ISRCTN31547763 https://doi.org/10.1186/ISRCTN31547763

Examination of a potential inflammatory response in the blood of individuals with ALSP and the effect of a stem cell transplant on this inflammatory response

Submission date
27/07/2022

Recruitment status
No longer recruiting

Registration date
09/08/2022

Overall study status
Ongoing

Last Edited
05/08/2022

Condition category
Nervous System Diseases

[ ] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The brain consists of gray matter and white matter. The white matter ensures the transmission of information to other brain areas and to the rest of the body. In individuals with the disease “Adult-onset Leukoencephalopathy with axonal Spheroids and Pigmented glia (ALSP)”, the white matter in the brain is damaged, leading to disrupted transmission of information. As a result, various complaints can arise, for example problems with memory or with walking. The damage to the brain is (partly) caused by diseased 'microglia'. Microglia are immune cells that remove harmful material from the brain. In ALSP patients, the microglia become diseased and disappear due to an error in the DNA. As a result, harmful material in the brain can no longer be properly cleaned up. In addition, the brain damage may trigger an inflammatory response in the body which is visible in the blood.
Early in the disease, the diseased microglia can be replaced with healthy microglia from a donor. This is done through a stem cell transplant, also known as a bone marrow transplant. The healthy donor microglia can properly clean up the harmful material in the brain. In this way new damage to the brain is prevented. Research in other white matter diseases shows that the healthy donor microglia also reduce the inflammatory response in the body. The aim of this study is therefore to investigate the presence of the inflammatory response in the body in individuals with ALSP by examination of their blood and to study whether a stem cell transplant reduces the inflammatory response. The results of this study may contribute to improved treatment of ALSP.

Who can participate?
All individuals with ALSP in whom the error in the DNA causing ALSP has been identified and are referred to the Amsterdam UMC, location VUmc or AMC and are considered to be eligible for stem cell transplant.

What does the study involve?
We want to take approximately fifteen milliliters of extra blood from subjects participating in this study over a period of five years during six regular blood draws. Regular blood draws take place as part of standard care for individuals with ALSP.

What are the possible benefits and risks of participating?
There is no direct benefit for the patients; there is only benefit for the ALSP patient population by increased knowledge. Risks and burdens of the study will be minimized by collecting blood samples only during venous blood sampling in the context of standard care.

Where is the study run from?
Amsterdam UMC (Netherlands)

When is the study starting and how long is it expected to run for?
July 2020 to July 2030

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Shanice Beerepoot, s.beerepoot@amsterdamumc.nl

Study website
https://www.vumc.com/departments/center-for-children-with-white-matter-disorders.htm

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
NL74275.029.20

Study information

Scientific Title
Systemic inflammation in ALSP patients and the effect of an allogenic hematopoietic stem cell transplantation on the inflammation

Acronym
ALSP-INFLAM

Study objectives
1. Cytokine profiles in blood of untreated patients with ALSP differ from cytokine profiles in blood of healthy individuals, revealing an increased production of proinflammatory cytokines
2. Treatment with an allogeneic hematopoietic stem cell transplantation decreases the levels of proinflammatory cytokines, reducing systemic inflammation in treated patients with ALSP over time

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/12/2020, Amsterdam UMC VUmc site Ethics Committee (De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands; +31 20 444 4444; metc@vumc.nl), ref: 2020.374

Study design
Longitudinal cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Observational study in untreated and treated patients with adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP)

Interventions
The procedure includes collection of ±15ml extra venous blood at the moment of venous blood sampling for standard clinical care during a period of 5 years (6 times in total). Primary analyses of plasma cytokines will be done by using a high-throughput, multiplex immunoassay.

Intervention Type
Other

Primary outcome measure
Cytokine profiles in blood before/without treatment, expressed in Normalized Protein eXpression (NPX) in Log2 scale, and cytokine profiles in blood over time (6 times over 5 years)

Secondary outcome measures
Clinical outcomes after treatment measured using patient records
1. Modified Rankin Scale score
2. Guys Neurological Disability score
3. Health Utilities Index score
4. Cognitive function
5. Total HDLS MRI score

Overall study start date
01/07/2020

Completion date
01/07/2030

Eligibility

Key inclusion criteria
1. Diagnosis of ALSP confirmed by a pathogenic CSF1R mutation
2. Aged 18 years or older
3. Capable of giving informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
15

Key exclusion criteria

1. No informed consent given by the patient
2. Cognitive capabilities are too low at inclusion of the study to give informed consent

Date of first enrolment
03/02/2022

Date of final enrolment
01/07/2025

Locations

Countries of recruitment
Netherlands

Study participating centre
Amsterdam UMC, VUmc site
De Boelelaan 1118
Amsterdam
Netherlands
1081 HV

Study participating centre
Amsterdam UMC, AMC site
Meibergdreef 9
Amsterdam
Netherlands
1105 AZ

Sponsor information

Organisation
Amsterdam UMC Location VUmc

Sponsor details
De Boelelaan 1118
Amsterdam
Netherlands
1081 HV
+31-20-5667508
n.wolf@amsterdamumc.nl

Sponsor type
Hospital/treatment centre

Website
http://www.vumc.nl/

ROR
https://ror.org/00q6h8f30

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/07/2031

Individual participant data (IPD) sharing plan
Unpublished anonymized data will be available on reasonable request from a qualified investigator after publication of the primary and secondary outcomes of this study

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 5	17/02/2022	29/07/2022	No	No