ISRCTN13397128 https://doi.org/10.1186/ISRCTN13397128

A study of potential treatment-responsive biomarkers and clinical outcomes in Hunter syndrome

Submission date
23/12/2025

Recruitment status
No longer recruiting

Registration date
15/01/2026

Overall study status
Completed

Last Edited
15/01/2026

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The primary objectives of the study were to characterize the progression of adaptive behavior, characterize the progression of neurocognition, and to assess levels of potential disease-related or treatment-responsive biomarkers in blood, urine,
and/or CSF samples from participants with mucopolysaccharidosis Type II (Hunter Syndrome or MPS II).

Who can participate?
Participants with a confirmed diagnosis of MPS II. This included genetic testing (looking for changes in the iduronate 2-sulfatase [IDS] gene) and lab tests showing iduronate-2-sulfatase (IDS) enzyme activity in the blood, white blood cells, or skin cells.

What does the study involve?
No new or experimental treatments were given in this study. This was a six-part, forward-looking (prospective), observational study done at multiple centers in different regions. The goal was to study biomarkers and look at how the disease affects people with MPS II, including both types: the kind that affects the brain (nMPS II) and the kind that does not (nnMPS II).

What are the possible benefits and risks?
Participants in the study did not receive any additional medical therapy for MPS II, and, as such, did not receive direct therapeutic benefit. However, there was a possible benefit from participation in the study via the included assessments of health status and information that may be used to request educational, medical, or other services.

Where is the study run from?
The study was sponsored by Denali Therapeutics Inc. and run from multiple medical institutes in the United States of America, The Netherlands, and the UK.

When is the study starting and how long is it expected to run for?
October 2019 to March 2024.

Who is funding the study?
Denali Therapeutics Inc.

Who is the main contact?
Clinical Trials Disclosures Group at Denali Therapeutics, clinical-trials-disclosures@dnli.com

Contact information

Type(s)
Public

Contact name
None Clinical Trials Disclosures Group

Contact details
161 Oyster Point Blvd.
South San Francisco
United States of America
94080
+1 650 296 2029
clinical-trials-disclosures@dnli.com

Type(s)
Scientific

Contact name
None Denali Medical Monitor

Contact details
161 Oyster Point Blvd.
South San Francisco
United States of America
94080
+1 650 296 2029
clinical-trials-disclosures@dnli.com

Type(s)
Principal investigator

Contact name
Dr Denali Medical Monitor

Contact details
161 Oyster Point Blvd.
South San Francisco
United States of America
94080
+1 650 296 2029
clinical-trials-disclosures@dnli.com

Additional identifiers

Integrated Research Application System (IRAS)
263187

ClinicalTrials.gov (NCT)
NCT04007536

Protocol serial number
DNLI-E-0001

Study information

Scientific Title
A prospective, longitudinal study of potential treatment-responsive biomarkers and clinical outcomes in Hunter syndrome

Study objectives
This study observed how mucopolysaccharidosis type II (MPS II) changes over time and looked for biomarkers that might respond to treatment. It included both the neuronopathic form (nMPS II), which affects the brain, and the non-neuronopathic form (nnMPS II), which does not. The goal was to better understand these biomarkers and how they relate to signs and symptoms of MPS II as the disease gets worse over time.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 30/09/2019, NHS HRA North East - Tyne & Wear South Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; +44 0207 1048084; nrescommittee.northeast-tyneandwearsouth@nhs.net), ref: 19/NE/0169

Study design
Six-part, prospective, multicenter, multiregional, observational study.

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Mucopolysaccharidosis II

Interventions
This was a six-part, prospective, multicenter, multiregional, observational study designed to evaluate biomarkers and assess the clinical outcomes of disease in patients with MPS II, including nMPS II and nnMPS II. Eligible participants were required to have a documented diagnosis of MPS II, which included genetic analysis (ie, mutation analysis of the iduronate 2-

sulfatase [IDS] gene) and biochemical assessment (eg, IDS enzyme activity in plasma, white blood cells, or fibroblasts). No experimental therapies were administered in this study.

Intervention Type
Other

Primary outcome(s)
1. Adaptive behavior measured using Vineland-3 8-subdomain Adaptive Behavior Raw Score (ABRS-8) at Baseline, Week 24, and Week 48

2. Adaptive behavior measured using Vineland-3 Adaptive Behavior Composite (ABC) Score at Baseline, Week 24, and Week 48

3. Neurocognition measured using Bayley Scales of Infant and Toddler Development, 3rd Edition (BSID-III) cognitive raw score at Baseline, Week 24, and Week 48

4. Neurocognition measured using Kaufman Assessment Battery for Children, 2nd Edition (KABC-II) score at Baseline, Week 24, and Week 48

5. Neurocognition measured using Wechsler Intelligence Scale for Children, Fifth Edition (WISC-V) score at Baseline and Week 48

