Understanding colchicine resistance in Familial Mediterranean Fever; exploring pathophysiological mechanisms and therapeutic options

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The primary objective is to identify what causes colchicine resistance in FMF. Additionally, we will try to identify potential interventions to overcome resistance

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Immune system disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON56532

Source
ToetsingOnline

Brief title
CRAFT

Condition

- Immune system disorders congenital
- Immune disorders NEC

Synonym
Familial Mediterranian Fever

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Novartis,SOBI en Novartis Pharma,Swedish Orphan International

Intervention

Keyword: colchicine, FMF, resistance

Outcome measures

Primary outcome

Within cases and controls we will determine intracellular levels of colchicine, assuming that cases will have lower intracellular colchicine levels as compared to controls. Additionally, we will perform genomics analysis on peripheral blood cells as well as transcriptomic analysis by single cell RNA-seq in order to identify potential differences in genetic profile and gene expression between cases and controls.

Secondary outcome

Are demographic factors like age, gender and body composition associated with colchicine response?

Study description

Background summary

Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disease mainly affecting immigrants from the Near-East and North-Africa. Untreated this disorder may lead to amyloidosis, organ failure and decreased quality of life. Most patient can adequately be treated with colchicine, however up to 10% of the FMF patients are intolerant or resistant this first line of treatment and have to be treated with IL-1 blocking drugs (Anakinra and Canakinumab). The disadvantages of these biologicals are primarily the need to inject the medication and the costs. Why patients are resistant to colchicine is still unknown although inability to reach adequate intracellular levels of colchicine is assumed to play a role.

Study objective

The primary objective is to identify what causes colchicine resistance in FMF. Additionally, we will try to identify potential interventions to overcome resistance

Study design

Case control study

Study burden and risks

Blood samples will be collected from each participant during the inclusion visit. When possible, blood samples will be taken in conjunction with blood sampling for clinical monitoring. In total we will collect 4 heparin tubes for all analysis. Additionally, participants are asked to fill out a questionnaire. The study can only be performed with subjects suffering from FMF. Apart from some discomfort during collection of blood, burden for participant is minimal. This study bears no risk for the participants.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Patients: Diagnosis of FMF (genetically confirmed). Insufficient control of symptoms despite use of colchicine
Controls: Diagnosis of FMF (genetically confirmed). In remission on colchicine

Exclusion criteria

pregnancy

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-09-2024
Enrollment:	100
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	05-02-2024
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL85047.078.23