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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
11/04/2019	Haematological Disorders	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Alain Fischer

Contact details
Unité d'Immunologie et d'Hématologie Pédiatriques
Hôpital Necker-Enfants Malades
149 rue de Sèvres
Paris
France
75015

Additional identifiers

ClinicalTrials.gov (NCT)
NCT01347346

Protocol serial number
GTG003.08

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)
Committee to Protect People (Comité de Protection des Personnes) - Ile de France 2 approved on 11th August 2009, (ref : 2009-04-01)

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

Primary study design
Interventional

Study type(s)
Treatment

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

Drug/device/biological/vaccine name(s)
Gene therapy

Primary outcome(s)
1. Safety of conditioning regimen (haematopoietic recovery within 6 weeks 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 1 x 106CD34+ cells per kg; retrospective undetectable (replication-competent lentiviruses)RCL; and cell viability equal to or greater than 70%, in accordance with the GMO 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 (as assessed by increased blood platelet counts, expected to rise above 50,000/mm3 and platelets size restoration)

Key secondary outcome(s))
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 (as assessed by clinical monitoring)

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. Unless desease severity indicates that one cannot wait for 3 months (score 5; refractory thrombocytopenia with platelets < 5000 with bleeding or severe autoimmunity)
5. Lack of HLA-genotypically identical bone marrow after 3 month search
6. Lack of a 10/10 or 9/10 antigen HLA-matched unrelated donor after 3 month search
7. Lack of a HLA-matched cord blood after 3 month search
8. Parental, guardian, patient signed informed consent/assessment
9. Willing to return for follow-up during the 2 year study and lifelong for off study review
10. Only for patients who have received previous allogenic haematopoietic stem cell transplant
10.1. Failed allogenic haematopoietic stem cell transplant
10.2. Contraindication to repeat allogenic transplantation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Sex
Male

Key exclusion criteria
1. Patient with HLA-genotypically identical bone marrow
2. Patient with 10/10 or 9/10 antigen HLA-matched unrelated donor or with HLA-matched cord blood
3. Contraindication to leukapheresis
3.1. Anaemia (Hb < 8g/dl)
3.2. Severe vascularitis
3.3. Refractory thrompopenia
3.3.1. Contraindication to bone marrow harvest
3.3.2. Contraindication to administration of conditioning medication
4. Human immunodeficiency virus (HIV) seropositive patient

Date of first enrolment
16/05/2011

Date of final enrolment
31/12/2013

Locations

Countries of recruitment
France

Study participating centre
Unité d'Immunologie et d'Hématologie Pédiatriques
Paris
France
75015

Sponsor information

Organisation
Genethon (France)

ROR
https://ror.org/03fj96t64

Funder(s)

Funder type
Industry

Funder Name
Genethon (France)

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?
Results article	results	21/04/2015	11/04/2019	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes