Real-World Characteristics and Treatment Patterns Among Patients With ATTR-CM Who Initiate Vutrisiran Treatment

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Conclusions

- Patients initiating vutrisiran as 2L (vs 1L) therapy had greater CV and overall comorbidity burden and more frequent use of concomitant HF therapies.
- Patients receiving vutrisiran following prior stabilizer therapy may have more complex clinical management needs, highlighting the importance of considering baseline disease burden and treatment history when making therapeutic decisions.

Introduction

- Transthyretin amyloidosis with cardiomyopathy (ATTR-CM) is a progressive disease caused by TTR amyloid deposits accumulating in the myocardium.[1]
- Management of ATTR-CM includes heart failure (HF) therapies and ATTR-specific disease-modifying therapies, including TTR stabilizer and TTR-silencing therapies.[1]
- Vutrisiran is an RNA interference therapeutic that decreases hepatic TTR synthesis to reduce the formation and deposition of pathogenic TTR amyloid.[2,3]
- Vutrisiran demonstrated clinical benefit in patients with ATTR-CM in the HELIOS-B clinical trial.[3]
- As vutrisiran use increases in clinical practice, real-world data are needed to better understand the characteristics and treatment patterns of patients initiating therapy.

Methods

Study Design and Data Source

- This retrospective cohort study used Truveta electronic health record (EHR) data from April 1, 2025, through April 30, 2026 (identification period).
- Adults with ATTR-CM who initiated vutrisiran during the identification period were eligible for inclusion.
- The index date was defined as the date of vutrisiran initiation. Baseline patient characteristics were assessed during the 6 months before index (baseline period).

Study Population

- Patients were included in the study if they were aged ≥18 years; had ATTR-CM (i.e., received vutrisiran, acoramidis, or tafamidis and had evidence of CM or HF); initiated vutrisiran during the identification period; and had ≥6 months of observable baseline data before vutrisiran initiation.
- Patients were classified according to line of therapy:
  - First-line (1L): No recorded prior TTR stabilizer treatment during baseline period.
  - Second-line (2L): Recorded prior treatment with a TTR stabilizer (tafamidis and/or acoramidis) during the baseline period.

Study Outcomes and Statistical Analysis

- This study descriptively analysed patient demographics at index; baseline clinical characteristics and comorbidities; baseline biomarkers (when available), including estimated glomerular filtration rate (eGFR) and N-terminal pro-B-type natriuretic peptide (NT-proBNP); baseline concomitant HF therapies and line of therapy for vutrisiran use.
- Continuous variables were reported using means and standard deviations (SDs) and/or medians and interquartile ranges (IQRs), as appropriate.
- Categorical variables were reported as counts and proportions.
- A descriptive comparison of baseline characteristics available for both Truveta and HELIOS-B populations was also conducted.

Results

Patient Population and Baseline Characteristics (Table)

- Among 1,001 vutrisiran initiators, 415 (41.5%) received vutrisiran as 1L and 586 (58.5%) as 2L therapy.
- Patients had a median age of approximately 78 years; 21.0% were female and 30.9% were Black or African American.
- Patients had a substantial comorbidity burden, with HF and arrhythmia/atrial fibrillation among the most common cardiovascular (CV) comorbidities.
- Loop diuretics were the most commonly used HF therapy (64.5%), followed by SGLT2 inhibitors (48.8%), beta-blockers (46.5%), and MRAs (42.0%).
- Compared with 1L patients, 2L patients generally had greater CV comorbidity burden, including higher prevalence of HF (86.3% vs 67.5%), arrhythmia (75.6% vs 60.0%), and atrial fibrillation (59.6% vs 46.3%), and higher median CCI (8 vs 7).
- Median eGFR at baseline was lower among 2L than 1L patients (55.6 vs 59.4 mL/min/1.73 m²), while median NT-proBNP was higher (2,140 vs 1,742 pg/mL).
- HF therapy use was generally higher among 2L than 1L patients, particularly for loop diuretics (75.4% vs 49.2%) and SGLT2 inhibitors (58.4% vs 35.2%).

