Polypharmacy and Potential for Drug–Drug Interactions Among Patients With ATTR-CM Initiating Tafamidis

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Scan to View

Conclusions

- **In this real-world cohort of patients treated with tafamidis there was a high prevalence of polypharmacy and concomitant medication use with potential for DDIs with tafamidis**
- **These factors warrant close monitoring for adherence, persistence, and clinically meaningful DDIs in patients with ATTR-CM treated with tafamidis**

Background and Rationale

- Patients with transthyretin amyloid cardiomyopathy (ATTR-CM) are typically older adults with multiple comorbidities and receive multiple cardiovascular and non-cardiovascular medications (1, 2)
- High medication burden may increase the risk of drug–drug interactions (DDIs) and complicate treatment management in ATTR-CM (2, 3)
- Tafamidis, an oral transthyretin stabilizer approved for ATTR-CM, carries the potential for DDIs as noted in its Prescribing Information, including interactions that can increase exposure to breast cancer resistance protein (BCRP) substrates such as statins (3-5)
- There is limited real-world evidence on medication burden and exposure to potential DDIs with tafamidis use

Objective

To assess the prevalence of polypharmacy and concomitant use of medications with potential DDIs among patients with ATTR-CM receiving tafamidis in real-world clinical practice

Methods

Study Design and Data Source

- In this retrospective observational study, we used de-identified patient-level claims data from the Komodo Healthcare Map database (January 2019–October 2025) to assess medication burden and potential drug-drug interaction exposure among patients with ATTR-CM with a claim for tafamidis
- The database contains longitudinal medical and prescription claims data for more than 325 million insured individuals across the United States (6)

Study Population

- Patients with ATTR-CM were included if they had a claim for tafamidis in the KRD during the study period
- Patients were not required to be newly initiated on tafamidis
- The first observed tafamidis claim in the database was defined as the index date

Medication Assessment Window

- Medications dispensed within 90 days following the index date were identified to evaluate medication burden and potential DDI risk

Statistical Analysis

- Baseline characteristics and medication use were summarized descriptively using means, medians, and proportions

Results

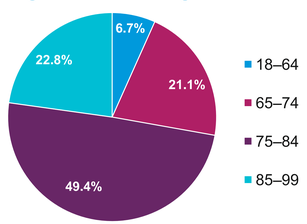
Baseline Demographics and Clinical Characteristics

- Among 7,623 patients with ATTR-CM initiating tafamidis as monotherapy, mean age was **78.1** years (SD 8.0), and most patients were **male** (78.5%) (**Table 1, Figure 1**)
- Patients were most commonly from the Northeast US
- Medicare was the predominant payor
- Index years were most frequently **2024** (29.3%) and 2023 (20.6%)
- The most common comorbid conditions were congestive heart failure (83.9%) and renal disease (36.3%) (data not shown)

Table 1. Patient Baseline Demographics

Characteristic	Tafamidis N=7,623	
	Mean	**SD**
Age	78.1	8.0
Sex	**N**	**%**
Female	1,439	18.9
Male	5,985	78.5
Other	199	2.6
Geographic region	**N**	**%**
Midwest	1,773	23.3
Northeast	2,906	38.1
South	1,901	24.9
West	1,042	13.7
Missing	1	0.01
Index year	**N**	**%**
2019	789	10.4
2020	700	9.2
2021	839	11.0
2022	1,031	13.5
2023	1,568	20.6
2024	2,230	29.3
2025	466	6.1
Payer	**N**	**%**
Commercial	713	9.4
Medicaid	117	1.5
Medicare	6,769	88.8
Missing	24	0.3

Figure 1. Patient Age at Index



- Most patients were aged **75–84 years** (49.4%), and 22.8% were aged 85–99 years (**Figure 1**)

Footnote: Percentages reflect the distribution of age categories among tafamidis-treated patients at the index date

Results (continued)

