Vutrisiran: Arthralgia

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SUMMARY

- In the HELIOS-A study, arthralgia events were reported in 13 (10.7%) patients in the vutrisiran arm, which were mostly mild or moderate in severity. None of the arthralgia events were serious, led to discontinuation of treatment, or increased over time.[1,2]
  - During the RTE period (as of August 26, 2021) of the HELIOS-A study, arthralgia was reported as an AE with very common frequency, defined as affecting more than 1 in 10 patients.[3]
- A cumulative post-marketing review of Alnylam's global safety database did not identify any new safety concerns involving arthralgia with the use of vutrisiran.[4]
- No additional information is available regarding arthralgia events and their management.

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CLINICAL DATA

Study Design

HELIOS-A was a phase 3, global, randomized, open-label study designed to evaluate the efficacy and safety of vutrisiran in patients with the polyneuropathy of hATTR. Patients were randomized (3:1) to receive either vutrisiran 25 mg every 3 months by subcutaneous injection (n=122) or patisiran 0.3 mg/kg every 3 weeks by IV infusion (as a reference group, n=42) for 18 months. This study used the placebo arm of the APOLLO study (NCT01960348) as an external control arm (n=77) for the primary endpoint and most other efficacy endpoints. The primary endpoint was the change from baseline in mNIS+7 at 9 months. After the 18-month treatment period was completed, all eligible patients, including those on patisiran, entered the RTE and were randomized 1:1 to receive either vutrisiran 25 mg every 3 months or vutrisiran 50 mg every 6 months by subcutaneous injection.[1,3]

Note: The decision was made not to further advance the vutrisiran 50 mg every 6 months dosing regimen due to the pharmacodynamics of serum TTR recovery seen at the end of the 6-month dosing interval.[3]

Through 18 months of the study, arthralgia events were reported in 13 (10.7%) patients in the vutrisiran arm, which were mostly mild or moderate in severity with 1 patient experiencing a severe AE. No cases of arthralgia were reported in the placebo arm. None of the arthralgia events were serious, led to discontinuation of treatment, or increased over time.[1,2]

After completion of the 18-month treatment period and during the RTE period (as of August 26, 2021), arthralgia was identified as an AE with very common frequency, defined as affecting more than 1 in 10 patients.[2]

No additional information is available regarding the incidence or management of arthralgia events reported with vutrisiran in the HELIOS-A study.

GLOBAL SAFETY DATABASE

A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any new safety concerns involving arthralgia with the use of vutrisiran.[4]

AMVUTTRA PRESCRIBING INFORMATION – RELEVANT CONTENT

For relevant labeling information, please refer to the following section of the AMVUTTRA Prescribing Information[5]:

- ADVERSE REACTIONS Section 6.1 Clinical Trial Experience

ABBREVIATIONS

AE = adverse event; hATTR = hereditary transthyretin amyloidosis; IV = intravenous; mNIS+7 = modified Neuropathy Impairment Score +7; RTE = randomized treatment extension; TTR = transthyretin.

Updated 28 May 2024

REFERENCES

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3. Obici L, Polydefkis M, Gonzalez-Duarte A, et al. HELIOS-A: 9-month results from the randomized treatment extension period of vutrisiran in patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy. Presented at: Italian Association for the Study of the Peripheral Nervous System (ASNP) Annual Meeting; May 25-27, 2023; Naples, Italy.
4. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTRSC02-2400004.
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