**Cardiac safety and tolerability, and effects on cardiac function of tafamidis in patients with non-V30M TTR-FAP**

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**Background:** Transthyretin familial amyloid polyneuropathy (TTR-FAP) is an autosomal dominant disease characterized by extracellular amyloid deposition in the nerves and heart. Orthotopic liver transplant (OLT) is recommended to remove the source of mutated TTR and stop amyloid deposition. However, progressive cardiomyopathy due to continuing amyloidosis has been described following OLT in patients with non-V30M mutations. Tafamidis prevents dissociation of TTR into monomers and formation of amyloid.

**Objectives:** To evaluate cardiac safety and tolerability of tafamidis in patients with non-V30M TTR-FAP.

**Methods:** Patients (N=21) with TTR-FAP due to non-V30M TTR mutations and no OLT history were studied in a phase 2 open-label trial. Cardiac assessments included ECG, 24-hour Holter monitoring, echocardiogram, and cardiac biomarkers (troponin I and NT-pro-BNP) at baseline and 6 and 12 months.

**Results:** Of the 21 patients enrolled, mean (SD) age, LVEF, troponin I, and NT-pro-BNP at baseline were 63.1 (9.86) years, 60.3 (9.96)%, 0.023(0.04) ng/mL, and 1248.9 (1529.4) pg/mL, respectively. Nine patients had a history of cardiac events. Six of these 9 experienced peripheral edema or dyspnea related to heart failure while on treatment, and 3 patients were hospitalized for other cardiovascular events (AV block, coronary stenosis, TIA). Eighteen patients completed the study, with no significant changes in troponin I, LVEF, or cardiac remodeling. NT-pro-BNP, while elevated at baseline, remained stable with no clinically relevant changes. The pattern of Holter monitoring abnormalities was similar at baseline and while on treatment (eg, atrial tachycardia, 52.4% [11/21] vs 44.4% [4/9]). The percentage of patients with normal heart rate variability (HRV) increased from 21% (4/19) at baseline to 42% (8/19) at month 12.

**Discussion:** This study showed no deleterious effects of tafamidis on cardiac function among a cohort of treated TTR-FAP patients. The number of patients with severe cardiac disease.

**Conclusion:** Cardiac safety and tolerability of tafamidis in patients with non-V30M TTR-FAP.

**Conclusions:** Tafamidis was safe and well tolerated in patients with non-V30M TTR-FAP.

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**Left atrial enlargement in sickle cell disease patients: remodelling associated with haematological parameters or index of left ventricular filling pressures**

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**Background:** Several arrhythmias were reported in myotonic dystrophy (MD). The most frequent would be conduction disturbances and ventricular arrhythmias. The purpose of the study was to evaluate the prevalence of atrial flutter and fibrillation (AF) in MD and the consequences.

**Methods:** 157 patients, 80 men and 77 women, aged from 16 to 70 years, mean age 41±14 years, at the inclusion, were consecutively recruited for a type 1 MD. Patients were asymptomatic at the inclusion, except 4 patients were followed during 4.5±3.5 years. ECG, left ventricular ejection fraction (LVEF) determination at echocardiography, Holter monitoring, signal-averaged ECG were obtained and repeated.

**Results:** 24 patients presented sustained (> 1 hour) AF or atrial flutter (n=8). The prevalence was 15%. Among these patients 2 presented a 1/1 atrial flutter associated with syncope. In one of them, 16 years old, cardiac defibrillator was implanted for a diagnosis of ventricular tachycardia, but the real diagnosis was made after inappropriate shocks. Atrial flutter ablation was performed in 4 patients but 3 of them developed AF. During follow-up, 21 patients died...
15% during the follow-up generally from cardiac and respiratory failure. 7 of them had AF (29%) and 14 had no AF (10.5%) (p < 0.01). Univariate analysis indicated that age greater than 40 years (death: 51±14 vs 40±14 in alive patients), ECG, occurrence of sustained AF or flutter and LVEF less than 45% were significant predictors of death. At multivariate analysis AF at ECG (relative risk RR 6.72) was independent predictor of death.

Conclusions: Atrial flutter and atrial fibrillation are frequent in MD and are associated with increasing mortality. Atrial flutter may present as a 1:1 atrial flutter (25%) with a poor tolerance and a risk of misdiagnosis.

Method and results: Two hundred and twenty consecutive patients with definite left-sided native valve IE according to the Duke criteria were included in this analysis. When compared with patients without CHF (n=144), new heart murmur, high comorbidity index, aortic valve IE, and severe valve regurgitation were more frequently observed in CHF patients (n=76, 34.5%). Aortic valve IE, elderly patients were more frequent in CHF patients. Congestive heart failure was independently predictive of in-hospital [OR 3.8 (1.7-9.0); P=0.0013] and 1 year mortality [HR 1.8 (1.1-3.0); P=0.007]. Early surgery was performed in 63% of CHF patients with a peri-operative mortality of 15%. In the CHF group, comorbidity index, anemia, uncontrolled infection, and major neurological events were multivariate predictors of 1 year mortality. Early surgery was independently associated with improved 1 year survival [HR 0.45 (0.22-0.93); P=0.03].

Conclusion: Native valve IE complicated by CHF is more frequent in aortic IE and is associated with severe regurgitation. Congestive heart failure is an independent predictor of in-hospital and 1 year mortality. In CHF patients, early surgery is independently associated with reduced mortality and should be widely considered to improve outcome.