Clinical Presentation and Treatment Landscape of Patients with Transthyretin Amyloidosis with Cardiomyopathy: A Real-World Study in Five European Countries and Japan

Caroline Morbach[1], Jin Endo[2], José González-Costello[3], Francesco Cappelli[4], William E. Moody[5], Elena Klimova[6], Gilbert Habib[7]

[1]Department of Clinical Research and Epidemiology, Comprehensive Heart Failure Center, and Department of Medicine I, University Hospital Würzburg, Würzburg, Germany; [2]Department of Cardiology, Keio University School of Medicine, Tokyo, Japan; [3]Department of Cardiology, IDIBELL, Bellvitge University Hospital, CIBER-CV, Barcelona, Spain; [4]Cardiomyopathy Unit, Careggi University Hospital, Florence, Italy; [5]Institute of Cardiovascular Sciences, University of Birmingham, Birmingham, UK; [6]Strategy, Insights, and Analytics, Alnylam Pharmaceuticals, London, UK; [7]Cardiology Department, La Timone Hospital, Marseille, France.

Conclusions

- A real-world study conducted with cardiologists across five European countries and Japan showed that patient characteristics were generally similar across countries and reflected the multi-organ impairment in transthyretin amyloidosis with cardiomyopathy (ATTR-CM)
- Most patients were considered as having partial or no response to their current treatment by the reporting physicians, and showed persistence or progression of heart failure symptoms, reflecting an unmet need for more available and effective treatment options in ATTR-CM

Introduction

ATTR-CM

- Transthyretin amyloidosis (ATTR) is a progressive, fatal systemic disease caused by misfolded transthyretin (TTR) protein accumulating as toxic amyloid fibrils in multiple organs,[1–4] and results from inherited *TTR* gene variants (hATTR) or with ageing in those with wild-type TTR (wtATTR)[1–4]
- ATTR has a heterogeneous clinical presentation of cardiac, neurological or other manifestations, or often with a mixed phenotype of cardiomyopathy and polyneuropathy[4]
- Patients with ATTR-CM experience progressive heart failure, arrhythmias, decline in health status and quality of life, and increased hospitalisations and mortality[1,5]
- Current treatment options for ATTR-CM remain limited, with TTR tetramer stabilisers being the only approved agents for ATTR-CM[6,7]

Objective

- To characterise the clinical presentation and treatment landscape of patients with ATTR-CM from real-world clinical practice across 6 different countries

Methods

- Primary market research study conducted with cardiologists in France, Germany, Italy, Japan, Spain, and the UK between September 2023 and October 2023, with supporting data from anonymised patient records
- Cardiologists were identified and approached through computer-assisted web interviews based on IQVIA OneKey. Qualifying criteria included cardiology as main speciality; ≥3 years practising medicine, ≥20% time in patient care, and ≥1 wtATTR-CM patient followed in the last 12 months
- Cardiologists completed a 45-minute online survey, reporting data for ≥1–6 patients with ATTR-CM they had seen in the previous 12 months
- Medical records based on data from patient record forms were aggregated and fully anonymised

Results

Data Sources

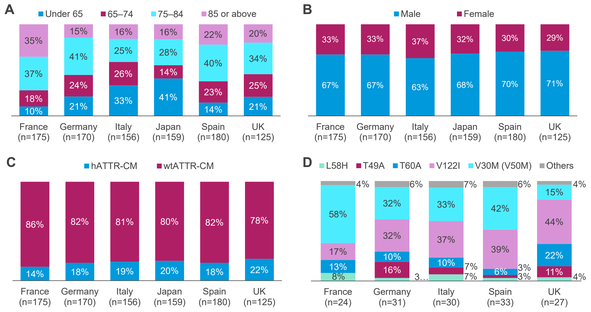
- Market research data were available from 242 cardiologists (France n=41, Germany n=41, Italy n=40, Japan n=46, Spain n=42, and the UK n=32) who contributed 965 patient record forms (France n=175, Germany n=170, Italy n=156, Japan n=159 Spain n=180, and the UK n=125)
- Participating cardiologists were mainly based in non-private settings (France 63%, Germany 73%, Italy 78%, Japan 100%, Spain 98%, UK 100%)

