Poster #R076

Donidalorsen for the Treatment of Hereditary Angioedema: 1-Year Results From the OASISplus Open-Label Extension Study

Raffi Tachdjian[1], Laura Bordone[2], Kenneth B Newman[2], Sabrina Treadwell[2], Tao Lin[2], Aaron Yarlas[2], Marc A Riedl[3], Danny M Cohn[4]

[1]Division of Allergy, Immunology, and Rheumatology, University of California, Los Angeles, Los Angeles, CA, USA; [2]Ionis, Carlsbad, CA, USA; [3]Division of Allergy and Immunology, University of California San Diego School of Medicine, La Jolla, CA, USA; [4]Department of Vascular Medicine, Amsterdam Cardiovascular Sciences, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

Introduction

- Hereditary angioedema (HAE) is a rare, debilitating disease characterized by recurrent, unpredictable, and potentially life-threatening attacks of tissue swelling[1,2]
- HAE attacks are associated with significant functional impairment, decreased psychological well-being, health-related quality of life (QoL), and work productivity[3,4]

Figure 1. Donidalorsen Mechanism of Action

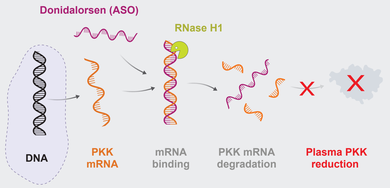
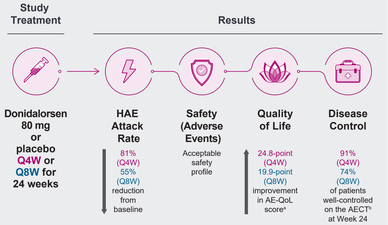


Figure created using BioRender (https://www.biorender.com/).
ASO, antisense oligonucleotide; mRNA, messenger RNA; PKK, prekallikrein; RNase H1, ribonuclease H1.

- Donidalorsen is an RNA-targeted antisense oligonucleotide that specifically and reversibly reduces plasma prekallikrein production in the liver[1]
- Donidalorsen is indicated for prophylaxis to prevent attacks of HAE in adult and pediatric patients 12 years of age and older[5]

Figure 2. Overview of the OASIS-HAE Study

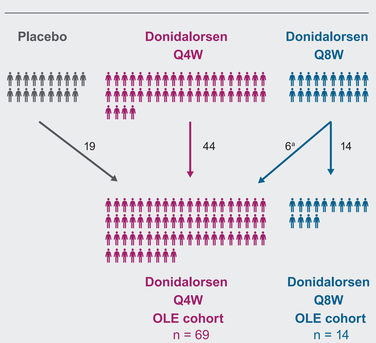


[a]Improvement in QoL is defined as a reduction in AE-QoL total score.
[b]Defined as an AECT total score ≥10.[6]
AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; HAE, hereditary angioedema; Q4W, once every 4 weeks; Q8W, once every 8 weeks; QoL, quality of life.

- In the phase 3 OASIS-HAE study, patients ≥12 years of age with HAE received donidalorsen 80 mg or placebo subcutaneously (SC) once every 4 weeks (Q4W) or 8 weeks (Q8W) for 24 weeks[7]
- Here, we report 1-year results for donidalorsen from the open-label extension (OLE) cohort of the ongoing OASISplus study (NCT05392114)

Study Design

Figure 3. OASISplus OLE Cohort



[a]Patients who were not attack free for ≥8 weeks (Weeks 16–24 in OASIS-HAE) received donidalorsen 80 mg SC Q4W.
OLE, open-label extension; Q4W, once every 4 weeks; Q8W, once every 8 weeks; SC, subcutaneously.

- Patients who completed the OASIS-HAE study or exited the study per protocol were eligible for enrollment in the OLE cohort of the OASISplus study
- Patients aged ≥12 years with HAE caused by C1 inhibitor (C1INH) deficiency (HAE-C1INH-Type1) or dysfunction (HAE-C1INH-Type2) were included in the study
- In the OASISplus OLE, patients received donidalorsen 80 mg SC per their original dosing schedule in OASIS-HAE
  - Patients who were not attack free for ≥8 weeks (Weeks 16–24 in OASIS-HAE) received donidalorsen 80 mg SC Q4W
- Endpoints reported here include
  - Incidence and severity of treatment-emergent adverse events (TEAEs; primary endpoint)
  - Rate of HAE attacks/month
  - Angioedema Quality of Life Questionnaire (AE-QoL)
    - Scored 0–100; higher scores indicate worse QoL[8]
  - Angioedema Control Test (AECT)
    - Scored 0–16 points; higher scores indicate greater disease control[6]
    - AECT ≥10 points indicated well-controlled disease[6]
  - Treatment Satisfaction Questionnaire for Medication, version II (TSQM-II)
    - Scored 0–100; higher scores indicate greater treatment satisfaction
- OLE data are shown from an interim January 27, 2025, data cutoff

