Demographic characteristics of the 1902 transthyretin amyloid cardiomyopathy patients treated by tafamidis through the French early access program

O. Lairez[1], P. Reant[2], G. Habib[3], J. Jeanneteau[4], J.C. Eicher[5], A. Jobbe Duval[6], B. Lequeux[7], F. Bauer[8], M. Bartoli[9], C. Noirot-Cosson[9], J. Rudant[9], M. Kharoubi[10], T. Damy[10]

[1]University Hospital of Toulouse, Department of Cardiology, Department of Nuclear Medicine, Cardiac Imaging Center, Toulouse, France; [2]Hôpital Haut-Levêque, Department of Cardiology, Centre hospitalo-universitaire de Bordeaux, Université de Bordeaux, INSERM 1045, IHU Lyric, CIC1401, Pessac, France; [3]La Timone Hospital, Department of Cardiology, Marseille, France; [4]Clinic Saint Joseph, Department of Cardiology, Trelaze, France; [5]Hôpital du Bocage, Department of Cardiology, Centre Hospitalo-Universitaire de Dijon, Dijon, France; [6]Hospital Louis Pradel of Bron, HCL, Department of Heart failure, Bron, France; [7]University Hospital of Poitiers, Department of Cardiology, Poitiers, France; [8]Normandie Univ, UNIROUEN, INSERM U1096, University Hospital of Rouen, Department of Cardiac Surgery, Rouen, France; [9]Pfizer, Medical department, 23–25 avenue du Dr. Lannelongue, Paris, France; [10]CHU Henri Mondor, Department of Cardiology, Referral Center for Cardiac Amyloidosis, GRC Amyloid Research Institute, Clinical Investigation Center 006, DHUA-TVB INSERM U955, Creteil, France

Funding Acknowledgement: Type of funding sources: Private company. Main funding source(s): Early access program sponsored by Pfizer

Background: Transthyretin amyloidosis (ATTR) is a rare and serious, systemic disease characterized by deposits of amyloid fibrils in various tissues and organs. Tafamidis meglumine is a potent and selective stabilizer of TTR, indicated since 2011 in the treatment of neurological forms of the disease. The French "Agence Nationale de Sécurité du Médicament et des produits de santé" (ANSM) granted a temporary recommendation for use (RTU) on November 28th 2018, based on ATTR-ACT, the pivotal trial results, and designed to enable use of tafamidis meglumine in ATTR cardiomyopathy (ATTR-CM) patients with NYHA I, II and III before marketing authorization. This RTU has been a unique opportunity in France to collect real world data of ATTR-CM patients treated by tafamidis meglumine.

Objective: We aimed to describe the characteristics of ATTR-CM patient treated by tafamidis in the setting of the RTU, over 2 years from November 28th 2018 to November 27th 2020.

Methods: Demographic and clinical data about the diagnosis pathway of patients included in the RTU were prospectively collected using questionnaires, as requested by ANSM to be completed by physicians at the time of tafamidis prescription. A second version of the inclusion form, introduced in May 2020, has allowed collection of additional clinical information.

Results: Overall, 1902 ATTR-CM patients have been included by 189 physicians from 107 centers. Nine centers included each at least 50 patients, accounting for 1092, or 57.4% of all patients. The median age of the patients was 82 years (IQR=9 years), 82% were male, and, 12.4%, 58.8% and 28.7% of patients had a NYHA class of I, II and III, respectively. For almost all patients, the diagnosis of restrictive/infiltrative heart failure was based on heart MRI and/or echocardiography (98.5%; among the 601 patients included from May 2020 28.8% had both exams, 69.7% echo only and 1.6% MRI only), the infiltrative nature of the cardiomyopathy had been confirmed by bone scintigraphy (99.3%), and the absence of light chains had been confirmed by protein electrophoresis or Bence Jones proteinuria (96.6%). Genetic test was performed in 1205 patients (69.4%). Out of the 884 patients who had a genetic test result available at the time of initial prescription, 762 (86.2%) were affected with the wild-type form and 122 (13.8%) with the hereditary form. Among the 601 patients included from May 2020, a hospitalization for cardiovascular condition within the 6 months preceding tafamidis initiation was reported for 22.3% of them, and tafamidis was initiated within 12 months after diagnosis for 92% of them (only 8% initiated the treatment beyond that period).

Conclusion: The RTU program has provided 1902 ATTR-CM patients with early access to tafamidis over 24 months, in France. Overall, as compared to patients included in ATTR-ACT, the pivotal trial, RTU patients were older, the proportion of wild-type was slightly higher, and NYHA distributions were similar.

Table 1: main characteristics of patients included in RTU according to ATTR-CM subtype

	ATTR-CM N=1902	ATTRwt (wild type) N=762	ATTRv (hereditary) N=122	Genetic test not done N=531	Result not yet available/missing N=487
Age, years, median (Q1, Q3)	82 (76, 85)	80 (76, 85)	74 (70, 80)	83 (79, 87)	82 (77, 85)
Male gender, n (%)	1565 (82.3%)	649 (85.2%)	84 (68.9%)	434 (81.7%)	398 (81.7%)
NYHA class					
I, n (%)	231 (12.4%)	91 (12.3%)	22 (18.3%)	51 (9.7%)	67 (14.0%)
II, n (%)	1094 (58.8%)	406 (55.0%)	52 (43.3%)	338 (64.4%)	298 (62.2%)
III, n (%)	534 (28.7%)	241 (32.7%)	43 (35.8%)	136 (25.9%)	114 (23.8%)
IV, n (%)	3 (0.2%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	0 (0.0%)
Missing	40	24	2	6	8