

Gene therapy for Tay-Sachs and related diseases

Submission date 12/09/2010	Recruitment status No longer recruiting	☒ Prospectively registered
Registration date 06/10/2010	Overall study status Completed	☐ Protocol
Last Edited 25/06/2020	Condition category Nutritional, Metabolic, Endocrine	☐ Statistical analysis plan
		☐ Results
		☐ Individual participant data
		☐ Record updated in last year

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

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Additional identifiers

Protocol serial number

HGM201

Study information

Scientific Title

Phase I/II open-label trial to determine the safety and tolerability of intracranial gene therapy in GM2 gangliosidosis using recombinant adeno-associated viral vectors

Acronym

SAVVY CHILD

Study objectives

Intracerebral and intraventricular rAAV vectors will safely deliver potentially therapeutic hexosaminidase A and B isozymes in patients with GM2 gangliosidosis.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Not provided at time of registration

Study design

Single-centre open-label interventional trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Tay-Sachs disease, Sandhoff disease

Interventions

Single interventional event: neurosurgical delivery of monocistronic rAAV vectors harbouring α and β human hexosaminidase transgenes by intracranial injection, depositing at 12 sites with supplementary infusion into cerebrospinal fluid spaces ~10¹² genome copies per locus delivered within 36 h. No placebo or interventional control group is possible.

At recruitment: intensive rapid neurological, motor development and neuropsychological evaluation with sample collection and banking.

Follow-up: safety and tolerance: clinical examination twice daily for 7 days after procedure, weekly for 1 month then every month for 6 months; every 2 months thereafter for 2 years to exclude signs of haemorrhage, systemic infection, immune reactions and encephalitis. CSF testing will be conducted as appropriate but pre-procedure and within 2 weeks of vector administration; thereafter at intervals alongside MRI (including DTwi and MR spectroscopy), to exclude leukoencephalopathy and incidental lesions before procedure and at day 7; further studies at 3, 6 12 and 24 months to evaluate necrosis and cortical conformation and thickness afterwards. Six monthly neuro-developmental (if relevant) and neuropsychological testing.

The total duration of the study will be 3 years.

Intervention Type

Other

Phase

Not Applicable

Primary outcome(s)

No acute or sub-acute events causing deterioration in neurological function or impaired structural integrity of central nervous system.

Key secondary outcome(s))

Secondary end-point criteria on which phase III efficacy studies will be predicated, will compare outcomes in siblings with disease in affected pedigrees with Tay-Sachs and related diseases, as well as population data on the natural course of GM2 gangliosidosis. Procedures include banking of biological samples and interval neuropsychological evaluation.

Completion date

28/02/2015

Eligibility**Key inclusion criteria**

1. Male and female infants and young subjects aged 3 months to 18 years
2. GM2 gangliosidosis confirmed by biochemical analysis and molecular analysis of cognate HEXA or HEXB genes in the presymptomatic phase with normal neuromotor development, physical examination and cerebral MR imaging

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Child

Lower age limit

3 months

Upper age limit

18 years

Sex

All

Key exclusion criteria

1. GM2 activator deficiency
2. Developmental regression or other features of symptomatic GM2 gangliosidosis
3. Clinical or radiological abnormalities of the central nervous system

Date of first enrolment

01/03/2012

Date of final enrolment

28/02/2015

Locations

Countries of recruitment

United Kingdom

England

Cyprus

Czech Republic

France

Germany

Greece

Israel

Italy

Netherlands

Poland

Portugal

Türkiye

Study participating centre

University of Cambridge

Cambridge

United Kingdom

CB2 0QQ

Sponsor information

Organisation

Cambridge University Hospitals NHS Foundation Trust (UK)

ROR

<https://ror.org/04v54gj93>

Funder(s)

Funder type

Government

Funder Name

Medical Research Council, Grant Ref: MR/K025570/1DPFS/DCS

Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Funder Name

Proposal in preparation collaboration with Institute Pasteur (coordinator: Prof. J.-M. Heard) in submission to European Union, Framework Package 7. Gene therapy of the brain in lysosomal storage diseases, Acronym: LSDGT. This will seek support for the industrial collaborator and preparation of the Investigational Medicinal Product - call

Funder Name

Q4 2010: Application to MRC & NIHR Efficacy and Mechanism Evaluation (EME) Programme jointly with the National Institute of Health Research to support Clinical Trial

Funder Name

Q4 2010 Application to Regional Clinical Research network for infrastructure support for clinical trial coordinator and nursing and ancillary healthcare staff

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration