Real-World Adherence and Persistence of Eplontersen in Patients with ATTR

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Conclusions

- **While adherence with eplontersen was high, 1 in 4 patients experienced a >60-day treatment gap at 12 months. Findings should be interpreted cautiously because of the small cohort size.**
- **Future studies should compare adherence and persistence across treatments for ATTR, including regimens with differing dosing frequencies and routes of administration.**

Introduction

- Hereditary transthyretin amyloidosis with polyneuropathy (ATTRv-PN) is a rare, progressive, multisystem disease characterized by transthyretin (TTR) amyloid deposition and progressive peripheral neuropathy.[1,2]
- Eplontersen is a TTR-directed antisense oligonucleotide administered subcutaneously every 4 weeks and has demonstrated efficacy in patients with ATTRv-PN.[3,4]
- Evidence describing adherence and persistence with eplontersen in routine clinical practice is needed to understand treatment patterns outside the clinical-trial setting.

Objective

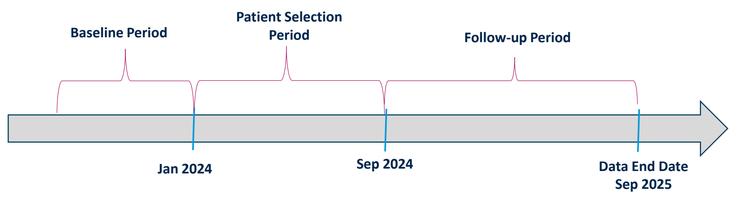
To estimate real-world adherence and persistence/discontinuation rates of patients treated with eplontersen

Methods

Study design and data source

- This was a retrospective observational cohort study using Optum's de-identified Market Clarity Data (Optum® Market Clarity) from January 1, 2024, to September 30, 2025.
- This study included patients who filled an eplontersen prescription between January 2024 and September 2024 and maintained continuous health plan enrollment for ≥6 months prior to treatment initiation (baseline period) and ≥12 months following initiation (follow-up period). **(Figure 1)**

Figure 1. Study design



Study outcomes and statistical analysis

- Baseline demographics and clinical characteristics were described using means (SDs), medians (IQRs), and counts and percentages, as appropriate.
- Eplontersen adherence was assessed using proportion of days covered (PDC). PDC was calculated as the proportion of days covered from the first eplontersen prescription fill through the end of supply of the last prescription fill, defined as (last prescription fill date + days' supply) − first prescription fill date.
- Adherence was defined as PDC ≥0.80 and calculated for the entire follow up period.
- Persistence at 12 months was evaluated using up to 60-day and 90-day allowable gaps between prescription fills. Patients without a gap exceeding the specified threshold were considered persistent. The rate of discontinuation was calculated as 100% minus the rate of persistence.

Results

Baseline patient characteristics

- Among the 24 patients included in the analysis, mean (SD) age was 73.8 (7.2) years, with a median age of 74 years (IQR, 69–78). **(Table 1)**
- Most patients were Black (19 of 24; 79.2%) and female (13 of 24; 54.2%), and all patients were Medicare beneficiaries (100%).
- Most patients (20 of 24; 83.3%) had evidence of polyneuropathy and cardiomyopathy, consistent with mixed phenotype.
- Patients had a substantial comorbidity burden, with a mean (SD) CCI of 4.6 (2.6) and median CCI of 5 (IQR, 2.5–6.0). Hypertension was present in 18 patients (75.0%). Arrhythmia and heart failure were both diagnosed in 15 patients (62.5%).

Treatment patterns and adherence

- During a mean (SD) follow-up of 452.0 days (82.4), patients received a mean of 12.8 eplontersen administrations (5.8), with a mean treatment duration of 357.9 days (162.9). **(Table 2)**
- The mean interval between eplontersen administrations was 30.6 days (1.7). The median interval between eplontersen administrations was 30.3 days (IQR, 29.9–31.0).
- Mean (SD) PDC was 0.93 (0.05) and median PDC was 0.93 (IQR, 0.91–0.95).
- Overall, 95.8% (23 of 24) of patients were adherent to eplontersen, defined as PDC ≥0.80.