Results

Patient Demographics and Disease Characteristics

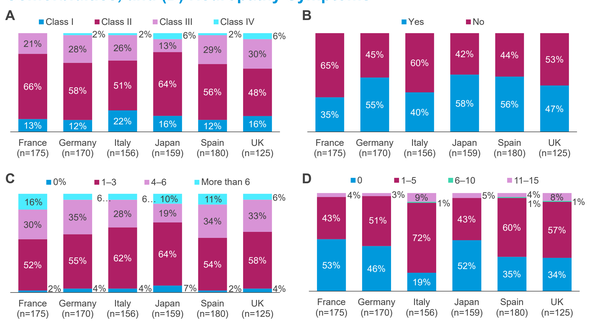
- Overall, most of the 965 patients with ATTR-CM were male (63–71%), aged ≥65 years (59–90%), and had wtATTR-CM (78–86%) (**Figure 1A–C**)
- Among patients with hATTR-CM, the most common *TTR* gene variants were V50M (V30M) and V122I (**Figure 1D**)

Figure 1. ATTR-CM Patient Distribution by (A) Age[a], (B) Gender, (C) Amyloidosis Type, and (D) *TTR* Variant[b,c]



[a]Age at most recent consultation; [b]Patients with hATTR-CM; [c]*TTR* variant data not available for Japan.

Figure 2. ATTR-CM Patient Distribution at Their Most Recent Consultation by (A) NYHA Class, (B) Presence of Heart Failure, (C) Comorbidities, and (D) Neuropathy Symptoms



Clinical Presentation at the Most Recent Consultation

- The most common clinical presentation in patients with ATTR-CM was heart failure (35–58%), with most patients in NYHA class II (48–66%) (**Figure 2A, 2B**)
- More than 90% of patients in each country had ≥1 comorbidity (**Figure 2C**)
- Neuropathy symptoms were reported by most patients with ATTR-CM across countries (48–81%) (**Figure 2D**)
- Reported symptoms and clinical presentations were generally similar across countries, with the most common including heart failure, dyspnoea/shortness of breath, fatigue, cardiomyopathy, arrhythmia, and muscle weakness (**Figure 3**)

Figure 3. Most Common Symptoms and Clinical Presentations Reported for Patients with ATTR-CM at Their Most Recent Consultation

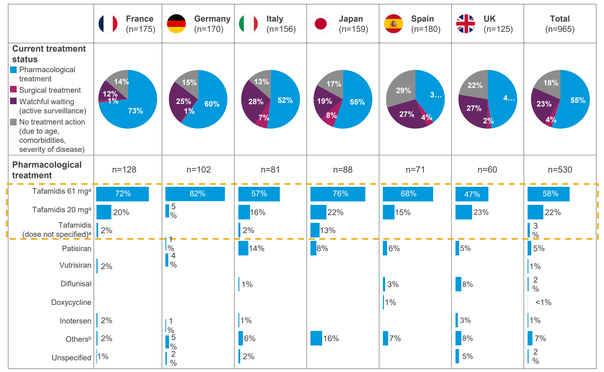
	France (n=175)	Germany (n=170)	Italy (n=156)	Japan (n=159)	Spain (n=180)	UK (n=125)
Heart failure	35%	55%	50%	58%	56%	47%
Dyspnoea/shortness of breath	51%	45%	40%	26%	54%	58%
Fatigue	45%	38%	40%	23%	41%	54%
Cardiomyopathy	36%	45%	50%	38%	39%	40%
Oedema	21%	23%	16%	25%	37%	32%
Arrhythmia	37%	32%	42%	35%	48%	34%
Carpal tunnel syndrome	20%	22%	30%	15%	22%	6%
Rhythm disturbance	20%	20%	29%	13%	27%	20%
Muscle weakness	23%	17%	47%	17%	21%	20%
Numbness	8%	21%	39%	6%	11%	26%
Cardiac disorders	11%	15%	18%	28%	22%	14%
Walking difficulty	13%	18%	22%	13%	19%	18%
Impaired balance	13%	12%	21%	8%	14%	17%
Orthostatic intolerance	9%	11%	24%	9%	23%	20%
Conduction disturbances	21%	11%	26%	15%	24%	19%