Results

Table 1. Patient Disposition and Demographics

	Donidalorsen Q4W	Donidalorsen Q8W	Total
Patients dosed[a]	69	14	83
Completed 1 year, n (%)	61 (88.4)	14 (100.0)	75 (90.4)
Main reason for discontinuation, n (%)			
Voluntary withdrawal	5 (7.2)	0	5 (6.0)
Any adverse event	3 (4.3)	0	3 (3.6)
Age, years, mean (SD)	38 (14.1)	30 (9.0)	37 (13.7)
Age category, years			
12–17	5 (7.2)	2 (14.3)	7 (8.4)
18–39	32 (46.4)	10 (71.4)	42 (50.6)
40–64	31 (44.9)	2 (14.3)	33 (39.8)
≥65	1 (1.4)	0	1 (1.2)
Sex, n (%)			
Male	29 (42.0)	9 (64.3)	38 (45.8)
Female	40 (58.0)	5 (35.7)	45 (54.2)
Race, n (%)			
White	62 (89.9)	14 (100.0)	76 (91.6)
American Indian/ Alaska Native	3 (4.3)	0	3 (3.6)
Black or African American	1 (1.4)	0	1 (1.2)
Asian	1 (1.4)	0	1 (1.2)
Multiple	1 (1.4)	0	1 (1.2)
Other[b]	1 (1.4)	0	1 (1.2)
BMI, kg/m², mean (SD)	27.8 (6.6)	26.9 (5.4)	27.6 (6.4)
Baseline HAE attack rates			
Mean (SD)	3.5 (2.1)	2.9 (2.1)	3.4 (2.1)
Median	3.0	2.3	3.0
Treatment duration, days			
Median	392.3	392.5	392.3
Min, max	55.9, 412.0	390.0, 411.0	55.9, 412.0

[a]The full analysis and safety sets included all dosed patients.
[b]Patients could select "Other" on the clinical report form and write in an answer.
BMI, body mass index; HAE, hereditary angioedema; max, maximum; min, minimum; Q4W, once every 4 weeks; Q8W, once every 8 weeks; SD, standard deviation.

- As of the data cutoff date (January 27, 2025), 75 of 83 (90%) randomized patients completed the study treatment through Week 52
- Early treatment discontinuation rates were low, with 3 (3.6%) patients discontinuing due to adverse events (1 [1.2%] was treatment-related), and 5 (6.0%) discontinuing voluntarily
- Median exposure to donidalorsen was 392.3 days

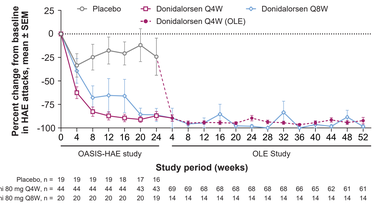
Table 2. Summary of Adverse Events

n (%)	Donidalorsen Q4W (n = 69)	Donidalorsen Q8W (n = 14)	Total (N = 83)
Any TEAE	64 (92.8)	11 (78.6)	75 (90.4)
Related to study drug[a]	19 (27.5)	3 (21.4)	22 (26.5)
Leading to discontinuation	3 (4.3)	0	3 (3.6)
Any serious TEAE	7 (10.1)	0	7 (8.4)
Related to study drug[a]	0	0	0
Severity of TEAE			
Mild	28 (40.6)	5 (35.7)	33 (39.8)
Moderate	31 (44.9)	5 (35.7)	36 (43.4)
Severe	5 (7.2)	1 (7.1)	6 (7.2)
Most common TEAEs (>10% of all patients)			
Influenza	13 (18.8)	2 (14.3)	15 (18.1)
Nasopharyngitis	11 (15.9)	4 (28.6)	15 (18.1)
Back pain	9 (13.0)	3 (21.4)	12 (14.5)
Headache	10 (14.5)	1 (7.1)	11 (13.3)
Upper respiratory tract infection	10 (14.5)	0	10 (12.0)
COVID-19	9 (13.0)	1 (7.1)	10 (12.0)

Safety set.
[a]Defined as "Related," "Possible," or missing relationship to study drug.
COVID-19, coronavirus disease 2019; Q4W, once every 4 weeks; Q8W, once every 8 weeks; TEAE, treatment-emergent adverse event.

