Contemporary Oral Medication Usage and Frequency in Patients With Transthyretin Cardiac Amyloidosis

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PURPOSE

- **We report oral medication use in patients with transthyretin cardiac amyloidosis (ATTR-CM) using 2 complementary sources: ATTRibute-CM study and real-world claims data**

INTRODUCTION

- ATTR-CM, a progressive disease caused by the destabilization and deposition of misfolded amyloid fibrils in the myocardium, is an increasingly recognized cause of heart failure (HF) with a higher prevalence in older patients, who also often experience comorbidities requiring concomitant medical therapy[1-5]
- Acoramidis is a next-generation, investigational treatment for ATTR-CM, with near-complete TTR stabilization (≥ 90%) and is administered orally twice daily (BID)[6]
- While medication use in clinical trials follows the study protocol, it is also important to analyze medication use in the real-world setting
- The first step is to characterize patients' current medication dosing schedules
- Here we report oral medication use in patients with ATTR-CM using 2 complementary sources: ATTRibute-CM study and real-world claims data

METHODS

- The study design of ATTRibute-CM (NCT03860935) has been described previously. Patients with ATTR-CM were randomly assigned 2:1 to receive 800 mg of acoramidis-HCl or matching placebo BID for 30 months[6]
  - Acoramidis demonstrated a significant improvement compared with placebo in the four-step primary hierarchical endpoint consisting of death from any cause, cumulative frequency of cardiovascular-related hospitalization, change from baseline in N-terminal pro-B-type natriuretic peptide level, and change from baseline in 6-minute walk distance over 30 months ($P < 0.0001$); acoramidis was generally well tolerated[6]
- Clinical trial data were obtained from ATTRibute-CM
  - Patients from acoramidis and placebo groups were pooled for this analysis
  - Baseline oral medication use was collected upon enrollment in ATTRibute-CM
- Real-world data were obtained from patients meeting stability criteria in the Optum Clinformatics Data Mart (**Figure 1**)
  - Patients who met the stability criteria were those who had: 1) At least 2 years of continuous enrollment with a minimum of 3 months look back and 12 months look forward from index diagnosis, during the study period of 2018-2021; 2) At least 28 days of continuous treatment for a given dosing frequency within the 12 month look forward period
- Results are reported descriptively

FIGURE 1. Optum Clinformatics Data Mart Patient Attrition

Inclusion/exclusion step	Excluded patient count	Remaining patients in cohort
Patients diagnosed with ATTR and/or treated with tafamidis between 2016 and 2022	20 750	
Exclude patients without HF/CM diagnosis within 2 years of ATTR	873	19 877
Exclude patients without at least one HF/CM diagnosis between 2018 and 2021	7761	12 116
Exclude patients with AL/MM before index diagnosis or within 18 months following index diagnosis	2708	9408
Exclude patients undergoing treatment on AL chemotherapy drugs anytime during 2016 and 2022	87	9321
Exclude patients with heart, liver, or kidney transplants on or before index diagnosis or within 12 months following index diagnosis	239	9082
Exclude patients with heart device implants on or before index diagnosis or within 12 months following index diagnosis	113	8969
Exclude patients that do not meet stability criteria	3368	5601
Final ATTR-CM patient cohort	5601	
Patients with chronic prescription medication of any dosing frequency during 1 year follow-up after index diagnosis	4739	
Patients with chronic prescription medication of any dosing frequency during 1 year follow-up after index diagnosis with days of supply ≥ 28 days within dosing frequency for a brand	4725	
Patients with chronic BID prescription medications during 1 year follow-up after index diagnosis	4166	

CONCLUSIONS

- **Patients with ATTR-CM take multiple oral medications administered BID for treatment of HF and other comorbidities**
- **As a BID medication, acoramidis, an investigational, novel treatment for ATTR-CM with robust efficacy on cardiovascular-related hospitalization, appears to consistently follow non-ATTR-CM pharmacotherapy strategies commonly implemented in the real-world**
- **These data suggest that acoramidis aligns with and would be easily implemented into patients' existing non-ATTR-CM pharmacotherapeutic regimens**
- **Further research should be undertaken to assess whether BID dosing in the ATTR-CM population impacts real-world medication adherence**

RESULTS

- Baseline demographics are shown in **Table 1**
  - ATTRibute-CM randomly assigned 632 patients with ATTR-CM (mean [±SD] age: 77.3 [6.55] years)
  - From a pool of 2.46 million patients with HF and CM identified in Optum's Clinformatics Data Mart, 12 116 patients met the criteria for ATTR-CM, and 5601 patients (mean [±SD] age: 76 [9.4] years) met the stability criteria (≥ 2 years of continuous enrollment and ≥ 28 days of continuous treatment)

