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Treatment Of Hereditary Angioedema: Safety, Efficacy, And Patient Preference After Switching To Donidalorsen (OASISplus Study)

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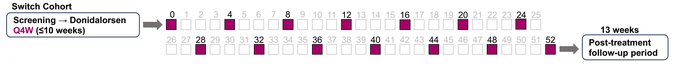
INTRODUCTION

- Hereditary angioedema (HAE) is a rare, chronic disease characterized by frequently severe and potentially fatal attacks of tissue swelling[1-3]
- HAE is most frequently caused by either C1 inhibitor (C1-INH) deficiency (HAE-C1INH-Type1) or dysfunction (HAE-C1INH-Type2), which leads to kallikrein-kinin system dysregulation[1-3]
- Donidalorsen is an investigational RNA-targeted antisense oligonucleotide that specifically reduces plasma prekallikrein production in the liver[4]
- The phase 3 OASIS-HAE study (NCT05139810) demonstrated the efficacy of donidalorsen 80 mg administered subcutaneously (SC) once every 4 weeks (Q4W) or every 8 weeks (Q8W) in patients with HAE[4]
- Here, we report interim results of patients with HAE who switched from a prior long-term prophylactic (LTP) treatment to donidalorsen (**Switch cohort**) in the ongoing OASISplus open-label extension study (NCT05392114)

METHODS

Figure 1. Study Design



Q4W, once every 4 weeks.

- Patients ≥12 years of age with HAE-C1INH-Type1 or HAE-C1INH-Type2 and on stable doses of lanadelumab, berotralstat, or C1-INH for ≥12 weeks switched, using a predefined algorithm without washout, to donidalorsen 80 mg Q4W:
  - Lanadelumab: The last dose of lanadelumab was administered 14 ± 3 days prior to first dose of donidalorsen
  - Berotralstat: Patients continued taking berotralstat for 14 ± 3 days after the first dose of donidalorsen
  - C1-INH: Patients continued taking C1-INH for 14 ± 3 days after the first dose of donidalorsen
- Primary endpoint: Incidence of treatment-emergent adverse events (TEAEs)
- Other endpoints:
  - Time-normalized rate of investigator-confirmed HAE attacks per month (HAE attack rate) over Weeks 0–52
  - Angioedema Quality of Life (AE-QoL) questionnaire total score at Week 16
  - Well-controlled disease, defined as an Angioedema Control Test (AECT) total score ≥10, at Week 16[5]
  - Treatment preference survey at Week 16
    - The de novo, ad hoc treatment preference survey was scored on a 5-point Likert-type preference scale, ranging from "strong preference" for donidalorsen to "strong preference" for the prior LTP
  - Treatment Satisfaction Questionnaire for Medication II (TSQM-II) at Week 16
- Interim results are reported from a February 2024 data cut

RESULTS

Table 1. Patient Demographics and Disposition

	Patients switching to donidalorsen 80 mg Q4W from:			
	Lanadelumab (n = 31)	Berotralstat (n = 11)	C1-INH (n = 22)	Total (N = 64)
Age, years, mean (SD)	40 (14)	46 (11)	41 (17)	42 (15)
Age, years, n (%)				
12–17 years old	1 (3)	0	3 (14)	4 (6)
≥18 years old	30 (97)	11 (100)	19 (86)	60 (94)
Sex, n (%)				
Male	17 (55)	3 (27)	6 (27)	26 (41)
Female	14 (45)	8 (73)	16 (73)	38 (59)
Race,[a] n (%)				
White	26 (84)	11 (100)	20 (91)	57 (89)
Multiple or other[b]	5 (16)	0	2 (9)	7 (11)
Patients enrolled, n	32	11	22	65
Patients dosed, n	31	11	22	64
Completed Week 16 of treatment, n (%)	28 (88)	10 (91)[c]	20 (91)	58 (89)
Early termination, n (%)				
Lack of efficacy	3 (10)	0	1 (5)	4 (6)
Serious adverse event	1 (3)	0	0	1 (2)
Lost to follow-up	1 (3)	0	0	1 (2)
Voluntary withdrawal	0	0	1 (5)	1 (2)
Other (not dosed)	1 (3)	0	0	1 (2)

[a]Race was self-reported by patients during screening. [b]Includes American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, multiple races, and "other." [c]One patient in the berotralstat group has not reached Week 16 of treatment but is ongoing in the study.
C1-INH, C1 inhibitor; Q4W, once every 4 weeks; SD, standard deviation.

