Gene Transfer Study of AAV9-CLN3 for Treatment NCL Type 3

ClinicalTrials.gov Identifier: NCT03770572

Recruitment Status : Recruiting
First Posted : December 10, 2018
Last Update Posted : December 10, 2018

See **Contacts and Locations**

Sponsor:

Nationwide Children's Hospital

Collaborator:

Amicus Therapeutics

Information provided by (Responsible Party):

Emily de los Reyes, Nationwide Children's Hospital

Study Description

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Brief Summary:

Open-label, single dose, dose-escalation clinical trial AAV9-CLN3 via intrathecal injection in NCL type 3 subjects

Condition or disease	Intervention/treatment	Phase
CLN3-Related **Neuronal Ceroid-Lipofuscinosis**	Biological: AAV9-CLN3	Phase 1 Phase 2

Detailed Description:

Open-label, dose escalation clinical trial including two study cohorts of NCL type 3 (CLN3 disease) subjects. Cohort 1 will evaluate a one-time low-dose via intrathecal injection of AAV-CLN3 and Cohort 2 evaluating a one-time high-dose intrathecal injection of AAV-CLN3 vector construct containing human CLN3 transgene. This study will be monitored by a Data Safety Monitoring Committee (DSMB). Cohort 2 subjects (high-dose) will proceed with treatment after evaluation by the DSMB of AAV9-CLN3 in Cohort 1 (low-dose) subjects. Both subject cohorts will participate in the ongoing study for a period of at least three years. Periodic assessments including clinical, laboratory, cognitive and medical imaging assessment will be performed. Participating subjects will be asked to participate in a separate long term follow-up study for a total duration of approximately 5 years from the time of completion of the active phase of the current study.

Study Design

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Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	7 participants
Allocation:	Non-Randomized
Intervention Model:	Single Group Assignment
Intervention Model Description:	

Single Treatment Group (AAV9-CLN3) - 2 Cohort Assignment (Low-dose, High-dose)

Dose escalation in this study will begin with low-dose, determined to be the minimal efficacious dose as determined in non-clinical studies. Dose escalation to a high-dose (2x the minimally effective dose (MED) as evaluated in Cohort 1) will proceed as part of Cohort 2 of the study upon demonstration of safety of the low-dose in Cohort 1 of the study.

Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Phase I/IIa Gene Transfer Clinical Trial for Juvenile **Neuronal Ceroid Lipofuscinosis**, Delivering the **CLN3** Gene by Self-Complementary AAV9
Actual Study Start Date :	November 13, 2018
Estimated Primary Completion Date :	December 2022
Estimated Study Completion Date :	December 2022

Resource links provided by the National Library of Medicine NIH NLM

Genetics Home Reference related topics:

CLN1 disease CLN10 disease CLN2 disease
CLN3 disease CLN4 disease CLN5 disease
CLN6 disease CLN7 disease CLN8 disease

MedlinePlus related topics: Genes and Gene Therapy

Genetic and Rare Diseases Information Center resources: Adult Neuronal Ceroid Lipofuscinosis
Ceroid Storage Disease
Neuronal Ceroid Lipofuscinosis
Neuronal Ceroid Lipofuscinosis 3

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment

Experimental: Cohort 1 AAV-CLN3 Low-Dose (Minimally Effective Dose (MED)	Biological: AAV9-CLN3 A single dose of AAV9-CLN3 will be delivered via an intrathecal injection.
Experimental: Cohort 2 AAV-CLN3 High-Dose (Escalated Dose, 2x, Minimally Effective Dose, MED)	Biological: AAV9-CLN3 A single dose of AAV9-CLN3 will be delivered via an intrathecal injection.

Outcome Measures

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Primary Outcome Measures ⓘ :

1. Safety: Incidence of any one Grade III or higher, unanticipated, treatment-related toxicity [Time Frame: 36 Months]
2. Efficacy: Change in rating as determined using the Unified Batten Disease Rating Scale (UBDRS) rating scale. The UBDRS is a clinical ratings instrument used specifically to assess motor, seizure, behavioral and functional capabilities. [Time Frame: 36 months]

Secondary Outcome Measures ⓘ :

1. QOL: Change in Quality of Life (QOL) as determined using the Pediatric Quality of Life (PedsQL™) scale. The PedsQL is used to assess physical, emotional, social, and school functioning of pediatric subjects in ranging from 2 years to 18 years of age.
   [Time Frame: 36 months]
2. Seizures: Change is seizure subscore as determined using Seizure subscale of the UBDRS scale. The UBDRS seizure subscale is used to assess seizure history, type, frequency, duration, and frequency of seizure-related injury. [Time Frame: 36 months]
3. Global impression: Change in disease severity using the UBDRS clinical global impression (CGI) subscale. The clinical global impression subscale includes assessment of motor, seizure, behavioral and functional measures in NCL subjects. [Time Frame: 36 months]