TABLE 1: Baseline Demographics of Patients in the (A) ATTRibute-CM Trial and (B) Optum Clinformatics Data Mart Analysis

(A)

	Overall safety population in ATTRibute-CM trial N = 632
Age, years, mean (SD)	77.3 (6.55)
Sex, n (%)	
Male	570 (90.2)
Female	62 (9.8)
Race or ethnic group, n (%)	
American Indian or Alska Native	1 (0.2)
Asian	13 (2.1)
Black or African American	30 (4.7)
Native Hawaiian or Other Pacific Islander	1 (0.2)
White	555 (87.8)
Other	6 (0.9)
Multiple races	2 (0.3)
Not reported	24 (3.8)

ATTR-CM, transthyretin cardiac amyloidosis; SD, standard deviation.

(B)

	Optum Clinformatics Data Mart analysis N = 5601
Age, years, mean (SD)	76 (9.40)
Sex, n (%)	
Male	3198 (57.1)
Female	2403 (42.9)
Race or ethnic group, n (%)	
Asian	126 (2.2)
Black	1058 (18.9)
Hispanic	459 (8.2)
White	3661 (65.4)
Unknown	24 (0.4)
None	273 (4.9)

TABLE 2: Oral Medication Use and Frequency in the ATTRibute-CM Trial, at Baseline[a]

	Overall safety population N = 632
Oral medication use at baseline,[a] number of patients, n (%)	
Daily oral use	612 (96.8)
BID or TID or QID	407 (64.4)
At least one BID	392 (62.0)
Most frequent drug class[b] administered BID,[a] number of patients, n (%)	
Antithrombotic agents	208 (32.9)
Diuretics	120 (19.0)
Beta-Blocking agents	88 (13.9)
Agents acting on the renin-angiotensin system	39 (6.2)
Drugs used in diabetes mellitus	37 (5.9)

[a]Only medications started before the first dose of study drug and continued on/after the day of first dose of study drug are included in the analysis.
[b]Medication class is based on the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) level 2 drug classification

- Oral Medication use and frequency in the ATTRibute-CM trial and Optum Clinformatics Data Mart are shown in **Table 2** and **3**, respectively
- In the ATTRibute-CM trial, the most frequent BID medications within these drug classes were apixaban, furosemide, metformin, metoprolol, and sacubitril-valsartan
- In the Optum Clinformatics Data Mart, the most frequent BID medications were apixaban, carvedilol, furosemide, metoprolol, and potassium chloride
- Patients in the Optum Clinformatics Data Mart had an average (SD) of 8.9 (4.1) unique medication brands per patient (minimum = 1 brand, maximum = 28 brands) and 7.3 (2.9) medication classes per patient (minimum = 1 medication class, maximum = 17 medication classes)

TABLE 3: Chronic (≥ 28 continuous days) Oral Medication Use and Frequency in Patients With ATTR-CM from Optum Clinformatics Data Mart

	Overall population N = 4725
Oral medication use, number of patients, n (%)	
Daily oral use	4690 (99.3)
BID or TID or QID	4351 (92.1)
At least one BID	4166 (88.2)
Most frequent drug class administered BID,[a,b] number of patients, n (%)	
Beta-Blocking agents	2051 (49.2)
Antithrombotic agents	1474 (35.4)
Diuretics	1325 (31.8)
Agents acting on the renin-angiotensin system	700 (16.8)
Drugs used in diabetes mellitus	606 (14.5)

[a]Top 5 drug classes with the most medication use (based on proportion of patients) are listed here.
[b]Medication class is based on the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) level 2 classification, mapped by NDC using mapping maintained by Definitive Healthcare

- Among patients in the ATTRibute-CM trial, the mean proportion of tablets taken of the expected number was high (approximately 97% in each treatment group and overall; **Table 4**)

TABLE 4: Adherence to Acoramidis During ATTRibute-CM Trial, Safety Population

	Acoramidis n = 421	Placebo n = 211	Overall N = 632
Mean percentage of tablets taken of expected number, %	97.1	97.0	97.1

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ABBREVIATIONS: AL, amyloid light-chain; ATTR-CM, transthyretin cardiac amyloidosis; BID, twice daily; CM, cardiomyopathy; HF, heart failure; MM, multiple myeloma; QID, four times daily; SD, standard deviation; TID, three times daily; TTR, transthyretin.

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