Persistence and discontinuation

- At 12 months, 25.0% (6 of 24) of patients met the discontinuation definition using a >60-day gap and 20.8% (5 of 24) using a >90-day gap. **(Figure 2)**

Results *continued*

Table 1. Baseline population characteristics

Baseline characteristics	Eplontersen-treated patients (N = 24)
Age, years	
Mean (SD)	73.8 (7.2)
Sex, n (%)	
Female	13 (54.2)
Race, n (%)	
Black	19 (79.2)
CCI	
Mean (SD)	4.5 (2.6)
Median (IQR)	5 (2.5–6.0)
Comorbidity, n (%)	
Arrhythmia	15 (62.5)
Heart failure	15 (62.5)
Hypertension	18 (75.0)
Atrial fibrillation	<11
Diabetes	<11

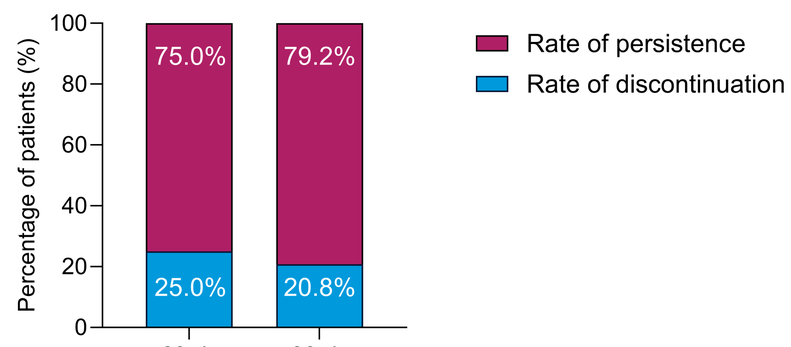
To protect patient confidentiality, counts <11 were suppressed in accordance with the Optum data-use agreement.
Abbreviations: CCI, Charlson Comorbidity Index; IQR, interquartile range; SD, standard deviation.

Table 2. Treatment patterns and adherence

Treatment measure	
Follow-up time in days, mean (SD)	452.0 (82.4)
Eplontersen administrations, mean (SD)	12.8 (5.8)
Treatment duration in days, mean (SD)	357.9 (162.9)
Gap between administrations in days, mean (SD)	30.6 (1.7)
PDC, mean (SD)	0.93 (0.05)
PDC ≥0.80, n (%)	23 (95.8)

PDC was calculated as the proportion of days covered by eplontersen prescription fills during follow-up. Adherence was defined as PDC ≥0.80.
Abbreviations: PDC, proportion of days covered; SD, standard deviation.

Figure 2. Eplontersen persistence and discontinuation at 12 months



Discussion and limitations

- This study examined the real-world adherence and persistence with eplontersen using a geographically diverse US claims database. However, the sample size was small and generalizability is limited.
- Eplontersen is administered monthly by a physician; therefore, the claims data used to assess adherence and persistence accurately reflect that the patient received the medication.
- While few patients being treated with eplontersen were included in this real-world analysis, treatment adherence was high, which aligns with studies of other ATTR treatments, such as vutrisiran.[5]
- The observed discontinuation rate in this analysis was lower than the discontinuation rates in patients treated with vutrisiran in a similar study.[5]
- Further research is needed to compare real-world adherence and persistence rates between ATTR therapies and to assess the relationships between adherence, persistence, and outcomes.

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If you are seeking additional scientific information related to Alnylam therapeutics, non-US HCPs should contact medinfo@alnylam.com. US HCPs may visit the Alnylam US Medical Affairs website at RNAiScience.com.

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Abbreviations: ATTR, transthyretin amyloidosis; ATTRv-PN, hereditary transthyretin amyloidosis with polyneuropathy; CCI, Charlson Comorbidity Index; HCP, healthcare professional; IQR, interquartile range; PDC, proportion of days covered; SD, standard deviation; TTR, transthyretin; US, United States.