Effects of Patisiran, an RNA Interference Therapeutic, on Regional Left Ventricular Myocardial Deformation in Hereditary Transthyretin Amyloidosis: The APOLLO Study

Masatoshi Minamisawa, MD[1], PhD, David Adams, MD[2], Arnt V. Kristen, MD[3], Giampaolo Merlini, MD[4], Michel S. Slama, MD[5], Angela Dispenzieri, MD[6], Rodney H. Falk, MD[1], Verena Karsten, PhD[7], Marianne Sweetser, MD[7], Jihong Chen, PhD[7], Richard Riese, MD[7], John Vest, MD[7], Scott D. Solomon, MD[1].

[1]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States (M.M., R. F., S.S.), [2]National Reference Center for FAP (NNERF)/ APHP/ INSERM U 1195/ CHU Bicêtre, Le Kremlin-Bicêtre, France, [3]Heidelberg University Hospital, Heidelberg, Germany, [4]IRCCS Policlinico San Matteo Hospital, University of Pavia, Italy, [5]Service de cardiologie-Hosptial Antoine-Beclere AP-HP, France, [6]Mayo Clinic, Rochester, MN, United States, [7]Alnylam Pharmaceuticals, Cambridge, MA, United States (V.K., M.S., J.C., R.R, J.V.)

Correspondence to: Scott Solomon, MD, Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115, USA. Tel. +1 (857) 307-1960; Fax 857-307-1944. E-mail ssolomon@bwh.harvard.edu

Background: Cardiac amyloidosis patients demonstrate reduced myocardial strain with relative sparing of the cardiac apex. In APOLLO, patisiran reduced NT-proBNP and left ventricular (LV) wall thickness and improved global longitudinal strain (GLS) relative to PBO in patients with hereditary transthyretin mediated (hATTR) amyloidosis.

Methods: An exploratory analysis from APOLLO, a randomized, double-blind, PBO-controlled Ph 3 trial in hATTR amyloidosis with polyneuropathy, assessed effects of patisiran on LV regional strain. Patients were randomized 2:1 to receive 0.3 mg/kg patisiran or PBO via IV infusion once every 3 weeks for 18 months. The prespecified cardiac subpopulation (n = 126) comprised patients with baseline LV wall thickness ≥ 13 mm and no history of hypertension or aortic valve disease. Patients underwent two-dimensional and speckle tracking echocardiography.

Results: At baseline, average strain was lowest in the basal segments with apical sparing. Patisiran reduced GLS (LSM difference ± SE; -1.36 ± 0.56 %, P=0.014) compared with PBO at 18 months, with the greatest reduction in LV strain was observed in the basal region, (overall LSM difference -2.08 ± 0.75%, P=0.006), and no significant differences in the mid and apical regions among groups.

Conclusions: Patisiran improved LV GLS driven primarily by improvements in the basal region, suggesting that basal regional longitudinal strain may be a more sensitive marker to evaluate treatments for the cardiomyopathy in hATTR amyloidosis.