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Utility of Genetic Testing to Identify Individuals Suspected of Having Hereditary ATTR (hATTR) Amyloidosis

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Objective: To evaluate the utility of genetic testing in individuals suspected of having hATTR amyloidosis.

Background: hATTR amyloidosis is a rare, rapidly progressive, life-threatening disease caused by mutations in the transthyretin (TTR) gene. Heterogeneous clinical presentation of hATTR amyloidosis includes sensory, motor and autonomic neuropathies, and cardiac dysfunction. Diagnosis may take several years as hATTR amyloidosis symptoms may overlap with other more common diseases.

Design/Methods: To potentially facilitate earlier diagnosis, Alnylam Pharmaceuticals sponsors Alnylam Act™, a third-party genetic screening program in the United States for individuals suspected of having hATTR amyloidosis. Program includes neuropathy and cardiomyopathy panels in addition to single gene (TTR) testing. While no patient-identifiable information is shared with the sponsor, reports of pathogenic or likely-pathogenic mutations (positive tests) identified in conjunction with reported hATTR amyloidosis symptoms are provided to the sponsor.

Results: From April to October 2017, 1489 individuals (>18 years of age) were tested, yielding 239 (16%) positive test results for pathogenic or likely pathogenic mutations related to hereditary neuropathies or cardiomyopathies. Among all individuals tested, TTR gene mutations were identified in 79 (5.3%) individuals and were associated with the following signs and symptoms: family history of hATTR amyloidosis (n=35; 44%), heart disease (n=30; 38%) and sensory and motor symptoms (n=21; 27%). Of the 30 individuals with positive TTR tests and heart disease, 6 (20%) individuals also had sensory and motor symptoms reported. Data highlighting frequency of other symptoms, including history of carpal tunnel syndrome, generalized fatigue, unintentional weight loss and ocular changes, will be presented.

Conclusions: The results suggest genetic testing is a valuable tool to facilitate an earlier hATTR amyloidosis diagnosis and could possibly minimize us of more invasive diagnostic tests, especially in patients with heart disease, as well as sensory and motor symptoms of unknown etiology.