Results *continued*

Table. Population Characteristics

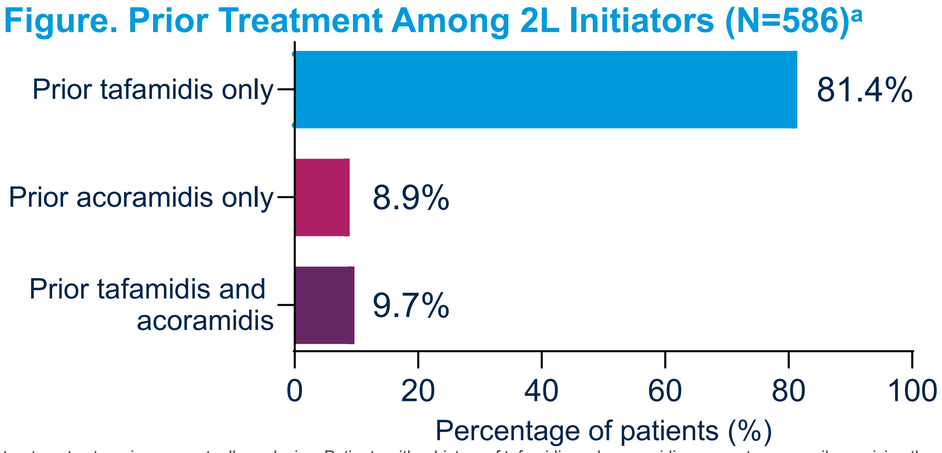
Characteristic	Truveta Vutrisiran total (N=1,001)	Truveta Vutrisiran 1L (n=415)	Truveta Vutrisiran 2L (n=586)	HELIOS-B Vutrisiran (N=81)[a]
Age, years				
Mean (SD)	76.8 (8.8)	75.6 (10.1)	77.8 (7.6)	74.8 (6.7)
Median (IQR)	78 (72–83)	77 (70–82)	78 (73–83)	NR
Sex, n (%)				
Female	210 (21.0)	103 (24.8)	107 (18.3)	1 (1.2)
Male	791 (79.0)	312 (75.2)	479 (81.7)	80 (98.8)
Baseline clinical characteristics, n (%)				
Polyneuropathy indication (any time)	494 (49.4)	211 (50.8)	283 (48.3)	NR[b]
Baseline polyneuropathy	324 (32.4)	147 (35.4)	177 (30.2)	NR[b]
Arrhythmia	692 (69.1)	249 (60.0)	443 (75.6)	NR[b]
Heart failure	786 (78.5)	280 (67.5)	506 (86.3)	326 (100)[b,c]
Atrial fibrillation	541 (54.0)	192 (46.3)	349 (59.6)	197 (60.4)[b]
Hypertension	671 (67.0)	256 (61.7)	415 (70.8)	185 (56.7)[b]
Diabetes	274 (27.4)	98 (23.6)	176 (30.0)	NR[b]
CKD (any stage)	366 (36.6)	133 (32.0)	233 (39.8)	NR[b]
Charlson Comorbidity Index				
Mean (SD)	7.8 (3.2)	7.1 (3.2)	8.3 (3.1)	NR[b]
Median (IQR)	8 (5–10)	7 (4–9)	8 (6–10)	NR[b]
Medications, n (%)				
Other medication use				
SGLT2 inhibitors	488 (48.8)	146 (35.2)	342 (58.4)	10 (3.1)[b]
MRA	420 (42.0)	151 (36.4)	269 (45.9)	NR[b]
Beta-blockers	465 (46.5)	155 (37.3)	310 (52.9)	NR[b]
Loop diuretics use	646 (64.5)	204 (49.2)	442 (75.4)	261 (80.1)[b]
Bumetanide	118 (11.8)	38 (9.2)	80 (13.7)	NR[b]
Furosemide	447 (44.7)	178 (42.9)	269 (45.9)	NR[b]
Torsemide	231 (23.1)	70 (16.9)	161 (27.5)	NR[b]
Baseline labs				
eGFR available, n (%)	756 (75.5)	283 (68.2)	473 (80.7)	81 (100)
Mean (SD), mL/min/1.73m²	57.2 (19.9)	59.6 (20.1)	55.7 (19.7)	67.0 (17.7)
Median (IQR), mL/min/1.73m²	57.4 (41.9–71.1)	59.4 (45.5–73.7)	55.6 (40.3–68.5)	65.0 (53.0–78.0)
NT-proBNP available, n (%)	523 (52.2)	194 (46.7)	329 (56.1)	81 (100)
Mean (SD), pg/mL	3,757.1 (4,834.6)	3,781.2 (4,924.7)	3,742.9 (4,788.2)	2,242.3 (1,590.4)
Median (IQR), pg/mL	1,992.0 (801.3–5,007.2)	1,742.0 (602.0–5,404.0)	2,140.0 (966.8–4,657.0)	1,822.0 (1,083.0–3,062.0)

