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Optimizing therapeutic strategies in VLCADD

Submission date	Recruitment status	[_] Prospectively registered
20/06/2017	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
22/06/2017	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
25/09/2018	Nutritional, Metabolic, Endocrine	

Plain English summary of protocol

Background and study aims
Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD) is an inherited disorder of that causes the body to be unable to break down certain fats. Patients are unable to use fat as an energy source and can develop symptoms during fasting, fever and extensive exercise. To prevent symptoms many countries screen for VLCADD in their newborn screening (NBS) programs over the last years. This resulted in the detection of patients at an early age, often before the development of symptoms. The only treatment is a strict low-fat diet with regular feedings, but this is not necessary for every patients. Some will never develop symptoms, even without a strict diet. A recent study showed that measurement of fat oxidation in skin cells is currently the best marker to predict if a patient will develop symptoms. The aim of this study is to use this test as a tool to choose the best diet for VLCADD patients.

Who can participate?
Anyone aged 10 to 99 years old who have a confirmed diagnosis of VLCADD

What does the study involve?
Participants attend regular visits (about once every one to two years) where they are examined by a multidisciplinary team consisting of a metabolic specialist, a research dietician, a neurologist, a physical therapists and a cardiologist. Before the study visits, participants are asked to fill in a three day food diary. During this visit an extensive medical questionnaire, neurological examination, and undergo heart tests. If necessary, patient records from the local metabolic center of the participant are collected (only after permission by the participant).

What are the possible benefits and risks of participating?
There are no benefits or risks with participating.

Where is the study run from?
Dutch Fatty Acid Oxidation Expertise Center, University Medical Center Utrecht (Netherlands)

When is the study starting and how long is it expected to run for?
October 2010 to June 2017

Who is funding the study?
Metakids (Netherlands)

Who is the main contact?
Dr Gepke Visser
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Study website
www.vetzuuroxidatie.nl

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
METC 10–430

Study information

Scientific Title
Observational study on the dietary habits and clinical outcome of Dutch VLCADD patients

Study objectives
LC-FAO flux (beta-oxidation (LC-FAO) flux score (rate of oleate oxidation)) can be used as a tool to select an individualized dietary strategy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Medical Ethics Committee of the University Medical Centre Utrecht, 07/12/2010, ref: METC 10–430/C

Study design
Retrospective observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

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

Health condition(s) or problem(s) studied
Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD) is an autosomal recessive inherited disorder of mitochondrial long-chain fatty acid beta-oxidation (OMIM 201475)

Interventions
For this observational study, all registered Dutch Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD) patients diagnosed before 2007 (when VLCADD was included in the Dutch newborn screening programmes (NBS) panel) are asked to visit the Dutch Fatty Acid Oxidation Expertise Center in the University Medical Center in Utrecht on a regular basis (around once every one to two years). Before the visit, participants are asked to fill in a three day food diary.

During visits, participants are interviewed and examined by a team of medical experts (metabolic specialists, a research dietician, a neurologist, a physical therapist and a cardiologist). Routine cardiac ultrasound and EKG is also performed during the visits. Information on previous symptoms and/ or lab results was collected from patient records from their local metabolic center (if this was mentioned during the interview). Participant's long-term dietary histories and their beta-oxidation (LC-FAO) flux score (rate of oleate oxidation) in cultured skin fibroblasts are evaluted in relation to clinical outcomes. This was in addition to their regular follow-up by their local metabolic specialist. Available data on diagnostic markers (including LC-FAO flux measured in fibroblasts) are collected and evaluated in relation to clinical outcome.

Intervention Type
Behavioural

Primary outcome measure
Clinical outcomes are measured using the Clinical Severity Score (CSS) during visits to the Dutch FAO (around everyone to two years).

Secondary outcome measures
Ability to work/ attend a regular school as reported by the patient or parents is measured using a standardized questionnaire at each visit to the Dutch FAO expertise center at the University Medical Center Utrecht.

Overall study start date
01/10/2010

Completion date
01/06/2017

Eligibility

Key inclusion criteria
1. Confirmed diagnosis based on deficient VLCADD enzymatic activity in lymphocytes and/or cultured fibroblasts
2. Presence of biallelic mutations in the ACADVL gene (OMIM 609575). The diagnosis should not be based on newborn screening.
3. Aged between 10 to 99 years old

Participant type(s)
Patient

Age group
All

Sex
Both

Target number of participants
Not limited, as many as possible

Key exclusion criteria
Diagnosis based on results of Newborn Screening

Date of first enrolment
01/01/2011

Date of final enrolment
01/01/2017

Locations

Countries of recruitment
Netherlands

Study participating centre

Dutch Fatty Acid Oxidation Expertise Center
Wilhelmina Children's Hospital
University Medical Center Utrecht
Lundlaan 6
Utrecht
Netherlands
3584 EA

Sponsor information

Organisation
University Medical Center Utrecht

Sponsor details
Heidelberglaan 100
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/0575yy874

Funder(s)

Funder type
Charity

Funder Name
Metakids

Results and Publications

Publication and dissemination plan
Manuscript will be submitted to American Journal of Clinical Nutrition.

Intention to publish date
01/08/2017

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Dr. Gepke Visser (gvisser4@umcutrecht.nl). Requests for participant data can also be made at the official fatty acid oxidation disorders registry www.fattyacidoxidation.org

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/01/2019		Yes	No