Poster 648

Improvements in Quality-of-Life in Patients with HAE Receiving Donidalorsen: Post Hoc Analysis from the OASIS-HAE Study

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BACKGROUND

- Hereditary angioedema (HAE) is a rare form of angioedema characterized by attacks of cutaneous and submucosal swelling[1]
- Patients with HAE are highly motivated to switch to improved dosing (e.g., route, frequency), reducing treatment burden and improving quality-of-life (QoL)[2]
- The Angioedema Quality of Life Questionnaire (AE-QoL) is a 17-item, disease-specific, 4-week recall, patient-reported questionnaire capturing the global impact of angioedema (AE) attacks on functioning and well-being[2]
- In the phase 3, double-blind, placebo-controlled OASIS-HAE study (NCT05139810), donidalorsen 80 mg, an antisense oligonucleotide targeting prekallikrein mRNA, administered every 4 weeks (Q4W) or every 8 weeks (Q8W), significantly improved overall health-related QoL (HRQoL) from Baseline (Week 0) to Week 24, as captured by AE-QoL total scores, versus placebo in patients with HAE[1]

OBJECTIVE

- To further explore the impact of donidalorsen, relative to placebo, on overall and specific HRQoL using post hoc analyses on data from OASIS-HAE

METHODS

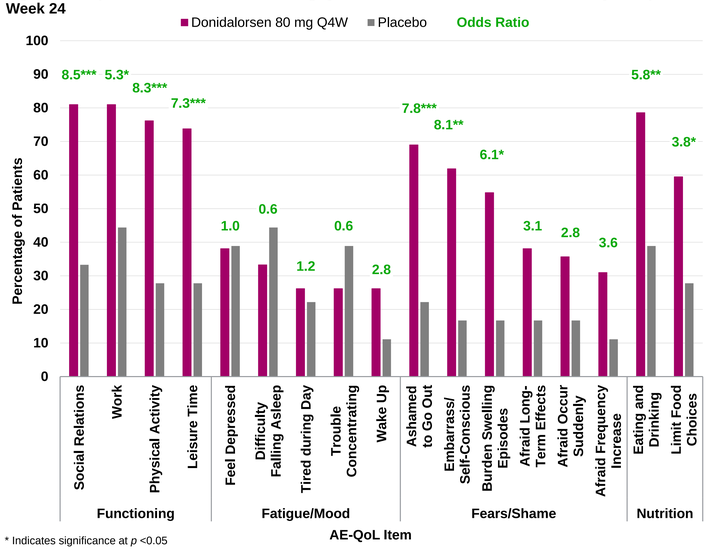
- In OASIS-HAE, patients with HAE received donidalorsen 80 mg or placebo subcutaneously Q4W or Q8W over 24 weeks
  - Analyses combined placebo groups from the 2 treatment arms of the OASIS-HAE study (“pooled placebo,” referred to hereafter as “placebo”)
- Analyses included all dosed patients (N = 90)
- All *p*-values are nominal and were not corrected for multiplicity of testing
- AE-QoL was administered at Baseline (Week 0) and at Week 24
  - All 17 AE-QoL items are scored using a 5-point response scale, with impact of AE attacks on QoL coded from 0 (“never”) to 4 (“very often”)
  - Total score, based on responses to all 17 items, is scaled from 0 to 100, with lower scores indicating better QoL
  - AE-QoL total score classified as “no HRQoL impact” at <24; “small HRQoL impact” from ≥24 to <39; and “moderate to large HRQoL impact” at ≥39[3]
- Item-level analysis for Q4W donidalorsen group at Week 24 included:
  - “No HRQoL impact,” defined by a response of “never” (0) for each AE-QoL item
  - Percentage of “no HRQoL impact” (i.e., patients responding "never") compared between Q4W donidalorsen group and placebo
  - Logistic regression, to model odds of having “no HRQoL impact” between Q4W and placebo groups
  - Fisher’s exact test (*p*-value <0.05) tested statistical significance between Q4W donidalorsen group and placebo
- Scale-level analysis for Q4W and Q8W donidalorsen groups at Baseline and Week 24 included:
  - Percentage of patients with AE-QoL total scores indicating “no HRQoL impact” (total score <24) and “any HRQoL impact” (total score ≥24) reported for each donidalorsen group and placebo
  - Logistic regression, to model odds of the dichotomous HRQoL outcome (i.e., “no HRQoL impact”) based on donidalorsen treatment groups with placebo as comparison group
  - Fisher’s exact test, to determine statistically significant differences (*p*-value <0.05)

