Patisiran: 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 patisiran have not been conducted to date.
- In the APOLLO study, patients that had participated in a clinical trial with an antisense oligonucleotide were required to have completed a 3-month wash-out prior to the start of study drug administration.[1]
- In the HELIOS-A study, patients that had received prior TTR-lowering treatment or participated in a gene therapy trial for hATTR were excluded.[2]
- In the APOLLO-B study, patients that had received prior TTR-lowering treatment or participated in a gene therapy trial for hATTR were excluded.[3]

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CLINICAL DATA

APOLLO Study

APOLLO was a multicenter, international, randomized (2:1), double-blind, placebo-controlled, phase 3 study designed to assess the efficacy and safety of IV patisiran 0.3 mg/kg every 3 weeks (n=148) versus placebo (n=77) in patients with the polyneuropathy of hATTR. The primary endpoint was the change from baseline in the mNIS+7 at 18 months.[4]

Exclusion Criteria

- Participated in a clinical trial with antisense oligonucleotide, must have completed a 3-month wash-out prior to start of study drug administration.
- Had a prior severe reaction to a liposomal product or a known hypersensitivity to oligonucleotides or any component of patisiran.

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 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 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.[5]

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.

APOLLO-B Study

APOLLO-B was a multicenter, randomized (1:1), double-blind, placebo-controlled, phase 3 study designed to evaluate the efficacy and safety of IV patisiran 0.3 mg/kg every 3 weeks (n=181) versus placebo (n=179) in patients with ATTR with cardiomyopathy, including both hATTR and wtATTR. The primary endpoint was the change from baseline in 6-MWT at 12 months.[6]

Exclusion Criteria

Patients were excluded from the study if the following criterion applied[3]:

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

ABBREVIATIONS

6-MWT = 6-minute walk test; ATTR = transthyretin amyloidosis; hATTR = hereditary transthyretin amyloidosis; IV = intravenous; mNIS+7 = modified Neuropathy Impairment Score +7; TTR = transthyretin; wtATTR = wild-type transthyretin amyloidosis.

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