

# The PHENOSAR trial: Antibiotic treatment of biopsy confirmed phenotypes in sarcoidosis: a proof of concept clinical trial

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This study has been transitioned to CTIS with ID 2024-513534-38-00 check the CTIS register for the current data. Investigate whether treatment with azithromycin has an inhibitory effect on the mTOR pathway and/or C. acnes, causing a reduction of the...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruiting
<b>Health condition type</b>	Respiratory disorders NEC
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON56424

### Source

ToetsingOnline

### Brief title

The PHENOSAR trial

### Condition

- Respiratory disorders NEC
- Skin and subcutaneous tissue disorders NEC

### Synonym

sarcoidosis

### Research involving

Human

## Sponsors and support

**Primary sponsor:** Sint Antonius Ziekenhuis

**Source(s) of monetary or material Support:** ZonMW

## Intervention

**Keyword:** inflammation, phenotype, sarcoidosis, therapy

## Outcome measures

### Primary outcome

The difference in inflammatory activation based on blood biomarkers and FDG-PET of patients which were treated with Doxycyclin and Azithormycin compared to patients treated with placebo

### Secondary outcome

Measure the presence of C.acnes in biopsies

Measure the activity of the signaling pathways in biopsies

## Study description

### Background summary

Sarcoidosis is a multisystemic disease of unknown origin, characterized by the formation of non-caseating granulomas. Sarcoidosis can be formed in every organ, but most often the lungs and lymph nodes are affected. There is no curative treatment for sarcoidosis, treatment is given to minimize risk of organ failure and to suppress inflammation. The first-choice treatment for sarcoidosis is prednisone, which is associated with numerous severe side-effects. Also the second and third-choice medication for sarcoidosis are associated with burdensome side effects. Recently, it was shown that the intracellular signaling pathway mTOR plays a role in the pathogenesis of sarcoidosis. Instead of inaccurate suppression of immune cells with immunosuppressive, specific inhibition of this mTOR pathway showed to be beneficial for some sarcoidosis patients. Inhibition of this pathway can be done by antibiotics with immunomodulatory properties, such as azithromycin, which comes with fewer side-effects compared to prednisone and methotrexate. Furthermore, this antibiotic also has an inhibiting effect on a largely studied

trigger of sarcoidosis, the *C. acnes* bacterium. Already considerable research has been done to the role of *C. acnes* in sarcoidosis pathogenesis and presence of this bacterium has been associated with a more progressive disease. Treatment of patients in whom *C. acnes* is present in and around the granuloma may benefit from treatment with azithromycin, which may possibly also decrease the possibility of a more progressive form later in life.

## **Study objective**

This study has been transitioned to CTIS with ID 2024-513534-38-00 check the CTIS register for the current data.

Investigate whether treatment with azithromycin has an inhibitory effect on the mTOR pathway and/or *C. acnes*, causing a reduction of the inflammatory activity which is found in sarcoidosis patients measured by blood biomarkers ACE and sIL-2R and by FDG-PET/CT

## **Study design**

Prospective cohort study.

## **Intervention**

The study population will be divided into two groups receiving either Doxycycline and Azithromycin or placebo for 3 months. Both groups will contain an equal amount of patient in which *C. acnes* can be detected in the tissue

## **Study burden and risks**

Risk: Adverse effects of study treatment.

Burden:

FDGPET-scan: at start and end of study.

Blood tests: at start and end of study; 40 mL per occasion

## **Contacts**

### **Public**

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Koekoekslaan 1  
Nieuwegein 3435CM  
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### **Scientific**

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## **Trial sites**

### **Listed location countries**

Netherlands

## **Eligibility criteria**

### **Age**

Adults (18-64 years)

Elderly (65 years and older)

### **Inclusion criteria**

Biopsy proven sarcoidosis.

No treatment indication for the sarcoidosis

in case of treatment, started at least 12 months ago. with stable dosis and no intention of changing this treatment during this study

Inflammatory activity according to FDG-PET scan

SUVmax above 3 in lungs and above 5 in mediastinum/hili

### **Exclusion criteria**

Increased duration of QT interval (>440ms for men and >450ms for women) on ECG

Hearing deficits, a possible side-effect of azithromycin use is hearing deficits, although the chance of this is very small

Being pregnant or breastfeeding at time of inclusion

Use of an investigational drug during the time between FDG-PET scan and screening.

## **Study design**

## Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

## Recruitment

NL	
Recruitment status:	Recruiting
Start date (anticipated):	23-03-2023
Enrollment:	40
Type:	Actual

## Medical products/devices used

Product type:	Medicine
Brand name:	Azithromycin
Generic name:	Azithormycin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	doxycycline
Generic name:	doxycycline
Registration:	Yes - NL intended use

## Ethics review

Approved WMO	
Date:	10-08-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	
Date:	05-01-2023

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-11-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-05-2024
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-10-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

## 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
EU-CTR	CTIS2024-513534-38-00
EudraCT	EUCTR2021-003057-29-NL
CCMO	NL73729.100.21