Autologous hematopoietic stem cell gene therapy in RAG-deficient severe combined immunodeficiency: pre-phase study

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Immunodeficiency syndromes
Study type	Observational invasive

Summary

ID

NL-OMON55430

Source
ToetsingOnline

Brief title
RAG gene therapy pre-phase

Condition

- Immunodeficiency syndromes

Synonym
severe combined immunodeficiency

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: ZonMW. EU

Intervention

Keyword: gene therapy, process evaluation, stem cell donors

Outcome measures

Primary outcome

Successful transduction of fresh CD34+ hematopoietic stem cells with a

lentiviral SIN vector encoding codon-optimized human RAG1 or RAG2 cDNA

(SIN-LV-RAG1 or RAG2 vector), defined as a vector copy number higher than 0.5.

Secondary outcome

Total number and percentage of viable CD34+ HSC after thawing of cryopreserved

transduced cells.

Failure to meet release criteria as defined in IMPD.

in vitro and/or in vivo functionality assays of transduced CD34+ HSC after

thawing.

Study description

Background summary

Severe combined immunodeficiency (SCID) is the most severe form of inherited primary immunodeficiency (PID). SCID due to RAG deficiency has an invariably fatal prognosis if untreated. The only currently available potentially curative treatment is allogeneic stem cell transplantation. Recently, successful application of (lentiviral) codon-optimized SIN vector mediated gene therapy in mouse models for RAG1 and RAG2-deficient SCID has been demonstrated. A phase 1/2 clinical trial is planned that will investigate safety and efficacy (i.e. engraftment and sustained reconstitution of humoral and cellular immunity) of gene therapy using lentiviral SIN vector encoding codon-optimized human RAG1 transduced autologous hematopoietic stem cells (HSC) in RAG1-deficient patients without a HLA-matched donor. A similar approach is currently under development

for patients with RAG2-deficient SCID.

Study objective

The purpose of this study is to evaluate the feasibility and efficiency of transducing freshly obtained CD34+ HSC from either mobilized peripheral blood or bone marrow of healthy donors using lentiviral SIN vectors encoding codon-optimized human RAG1 or RAG2 cDNA.

Study design

Test runs in the LUMC clean room facility of lentiviral vector transduction procedures on fresh HSC material obtained from mobilized peripheral blood or bone marrow of healthy donors.

Study burden and risks

No potential subject benefit or risk from participation in this study. Burden consists of the collection of an extra 20 ml of bone marrow or a lengthening of the stem cell collection apheresis duration during procedures that are part of standard donor care.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Selection as stem cell donor for a family member;
- In case of stem cells from mobilized peripheral blood: completion of G-CSF mobilization procedure for collection of CD34+ HSC from G-CSF mobilized peripheral blood;
Age > 18 years;
Able to comprehend and give signed informed consent.

Exclusion criteria

Any condition precluding stem cell donation
Pregnancy

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-12-2018

Enrollment:	8
Type:	Actual

Ethics review

Approved WMO Date:	31-10-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	03-10-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	21-06-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL66901.058.18