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RNAi Therapy in ATTRv Amyloidosis with Polyneuropathy (HELIOS-A): Patient-reported Experiences and Preferences

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Conclusions

- **Most patients receiving subcutaneous (SC) vutrisiran every 3 months (Q3M) or intravenous (IV) patisiran every 3 weeks (Q3W) in the HELIOS-A study report favorable experiences regarding convenience**
- **At Month 18, a larger proportion of patients rated the frequency of dosing and duration of administration to be quite a bit/extremely convenient in the Q3M SC vutrisiran arm vs the Q3W IV patisiran arm**
- **The vast majority of patients switching from patisiran to vutrisiran in the randomized treatment extension (RTE) preferred the administration of Q3M/every 6 months (Q6M) SC vutrisiran rather than Q3W IV patisiran at Month 9**
  - **More than half of patients who preferred vutrisiran had a quite/extremely strong preference for it**
  - **Frequency of administration was the primary reason given for vutrisiran preference**
  - **Location of treatment administration had limited impact on patient preference**
  - **Patisiran administration may have had a higher burden than vutrisiran administration due to the additional premedications used to minimize the risk of infusion-related reactions**

Background and Rationale

Background

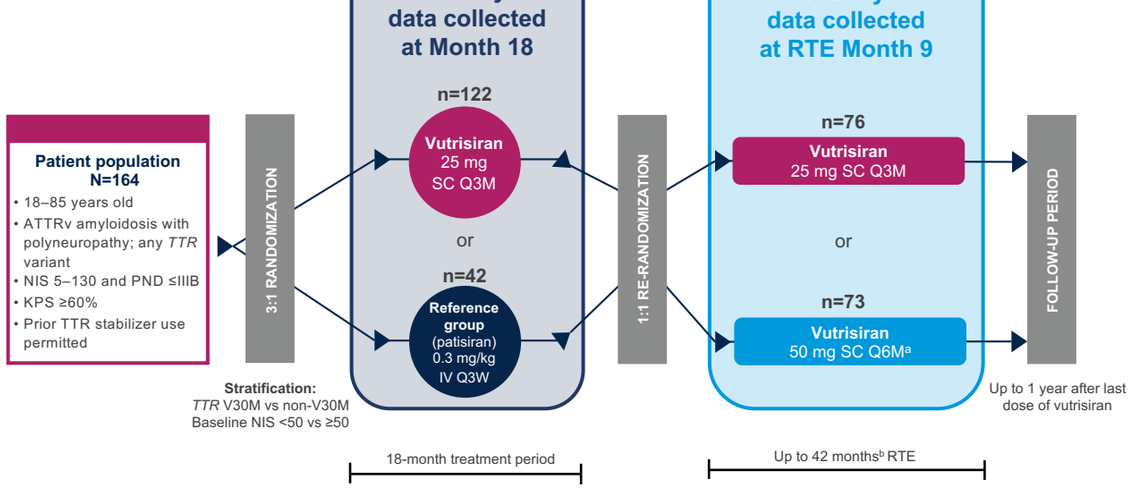
- ATTRv amyloidosis is a rare, underdiagnosed, rapidly progressive, debilitating, and fatal disease caused by variants in the *TTR* gene that result in misfolded transthyretin (TTR) accumulating as amyloid deposits in multiple organs and tissues[1–4]
- Vutrisiran and patisiran are approved RNAi therapeutics for ATTRv amyloidosis with polyneuropathy, based on the Phase 3, open-label HELIOS-A study[5–7] and the Phase 3, placebo-controlled APOLLO study[8–10], respectively
- Vutrisiran is administered subcutaneously (Q3M)[6,7] and patisiran is administered intravenously (Q3W)[9,10]

Objective

- To evaluate patient experiences with, and preferences for, vutrisiran and patisiran in HELIOS-A

Methods

Figure 1. Study design



[a]The vutrisiran 50 mg Q6M dose was discontinued during the RTE period of this study, and all patients receiving vutrisiran 50 mg Q6M were transitioned to the 25 mg Q3M dose 24 weeks after their last dose. Hence, data from both dose regimens were pooled for this analysis. [b]Patients completed the study following 18 months of the RTE period.