6. Cross-sectional CSF HS level measured using the sum of HS D0A0, D0A6, D0S0, and D2S6 at Week 1

7. Cross-sectional CSF DS measured using D0a4 at Week 1

8. Urine HS level measured using the sum of HS D0A0, D0A6, D0S0, D2S6, and normalized to urine creatinine) and percent change in urine HS from first observation to last observation at each visit over 78 weeks

9. Urine DS (D0a4) level (normalized to urine creatinine) and percent change in urine DS measured using urine test at each visit over 78 weeks

10. Sum of urine HS and DS level (normalized to urine creatinine) and percent change in sum of urine HS and DS measured using urine test at each visit over 78 weeks

11. Total urine glycosaminoglycans (GAGs) level measured using a colorimetric assay and normalized to urine creatinine) and percent change in total urine GAGs at each visit over 78 weeks

12. Serum HS level measured using the sum of HS D0A0, D0A6, D0S0, and D2S6 and percent change in serum HS at each visit over 78 weeks

13. Serum DS level and percent change in serum DS measured using D0a4 at each visit over 78 weeks

14. Sum of serum HS and DS level and percent change in sum of serum HS and DS measured using previously measured serum HS and DS levels at each visit over 78 weeks

Key secondary outcome(s))

Completion date
01/03/2024

Eligibility

Key inclusion criteria
Key Inclusion Criteria (Part 1):
1. Participants aged 2 through 10 years
2. nMPS II subgroup: participants with a development quotient (DQ) <85 and/or a decline of at least 7.5 points in DQ, assessed at least 6 months apart, or with the same genetic mutation as a blood relative with confirmed nMPS II

Key Inclusion Criteria (Part 2):
1. Participants aged 2 through 30 years
2. nMPS II subgroup: patients with an age-adjusted DQ <85 and/or a decline of 10 points or more in DQ in the previous 6 months or more, or with the same genetic mutation as a blood relative with confirmed nMPS II
3. Scheduled to undergo general anesthesia or CSF sampling for non-study-related medical reasons and parent(s)/legally authorized representative consent to donate CSF for research purposes during that procedure, or an adult patient is able to provide consent and agrees to participation in the study for CSF collection/donation

Key Inclusion Criteria (Part 3):
1. nMPS II participants aged <8 years

Key Inclusion Criteria (Part 4):
1. nnMPS II participants aged 6 to 17 years

Key Inclusion Criteria (Part 5):
1. Participants aged ≤ 3 years
2. Have undetermined MPS II phenotype
3. Do not have a large deletion(s) or rearrangement(s) in the IDS gene or other definitive mutation indicative of nMPS II
4. Do not have a DQ < 85 at the screening/baseline neurocognitive assessment and/or a documented decline of at least 7.5 points in DQ in the previous 6 to 18 months
5. Do not have the same IDS gene variant as a blood relative with confirmed nMPS II or nnMPS II

Key Inclusion Criteria (Part 6):
1. nMPS II participants aged 1 to 17 years
2. Have received an MPS II gene therapy or allogeneic HSCT > 12 months prior to screening
3. Have a post-HSCT or post-gene therapy DQ < 85 at the screening/baseline neurocognitive assessment and/or a documented decline of at least 7.5 points in DQ in the previous 6 to 18 months

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Mixed

Lower age limit
0 years

Upper age limit
30 years

Sex
All

Total final enrolment
18

Key exclusion criteria
1. Have unstable medical condition that would make participation in the study unsafe or would interfere with necessary medical care
2. Have received any central nervous system (CNS)-targeted MPS II investigational therapy within the previous 6 months

Date of first enrolment
23/10/2019

Date of final enrolment
01/03/2023

Locations

Countries of recruitment
United Kingdom

England

Netherlands

United States of America

Study participating centre
Birmingham Children's Hospital
-
Birmingham
England
B4 6NH

Study participating centre
Greater Manchester NHS Genomic Medicine Centre
Genomic Diagnostics Laboratory

Manchester Ctr for Genomic Medicine
St Marys Hospital, Oxford Road
Manchester
England
M13 9WL

Study participating centre
UCSF Benioff Children's Hospital
Oakland
United States of America
94609

Study participating centre
UNC Children's Research Institute
Chapel Hill
United States of America
27514

Study participating centre
UPMC | Children's Hospital of Pittsburgh
Pittsburgh
United States of America
15224

Study participating centre
Erasmus Medical Center
Rotterdam
Netherlands
3015 GD

Sponsor information

Organisation
Denali Therapeutics (United States)

ROR
https://ror.org/00pprn321

Funder(s)

Funder type
Not defined

Funder Name
Denali Therapeutics

Alternative Name(s)
DENALI, Denali Therapeutics Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Plain English results			29/12/2025	No	Yes