Patient-Reported Disease Control, Work Productivity, and Activity Impairment in Hereditary Angioedema: Insights from OASIS-HAE

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BACKGROUND

- Hereditary angioedema (HAE) is a rare form of angioedema characterized by episodes of localized severe swelling in the body[1]
- HAE attacks significantly impair patient quality of life (QoL), affecting both physical and psychological well-being, due to the severity of symptoms and the unpredictability of attacks[2]
- The negative impact of HAE on QoL has been well-established;[1-4] however, further inquiry into how HAE impacts specific areas of patients' daily lives is warranted

OBJECTIVE

- To evaluate the relationship between patient-reported disease control and work/school productivity and activities among patients with HAE

METHODS

Data Source

- Post-hoc analyses of the 24-week, phase 3 OASIS-HAE study (NCT05139810) of donidalorsen, a novel prekallikrein-directed antisense oligonucleotide for treatment of HAE, versus placebo (n=90, pooled sample)[5]

Patient-Reported Outcome Assessments (Administered at Baseline and Week 24)

- Angioedema Control Test (AECT): a 4-item measure of angioedema symptom frequency/severity in the past month[6]
  - Scores range 0-16; higher scores indicate greater control
- Work Productivity and Activity Impairment plus Classroom Impairment Questionnaire (WPAI+CIQ): a 10-item measure of the impact of a specific health condition on employment/school impairment, work/school productivity, absence, and regular activities[7]
  - Scores are calculated as the mean of weekly domain scores (absenteeism, presenteeism, overall productivity impairment, activity impairment) over a 4-week period, and are presented as the percentage impairment or productivity loss
  - Higher scores indicate greater impairment and less productivity

Statistical Analyses

- Subgroups were defined at Week 24 as 1) poorly versus well-controlled (AECT<10 versus AECT≥10),[8] and 2) less-than-complete versus complete control (AECT<16 versus AECT=16)
- Better disease control (higher AECT scores) was hypothesized to be associated with less work/school and activity impairment (lower WPAI+CIQ scores)
- Mean scores across disease control subgroups were compared using t-tests and associated Cohen's d effect sizes at Week 24

$$d = \frac{\text{mean}_{\text{group1}} - \text{mean}_{\text{group2}}}{\text{standard deviation}_{\text{pooled}}} \quad [9]$$

RESULTS

### Table 1. Mean Differences in WPAI+CIQ Domain Scores By Disease Control Subgroups at Week 24

Poorly Controlled versus Well-Controlled Disease

	AECT<10			AECT≥10			Mean Difference (95% CI)	p-value
	n	Mean	SD	n	Mean	SD		
Absenteeism	11	8.1	14.2	52	2.0	6.2	6.1 (-3.5, 15.7)	0.190
Presenteeism	10	29.8	20.1	52	4.2	9.2	**25.6** (11.1, 40.1)	**0.003**
Overall Productivity Impairment	10	34.9	24.6	52	5.8	9.9	**29.1** (11.4, 46.8)	**0.005**
Activity Impairment	17	42.2	26.0	65	7.7	16.5	**34.5** (20.7, 48.4)	**<0.001**

Less-Than-Complete versus Complete Disease Control

	AECT<16			AECT=16			Mean Difference (95% CI)	p-value
	n	Mean	SD	n	Mean	SD		
Absenteeism	35	4.7	10.1	28	1.1	4.7	3.6 (-0.3, 7.5)	0.067
Presenteeism	34	12.9	17.7	28	2.8	7.7	**10.1** (3.4, 16.9)	**0.004**
Overall Productivity Impairment	34	16.0	20.0	28	3.8	8.8	**12.2** (4.5, 19.8)	**0.003**
Activity Impairment	46	20.5	24.7	36	7.6	19.6	**12.9** (2.9, 22.9)	**0.012**

Abbreviations: AECT, Angioedema Control Test; CI, confidence interval; SD, standard deviation; WPAI+CIQ, Work Productivity and Activity Impairment plus Classroom Impairment Questionnaire.

Notes: n represents the number of patients within each subgroup who provided scores for each WPAI domain. WPAI domain scores are percentage impairment or productivity loss; greater scores indicate greater impairment/less productivity. Bolded values indicate significant differences between subgroups at $p<0.05$.

Figure 1. Comparing the Magnitude of Mean Differences in WPAI+CIQ Domain Scores by Disease Control Group
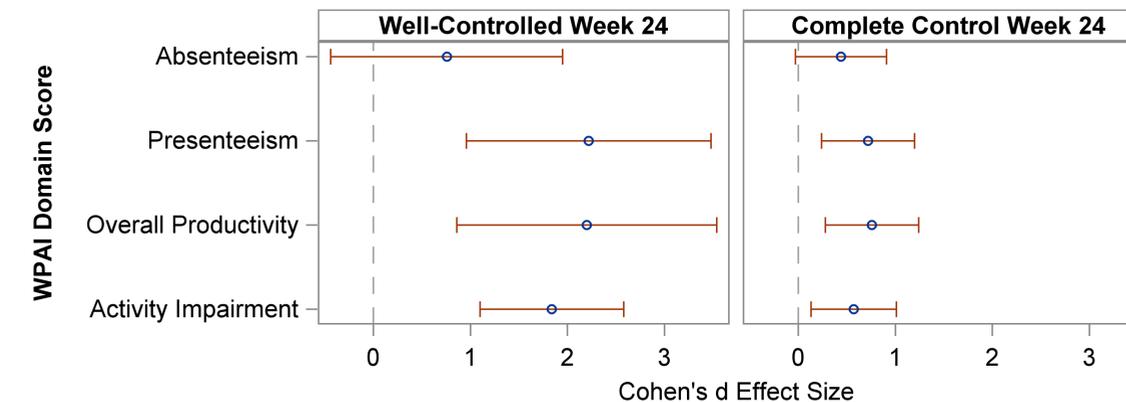
Abbreviations: WPAI+CIQ, Work Productivity and Activity Impairment plus Classroom Impairment Questionnaire.
Note: Magnitude of mean difference (Cohen's d) can be interpreted as $d<0.2$: negligible; 0.2 to 0.49: small; 0.5 to 0.79: medium; ≥0.8: large[9]

At Week 24, significant differences in mean scores were observed for both disease control subgroups across all WPAI+CIQ domains, except absenteeism

- Patients with well-controlled disease had significantly more favorable mean scores on presenteeism, overall productivity impairment, and activity impairment domains (all $p<0.05$) than those with poorly controlled disease; scores for the absenteeism domain were in the hypothesized direction, but did not reach statistical significance (**Table 1**)
  - Effect sizes for significant domains were large (all $d>1.80$) (**Figure 1**)
- Patients with complete disease control had significantly more favorable mean scores on presenteeism, overall productivity impairment, and activity impairment domains (all $p<0.05$) than those with less-than-complete control; absenteeism domain scores did not reach statistical significance (**Table 1**)
  - Effect sizes for significant domains were medium-sized ($d=0.57$ to 0.76) (**Figure 1**)

CONCLUSIONS

- In the OASIS-HAE clinical study, patients with HAE with well- or completely-controlled disease experienced significantly less impairment on work/school productivity and activities
  - Patients did not need complete control over their HAE to experience benefits
- This study provides continuing evidence that the symptoms of HAE can significantly impair daily activities and engagement in work/school for patients

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DISCLOSURES