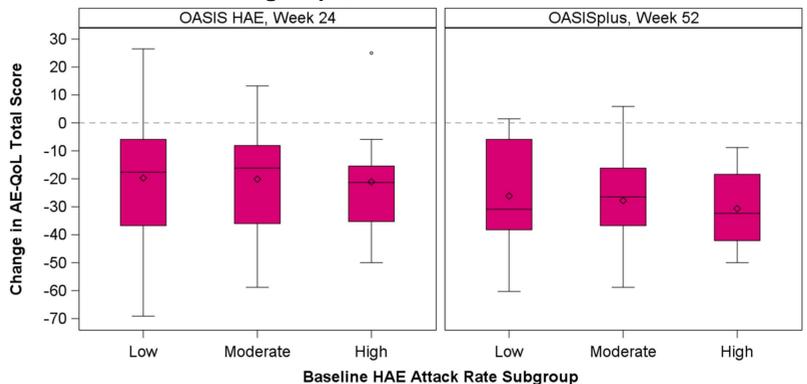
\* Based on omnibus ANOVA model. Abbreviations: AE-QoL, Angioedema Quality of Life Questionnaire; HAE, hereditary angioedema; SD, standard deviation. Note(s): Bolded values indicate significance at  $p < 0.05$ . Baseline 4-week HAE attack rate subgroups are defined as: low (2 or less), moderate (> 2 to 5), and high (> 5).

**Figure 1. Distribution of Change in AECT Total Score by Baseline HAE Attack Rate Subgroups, Across Cohorts**



Abbreviations: AECT, Angioedema Control Test; HAE, hereditary angioedema. Note(s): Baseline HAE attack rate subgroups are defined as: low (2 or less), moderate (> 2 to 5), and high (> 5).

**Figure 2. Distribution of Change in AE-QoL Total Score by Baseline HAE Attack Rate Subgroups, Across Cohorts**



Abbreviations: AE-QoL, Angioedema Quality of Life Questionnaire; HAE, hereditary angioedema. Note(s): Baseline HAE attack rate subgroups are defined as: low (2 or less), moderate (> 2 to 5), and high (> 5).

## CONCLUSIONS

- Patients with HAE who were treated with donidalorsen experienced large improvements in subjective disease control and QoL regardless of baseline HAE attack rate
- Improvements in subjective disease control and QoL in OASIS-HAE were maintained as participants transitioned into OASISplus
- While mean differences in scores varied slightly across attack rate subgroups, most differences were not statistically significant
  - In the OASISplus cohort, omnibus ANOVA testing was statistically significant, but post hoc tests were not
  - Lack of significant findings could be due to sample size imbalances across subgroups, which impacted the power to detect differences

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## DISCLOSURES

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