RESULTS

- Week 24 assessments were completed by 42 (Q4W), 22 (Q8W), and 18 (placebo) patients
- A significantly larger percentage of patients treated with Q4W donidalorsen compared to placebo (all $p < 0.05$) responded “never” to 9 out of 17 AE-QoL items (Figure 1)
  - Items showing statistically significant differences included all Functioning domain items (Social Relations, Work, Physical Activity, Leisure Time); 3 Fears/Shame domain items (Ashamed to Go Out, Embarrass/Self-Conscious, Burden Swelling Episodes); and all Nutrition domain items (Eating and Drinking, Limit Food Choices)
  - Items not showing statistically significant differences included those in the Fatigue/Mood domain (Depression, Sleep Problems, Concentration Problems) and items related to fears of long-term treatment side effects, suddenly occurring attacks, or more frequent attacks

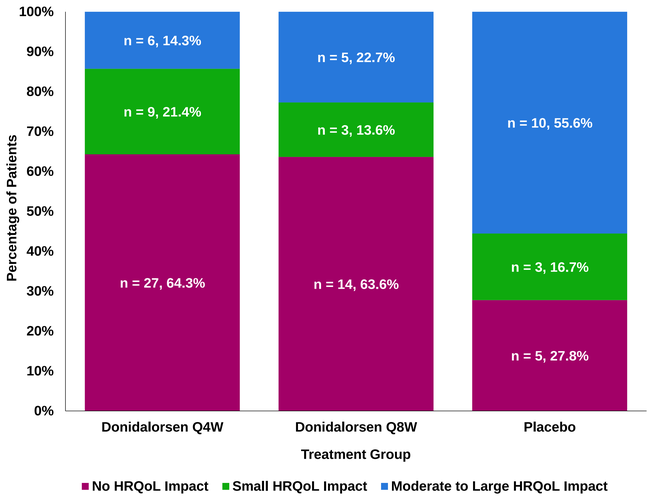
- At Baseline, the percentage of patients indicating no HRQoL impact (i.e., AE-QoL total score <24) did not differ between donidalorsen Q4W (13.3%) or Q8W (8.7%) compared to placebo (9.1%; all $p = 1.000$)
- At Week 24, a significantly larger percentage of patients receiving donidalorsen Q4W (64.3%, OR [95% CI] = 4.7 [1.5 – 17.0], $p = 0.012$) or Q8W (63.6%, OR [95% CI] = 4.5 [1.2 – 18.9], $p = 0.031$) indicated no impact compared to placebo (27.8%) (Figure 2)

Figure 1. Proportion of Donidalorsen 80 mg Q4W and Placebo Patients with No HRQoL Impact† at Week 24



* Indicates significance at $p < 0.05$
** Indicates significance at $p < 0.01$
*** Indicates significance at $p < 0.001$
† No HRQoL impact is defined by “never” (0) response.
Note: Odds ratios are presented above each AE-QoL item.
Abbreviations: AE-QoL, Angioedema Quality of Life Questionnaire; HRQoL, health-related quality of life; Q4W, every 4 weeks

Figure 2. Categorized AE-QoL Total Scores Comparing Donidalorsen 80 mg Q4W and Donidalorsen 80 mg Q8W to Placebo, at Week 24



Note: No HRQoL impact is defined by AE-QoL total score <24. Small HRQoL impact is defined by AE-QoL total score ≥24 and <39. Moderate to large HRQoL impact is defined by AE-QoL total score ≥39.
Abbreviations: AE-QoL, Angioedema Quality of Life Questionnaire; HRQoL, health-related quality of life; Q4W, every 4 weeks; Q8W, every 8 weeks

CONCLUSIONS

- Treatment with donidalorsen Q4W, compared with placebo, resulted in significantly less QoL impairment, particularly decreasing impacts on social relations, work, physical activity, leisure, shame and self-consciousness about appearance, burden related to swelling episodes, and nutrition
  - A significantly larger percentage of patients treated Q4W responded “never” to 9 AE-QoL items, compared to the placebo group
    - More patients in the Q4W group responded “never” for all Functioning domain items and all Nutrition domain items
    - Outcomes for several items from the Fears/Shame domain also significantly favored donidalorsen treatment
  - No statistically significant treatment group differences were found for any of the items in the Fatigue/Mood domain
- At Week 24, patients with HAE treated with donidalorsen had better global QoL compared to patients in the placebo group
  - 64.3% of patients receiving donidalorsen Q4W and 63.6% of patients receiving donidalorsen Q8W indicated no HRQoL impact compared to 27.8% of patients receiving placebo
- These post hoc analyses provide evidence that donidalorsen is associated with better overall QoL compared to placebo
  - Patients treated Q4W with donidalorsen, compared to placebo, had significantly less impairments on the majority of assessed QoL domains

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.