

Characteristics and Treatment Patterns in Patients With ATTR-CM Treated With Vutrisiran in Clinical Practice

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Conclusions

- This retrospective US claims study revealed vutrisiran use across a broad range of patients with ATTR-CM in real-world clinical practice.
- Patients with ATTR-CM initiating vutrisiran were more diverse than those in the HELIOS-B clinical trial in terms of sex, race, ethnicity, and loop diuretic use, with a higher prevalence of CV and non-CV comorbidities.
- Vutrisiran was used as first-line therapy by approximately 1 in 3 patients, while others received background TTR stabilizer therapy before vutrisiran.

Introduction

- Transthyretin (TTR) amyloid cardiomyopathy (ATTR-CM) is a progressive and fatal disease, caused by the accumulation of amyloid deposits in the myocardial interstitium, which manifests as cardiac and extracardiac symptoms **(1-2)**.
- Management of ATTR-CM includes the use of heart failure (HF) therapies, as well as ATTR-specific therapies, including TTR stabilizers (ie, tafamidis and acoramidis) and the TTR silencer (vutrisiran) **(2)**.
- Vutrisiran is an RNA interference therapeutic that decreases hepatic TTR synthesis to reduce the formation of pathogenic TTR amyloid **(1)**.
- The HELIOS-B clinical trial showed that vutrisiran reduced all-cause mortality and recurrent cardiovascular (CV) events versus placebo while maintaining functional capacity and quality of life in patients with ATTR-CM **(1)**.
- Given the United States (US) Food and Drug Administration (FDA) approved vutrisiran for the treatment of ATTR-CM in March 2025 **(3)**, real-world data on vutrisiran use in clinical practice is limited.

Aim

- To characterize the patient population who received vutrisiran for the treatment of ATTR-CM in real-world clinical practice following its FDA approval.

Methods

Study Design and Data Source

- This retrospective cohort study used data from Optum's deidentified Clinformatics® Data Mart Database from October 1, 2022, through September 30, 2025 (study period).
- Optum Clinformatics® encompasses administrative health claims for members of large commercial and Medicare Advantage health plans.
- The identification period spanned April 1, 2025, through September 30, 2025.
- The index date was defined as the first observed vutrisiran administration.
- Patient characteristics were evaluated during a 6-month baseline period, including the index date, with no follow-up analyses.

Study Population

- Patients were included in the study if they
 - initiated treatment with vutrisiran during the identification period;
 - had baseline evidence of ATTR-CM, defined by *ICD-10-CM* diagnosis codes for (1) wild-type ATTR (ie, E85.82), or (2) other types of amyloidosis, excluding light chain and secondary systemic amyloidosis, combined with a CM or HF diagnosis code within 730 days.

Methods (continued)

- Patients were excluded from the study if they
 - had evidence of pregnancy, cerebral amyloid angiopathy, light chain amyloidosis, or hematopoietic stem cell transplant during the study period;
 - were aged less than 18 years;
 - had less than 180 days of pre-index continuous enrollment.

Study Outcomes

- Baseline demographics, clinical characteristics, HF treatments, and index vutrisiran line of therapy were analyzed descriptively.
- Continuous variables were reported as mean (SD) and median (IQR); categorical variables were reported as count (%).

Results

Patient Attrition

- Among the 305 patients who initiated vutrisiran during the identification period, 279 patients had pre-index ATTR-CM evidence.
- Following the application of the other exclusion criteria, 201 patients were included in the final study population.

Baseline Patient Characteristics

- A descriptive comparison of baseline characteristics available for both Optum and HELIOS-B populations is presented in **Tables 1-2**.

Demographics

- The mean (SD) age of patients was 78.4 (7.7) years, and most patients were male (75%) **(Table 1)**.
- The majority of patients were White (57%), and non-Hispanic (72%), with a notable proportion of Black patients (29%) **(Table 1)**.
- Patients predominantly had Medicare insurance (n = 194; 97%).

