Real-World Adherence and Persistence With Vutrisiran, an RNA Interference Therapeutic for the Treatment of Transthyretin Amyloidosis

Heffernan M, MD, PhD[1]; Patel A, MS[2]; Kauf TL, PhD[2]

[1] Halton Healthcare, Oakville, ON, Canada; [2] Alnylam Pharmaceuticals, Cambridge, MA, USA

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Conclusions

- **Real-world adherence and persistence with vutrisiran was high, with most patients still treated with vutrisiran after 12 months**
- **These findings may help inform clinical decision-making for the treatment of ATTR**

Background

- Transthyretin (TTR) amyloidosis (ATTR) is a progressive, debilitating, and fatal disease, caused by the buildup of amyloid deposits of misfolded TTR protein(1)
- Cardiomyopathy (CM) may arise as a result of TTR deposits in the myocardium; ATTR with cardiomyopathy (ATTR-CM) can lead to congestive heart failure and death(1, 2)
- Until the approval of acoramidis in November 2024 (3) and vutrisiran in March 2025 (4), tafamidis was the only United States (US) Food and Drug Administration-approved treatment for ATTR-CM;(5) however, while adherence to oral tafamidis is high,(6-8) previous research has shown high discontinuation rates after 12 months(9)
- Given that patients with ATTR-CM are frequently burdened by oral polypharmacy,(10) daily oral dosing required by tafamidis and acoramidis may adversely influence adherence with ATTR stabilizers(8, 10)
- Vutrisiran, an RNA interference therapeutic for ATTR-CM that requires 4 subcutaneous doses per year,(11) may benefit treatment persistence

Objective

To assess the real-world adherence and persistence among patients with ATTR receiving vutrisiran

Methods

Study design and data source

•This was a retrospective, observational cohort study using patient-level, US medical claims data from Optum's de-identified Clinformatics Data Mart Database from October 1, 2021, to March 31, 2025

Study population

- Adults (≥18 years) were eligible for inclusion if they had ≥1 outpatient claim for vutrisiran between May 2022 and March 2025 and maintained continuous health plan enrollment for ≥6 months prior to treatment initiation (baseline period) and 12 months following initiation (follow-up period)
- Adults were followed from vutrisiran initiation to the end of health plan enrollment, death, or last date of available data, whichever came first
- National Drug Codes (NDC) and Current Procedural Terminology (CPT) codes were used to select patients receiving vutrisiran

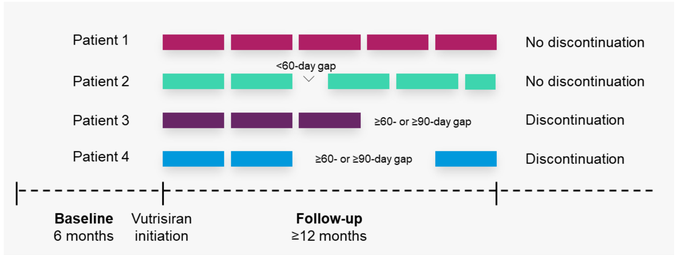
Statistical analysis

•Baseline patient demographic and clinical characteristics were analyzed descriptively

Methods (cont.)

- Proportion of days covered (PDC) was used to assess treatment adherence; PDC was defined as the proportion of days covered by a vutrisiran administration out of all the days between first and last administration dates, or up to a ≥60- or 90-day gap period not covered by a vutrisiran administration
- Patients were considered adherent if PDC ≥0.8
- Discontinuation rates were used to assess persistency with vutrisiran; discontinuation was defined as the time between the index date and date of first discontinuation, indicated by a ≥60-day period gap between the end of a vutrisiran treatment period and the receipt of a subsequent dose **(Figure 1)**. A sensitivity analysis using a ≥90-day gap was also conducted
- Rates of discontinuation of vutrisiran at 12 months were reported as the percentage of patients experiencing this outcome. Rates of persistence were calculated as 100% minus the rate of discontinuation

Figure 1. Study definition of vutrisiran discontinuation



The bars represent the 90-day treatment period covered by each vutrisiran administration over the course of follow-up for 4 hypothetical patients. Patients 1 and 2 do not meet discontinuation criteria while Patient 3 and Patient 4 do.

