Vutrisiran: Use in Patients with Heart Transplant

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SUMMARY

- In the HELIOS-A study, there were 3 patients with a medical/surgical history of heart transplant: 2 were enrolled in the vutrisiran arm and 1 in the patisiran arm.[1]
- 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.[2]
- Post-marketing data did not identify any specific pattern or new safety concerns with vutrisiran and heart transplantation.[3]
- No additional data are available regarding the use of vutrisiran in patients with heart transplant.

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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.[4]

Baseline History

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.[1]

No additional data are available regarding the use of vutrisiran in patients with heart transplant in the HELIOS-A study.

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]

Relevant 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.[2]

Primary Endpoint

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

GLOBAL SAFETY DATABASE

Post-marketing data did not identify any specific pattern or new safety concerns with vutrisiran and heart transplantation.[3]

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.

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5. Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. *N Engl J Med*. August 2024. doi:10.1056/NEJMoa2409134