Clinical Characteristics

- Overall, 25% of patients were diagnosed with ATTR-CM plus polyneuropathy **(Table 1)**.
- Patients had a moderate-to-high comorbidity burden, with 64% having a Charlson Comorbidity Index of at least 4 (n = 129).
- Prevalence of CV comorbidities was high, with hypertension in 82% of patients, HF in 78%, and atrial fibrillation in 77%; 26% of patients had been hospitalized for HF at baseline **(Table 1)**.
- Diabetes was present in 41% of patients **(Table 1)**.
- A total of 38% of patients had evidence of chronic kidney disease (n = 77), including 31% with chronic kidney disease stage 3 (n = 63).

Results (continued)

Table 1. Baseline Demographics and Clinical Characteristics for Patients With ATTR-CM Initiating Vutrisiran

	Optum Clinformatics® N = 201	HELIOS-B N = 81 ^a
Age, mean (SD), years	78.4 (7.7)	74.8 (6.7)
Sex, n (%)		
Male	150 (75%)	80 (99%)
Race, n (%) ^b		
Asian	< 11 (< 5%)	0 (0%)
Black	58 (29%)	14 (17%)
White	115 (57%)	67 (83%)
Ethnicity, n (%) ^b		
Hispanic	< 11 (< 5%)	< 11 (< 14%)
Non-Hispanic	145 (72%)	80 (99%)
Concurrent polyneuropathy, n (%)	51 (25%)	27 (33%)
CV comorbidities, n (%) ^c		
Atrial fibrillation	154 (77%)	197 (60%) ^d
HF	156 (78%)	326 (100%) ^{d,e}
Hypertension	164 (82%)	185 (57%) ^d
Prior HF hospitalization	53 (26%)	25 (31%)
Diabetes, n (%)	83 (41%)	56 (17%) ^d

Abbreviations: ATTR-CM, transthyretin amyloid cardiomyopathy; CMS, Centers for Medicare and Medicaid Services; CV, cardiovascular; HF, heart failure; *ICD-10-CM*, *International Classification of Diseases, Tenth Revision*, *Clinical Modification*; SD, standard deviation; US, United States.
Cells with n < 11 were suppressed to comply with Optum's and CMS's policies and protect data privacy.
^aData from the HELIOS-B clinical trial (NCT04153149), restricted to US patients who received vutrisiran (N = 81; unpublished).
^bValues for other, missing, or unknown data are not presented.
^cEvidence of CV comorbidities were defined by *ICD-10-CM* diagnosis codes.
^dData from the HELIOS-B clinical trial (NCT04153149), based on the multinational patient population who received vutrisiran (N = 326) **(2)**.
^eAll patients in the HELIOS-B population had HF, as it was an inclusion criterion for the trial **(1)**.

Previously Prescribed HF Treatments

- Most patients used loop diuretics (60%), with 30% using furosemide, 17% using torsemide, and 12% using bumetanide **(Table 2)**.
- Patients had a low-to-moderate diuretic burden, with a median furosemide equivalent dose of 20 mg (IQR, 0-40 mg) **(Table 2)**.
- Additionally, 51% of patients used beta-blockers, 45% used sodium-glucose cotransporter 2 inhibitors, and 39% used mineralocorticoid receptor antagonists **(Table 2)**.

