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Gene therapy for Wiskott-Aldrich Syndrome (WAS)

Submission date	Recruitment status	[ ] Prospectively registered
03/05/2011	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
20/05/2011	Completed	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
16/03/2018	Haematological Disorders	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT01347242

Secondary identifying numbers
GTG002.07

Study information

Scientific Title
Phase I/II clinical trial of haematopoietic stem cell gene therapy for the Wiskott-Aldrich Syndrome

Study objectives
Studying the safety and efficacy of an ex vivo gene therapy using a lentiviral vector containing the human Wiskott-Aldrich Syndrome protein gene in patients with WAS

Ethics approval required
Old ethics approval format

Ethics approval(s)
Gene Therapy Advisory Committee (GTAC) (UK), 21/12/2009, GTAC 146

Study design
Open-labelled non-randomised single-centre phase I/II cohort study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Wiskott-Aldrich Syndrome

Interventions
Ex vivo gene therapy using patient's autologous CD34+ cells transduced with a lentiviral vector containing the human WASP gene.

Patients undergo either a bone marrow harvest or a leukapheresis. They then receive a conditioning myeloablative regimen while CD34+ cells are selected in their bone marrow and transduced with the lentiviral vector (3 days). Patients then receive their transduced CD34+ cells (as in autologous bone marrow transplantation).

There are no real doses, simply quantity of CD34+ cells transduced will depend on the amount of bone marrow harvest and quality of transduction. This is part of the parameters that are being assessed in the trial.

Duration of the study follow-up is 2 years.

Intervention Type
Drug

Phase
Phase I/II

Primary outcome measure
1. Safety of conditioning regimen (haematopoietic recovery within 6 weeks as assessed by absolute neutrophil count (ANC) above 0.5 x 109 /l)
2. Safety of the transduction procedure [as assessed by availability of greater than 0.5 x 106 cells per kg after transduction; undetectable replication-competent lentiviruses (RCL) (determined retrospectively); and cell viability after transduction equal to or greater than 50%, in accordance with the final product release criteria]
3. Engraftment of genetically corrected haematopoietic progenitors and/or differentiated cells in peripheral blood and/or in bone marrow (as assessed by evidence of vector sequences or transgene expression in the cells)
4. Reconstitution of cell mediated and humoral immunity (as assessed by evidence of changes in T cell function and circulating immunoglobulin levels)
5. Correction of microthrombocytopenia (if not previously splenectomised, and as assessed by increased blood platelet counts, expected to rise above 50,000/mm3)

Secondary outcome measures
1. Reduction in frequency of infections (evaluated from 2nd year after treatment by clinical history, complete physical examinations, haematological and microbiological tests)
2. Resolution/reduction of autoimmunity (a decrease from baseline observations assessed by clinical examination)
3. Improvement in eczema (a decrease from baseline observations assessed by clinical examination)
4. Reduction in bruising and bleeding episodes when present (as assessed by clinical monitoring)

Overall study start date
23/02/2010

Completion date
31/12/2013

Eligibility

Key inclusion criteria
1. Males of all ages
2. Severe WAS (clinical score 3 5) or absence of WAS protein in peripheral blood mononuclear cells determined by Western blotting and flow cytometry
3. Molecular confirmation by WAS gene DNA sequencing
4. Lack of HLA-genotypically identical bone marrow or of a 10/10 antigen HLA-matched unrelated donor or cord blood after 3 month search
5. Parental, guardian, patient signed informed consent/assessment
6. Willing to return for follow-up during the 2 year study and the 3 year long-term off study review

7. Only for patients who have received previous allogenic haematopoietic stem cell transplant:
7.1. Failed allogenic haematopoietic stem cell transplant
7.2. Contraindication to repeat allogeneic transplantation for example severe graft versus host disease

Participant type(s)
Patient

Age group
Adult

Sex
Male

Target number of participants
5

Key exclusion criteria
1. Patient with HLA-genotypically identical bone marrow
2. Patient with 10/10 antigen HLA-matched unrelated donor or cord blood
3. Contraindication to leukapheresis
3.1. Anaemia (Hb < 8g/dl)
3.2. Cardiovascular instability
3.3. Severe coagulopathy
3.3.1. Contraindication to bone marrow harvest
3.3.2. Contraindication to administration of conditioning medication
3. Human immunodeficiency virus (HIV) positive patient

Date of first enrolment
23/02/2010

Date of final enrolment
31/12/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Institute of Child Health
London
United Kingdom
WC1N 1EH

Sponsor information

Organisation
Genethon (France)

Sponsor details
1 bis, rue de l'Internationale
Evry
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91000

Sponsor type
Industry

Website
http://www.genethon.fr

ROR
https://ror.org/03fj96t64

Funder(s)

Funder type
Industry

Funder Name
Genethon (France)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?

Results article	results	14/09/2017	Yes	No