Longterm Follow-up of Subjects With Cerebral Adrenoleukodystrophy Who Were Treated With Lenti-D Drug Product

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This study has been transitioned to CTIS with ID 2024-513904-33-00 check the CTIS register for the current data. • Monitor for long-term safety of the eli-cel administered in parent clinical studies• Monitor for long-term efficacy of eli-cel...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neurological disorders congenital
Study type	Interventional

Summary

ID

NL-OMON54368

Source
ToetsingOnline

Brief title
LTF-304

Condition

- Neurological disorders congenital

Synonym
CALD, cerebral adrenoleukodystrophy

Research involving
Human

Sponsors and support

Primary sponsor: bluebird bio, Inc.
Source(s) of monetary or material Support: Biotechnology Industry (bluebird bio;Inc.)

Intervention

Keyword: Gene therapy, Hematopoietic stem cell transplantation, Long-Term follow-up, X-linked adrenoleukodystrophy

Outcome measures

Primary outcome

1. Safety Endpoints include:

- Proportion of subjects who experience graft versus host disease (GVHD)

- Proportion of subjects who undergo subsequent stem cell transplantation (i.e.

second HSC infusion)

- All drug product-related AEs through 15 years post-drug product infusion

- All serious adverse events (SAEs) through 15 years post-drug product infusion

(regardless of relatedness to drug product)

- Immune-related AEs and new or worsening hematologic or neurologic disorders

or malignancies through 15 years post-drug product infusion

- Incidence of vector-derived RCL, assessed from archived samples as clinically

indicated.

- The number of subjects with insertional oncogenesis (myelodysplasia,

leukemia, lymphoma, etc.)

- The number of subjects with persistent oligoclonality

2. Efficacy Endpoints include:

-MFD-free survival

Secondary outcome

Secondary efficacy endpoints include the following:

- Overall survival.

- Change from Baseline (defined in parent study) in NFS.

- Gadolinium enhancement (GdE) status.

Study description

Background summary

To overcome the limitations of allogeneic hematopoietic stem cell transplantation (allo-HSCT), bluebird bio has developed a hematopoietic stem cell (HSC) gene therapy strategy aiming to perform autologous transplantation of cells that have been transduced ex vivo with an LVV that encodes for a functional gene product.

Subjects who receive eli-cel in Study ALD-102 or Study ALD-104 are initially followed for approximately 2 years post-drug product infusion under their respective parent study protocols.

The US Food and Drug Administration (FDA) (FDA 2020) and European Medicines Agency (EMA) (EMA 2009) recommend long-term follow-up for subjects treated with gene therapy drug products in order to monitor for selected adverse events (AEs) as well as durability of clinical response. Accordingly, Study LTF-304 is being conducted as a long-term observational safety and efficacy follow-up study for subjects who have received eli-cel in parent clinical studies.

Study objective

This study has been transitioned to CTIS with ID 2024-513904-33-00 check the CTIS register for the current data.

• Monitor for long-term safety of the eli-cel administered in parent clinical studies
• Monitor for long-term efficacy of eli-cel administered in parent clinical studies

Study design

This is a multi-center, long-term safety and efficacy follow-up study for subjects with cerebral adrenoleukodystrophy (CALD) who have received eli-cel in parent clinical studies.

Eli-cel is defined as an autologous CD34+ cell-enriched population that

contains cells transduced with Lenti-D lentiviral vector encoding the human adrenoleukodystrophy protein. In parent studies, male subjects with CALD are infused on a single occasion with eli-cel, and then followed for 24 (±1) month for safety and efficacy.

The US Food and Drug Administration (FDA) and European Medicines Agency (EMA) recommend long-term follow-up for subjects treated with gene therapy drug products to monitor for selected adverse events (AEs), as well as durability of clinical response.
Therefore, after subjects have completed the parent clinical studies, they will be asked to participate in a long-term follow-up Study LTF-304, in which they will be followed every 4 months through their post-drug product infusion Year 10 Visit, and then every 6 months from the Year 10.5 Visit through their post-drug product infusion Year 15 Visit.

Intervention

Not applicable as no investigational medicinal product (IMP) will be administered to the patients.

Study burden and risks

The majority of the burden and risks are those associated to the procedures that participants will undertake.
Risks associated to the investigational procedures are the following: pain and discomfort associated to blood sample and to potential bone marrow biopsies.
Risks associated to MRI are the following: adverse effects associated to the contrast agents (gadolinium) and adverse effects to sedation or potential general anaesthesia.
Additionally, there are specific potential risks associated with the gene therapy. Those risks will be closely monitored during this long-term efficacy and safety follow-up study.

This study is conducted in order to monitor the disease status of participants and look for any possible long-term side effects. There may be no direct benefit to participants from participating in this study. It is possible that if any long-term side effects do occur, the monitoring patients receive while on this study will ensure they receive proper treatment earlier than they might have otherwise.
This study may help researchers understand more fully whether gene transfer to treat CALD is safe and effective.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

1.Provision of written informed consent for this study by the subject or subject*s parent(s)/legal guardian(s) and written informed assent by subject, if applicable
2.Have received eli-cel in a parent clinical study
3.Able to comply with study requirements

Exclusion criteria

There are no exclusion criteria for this Study.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-02-2022
Enrollment:	3
Type:	Actual

Ethics review

Approved WMO Date:	28-04-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-09-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-09-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-12-2021

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-01-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-09-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-09-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-01-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-02-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-10-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-11-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
EU-CTR	CTIS2024-513904-33-00
EudraCT	EUCTR2015-002805-13-NL
ClinicalTrials.gov	NCT02698579
CCMO	NL76175.000.21