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## **P352 EXPLORATORY ANALYSES FROM APOLLO-B, A PHASE 3 STUDY OF PATISIRAN IN PATIENTS WITH ATTR AMYLOIDOSIS WITH CARDIOMYOPATHY**

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► **To cite this version:**

F Cappelli, P Kale, Mathew Maurer, Marianna Fontana, M Grogan, et al.. P352 EXPLORATORY ANALYSES FROM APOLLO-B, A PHASE 3 STUDY OF PATISIRAN IN PATIENTS WITH ATTR AMYLOIDOSIS WITH CARDIOMYOPATHY. 54th Congress of the Italian Association of Hospital Cardiologists (ANMCO), May 2023, Rimini, Italy. pp.D181-D182, 10.1093/eurheartj-suppl/suad111.425 . hal-04428722

**HAL Id: hal-04428722**

**<https://hal.science/hal-04428722>**

Submitted on 31 Jan 2024

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Abstract citation ID: suad111.425

**P352 EXPLORATORY ANALYSES FROM APOLLO-B, A PHASE 3 STUDY OF PATISIRAN IN PATIENTS WITH ATTR AMYLOIDOSIS WITH CARDIOMYOPATHY**

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**Introduction:** Transthyretin-mediated (ATTR) amyloidosis is a progressive and fatal disease. Patients with hereditary or wild-type ATTR amyloidosis frequently develop cardiomyopathy (CM). Patisiran, an IV RNAi therapeutic that inhibits synthesis of wt and variant TTR, is approved for the treatment of hATTR amyloidosis with polyneuropathy.

**Methods:** In APOLLO-B, patients were 18-85 yrs old with evidence of cardiac amyloidosis by echocardiography, ATTR amyloid deposition on tissue biopsy or fulfilling nonbiopsy diagnostic criteria for ATTR amyloidosis with CM, and had prior hospitalization for heart failure (HF) due to ATTR amyloidosis or clinical evidence of HF. Patients were randomized 1:1 to patisiran IV 0.3 mg/kg or placebo Q3W for 12 months. The primary endpoint was change from baseline in 6-MWT at Month 12 (M12) with patisiran vs placebo. Exploratory parameters at M12 included changes in cardiac biomarkers, echocardiography and Tc scintigraphy.

**Results:** APOLLO-B enrolled 360 patients (patisiran, n=181; placebo, n=179); median age, 76.0 yrs; male, 89%; wtATTR, 80%; on tafamidis at baseline, 25%. Patisiran showed a significant benefit compared with placebo in 6-MWT (median [95% CI] change from baseline: patisiran, -8.15 [-16.42, 1.50]; placebo, -21.35 [-34.05, -7.52]; HL estimate of median difference: 14.69 [0.69, 28.69]; p=0.0162). Patisiran demonstrated favorable trends in change from baseline of NT-proBNP (mean fold change ratio [95% CI]: 0.80 [0.73, 0.89]; p=1.825×10<sup>-5</sup>) and troponin I (mean fold change ratio [95% CI]: 0.87 [0.80, 0.95]; p=0.0011) at M12 vs placebo. Patisiran also demonstrated a trend towards benefit in change from baseline of most evaluated echocardiographic parameters at M12 vs placebo. Patisiran-treated patients evaluable for scintigraphy (n=37) experienced a reduction (37.8%) or no change (62.2%) in Perugini grade at M12 compared with baseline. Among placebo patients (n=28) at M12, none experienced a reduction from baseline in Perugini grade, and 1 (3.6%) increased in grade. Patisiran demonstrated an acceptable safety profile; AEs were mostly mild or moderate in severity, and there were no cardiac safety concerns.

**Conclusions:** Exploratory analyses after 12 months provide further evidence for the potential benefit of patisiran treatment on cardiac biomarkers and manifestations of cardiac amyloid involvement in patients with ATTR amyloidosis. The long-term impact of patisiran will be assessed in the ongoing APOLLO-B open-label extension.