Table 2. Baseline HF Treatments for Patients With ATTR-CM Initiating Vutrisiran

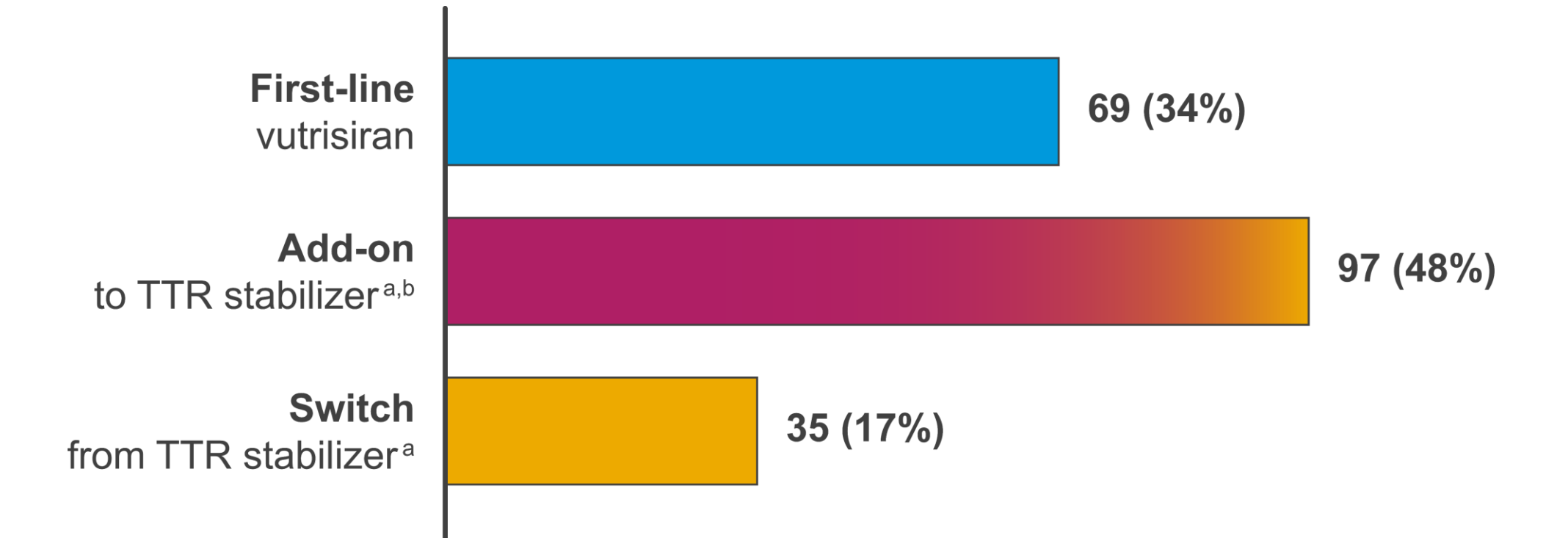
	Optum Clinformatics® N = 201	HELIOS-B N = 326 ^a
Loop diuretic use, n (%)	120 (60%)	261 (80%)
Bumetanide	25 (12%)	NR
Furosemide	61 (30%)	NR
Torsemide	34 (17%)	NR
None	81 (40%)	65 (20%)
FED, median (IQR), mg	20 (0-40)	40 (10-60)
Other medication use, n (%)		
Beta-blocker	102 (51%)	NR
MRA	78 (39%)	NR
SGLT-2 inhibitor	90 (45%)	< 11 (< 3%)

Abbreviations: ATTR-CM, transthyretin amyloid cardiomyopathy; FED, furosemide equivalent dose; HF, heart failure; IQR, interquartile range; MRA, mineralocorticoid receptor antagonist; NR, not reported; SGLT-2, sodium-glucose cotransporter 2.
Cells with n < 11 were suppressed to protect data privacy.
Percentages may not sum to 100% due to rounding.
^aData from the HELIOS-B clinical trial (NCT04153149), based on the multinational patient population who received vutrisiran (N = 326) **(1)**.

Vutrisiran Line of Therapy

- Vutrisiran initiations generally increased from April 2025 (n = 15; 7%) to September 2025 (n = 39; 19%).
- Vutrisiran was the first-line therapy for 34% of patients **(Figure)**.
- Vutrisiran was most commonly used as an add-on to a TTR stabilizer therapy (48%) **(Figure)**.
- Vutrisiran was used to switch from a TTR stabilizer therapy for 17% of patients **(Figure)**.

Figure. Index Vutrisiran Line of Therapy



Abbreviations: TTR, transthyretin.
Due to limited post-index data toward the end of the study period, second-line therapy patterns may have been misclassified; add-on and switch estimates may be subject to minor variations.
^aTTR stabilizer treatments included tafamidis alone, acoramidis alone, or a combination of both.
^bAdd-on line of therapy was represented as a gradient to reflect potential misclassification of add-on versus switch use.

References:

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Abbreviations:

ATTR-CM, transthyretin amyloid cardiomyopathy; CMS, Centers for Medicare and Medicaid Services; CV, cardiovascular; FDA, Food and Drug Administration; FED, furosemide equivalent dose; HF, heart failure; *ICD-10-CM*, *International Classification of Diseases, Tenth Revision*, *Clinical Modification*; IQR, interquartile range; MRA, mineralocorticoid receptor antagonist; NR, not reported; RNA, ribonucleic acid; SD, standard deviation; SGLT-2, sodium-glucose cotransporter 2; TTR, transthyretin; UK, United Kingdom; US, United States.

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