Eligibility Criteria

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Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	3 Years to 10 Years (Child)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- CLN3 diagnosis, confirmed by the presence of a mutation in the CLN3 gene as determined by gene sequencing from a laboratory certified by the Clinical Laboratory Improvement Act/Amendment (CLIA) or an equivalent organization.
- Age ≥3 years through 10 years of age
- UBDRS physical impairment score of ≤7
- Mobility: Independently walking for a distance of at least 50 feet

Exclusion Criteria:

- Presence of another neurologic, metabolic or immunologic disease
- Presence of another neurological illness resulting in cognitive decline
- Recent generalized motor status epilepticus
- Prior corneal or intraocular surgery
- Active viral infection or severe bacterial infection
- Hepatic laboratory values (ALT) outside of the protocol required range
- Pre-existing Anti-AAV9 antibody titers above the protocol-required limit
- Clinically significant abnormal laboratory values as defined in the protocol
- Prior stem cell or bone marrow or organ transplantation
- Recent Chemotherapy, radiotherapy or other immunosuppression therapy
- Current use of cannabinoids and any by-products
- Contraindications for intrathecal injection procedure
- Contraindications for MRI scans
- Recent participation in a clinical trial of an investigational treatment

Contacts and Locations

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Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03770572***

Contacts

Contact: Lisa Moffitt, RN 614-722-2650 lisa.moffitt@nationwidechildrens.org

Locations

United States, Ohio

Nationwide Children's Hospital **Recruiting**
Columbus, Ohio, United States, 43201

Sponsors and Collaborators

Nationwide Children's Hospital

Amicus Therapeutics

Investigators

Principal Investigator: Emily de los Reyes, MD Nationwide Children's Hospital

More Information

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Publications:

Schulz A, Kohlschütter A, Mink J, Simonati A, Williams R. NCL diseases - clinical perspectives. Biochim Biophys Acta. 2013 Nov;1832(11):1801-6. doi: 10.1016/j.bbadis.2013.04.008. Epub 2013 Apr 17.

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Munroe PB, Mitchison HM, O'Rawe AM, Anderson JW, Boustany RM, Lerner TJ, Taschner PE, de Vos N, Breuning MH, Gardiner RM, Mole SE. Spectrum of mutations in the Batten disease gene, CLN3. Am J Hum Genet. 1997 Aug;61(2):310-6.

Drack AV, Mullins RF, Pfeifer WL, Augustine EF, Stasheff SF, Hong SD. Immunosuppressive Treatment for Retinal Degeneration in Juvenile Neuronal Ceroid Lipofuscinosis (Juvenile Batten Disease). Ophthalmic Genet. 2015;36(4):359-64. doi: 10.3109/13816810.2014.886271. Epub 2014 Feb 19.

Kwon JM, Adams H, Rothberg PG, Augustine EF, Marshall FJ, Deblieck EA, Vierhile A, Beck CA, Newhouse NJ, Cialone J, Levy E, Ramirez-Montealegre D, Dure LS, Rose KR, Mink JW. Quantifying physical decline in juvenile neuronal ceroid lipofuscinosis (Batten disease). Neurology. 2011 Nov 15;77(20):1801-7. doi: 10.1212/WNL.0b013e318237f649. Epub 2011 Oct 19.

Adams HR, Mink JW; University of Rochester Batten Center Study Group. Neurobehavioral features and natural history of juvenile neuronal ceroid lipofuscinosis (Batten disease). J Child Neurol. 2013 Sep;28(9):1128-36. doi: 10.1177/0883073813494813. Review.

Ostergaard JR, Rasmussen TB, Mølgaard H. Cardiac involvement in juvenile neuronal ceroid lipofuscinosis (Batten disease). Neurology. 2011 Apr 5;76(14):1245-51. doi: 10.1212/WNL.0b013e31821435bd.

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Responsible Party:	Emily de los Reyes, Professor of Neurology, Nationwide Children's Hospital
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First Posted:	December 10, 2018 Key Record Dates
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Last Verified:	December 2018

Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No

Keywords provided by Emily de los Reyes, Nationwide Children's Hospital:

CLN3

Batten Disease (Juvenile Onset)

Spielmeyer-Sjogren disease

Vogt-Spielmeyer disease

Additional relevant MeSH terms:

Neuronal Ceroid-Lipofuscinoses
Heredodegenerative **Disorders**, Nervous System
Neurodegenerative **Diseases**
Nervous System **Diseases**
Genetic **Diseases**, Inborn

Lipidoses
Lipid Metabolism, Inborn Errors
Metabolism, Inborn Errors
Lipid Metabolism **Disorders**
Metabolic **Diseases**