Identifying disease specific pathways and modifiers in Phospholamban r14del cardiomyopathy

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Our main objective is to identify disease modifiers in PLN r14del cardiomyopathy by studying patients are different ends of the PLN r14del cardiomyopathy disease spectrum with respect to differences in the circulating proteome and metabolome and in...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Congenital cardiac disorders
Study type	Observational invasive

Summary

ID

NL-OMON49612

Source
ToetsingOnline

Brief title
DECIPHER-PLN part 1

Condition

- Congenital cardiac disorders
- Cardiac and vascular disorders congenital

Synonym
PLN heart disease, PLN r14del cardiomyopathy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Astra Zeneca

Intervention

Keyword: Biomarkers, Cardiology, Genetic heartdisease, Phospholamban

Outcome measures

Primary outcome

Differences between patients at different disease stages in terms of:

- Phenotypic/functional differences in cardiomyocytes derived from iPSC

- Circulating proteome at baseline and follow-up

- Circulating metabolome at baseline and follow-up

- Circulating cardiac biomarkers at baseline and follow-up

Secondary outcome

n.v.t.

Study description

Background summary

The r14del mutation of the Phospholamban (PLN) gene can result in a cardiomyopathy and is the most frequently found genetic mutation in patients with a cardiomyopathy in the Netherlands. Until date, over 1150 carriers have been identified, with the majority being resident in the Northern parts of the Netherlands. Subjects with a heterozygous PLN r14del mutation show a wide variety in phenotype. The majority of patients present with arrhythmias around their 40*s to 50*s or subtle ECG changes, but large differences are seen. Within the same family, patients can present either with sudden death or overt heart failure in their 20*s requiring a heart transplant or remain completely asymptomatic until their 70*s. So far, no modifiers (genetic or environmental) have been identified.

Study objective

Our main objective is to identify disease modifiers in PLN r14del cardiomyopathy by studying patients are different ends of the PLN r14del cardiomyopathy disease spectrum with respect to differences in the circulating proteome and metabolome and in cardiomyocytes derived from induced pluripotent

stem cells (iPSC-CM)

Study design

Non-therapeutic study, exploring PLN r14del cardiomyopathy patients, two visit research.

Study burden and risks

The burden and risk associated with this study is minimal and may only include complications of the skin punch biopsy and venipuncture. It will not provide a direct benefit to the patients, but may prove beneficial to both the research and the patient community with potential new insights in PLN r14del cardiomyopathy pathogenesis and new treatment approaches.

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

• A minimum age of 18.
• Genetically confirmed r14del mutation in PLN.
• Of adequate communication.
• Informed consent is obtained.

Exclusion criteria

• Aetiology of heart failure other than PLN r14del cardiomyopathy.
• Extensive skin disorder precluding a biopsy from unaffected skin area.
• Known allergy for local anaesthetics.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-11-2020
Enrollment:	90
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	10-09-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-09-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-03-2025
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL73975.042.20