Vutrisiran: Use in Patients with Heart Transplant

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 AMVUTTRA® (vutrisiran) 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

- Clinical trials to evaluate vutrisiran treatment in patients who underwent heart transplant have not been conducted to date.
  - In the HELIOS-A study, an analysis of the efficacy and safety of vutrisiran in clinical study participants with a past medical history of heart transplant is not available.
  - In the HELIOS-B study, patients were excluded if they had a prior or anticipated (during the first 12 months after randomization) heart transplant or implantation of left-ventricular assist device.[1]
- A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any safety concerns regarding the use of vutrisiran in patients with heart transplant.[2]

INDEX

CLINICAL DATA

HELIOS-A

HELIOS-A was a phase 3, global, randomized, open-label study designed to evaluate the efficacy and safety of vutrisiran in patients with hATTR-PN. 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 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.[3]

There were 3 patients enrolled in HELIOS-A that had a medical/surgical history of heart transplant: 2 were enrolled in the vutrisiran arm and 1 in the patisiran arm.[4]

HELIOS-B

HELIOS-B was a phase 3, global, randomized, double-blind, placebo-controlled, multicenter study designed to evaluate the efficacy and safety of vutrisiran in patients with ATTR-CM, including both

hATTR and wtATTR. Patients were randomized (1:1) to receive either vutrisiran 25 mg (n=326) or placebo (n=329) every 3 months by subcutaneous injection for up to 36 months. The primary endpoint was the composite endpoint of all-cause mortality and recurrent CV events (CV hospitalizations and urgent heart failure visits) at the end of the double-blind exposure period in the overall population and in the vutrisiran monotherapy population (patients not receiving tafamidis at baseline).[5]

Select Exclusion Criteria

Patients were excluded from enrolling in the study if they had a prior or anticipated (during the first 12 months after randomization) heart, liver, or other organ transplant or implantation of left-ventricular assist device.[1]

Primary Endpoint

Treatment with vutrisiran reduced the risk of the primary composite endpoint of all-cause mortality and recurrent CV events when compared with placebo in the overall population (HR 0.72; 95% CI 0.56, 0.93; P=0.01) and monotherapy population (HR 0.67; 95% CI 0.49, 0.93; P=0.02). Heart transplantation and implantation of a left ventricular assist device were treated as deaths in the efficacy analyses that included death from any cause. During the double-blind exposure period, 3 patients in the vutrisiran arm and 4 patients in the placebo arm had a heart transplantation.[5]

GLOBAL SAFETY DATABASE

A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any safety concerns regarding the use of vutrisiran in patients with heart transplant.[2]

ABBREVIATIONS

ATTR-CM = transthyretin amyloidosis with cardiomyopathy; CI = confidence interval; CV = cardiovascular; hATTR = hereditary transthyretin amyloidosis; hATTR-PN = hereditary transthyretin amyloidosis with polyneuropathy; HR = hazard ratio; IV = intravenous; mNIS+7 = modified Neuropathy Impairment Score +7; wtATTR= wild-type transthyretin amyloidosis.

Updated 19 February 2026

REFERENCES

1. Protocol for: Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. *N Engl J Med*. 2025;392(1):33-44. doi:10.1056/NEJMoa2409134
2. Alnylam Pharmaceuticals. Data on file. MED-ALL-VUTRI-2600002.
3. Adams D, Tournev IL, Taylor MS, et al. Efficacy and safety of vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial. *Amyloid*. 2023;30(1):18-26. doi:10.1080/13506129.2022.2091985
4. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTRSC02-2200006.
5. Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. *N Engl J Med*. 2025;392(1):33-44. doi:10.1056/NEJMoa2409134