Vutrisiran: Post-Orthotopic Liver Transplant

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SUMMARY

- In the HELIOS-A and HELIOS-B studies, patients were excluded if they had a liver transplant or were likely to undergo liver transplantation during the study period.[1,2]

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AMVUTTRA PRESCRIBING INFORMATION – RELEVANT CONTENT

The CLINICAL PHARMACOLOGY section provides the following information[3]:

Pharmacokinetics: Specific Populations

No clinically significant differences in the pharmacokinetics of vutrisiran were observed based on age, sex, race, mild and moderate renal impairment (eGFR≥30 to <90 mL/min/1.73 m^2), or mild (total bilirubin ≤1 x ULN and AST >1 x ULN, or total bilirubin >1.0 to 1.5 x ULN and any AST) and moderate (total bilirubin >1.5 to 3 × ULN and any AST) hepatic impairment. Vutrisiran has not been studied in patients with severe renal impairment, end-stage renal disease, severe hepatic impairment, or in patients with prior liver transplant.

CLINICAL DATA

Phase 3 HELIOS-A Study

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.[1]

Exclusion Criteria

Patients were excluded from the study if any of the following criteria applied[1]:

- Had a liver transplant or were likely to undergo liver transplantation during the 18-month treatment period of the study

Phase 3 HELIOS-B Study

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).[4]

Exclusion Criteria

Patients were excluded from the study if any of the following criteria applied[2]:

- Prior or anticipated (during the first 12 months after randomization) heart, liver, or other organ transplant or implantation of left-ventricular assist device

ABBREVIATIONS

AST = aspartate aminotransferase; ATTR-CM = transthyretin amyloidosis with cardiomyopathy; CV = cardiovascular; eGFR = estimated glomerular filtration rate; hATTR = hereditary transthyretin amyloidosis; hATTR-PN = hereditary transthyretin amyloidosis with polyneuropathy; IV = intravenous; mNIS+7 = modified neuropathy impairment score +7; ULN = upper limit of normal; wtATTR = wild-type transthyretin amyloidosis.

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REFERENCES

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2. 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
3. AMVUTTRA (vutrisiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.
4. 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