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Gene therapy for Tay-Sachs and related diseases

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Timothy Cox

Contact details
Department of Medicine
University of Cambridge
Box 157, Level 5
Addenbrooke's Hospital
Cambridge
United Kingdom
CB2 0QQ
+44 (0)1223 336864
tmc12@medschl.cam.ac.uk

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 ß 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, 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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes