Abstract #494

An Open-label Trial with Donidalorsen in Hereditary Angioedema Patients with Normal C1-inhibitor

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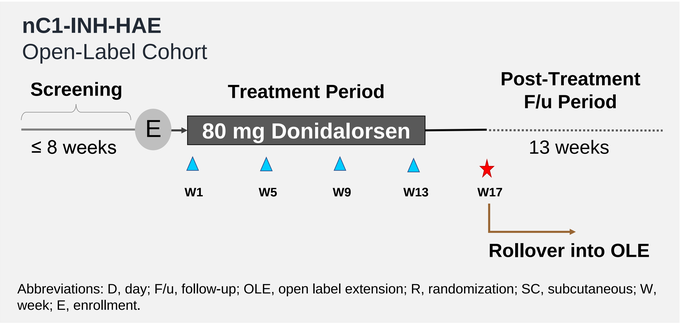
Rationale

- Hereditary angioedema with normal C1-inhibitor (nC1-INH-HAE) is a very rare condition, characterized by recurrent and unpredictable swellings which are disabling and potentially fatal
- There are currently no approved prophylactic treatments for this condition
- In a phase 2 study, we assessed efficacy and safety following treatment with oligonucleotide antisense therapy targeted against plasma prekallikrein (donidalorsen/PKK-L_{Rx}) in patients with nC1-INH-HAE

Methods

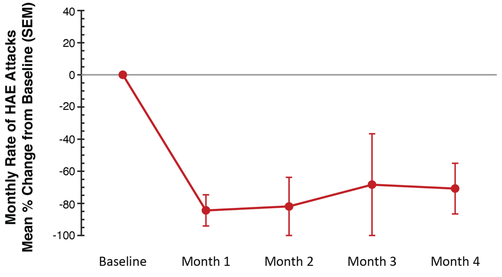
- Patients with nC1-INH-HAE were eligible if they had:
  - one of the established mutations associated with nC1-INH-HAE in the genes encoding for factor XII, plasminogen orangiopoietin-1 OR
  - a clinical diagnosis of bradykinin-mediated angioedema confirmed with threshold-stimulated kallikrein activity and an investigator confirmed response to acute use of a bradykinin targeted treatment
- All patients had two or more angioedema attacks during the run-in period which lasted maximally eight weeks
- Eligible patients received four unblinded doses of 80 mg donidalorsen every 4 weeks over a 16-week treatment period
- The primary endpoint was the time-normalized number of angioedema attacks per month during the treatment period compared to baseline

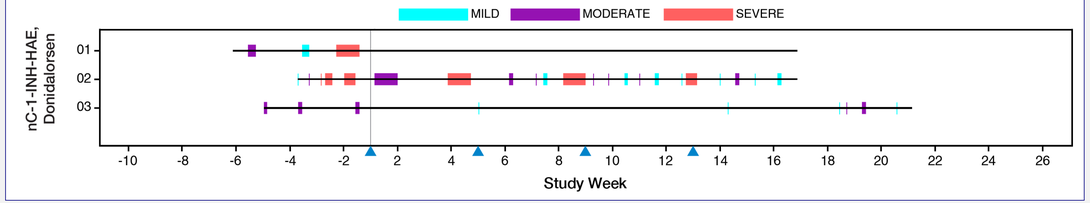


Abbreviations: D, day; F/u, follow-up; OLE, open label extension; R, randomization; SC, subcutaneous; W, week; E, enrollment.

Results

- Three patients met the eligibility criteria for enrollment based on the results of the threshold-stimulated kallikrein activity assay
- The mean monthly attack rate was 4.23 (95% confidence interval [CI] -2.56 to 11.03) at baseline and 1.52 during the treatment period (95% CI -3.99 to 7.04); mean difference -76% (95% confidence interval: -146.45 to -5.59)
- The treatment was well tolerated with no severe adverse events





Conclusion

Prophylactic treatment with plasma prekallikrein oligonucleotide antisense therapy in patients with nC1-INH-HAE was well tolerated and resulted in significantly improved disease control

American Academy of Allergy Asthma & Immuology, Annual Meeting, Phoenix, AZ, February 25-28, 2022

Funding source: Ionis Pharmaceuticals, Inc.