Vutrisiran: Transition from Antisense Oligonucleotide

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SUMMARY

- Clinical trials designed to evaluate the transition from an antisense oligonucleotide (e.g., inotersen, eplontersen) to vutrisiran have not been conducted to date.
- In the HELIOS-A and HELIOS-B studies, patients that had received prior TTR-lowering treatment or participated in a gene therapy trial for hATTR were excluded.[1,2]

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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.[3]

Exclusion Criteria

Patients were excluded from the study if the following criterion applied[1]:

- Received prior TTR-lowering treatment or participated in a gene therapy trial for hATTR

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).[4]

Exclusion Criteria

Patients were excluded from the study if the following criterion applied[2]:

- Received prior TTR-lowering treatment or participated in a gene therapy trial for hATTR

ABBREVIATIONS

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

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