- Most TEAEs were mild or moderate in severity and non–treatment-related
- The most common TEAEs were influenza, nasopharyngitis, back pain, headache, upper respiratory tract infection, and COVID-19
- The most common treatment-related TEAE was injection-site discoloration (Q4W, 6%; Q8W, 7%)

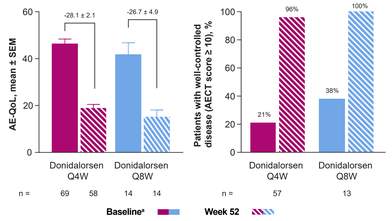
Figure 4. HAE Attack Rate Through Week 52



Doni, donidalorsen; HAE, hereditary angioedema; OLE, open-label extension; Q4W, once every 4 weeks; Q8W, once every 8 weeks; SEM, standard error of the mean.

- Over Weeks 0–52, the mean HAE attack rate decreased from OASIS-HAE baseline by 94% in both groups

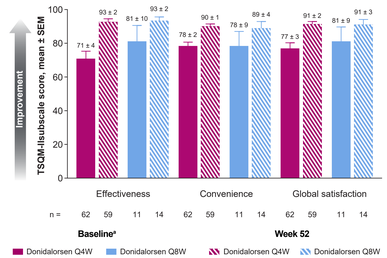
Figure 5. (A) AE-QoL Total Scores and (B) Percentage of Patients With Well-Controlled Disease (AECT ≥10) at OASIS-HAE Baseline and Week 52 of OASISplus



Mean ± SEM reductions in AE-QoL total score from baseline to Week 52 of OASISplus are presented above the bars. A minimal clinically important difference is ≥6 points.[9]
[a]Week 0 in the OASIS-HAE study.
AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; Q4W, once every 4 weeks; Q8W, once every 8 weeks; SEM, standard error of the mean.

- Patients reported clinically meaningful (≥6 points) improvements in mean AE-QoL total score (Q4W, 28.1 points; Q8W, 26.7 points)
- At Week 52, 97% of patients reported well-controlled disease on the AECT (total score ≥10)[9]

Figure 6. TSQM-II Scores at OASIS-HAE Baseline and at Week 52

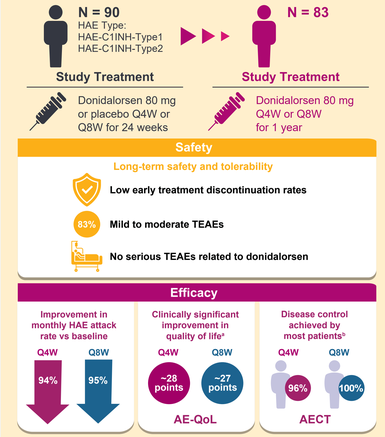


[a]Week 0 of the OASISplus study.
Q4W, once every 4 weeks; Q8W, once every 8 weeks; SEM, standard error of the mean; TSQM-II, Treatment Satisfaction Questionnaire for Medication, version II.

- Treatment satisfaction scores were high (≥88 points) across all domains at Week 52 for both dosing groups
- Due to few reported side effects at Week 52, the side effects subscale score was inconclusive

Conclusions

- At 1 year, donidalorsen had acceptable safety and led to a sustained reduction in HAE attack rate and corresponding improvements in patient-reported QoL, disease control, and treatment satisfaction, supporting its potential for long-term management of HAE



[a]Improvement in QoL is defined as a ≥6-point reduction in AE-QoL total score.[9]
[b]Well-controlled disease on the AECT is defined as a total score ≥10.[6]
AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; HAE, hereditary angioedema; Q4W, once every 4 weeks; Q8W, once every 8 weeks; QoL, quality of life; TEAE, treatment-emergent adverse event.

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DISCLOSURES

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ucladoc@gmail.com