Results

Baseline characteristics

•Among the 112 patients receiving vutrisiran included in the analysis, mean (SD) age was 72.3 (8.9) years, 64.3% were male, and 84.8% had Medicare coverage **(Table)**. Most patients (86.6%) had a diagnosis of ATTR with CM and polyneuropathy (PN)

•The majority of patients (70.5%) initiated vutrisiran in 2023

•The mean (SD) duration of follow-up was 613.8 days (157.5). The median (1st quartile [Q1], 3rd quartile [Q3]) follow-up duration was 616.5 days (449.5, 759.0)

•The mean (SD) duration of vutrisiran treatment was 572.1 days (207.8). The median (Q1, Q3) treatment duration was 540 days (450, 720)

Adherence

•Over the treatment period, mean (SD) and median (Q1, Q3) PDC were 0.96 (0.10) and 0.99 (0.97, 1.00), respectively

•Most (93.8%) patients were adherent to vutrisiran **(Figure 2)**

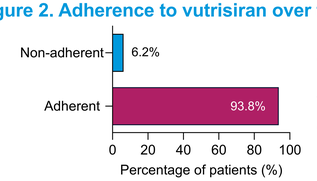
Results (cont.)

Table. Baseline characteristics

Characteristic	N=112
Age category, N (%), years	
18–64	21 (18.8%)
65–74	42 (37.5%)
75–84	43 (38.4%)
85–99	6 (5.4%)
Race, N (%)	
Black	66 (58.9%)
White	30 (26.8%)
Missing/Other	16 (14.3%)
Geographic region, N (%)	
Mid-West	21 (18.8%)
North-East	11 (9.8%)
South	55 (49.1%)
West	22 (19.6%)
Missing	3 (2.7%)
Payor, N (%)	
Commercial	16 (14.3%)
Medicare	95 (84.8%)
Missing/Unknown	1 (0.9%)
Diagnosis, N (%)	
CM only	6 (5.4%)
PN only	7 (6.3%)
CM + PN	97 (86.6%)
Unknown	2 (1.8%)
CCI, mean (SD)	4.23 (2.63)
Medication at baseline, N (%)	
Tafamidis	32 (28.6%)
Inotersen	4 (3.6%)
Diflunisal	3 (2.7%)
Doxycycline	8 (7.1%)

Abbreviations: CCI, Charlson Comorbidity Index; CM, cardiomyopathy; PN, polyneuropathy; SD, standard deviation

Figure 2. Adherence to vutrisiran over treatment period



Patients were considered adherent if PDC ≥0.8
Abbreviations: PDC, proportion of days covered

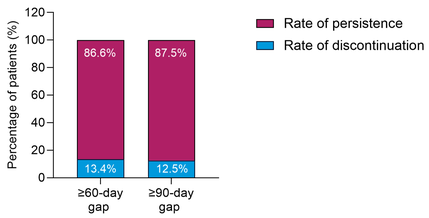
Persistence

•Median time (Q1, Q3) to discontinuation of vutrisiran, defined by a ≥60- or 90-day gap, was 553.0 (443.0, 752.0) and 559.5 (445.0, 763.5) days, respectively

•Discontinuation of vutrisiran at 12 months was observed in 13.4% of patients when discontinuation was classified based on a ≥60-day gap **(Figure 3)**

•Similar discontinuation rates were observed when discontinuation was defined using ≥90-day gap (12.5% at 12 months) **(Figure 3)**

Figure 3. Rates of persistence and discontinuation at 12 months



The rate of persistence was calculated as 100% minus the rate of discontinuation

Discussion

•This is the first study to examine the real-world adherence and persistence with vutrisiran using a geographically diverse, US claims database. However, generalizability to a patient population outside the US may be limited

•Vutrisiran can only be administered by a healthcare professional; therefore, the claims data used to assess adherence and persistence accurately reflect that the patient received the medication

•During the study timeframe, vutrisiran was only approved in the US for ATTR-PN;(4) therefore, it is assumed its use in this cohort was specifically for PN manifestations

•Vutrisiran has demonstrated efficacy and an acceptable safety profile in Phase 3 clinical trials for ATTR;(11,12) this study complements the evidence from those trials

•Less frequent dosing may reduce the burden of oral polypharmacy on patients and improve adherence and persistence(10,13)

•Further research is needed to compare real-world adherence and persistence rates between ATTR-CM therapies and to assess the relationship between adherence, persistence, and outcomes

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Abbreviations: ATTR, transthyretin amyloidosis; ATTR-CM, transthyretin amyloidosis with cardiomyopathy; ATTR-PN, transthyretin amyloidosis with polyneuropathy; CM, cardiomyopathy; CPT, Current Procedural Terminology; NDC, National Drug Codes; PDC, proportion of days covered; US, United States; SD, standard deviation; TTR, transthyretin

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