Medication Burden

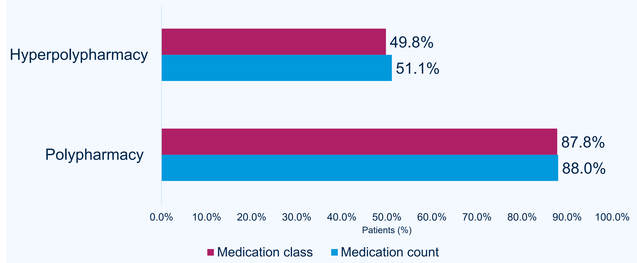
- Among tafamidis-treated patients the mean number of oral medications dispensed within 90 days of the index tafamidis claim was 9.13 (SD 4.55), with a median of 9 (Q1–Q3: 6–11) (**Table 2**)
- The mean number of distinct oral medication classes was 8.89 (SD 4.20), with a median of 8 (Q1–Q3: 6–11) (**Table 2**)

Table 2. Medication Use in Patients Initiating Tafamidis

Characteristic	Tafamidis N=7,623	
Measure	**Oral Medication**	**Medication Class**
Mean (SD)	9.1 (4.6)	8.9 (4.2)
Median	9	8
Range (Q1–Q3)	6–11	6–11
Minimum–Maximum	1–64	1–48

Footnote: Oral medication count = number of unique oral medications dispensed within 90 days of the index tafamidis claim. Medication class count = number of distinct therapeutic classes represented within the same period

Figure 2. Polypharmacy and Hyperpolypharmacy Among ATTR-CM Patients Initiating Tafamidis



Footnote: Blue = total oral medication count; Pink = distinct oral medication class count, assessed within 90 days following the index tafamidis claim. Polypharmacy ≥5; hyperpolypharmacy ≥9

Polypharmacy and Hyperpolypharmacy

Medication Count

- Based on total oral medication count within 90 days, polypharmacy (≥5 medications) was observed in **88.0%** ATTR-CM patients (**Figure 2**)
- Hyperpolypharmacy (≥9 medications) was observed in **51.1%** patients (**Figure 2**)

Medication Class Count

- Based on distinct oral medication classes polypharmacy (≥5 medication classes) was observed in **87.8%** and hyperpolypharmacy in **49.8%** ATTR-CM patients (**Figure 2**)

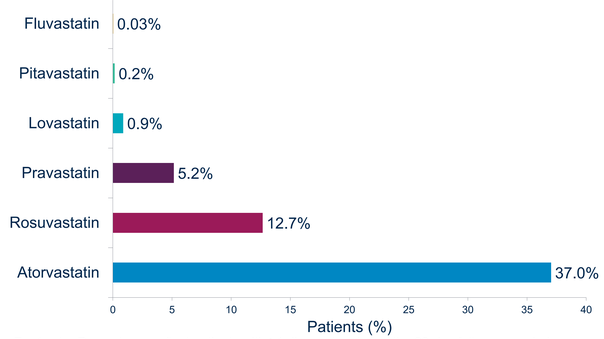
Concomitant Medications

- The most frequently dispensed medication classes included loop diuretics (62.4%) and statins (60.6%) beta blockers (49.2%), and direct factor Xa inhibitors (46.9%), consistent with management of heart failure and related cardiovascular conditions

Observed Use of Medications with Potential DDIs

- Among individual statins, atorvastatin (37.0%) and rosuvastatin (12.7%) were most frequently dispensed (**Figure 3**)
- Rosuvastatin, a BCRP substrate referenced in the tafamidis Prescribing Information, was dispensed to 12.7% of patients (**Figure 3**)
- Simvastatin (5.9%) and pravastatin (5.2%) were less commonly used

Figure 3. Distribution of BCRP Substrate Use Among ATTR-CM Patients Initiating Tafamidis



Footnote: Percentages reflect patients with ≥1 dispensing during the 90-day follow-up period

Strengths and Limitations

Strengths:

- Large national real-world cohort of patients with ATTR-CM receiving tafamidis
- Comprehensive characterization of medication burden and polypharmacy in patients with ATTR-CM initiating tafamidis

Limitations:

- Claims data do not confirm whether medications were taken as prescribed
- Findings may not generalize to populations outside U.S. health plans

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Disclosures: Ankur Patel, and Teresa Kauf are employed by Alnylam Pharmaceuticals and hold company stocks

Abbreviations: ATTR, transthyretin-mediated amyloidosis; ATTR-CM, transthyretin amyloid cardiomyopathy; BCRP, breast cancer resistance protein; DDI, drug–drug interaction; FU, follow-up; KRD, Komodo Research Database; Q1, first quartile; Q3, third quartile; SD, standard deviation; TTR, transthyretin; US, United States

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