Evaluation of disease progression in patients with ATTR amyloidosis with cardiomyopathy following treatment with patisiran: post-hoc analysis of the APOLLO-B study

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Introduction: Transthyretin-mediated (ATTR) amyloidosis is a progressive, fatal disease in which cardiac deposition of transthyretin (TTR) amyloid commonly manifests as cardiomyopathy. Patisiran, an RNA interference therapeutic that reduces TTR synthesis, is approved for the treatment of hereditary ATTR amyloidosis with polyneuropathy. The Phase 3 APOLLO-B study (NCT03997383) evaluated the clinical efficacy and safety of patisiran in patients with ATTR amyloidosis with cardiomyopathy (CM).

Purpose: This post-hoc analysis evaluated disease progression in APOLLO-B patients following treatment with patisiran vs placebo, based on the European Society of Cardiology (ESC) expert consensus on monitoring patients with ATTR amyloidosis with CM every 6–12 months using three domains: Clinical/Functional, Laboratory Biomarker, and Imaging/Electrocardiography (ECG).

Methods: Patients with ATTR amyloidosis with CM were randomised (1:1) to intravenous patisiran 0.3 mg/kg or placebo every 3 weeks for 12 months. Disease progression was defined at Month 12 (M12) relative to baseline using Clinical/Functional criteria (≥1 heart failure-related hospitalisation, increased New York Heart Association class ≥1, decline in Kansas City Cardiomyopathy Questionnaire ≥5, or decline in 6-minute walk test ≥30 metres), Laboratory Biomarker criteria (increased N-terminal prohormone B-type natriuretic peptide ≥30% and absolute change ≥300 ng/L, troponin I ≥30%, or ATTR disease stage ≥1), and Imaging/ECG criteria (conduction disturbances or change in left ventricular wall thickness ≥2 mm, change in diastolic dysfunction grade ≥1, or change in systolic function measurements). One marker from each domain provides the minimum criteria for disease progression.

Results: At M12, the patisiran group (N = 180) had improved odds of no disease progression compared with the placebo group (N = 178; odds ratio [OR] 1.4; 95% confidence interval [CI] 0.77, 2.55) (Figure). The patisiran group had beneficial changes in Clinical and Functional markers vs placebo at M12 (OR 1.58; 95% CI 1.03, 2.42). Patisiran also showed favourable changes in Laboratory Biomarkers vs placebo at M12 (OR 2.14; 95% CI 1.33, 3.43) and a favourable trend in Imaging/ECG vs placebo at M12 (OR 1.31; 95% CI 0.80, 2.15).

Conclusion: In this post-hoc analysis of APOLLO-B, fewer patisiran-treated patients had disease progression with respect to clinical, functional, and biomarker parameters vs placebo. The risk of disease progression was lower by Clinical/Functional and Laboratory Biomarker composite criteria, and trended lower by individual criterion from the ESC consensus statement among patisiran-treated patients at 12 months vs placebo patients. Long-term follow-up will further assess the impact of patisiran in patients with ATTR amyloidosis with CM.

![Figure 1](https://academic.oup.com/eurheartj/article-lookup/doi/10.1093/eurheartj/ehad655)