Vutrisiran: Dosage & Administration Schedule Used in Phase 3 Studies

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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.

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SUMMARY

- The recommended dosage of AMVUTTRA is 25 mg administered by subcutaneous injection once every 3 months.[1]
- As part of the HELIOS-A study protocol, vutrisiran 25 mg was administered subcutaneously every 3 months, defined as every 12 weeks.[2]
  - During the 18-month Treatment Period, a ± 3-day dosing window was allowed. During the RTE period, a ± 7 day dosing window was allowed.[2]
- As part of the HELIOS-B study protocol, vutrisiran 25 mg was administered subcutaneously every 3 months, defined as every 12 weeks, for up to 36 months starting on day 1 of the double-blind period and for up to 2 years starting on day 1 of the OLE period.[3]
  - A ± 7-day dosing window was allowed.[3]

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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] After the 18-month treatment period was completed, all eligible patients, including those on patisiran, entered the RTE and were randomized 1:1 to receive either vutrisiran 25 mg every 3 months or vutrisiran 50 mg every 6 months by subcutaneous injection.[4,5]

At Month 9 of the RTE period, the non-inferiority in serum TTR mean percent reduction was met with vutrisiran 50 mg every 6 months compared with vutrisiran 25 mg every 3 months; however, the decision was made not to pursue the vutrisiran 50 mg every 6 months dosing regimen due to the pharmacodynamics of serum TTR recovery seen at the end of the 6-month dosing interval.[5,6] As a result, a protocol amendment was made and all patients receiving vutrisiran 50 mg every 6 months were transitioned to vutrisiran 25 mg every 3 months at their next scheduled dosing visit (24 weeks after the last 50 mg dose).[2]

Vutrisiran Dosage and Administration Schedule

As part of the HELIOS-A study protocol, vutrisiran 25 mg was administered subcutaneously every 3 months, defined as every 12 weeks. During the 18-month Treatment Period, a ± 3-day dosing window was allowed. During the RTE period, a ± 7-day dosing window was allowed. Patients who were randomized to receive vutrisiran 50 mg every 6 months as part of the RTE period prior to the protocol amendment received the dose every 24 weeks ± 7 days.[2]

If a patient did not receive a dose of vutrisiran within the specified dosing window, the Investigator would consult with the Medical Monitor. After such consultation, the dose could be administered with up to an 8-week delay or as determined by the Medical Monitor. If a dose was administered with a delay, the next dose would then resume following the original schedule. In all cases, the dose was to be administered as close as possible to the scheduled timepoint.[2]

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). After the double-blind treatment period, all eligible patients remaining on the study were allowed to receive vutrisiran in an ongoing OLE.[7]

Vutrisiran Dosage and Administration Schedule

As part of the HELIOS-B study protocol, vutrisiran 25 mg was administered subcutaneously every 3 months, defined as every 12 weeks, for up to 36 months starting on Day 1 of the double-blind period and for up to 2 years starting on Day 1 of the OLE period. A ± 7-day dosing window was allowed.[3]

If a patient did not receive a dose of vutrisiran within the specified dosing window, the Investigator would consult with the Medical Monitor. After such consultation, the dose could be administered with up to an 8-week delay or as determined by the Medical Monitor. If a dose was administered with a delay, the next dose would then resume following the original schedule. In all cases, the dose was to be administered as close as possible to the scheduled timepoint.[3]

AMVUTTRA PRESCRIBING INFORMATION – RELEVANT CONTENT

The DOSAGE AND ADMINISTRATION section provides the following information[1]:

Recommended Dosage

The recommended dosage of AMVUTTRA is 25 mg administered by subcutaneous injection once every 3 months.

Missed Dose

If a dose is missed, administer AMVUTTRA as soon as possible. Resume dosing every 3 months from the most recently administered dose.

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; OLE = open-label extension; RTE = randomized treatment extension; TTR = transthyretin; wtATTR = wild-type transthyretin amyloidosis.

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7. 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