- As of February 2024, 56 of 64 dosed patients (88%) were ongoing in the study
- Mean donidalorsen exposure was 263 days

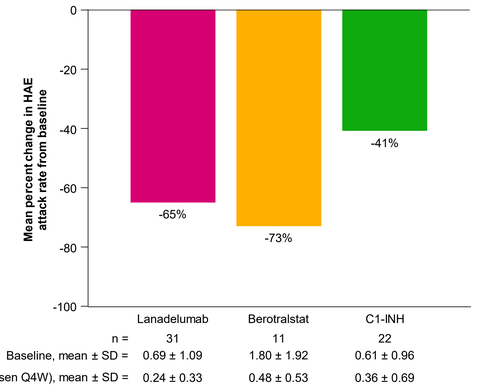
Table 2. Incidence and Severity of TEAEs

	Donidalorsen Q4W (N = 64)
Any TEAE,[a] n (%)	50 (78)
Related to study drug	21 (33)
Leading to discontinuation	1 (2)
Any serious TEAE, n (%)	1 (2)
Related to study drug	0
Severity of TEAEs, n (%)	
Mild	19 (30)
Moderate	26 (41)
Severe	5 (8)
Severity of TEAEs related to study drug, n (%)	
Mild	15 (23)
Moderate	5 (8)
Severe	1[b] (2)
Most common TEAEs[a] (≥10% of all patients), n (%)	
Upper respiratory tract infection	14 (22)
Nasopharyngitis	12 (19)
Injection-site erythema	9 (14)
Injection-site pruritus	7 (11)
Headache	7 (11)

[a]TEAE is defined as any adverse event starting or worsening on or after the first dose of donidalorsen.
[b]The TEAE was a headache, and no action was taken with the study drug
Q4W, once every 4 weeks; TEAE, treatment-emergent adverse event

- One TEAE that was not related to study drug led to treatment discontinuation
- No serious TEAEs were related to donidalorsen, and most TEAEs were at most mild or moderate in severity

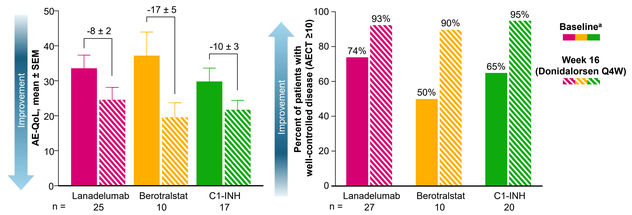
Figure 2. Time-Normalized Number of HAE Attacks Per Month (Weeks 0–16)



Baseline HAE attack rate during the screening period for the Switch cohort.
C1-INH, C1 inhibitor; HAE, hereditary angioedema; SD, standard deviation.

- Patients with HAE who switched from prior LTPs to donidalorsen Q4W had a mean 62% reduction from baseline in HAE attack rate

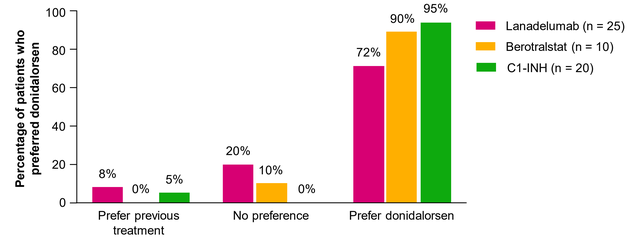
Figure 3. Patient-Reported Outcomes at Baseline and Week 16



[a]Week 0 in the OASISplus study.
AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; C1-INH, C1 inhibitor; Q4W, once every 4 weeks; SEM, standard error of the mean.

- Regardless of their prior LTP treatment, on average, patients who switched to donidalorsen reported clinically significant improvements (≥6-point reduction[6]) in AE-QoL total score from baseline to Week 16
- More patients self-reported disease control after switching to donidalorsen

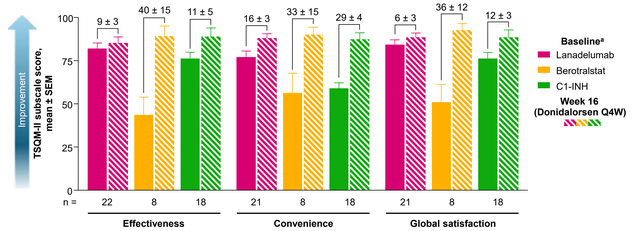
Figure 4. Patient-Reported Treatment Preference at Week 16



C1-INH, C1 inhibitor.

- Most patients preferred treatment with donidalorsen, regardless of their previous treatment
  - Overall, 84% of patients preferred donidalorsen, with 66% expressing a strong preference
- Patients most frequently selected the following reasons for their treatment preference:
  - **Lanadelumab**: Less injection-site pain or reactions with donidalorsen
  - **Berotralstat**: Better disease control with donidalorsen
  - **C1-INH**: Less time for administration with donidalorsen

Figure 5. Patient-Reported Treatment Satisfaction at Baseline and Week 16



[a]Baseline assessment during the screening period for the switch cohort.
C1-INH, C1 inhibitor; Q4W, once every 4 weeks; SEM, standard error of the mean; TSQM-II, Treatment Satisfaction Questionnaire for Medication II.

- Patients reported greater effectiveness, convenience, and satisfaction scores on the TSQM-II at Week 16 of donidalorsen treatment compared with their pre-switch baseline assessment

CONCLUSIONS

- In this cohort of patients in the OASISplus study who switched from a previous LTP to donidalorsen 80 mg SC Q4W:

Safety and Tolerability

- Donidalorsen had an acceptable safety and tolerability profile

Efficacy

- By Week 16, patients had a mean 62% reduction from baseline in HAE attack rate

Quality of Life and Disease Control

- Patients reported improved quality of life and disease control

Treatment Preferences and Satisfaction

- The large majority of patients preferred donidalorsen over their previous LTP, and patients were more satisfied with donidalorsen than their previous LTP

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DISCLOSURES

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