Impact of Patisiran on Overall Health Status in hATTR Amyloidosis: Results from the APOLLO Trial

Senda Ajroud-Driss, David Adams, Teresa Coelho, Michael Polydefkis, Alejandra Gonzalez-Duarte, Dianna Quan, Arnt Kristen, John L Berk, Angela M Partisano, Jared Gollob, Marianne T Sweetser, Jihong Chen, Sonalee Agarwal, Ole B Suhr

1Northwestern University, 2National Reference Center for FAP (NNERF)/ APHP/ INSERM U 1195/ CHU Bicêtre, 3Hospital de Santo Antonio, 4Johns Hopkins, 5Instituto Nacional de Ciencias Médicas y Nutrición, Salvador Zubirán, 6University of Colorado, 7Heidelberg University Hospital, 8Boston University, 9Alnylam Pharmaceuticals, 10Umea University

Objective: Here, we further evaluate the impact of patisiran on overall health in patients enrolled in APOLLO.

Background: Hereditary transthyretin-mediated (hATTR) amyloidosis is a multisystem, life-threatening disease resulting in heterogenous manifestations including neuropathy and cardiomyopathy, significantly impacting quality of life (QoL). In the Phase 3 APOLLO study, patisiran, an investigational RNAi therapeutic for hATTR amyloidosis, resulted in significant improvement in neuropathy and QoL (measured by Norfolk QoL-DN), and was generally well-tolerated.

Design/Methods:
APOLLO was a randomized (2:1), double-blind, placebo-controlled study of patisiran 0.3 mg/kg or placebo IV q3W in hATTR amyloidosis patients with polyneuropathy (NCT01960348). Overall health status was an exploratory endpoint assessed using EuroQOL-5-dimension 5-level (EQ-5D-5L), a standardized measure of health status based on 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, and the EuroQoL visual analogue scale (EQ-VAS), a patient's global impression of their overall health. Preservation was defined as no change in score.

Results: APOLLO enrolled 225 patients: mean age 60.5-years (24-83), 74% males and 43% with V30M mutation. At 18 months, the patisiran group showed overall improvement in health status assessed by EQ-5D index scores and EQ-VAS, compared to the placebo group; improvement was observed as early as 9 months. A larger proportion of patients on patisiran than placebo, respectively, showed preservation or improvement relative to baseline in each domain: mobility, 70% vs 22%; self-care, 66% vs 21%; usual activities, 72% vs 25%; pain/discomfort, 73% vs 31%; anxiety/depression, 81% vs 45%. While overall health, EQ-VAS, improved (increased by average 2.4 points) in patients on patisiran, overall health in patients on placebo declined by average of 7.1 points, indicating a 9.5 point difference (p=0.0004).

Conclusions: Patisiran improved overall health status as measured by EQ-5D-5L in a manner similar to Norfolk QoL-DN, showing an improvement in overall health status compared to placebo in patients with hATTR amyloidosis.