Patisiran: Ocular Adverse Events

The following information is provided in response to your unsolicited inquiry. It is intended to provide you with a review of the available scientific literature and to assist you in forming your own conclusions in order to make healthcare decisions. This document is not for further dissemination or publication without authorization.

The full Prescribing Information for ONPATTRO® (patisiran) is provided here. Alnylam Pharmaceuticals does not recommend the use of its products in any manner that is inconsistent with the approved Prescribing Information. This resource may contain information that is not in the approved Prescribing Information.

If you are seeking additional scientific information related to Alnylam medicines, you may visit the Alnylam US Medical Affairs website at RNAiScience.com.

SUMMARY

- In the APOLLO study (N=225), ocular AEs were observed in 41 patients (27.7%) in the patisiran group and 20 patients (26.0%) in the placebo group.[1]
- In the pooled population (N=224) including data from the completed Phase 2 OLE, completed phase 3 APOLLO, and Global OLE (as of January 27, 2021) studies, 101 patients (45.1%) reported ocular AEs, including night blindness in 2 patients (0.9%).[2]
- A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any new safety concerns involving ocular AEs related to patisiran.[2]

INDEX

CLINICAL DATA

APOLLO Study

APOLLO was a multicenter, international, randomized (2:1), double-blind, placebo-controlled, phase 3 study designed to assess the efficacy and safety of IV patisiran 0.3 mg/kg every 3 weeks (n=148) versus placebo (n=77) in patients with hATTR-PN. The primary endpoint was the change from baseline in the mNIS+7 at 18 months.[3]

During the study, the proportion of patients with ocular AEs was similar across treatment groups. Ocular AEs were observed in 41 patients (27.7%) in the patisiran group and 20 patients (26.0%) in the placebo group. Ocular AEs reported in ≥2% of patients in either group are presented in **Table 1**.[1]

Table 1. Ocular AEs Reported in ≥2% of Patients in the APOLLO Study.[1]

System Organ Class, n (%) Preferred Term	Placebo (N=77)	Patisiran 0.3 mg/kg (N=148)
Eye disorders	20 (26.0)	41 (27.7)
Cataract[a]	5 (6.5)	11 (7.4)
Conjunctival hemorrhage	3 (3.9)	1 (0.7)
Dry eye	2 (2.6)	7 (4.7)
Vision blurred	1 (1.3)	4 (2.7)

System Organ Class, n (%) Preferred Term	Placebo (N=77)	Patisiran 0.3 mg/kg (N=148)
Visual acuity reduced	2 (2.6)	1 (0.7)

[a]Includes preferred terms: cataract, cataract subcapsular, and cataract nuclear.
Abbreviations: AE = adverse event.

In the APOLLO study, visual acuity, intraocular pressure, visual field deviation, slit lamp biomicroscopy, and dilate indirect ophthalmoscopy were evaluated. No clinically notable trends were observed in the patisiran and placebo groups. In both treatment groups, the mean values of visual acuity, intraocular pressure, visual field deviation, and electroretinography results remained stable over the course of the study.[1]

Pooled Population

In the pooled population (N=224) including data from the completed Phase 2 OLE, completed phase 3 APOLLO, and Global OLE (as of January 27, 2021) studies, 101 patients (45.1%) reported ocular AEs, including night blindness reported in 2 patients (0.9%).[2]

Overall, ocular AEs reported in APOLLO and the pooled population were consistent with AEs expected in patients with hATTR and with the age of the patients in the studies.[1]

GLOBAL SAFETY DATABASE

A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any new safety concerns involving ocular AEs related to patisiran.[2]

ONPATTRO PRESCRIBING INFORMATION – RELEVANT CONTENT

The ADVERSE REACTIONS section provides the following information[4]:

Clinical Trials Experience

Ocular adverse reactions that occurred in 5% or less of ONPATTRO-treated patients in the controlled clinical trial, but in at least 2% of ONPATTRO-treated patients, and more frequently than on placebo, include dry eye (5% vs. 3%), blurred vision (3% vs. 1%), and vitreous floaters (2% vs. 1%).

The CLINICAL PHARMACOLOGY section provides the following information[4]:

Pharmacodynamics

Serum TTR is a carrier of retinol binding protein, which is involved in the transport of vitamin A in the blood. Mean reductions in serum retinol binding protein of 45% and serum vitamin A of 62% were observed over 18 months [see Warnings and Precautions (5.2)].

The WARNINGS AND PRECAUTIONS section provides the following information[4]:

Reduced Serum Vitamin A Levels and Recommended Supplementation

ONPATTRO treatment leads to a decrease in serum vitamin A levels. Supplementation at the recommended daily allowance of vitamin A is advised for patients taking ONPATTRO. Higher doses than the recommended daily allowance of vitamin A should not be given to try to achieve normal serum vitamin A levels during treatment with ONPATTRO, as serum vitamin A levels do not reflect the total vitamin A in the body.

Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g., night blindness).

ABBREVIATIONS

AE = adverse event; hATTR = hereditary transthyretin amyloidosis; hATTR-PN = hereditary transthyretin amyloidosis with polyneuropathy; IV = intravenous; mNIS+7 = modified Neuropathy Impairment Score +7; OLE = open-label extension; TTR = transthyretin.

Updated 14 January 2025

REFERENCES

1. Onpattro : EPAR – Public assessment report. European Medicines Agency. Published October 30, 2018. Accessed January 14, 2025. https://www.ema.europa.eu/documents/assessment-report/onpattro-epar-public-assessment-report.pdf.
2. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTR02-2400049.
3. Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi therapeutic, for hereditary transthyretin amyloidosis. *N Engl J Med*. 2018;379(1):11-21. doi:10.1056/NEJMoa1716153
4. ONPATTRO (patisiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.