Figure 2. Patient experience and preference surveys

Patient Experience Survey

Questions	Response options
Q1: "*How convenient is the **dosing schedule** of your current clinical study drug regimen? (i.e., duration of time between administrations)?*"	• Not at all convenient • A little convenient • Somewhat convenient • Quite a bit convenient • Extremely convenient
Q2: "*How convenient is the **time required to receive an administration** from start to finish? Include in your consideration the time needed to receive premedications/preparations of a dose before administration.*"	

Assessments: Day 1, Month 9, and **Month 18** (only Month 18 responses shown)
Respondents: **All patients who completed the Month 18 assessment in the vutrisiran and patisiran arms of HELIOS-A**

Patient Preference Survey

Questions	Response options
Q1: "*Considering the treatments that you have received during the clinical study, **which method of administration do you prefer**?*"	• Patisiran IV delivery every 3 weeks • ALN-TTRSC02 (vutrisiran) SC delivery every 3 months • ALN-TTRSC02 (vutrisiran) SC delivery every 6 months • No preference
Q2: "*If you prefer one of the administration routes listed above, **how strong is your preference**?*"	• Not at all strong • A little strong • Somewhat strong • Quite strong • Extremely strong
Q3: "*Select two statements that **best describe why you prefer the administration method** you selected in Q1.*"	Up to two out of five responses: • Feel more comfortable during administration • Prefer the time needed to receive one administration • Feel less emotional anxiety or distress when receiving an administration • Prefer the frequency of administration (i.e., time between administrations) • Prefer the location of administrations (i.e., infusion center, doctor's office, home) • Free text field (other)

Assessments: **Month 9 of RTE**
Respondents: **Patients who received patisiran** during the 18-month treatment period and **switched to vutrisiran[a] during the RTE period**

[a]The vutrisiran 50 mg Q6M dose was discontinued during the RTE period of this study, and all patients receiving vutrisiran 50 mg Q6M were transitioned to the 25 mg Q3M dose 24 weeks after their last dose. Hence, data from both dose regimens were pooled for this analysis.

Results

Number of Survey Respondents

Patient Experience Survey

Month 18 survey respondents
113/122 (93%) patients (vutrisiran)
38/42 (90%) patients (patisiran)

Patient Preference Survey

RTE Month 9 survey respondents
27/37 (73%) patients
(patisiran to vutrisiran switch)

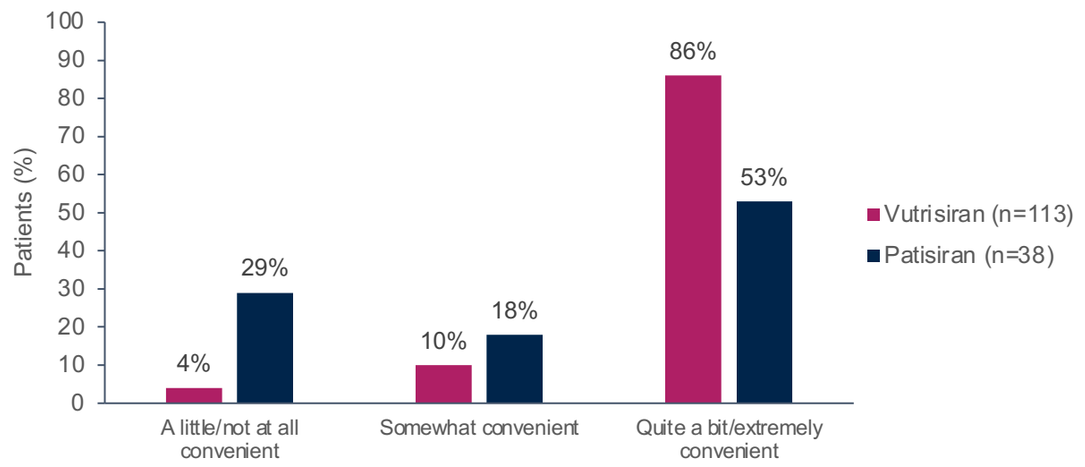
Results (cont'd)

HELIOS-A Patient Experience Survey: Baseline to Month 18

Patient-rated Convenience of Dosing Schedule at Month 18

- A larger proportion of patients treated with vutrisiran vs patisiran rated their dosing schedule to be quite a bit/extremely convenient at Month 18 (**Figure 3**)

Figure 3. HELIOS-A Patient Experience Survey: Patient-rated convenience of dosing schedule at Month 18[a]

