A Non-Interventional Mechanistic Study to Characterize Biomarkers for Mitochondrial Dysfunction and Inflammation in Subjects with Mitochondrial Disorder and Cardiomyopathy, and Healthy Volunteers

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To explore, whether markers of mitochondrial dysfunction measured in isolated PBMCs or immune cell subpopulations differ between subjects with mitochondrial disorders and cardiomyopathy and healthy volunteers.

Ethical review	Approved WMO
Status	Completed
Health condition type	Heart failures
Study type	Observational invasive

Summary

ID

NL-OMON51060

Source
ToetsingOnline

Brief title
Biomarkers in mitochondrial patients and healthy volunteers

Condition

- Heart failures
- Metabolic and nutritional disorders congenital

Synonym
cardiomyopathy, energy metabolism disease, mitochondrial diseases

Research involving
Human

Sponsors and support

Primary sponsor: OMEICOS Therapeutics GmbH
Source(s) of monetary or material Support: Pharmaceutical company

Intervention

Keyword: Biomarker, Mitochondrial Disease, Mitochondrial Dysfunction

Outcome measures

Primary outcome

The difference in performance of mitochondrial function assays between MitoD

subjects and HV subjects

Secondary outcome

Difference in blood serum/plasma markers associated with inflammation and

oxidative stress (IL-6, hs-CRP, PTX-3, and GDF-15) between MitoD subjects and

HV subjects

Study description

Background summary

OMT-28 is a fully synthetic small molecule that belongs to the family of 17,18-epoxyeicosatetraenoic acid (17,18-EEQ) analogs, a natural metabolite of the omega-3 fatty acid eicosapentaenoic acid (EPA).1,2 The safety of various doses of OMT-28 was studied in toxicology studies in various species, as well as in a First-in-Human study including a Single-Ascending-Dose (SAD) and Multiple-Ascending-Dose (MAD) part, and a Phase 2a Proof-of-Concept (PoC) study (PROMISE-AF) in subjects with atrial fibrillation.3 Recent non-clinical studies showed the potential of OMT-28 to positively affect mitochondrial function and survival. Therefore, OMT-28 is currently being developed for the treatment of cardiomyopathy in subjects with mitochondrial diseases and in subjects with coronary artery disease.

Subjects with mitochondrial disorder and cardiomyopathy might benefit from treatment with OMT-28, due to the potential positive effects of OMT-28 on mitochondrial function and survival.4,5 This non-interventional study aims to characterize these subjects using different markers of mitochondrial function and inflammation, and to assess using ex-vivo assays in blood the potential effect of OMT-28 on mitochondrial function.
The aim of this non-interventional study is to characterize subjects regarding their levels of mitochondrial dysfunction and inflammation markers, and to identify those subjects who might benefit most from OMT-28 treatment based on the ex-vivo blood assay results. The results of this study are supposed to guide the design of future clinical interventional studies with OMT-28.

Study objective

To explore, whether markers of mitochondrial dysfunction measured in isolated PBMCs or immune cell subpopulations differ between subjects with mitochondrial disorders and cardiomyopathy and healthy volunteers.

Study design

This is a non-interventional study with a cross-sectional design. Subjects will not be exposed to treatment.

Study burden and risks

Neither MitoD patients nor HVs will directly benefit from this study. MitoD patients might benefit indirectly, as OMT-28 is evaluated as a potential treatment for MitoD. As all study assessments are considered minimally invasive, the benefit-risk evaluation is considered acceptable for the participants. This is an exploratory, non-interventional study to characterize the markers of mitochondrial dysfunction, inflammation and cardiac dysfunction in MitoD subjects and healthy volunteers. The distribution and variability of these biomarkers are unknown in these populations
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Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

All subjects
1. Adults between 18 and 75 years, inclusive at screening
2. Body mass index (BMI) 18.0 to 30.0 kg/m2, inclusive at screening
3. Ability and willingness to abstain from alcohol at study visit
4. Subject (and/or parent/legal guardian) has voluntarily signed consent form.
5. Willingness and ability to comply with all study procedures.
6. Ability to communicate with the investigator in Dutch or English

Subjects of cohort 1 with Mitochondrial Disorder (in addition)
7. Diagnosis of Mitochondrial Disorder, confirmed by:
a. Genetic testing at any time prior to screening showing m.3243A>G mutation
b. Newcastle Mitochondrial Disease Scale (NMDAS) score *11

8. Any current cardiomyopathy (e.g., LVH, reduced systolic function or strain, ECG abnormalities consistent with cardiac involvement etc.).

Subjects of cohort 2 Healthy Volunteers (in addition)
9. Judged to be in good health in the opinion of the Investigator on the basis of a medical evaluation that reveals the absence of any clinically relevant abnormality

10. Matching to MitoD group for age (+/- 5 years), gender, and BMI (+/- 3 kg/m2).

Exclusion criteria

2. Women with positive urine hCG test at screening
3. Subject has a hemoglobin values outside the normal limits (as per local lab)
4. Subject has received drug therapy with any cytostatic, sGC stimulator/activator or nitrate agent during the last 3 months
5. Subjects with severe aortic valve stenosis
6. Subject has received drug therapy with Metformin during last 3 months
7. Significant psychiatric or neurological disorder that would inhibit the subject from being compliant with study procedures
15. Positive nasopharyngeal rapid antigen test for SARS-CoV-2 at admission to the clinical research center
16. Subject has received any vaccination in the last 2 weeks prior to Visit 1

Subjects of cohort 2 Healthy Volunteers (in addition)
17. Subject has acute decompensated hepatic, gastrointestinal, respiratory, cardiovascular, metabolic, immunological, or hormonal disorders.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	13-10-2021
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	01-08-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 21411
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL77982.056.21

Study results

Date completed:	19-11-2021
Results posted:	25-07-2022

First publication
23-06-2022