The top three most common symptoms for each country are highlighted.

ATTR-CM Treatment Patterns and Response

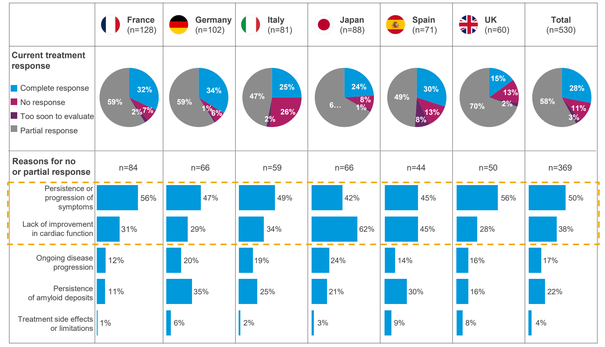
- The proportion of patients receiving pharmacological treatment ranged from 39% in Spain to 73% in France (**Figure 4**)
  - Across countries, 13–29% of patients were not receiving any form of treatment action or active surveillance due to age, comorbidities, or disease severity
  - Of patients on TTR-targeted treatments, the majority received tafamidis 61 mg (ranging from 47% in the UK to 82% in Germany)
- Across countries, cardiologists reported an inadequate response (i.e., no or partial response) to treatment for most patients (62–83%), with reports of persistence or progression of symptoms in 42–56% of patients and lack of improvement in cardiac function in 28–62% of patients (**Figure 5**)

Figure 4. Treatment Status of Patients with ATTR-CM



[a]Tafamidis is an approved treatment in some countries and available under early access programmes and compassionate use programmes in Spain and the UK; [b]Others includes diuretics (e.g., furosemide), alpha- and beta-blockers, angiotensin receptor-neprilysin inhibitor, aldosterone antagonist, cardiac glycoside, SGLT2/SGLT2i, mineralocorticoid receptor antagonist, antiepileptic, implants, and vasopressin receptor antagonists.

Figure 5. Response to Treatment in Patients with ATTR-CM as Perceived by the Reporting Physician



Definitions: 'Persistence or progression of symptoms', symptoms such as fatigue, shortness of breath, oedema, arrhythmias, etc.; 'Lack of improvement in cardiac function', assessed by measures such as ejection fraction, cardiac output, or exercise tolerance; 'Ongoing disease progression', underlying amyloid deposits continue to accumulate or cause further damage to the heart leading to disease progression, worsening of cardiac function, or development of additional complications; 'Persistence of amyloid deposits', existing amyloid deposits in the heart not fully eliminated or cleared. Residual deposits may persist, potentially affecting cardiac structure and function even if the treatment is effective in slowing down or halting further deposition; 'Treatment side effects or limitations', medication intolerance, adverse reactions, or the need for dose adjustments.

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Abbreviations: ATTR, transthyretin amyloidosis; ATTR-CM, ATTR with cardiomyopathy; hATTR, hereditary ATTR; GP, general practitioner; HCP, healthcare professional; NYHA, New York Heart Association; SGLT2, sodium–glucose cotransporter-2; SGLT2i, sodium–glucose cotransporter-2 inhibitor; TTR, transthyretin; wtATTR, wild-type ATTR.

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