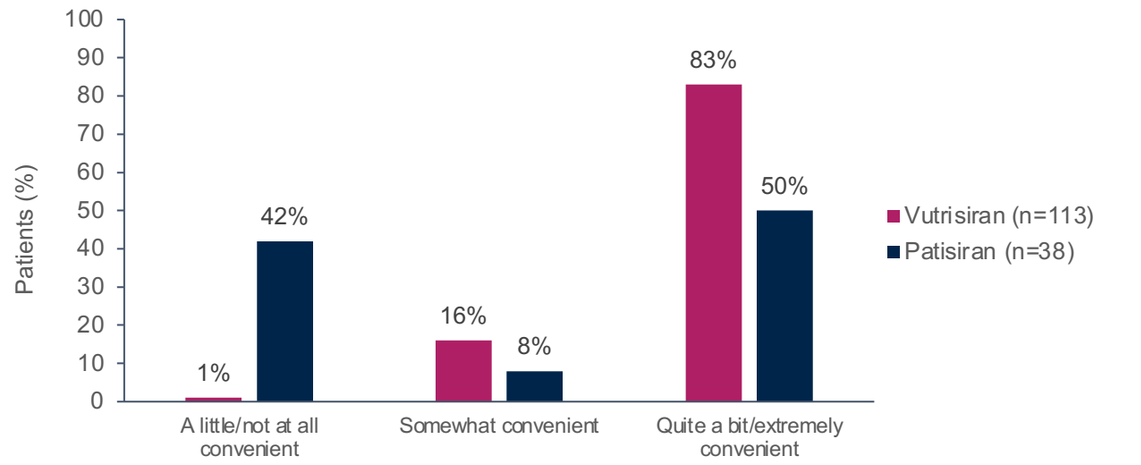


[a]Survey question (Q1): "How convenient is the dosing schedule of your current clinical study drug regimen? (i.e., duration of time between administrations)?"

Patient-rated Convenience of Time Required to Receive Administration at Month 18

- A larger proportion of patients treated with vutrisiran vs patisiran rated the time required to receive their drug administration to be quite a bit/extremely convenient at Month 18 (**Figure 4**)

Figure 4. HELIOS-A Patient Experience Survey: Patient-rated convenience of time to receive administration at Month 18[a]

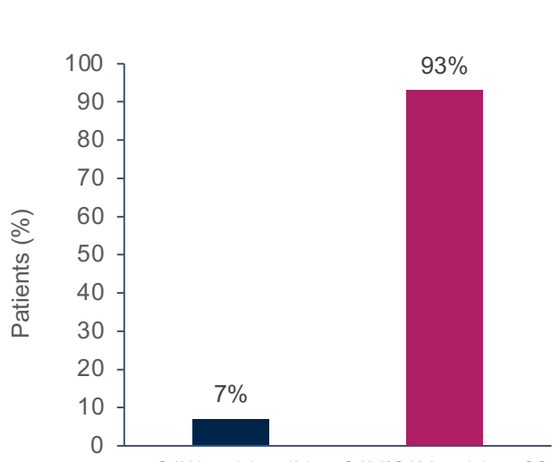


[a]Survey question (Q2): "How convenient is the time required to receive an administration from start to finish? Include in your consideration the time needed to receive premedications/preparations of a dose before administration."

HELIOS-A Patient Preference Survey: HELIOS-A Month 18 to RTE Month 9

Patient Preference of Administration Method at RTE Month 9

Figure 5. HELIOS-A Patient Preference Survey: Patient preference of administration method at Month 9 RTE (n=27)[a]



- The vast majority of patients preferred the Q3M/Q6M SC method of vutrisiran administration compared with the Q3W IV method of patisiran administration at Month 9 of the RTE (**Figure 5**)

[a]Survey question (Q1): "Considering the treatments that you have received during the clinical study, which method of administration do you prefer?"
[b]The vutrisiran 50 mg Q6M dose was discontinued during the study so data from patients receiving the 50 mg Q6M and 25 mg Q3M doses were pooled.

Patient Preference for SC Vutrisiran at RTE Month 9

- Most patients favoring the SC method of administration for vutrisiran had a strong preference for this choice (**Figure 6**)
- The most common reason for this preference was the frequency of administration (**Figure 6**)

Figure 6. Patient Preference Survey: Patients preferring the SC method of vutrisiran administration at Month 9 RTE (n=25)[a]

[a]The vutrisiran 50 mg Q6M dose was discontinued during the RTE period of this study, and all patients receiving vutrisiran 50 mg Q6M were transitioned to the 25 mg Q3M dose 24 weeks after their last dose. Hence, data from both dose regimens were pooled for this analysis.
[b]Survey question (Q2): "If you prefer one of the administration routes listed above, how strong is your preference?"
[c]Survey question (Q3): "Select two statements that best describe why you prefer the administration method you selected in Q1." Up to two statements could be chosen.

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Abbreviations: ATTRv, hereditary transthyretin (v for variant); IV, intravenous; KPS, Karnofsky Performance Status; NIS, Neuropathy Impairment Score; PND, polyneuropathy disability; Q3M, every 3 months; Q3W, every 3 weeks; Q6M, every 6 months; RTE, randomized treatment extension; SC, subcutaneous.

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