[a] Unless otherwise indicated, data are from the HELIOS-B clinical trial (NCT04153149), restricted to US patients who received vutrisiran (N = 81; unpublished).
[b] At the time of publication, results for the HELIOS-B US vutrisiran subgroup (N=81) were not available for all parameters used in the Truveta analysis. Data from the HELIOS-B multinational vutrisiran population (N = 326) are reported for these parameters instead, where available.[3]
[c] All patients in the HELIOS-B population had HF, as it was an inclusion criterion for the trial.[3]
Abbreviations: 1L, first-line; 2L, second-line; ATTR-CM, transthyretin amyloidosis with cardiomyopathy; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; MRA, mineralocorticoid receptor antagonist; NR, not reported; NT-proBNP, N-terminal pro-B-type natriuretic peptide; SD, standard deviation; SGLT2, sodium-glucose cotransporter 2.

Prior Treatment Among 2L Vutrisiran Initiators (Figure)

- Among 586 2L initiators, most had previously received tafamidis only (81.4%); 8.9% had received acoramidis only and 9.7% had received both.

Figure. Prior Treatment Among 2L Initiators (N=586)[a]



[a] Prior treatment categories are mutually exclusive. Patients with a history of tafamidis and acoramidis were not necessarily receiving these treatments concomitantly. The analysis did not distinguish between patients who switched from a TTR stabilizer to vutrisiran and those who added vutrisiran to ongoing stabilizer therapy.
Abbreviations: 2L, second-line; TTR, transthyretin.

Discussion and limitations

- In this analysis of real-world EHR data, patients initiating vutrisiran therapy had substantial comorbidity and HF medication use, which was higher in 2L vs 1L vutrisiran initiators.
- EHR data may be incomplete, inconsistently coded, or subject to misclassification, potentially limiting accuracy and generalizability.

Acknowledgments: Medical writing support, under the guidance of the authors, was provided by Kate Rogers of Genesis Research Group, London, UK, and was funded by Alnylam Pharmaceuticals in accordance with Good Publication Practice (GPP 2022) guidelines.

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Presented at: International Symposium of Amyloidosis (ISA) 2026, Nov 15–18, 2026, Montevideo, Uruguay.

Disclosures: SSM has received advisory, consulting, and/or speaking Honoraria from Akimbo Health, Alnylam, BridgeBio, Cytokinetics, Novo Nordisk, and Pfizer. BC and TLK are employees of Alnylam Pharmaceuticals Inc. VN has received speaking Honoraria from BridgeBio and Pfizer.

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Abbreviations: 1L, first-line; 2L, second-line; ATTR-CM, transthyretin amyloidosis with cardiomyopathy; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HCP, heathcare professional; HF, heart failure; IQR, interquartile range; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-B-type natriuretic peptide; SD, standard deviation; SGLT2, sodium-glucose cotransporter 2; US, United States.