Analysis of NT-proBNP Baseline Levels in APOLLO as a Predictor of Survival in Hereditary Transthyretin-mediated (hATTR) Amyloidosis

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INTRODUCTION Hereditary transthretin amyloidosisis (hATTR) is a multisystemic, fatal disease resulting TTR amyloid deposition. Clinical manifestations include neuropathy as well as cardiomyopathy, a major cause of death. NT-proBNP, cardiac biomarker, has shown prognostic value in cardiac diseases clinically validated. For hATTR and wild-type ATTR,survival in patients with NT-proBNP levels >3000ng/L was linked with poorer survival.

METHODE APOLLO, phase 3, randomized (2:1), double-blind study of patisiran 0.3mg/kg or placebo IV q3W in patients with hATTR with polyneuropathy. 56% of patients had cardiac involvement defined by prespecified criteria: left ventricular (LV) wall thickness ≥ 13mm and absence of aortic valve disease or hypertension. n=225: mean age 61 years, 57% non-V30M mutation, NT-proBNP median 756,4 ng/L. To assess the prognostic significance of baseline factors on survival, a Cox regression analyses were conducted. NT-proBNP was evaluated as a continuous variable following logarithmic transformation as well as a binary variable using a cut off value of 3000 ng/mL.

RESULTATS Median survival follow-up duration was 18.7 months. 13 deaths not related to the treatment, 6 (8%) PB0 arm and 7 (5%) in patisiran arm. NT-proBNP was the key significant factor predictive of survival based on univariate and multivariate analyses. The risk of death increased with higher baseline NT-proBNP (hazard ratio =2.9 [95% CI: 1.8, 4.8, p-value=8.7x10-7] per unit increment in log(NT- proBNP). Patients with NT-proBNP > 3000 ng/L (n=29) had a 19.3-fold [95% CI 5.9, 62.8, p-value=8.7x10- 7] increased risk for mortality compared with those below 3000 ng/L (n=196).

CONCLUSION Based on the data from APOLLO, baseline NT-proBNP serum levels in hATTR patients are predictive of survival. These data underscore the importance of diagnosing and treating patients early in the course of the disease