Biogen - NURTURE

An Open-Label Study to Assess the Efficacy, Safety, Tolerability, and Pharmacokinetics of Multiple Doses of ISIS 396443 Delivered Intrathecally to Subjects With Genetically Diagnosed and Presymptomatic Spinal Muscular Atrophy.

Summary

This is a Phase 2 clinical trial to test the safety and efficacy of Nusinersen in infants with genetically diagnosed and presymptomatic SMA. This study also aims to examine the effects of Nusinersen in infants.

Study Number: NCT02386553

Description by Biogen

The primary objective of the study is to examine the efficacy of multiple doses of Nusinersen administered intrathecally in preventing or delaying the need for respiratory intervention or death in infants with genetically diagnosed and pre-symptomatic spinal muscular atrophy (SMA). Secondary objectives of this study are to examine the effects of Nusinersen in infants with genetically diagnosed and presymptomatic SMA.

Primary Outcome Measures

- Time to death or respiratory intervention
  [Time Frame: Up to Day 2891]

The time will be the age of the participant at the first occurrence of either a respiratory intervention or death. Respiratory intervention is defined as invasive or noninvasive ventilation for 6 hours/day continuously for 7 or more days OR tracheostomy.

Secondary Outcome Measures

- Percentage of participants developing clinically manifested spinal muscular atrophy (SMA).
  [Time Frame: At 13 and 24 months of age]

AUSNMD

Trial Status
Fully recruited

Locations
Brisbane - Queensland Children's Hospital, Trial complete /terminated, Melbourne - Melbourne Children's Campus, Fully recruited

Trial Sponsor
Biogen

Age
Less than 6 weeks

SMASubtype
Type 1

SMN2 Copy Numbers Required
2 or more

Mode of delivery
IT

MRI
No

Phase
2

Length Of Participation
8 years

Recruitment Target
25

Therapeutic Category
SMN2 Gene upregulation

- Percentage of participants alive [Time Frame: At 13 months, and 2, 3, 4, 5, 6, 7 and 8 years of age]
- Percentage of participants who attained motor milestones assessed as part of the Hammersmith Infant Neurological Examination (HINE) [Time Frame: At 13 and 24 months of age]
- Percentage of participants who attained motor milestones as assessed by World Health Organization (WHO) criteria [Time Frame: Up to Day 2891]
- Change from Baseline in the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) motor function scale [Time Frame: Up to Day 2891]
- Change from Baseline in Hammersmith Functional Motor Scale - Expanded (HFMSE) [Time Frame: Up to Day 2891]
- Change from Baseline in weight for age/length [Time Frame: Up to Day 2891]
- Change from Baseline in head circumference [Time Frame: Up to Day 2891]
- Change from Baseline in chest circumference ratio [Time Frame: Up to Day 2891]
- Change from Baseline in head to chest circumference ratio [Time Frame: Up to Day 2891]
- Change from Baseline in arm circumference ratio [Time Frame: Up to Day 2891]
- Incidence of adverse events (AEs) and/or serious adverse events (SAEs) [Time Frame: Up to Day 2891]
- Change from Baseline in clinical laboratory parameters [Time Frame: Up to Day 2891]
- Assessed by the following laboratory tests: Hematology: red blood cells, hemoglobin, hematocrit, platelets, white blood cells, white blood cell differential, Blood chemistry: total protein, albumin, creatinine, cystatin C, creatine phosphokinase, blood urea nitrogen, total bilirubin (direct and indirect), alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, glucose, calcium, phosphorous, chloride, sodium, potassium. Urinalysis: specific gravity, pH, protein, glucose, ketones,

bilirubin, red blood cells, white blood cells, epithelial cells, bacteria, casts, crystals

- Change from Baseline in electrocardiograms (ECGs) [Time Frame: Up to Day 2891]
- Change from Baseline in vital signs [Time Frame: Up to Day 2891]
- Vital sign will be assessed by: temperature, pulse rate, resting systolic and diastolic blood pressure, and respiratory rate.
- Change from Baseline in neurological examinations [Time Frame: Up to Day 2891]
- Cerebrospinal fluid (CSF) and plasma Nusinersen concentrations. [Time Frame: Up to Day 2801]

Can I take part?

Inclusion Criteria

- Age 6 weeks at first dose
- Genetic documentation of 5q SMA homozygous gene deletion or mutation or compound heterozygous mutation.
- Genetic documentation of 2 or 3 copies of survival motor neuron 2 (SMN2).
- Ulnar compound muscle action potential (CMAP) 1 mV at Baseline.
- Gestational age of 37 to 42 weeks for singleton births; gestational age of 34 to 42 weeks for twins.

Exclusion Criteria

- Hypoxemia (oxygen saturation <96% awake or asleep without any supplemental oxygen or respiratory support).
- Any clinical signs or symptoms at Screening or immediately prior to the first dosing (Day 1) that are, in the opinion of the Investigator, strongly suggestive of SMA.
- Clinically significant abnormalities in hematology or clinical chemistry parameters.

- Treatment with an investigational drug given for the treatment of SMA biological agent, or device. Any history of gene therapy, prior antisense oligonucleotide (ASO) treatment, or cell transplantation.

Other inclusion/exclusion criteria apply.

For contact details and to find out more, please refer to ausnmd.org.

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