APOLLO Phase 3 Clinical Trial Overview

The APOLLO Phase 3 study (N=225) was a randomized, double-blind, placebo-controlled, global study designed to evaluate the efficacy and safety of ONPATTRO™ (patisiran) lipid complex injection in people with hereditary transthyretin-mediated (hATTR) amyloidosis with polyneuropathy. Relative to placebo, data from APOLLO showed that treatment with ONPATTRO resulted in improvement in polyneuropathy, as measured by the modified Neuropathy Impairment Score (mNIS+7) – with reversal of neuropathy impairment in a majority of patients – and improved quality of life, reduced autonomic symptoms, and improved activities of daily living.[1] The study was the largest controlled study of hATTR amyloidosis and was completed in August 2017. Patients who completed the trial were eligible to screen for the global open-label extension study.

Primary Endpoint:

The primary outcome measure of APOLLO was the difference between treated and placebo groups in the change from baseline of the modified Neuropathy Impairment Score+7 (mNIS+7) at 18 months.

modified Neuropathy Impairment Score+7 (mNIS+7)	A composite neurologic impairment score, including sensory, motor, and autonomic manifestations. An increase in mNIS+7 score over time means the neuropathy is worsening.

Secondary Endpoints:

Other secondary endpoints included the difference between ONPATTRO and placebo groups in the change from baseline after 18 months in terms of quality of life, motor function and autonomic function. Clinical evaluations of these outcomes included:

Norfolk Quality of Life-Diabetic Neuropathy (QOL-DN) Score	A comprehensive quality of life questionnaire for patients that includes domains relating to small fiber, large fiber, and autonomic nerve function, symptoms of polyneuropathy, and activities of daily living.[2]
Timed 10-meter walk (10-MWT)	A test of mobility, in which the time it takes for a patient to walk 10 meters is measured.
NIS-weakness (NIS-W)	A tool that evaluates weakness within a broad group of muscles, including those of the head and limbs.[3]
Composite Autonomic Symptom Score (COMPASS) 31	A self-assessment instrument used by patients to report autonomic symptoms such as dizziness, constipation, diarrhea, nausea/vomiting, and incontinence.[2,4]
Modified Body Mass Index (mBMI)	mBMI is a measure of nutritional status that combines serum albumin and body mass index.[5]
Rasch-built Overall Disability Scale (R-ODS)	A tool to assess activity and social participation limitations in patients comprised of a 24-item linearly weighted scale.[6]
EuroQoL 5 Dimensions 5 Levels (EQ-5D-5L)	EQ-5D-5L is an instrument used to measure health in five dimensions: mobility (walking), self-care (washing or dressing), usual activities, pain/discomfort, and anxiety/depression.[7]

Efficacy Results

At 18 months, ONPATTRO-treated patients demonstrated improvement in the primary endpoint with a mean 6.0-point decrease (improvement) in mNIS+7 score from baseline compared to a 28.0-point mean increase (worsening) for patients in the placebo group, resulting in a 34.0-point mean difference relative to placebo. This means, on average, placebo-treated patients continued to experience progression of their neuropathy.[1] Additionally, patients treated with ONPATTRO experienced significant benefit versus placebo for all other secondary efficacy endpoints including measures of activities of daily living, walking ability, nutritional status, and autonomic symptoms.[1]

- 56 percent of ONPATTRO-treated patients at 18 months of treatment experienced reversal of neuropathy impairment (a decrease from baseline in mNIS+7), compared to four percent of patients who received placebo.[1]
- As measured by the Norfolk Quality of Life Diabetic Neuropathy (QoL-DN) Score, 51 percent of patients treated with ONPATTRO experienced improvement in quality of life at 18 months relative to their own baseline, compared with 10 percent of placebo-treated patients.[1]

Safety Results

The most common adverse events that occurred more frequently with ONPATTRO than with placebo were upper respiratory tract infections and infusion-related reactions. To reduce the risk of infusion-related reactions, patients received premedications prior to infusion.

ONPATTRO is approved by the U.S. Food and Drug Administration for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. For more information about ONPATTRO and to view the full Prescribing Information, please visit www.ONPATTRO.com.

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