The PREDMETH trial: Effectiveness of methotrexate versus prednisone as first-line therapy for pulmonary sarcoidosis - A randomized controlled trial

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This study has been transitioned to CTIS with ID 2024-514055-15-00 check the CTIS register for the current data. Primary: • Investigate the effectiveness and tolerability of methotrexate as first-line therapy in patients with pulmonary sarcoidosis...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON49109

Source
ToetsingOnline

Brief title
PREDMETH trial

Condition

- Respiratory disorders NEC

Synonym
Besnier-Boeck-Schaumann disease of the lung, Pulmonary sarcoidosis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Longfonds

Intervention

Keyword: lung, methotrexate, prednisone, sarcoidosis

Outcome measures

Primary outcome

The change in hospital-measured Forced Vital Capacity (FVC) between baseline

and 24 weeks...

Secondary outcome

Other pulmonary function parameters, biomarkers, adverse events, quality of

life.

Study description

Background summary

Sarcoidosis is a multisystem, granulomatous disorder, most commonly affecting the lungs. Symptom burden is high, and quality of life (QoL) and social participation are negatively affected. In patients with pulmonary sarcoidosis, treatment is recommended in case of significant symptoms and/or impaired or deteriorating lung function. Evidence-based treatment recommendations are limited, outdated and largely based on expert opinion.
Prednisone is currently the first-choice therapy in pulmonary sarcoidosis and leads to short-term improvement of lung function. Unfortunately, prednisone has major side-effects and is associated with impaired QoL. Methotrexate is presently considered second-line therapy, and appears to have fewer side-effects. We hypothesize that first-line treatment with methotrexate is as effective as prednisone, with fewer side-effects and better QoL

Study objective

This study has been transitioned to CTIS with ID 2024-514055-15-00 check the CTIS register for the current data.

Primary:
• Investigate the effectiveness and tolerability of methotrexate as first-line

therapy in patients with pulmonary sarcoidosis compared with prednisone.
Secondary:
• Examine (immunological) biomarkers of disease progression and chronicity.
• Assess whether response to therapy can be predicted in individual patients.
• Gain more insights into the underlying disease mechanism and potential new targets

Study design

Phase 4, prospective, randomized, open-label, multi-center, single country, non-inferiority trial.
Randomization 1:1 to oral prednisone (start 40 mg daily, to be tapered to 10 mg daily) or oral methotrexate (15 mg weekly to be increased to 25 mg weekly) for 24 weeks. Thereafter continuation of trial for 18 months on regular treatment (investigator decision). 138 randomized patients.

Intervention

Treatment with prednisone or methotrexate.

Study burden and risks

Risk: Adverse effects of study treatment.
Burden:
Physical examination: every visit (=6 times).
Blood tests: every visit 80 mL per occasion
Pulmonary function: every visit.
FVC measurement at home: weekly, 24 weeks.
Questionnaires: King*s Sarcoidosis Questionnaire, General Rating of Change, EQ-5D-5L, Patient Experience and Satisfaction with Medication Questionnaire, VAS of Dyspnea, Cough, Fatigue, Complaints, MRC Dyspnea Scale, Fatigue Assessment Scale: every visit.
VAS at home: symptoms and side effects: weekly, 24 weeks.

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

- Diagnosis of sarcoidosis according to the ATS/ERS/WASOG criteria (7), in case of absent histology a diagnosis of sarcoidosis can also be established in a multidisciplinary team meeting in a sarcoidosis expert center based on a highly suggestive clinical and radiological picture (18, 19)
- Age >=18 years
- A pulmonary indication for treatment and parenchymal involvement on X-ray or CT-scan conducted within three months before inclusion (determined by the treating physician and conform current guidelines).
- A forced vital capacity (FVC) of <=90% of predicted, or a diffusion capacity of the lung for carbon monoxide (DLCO) <=70% of predicted, or >=5% FVC decline/>=10% DLCO decline in the past year. For pulmonary functions tests GLI reference values are used.

Exclusion criteria

- Any condition or circumstance that, in the opinion of the investigator, may make a subject unlikely or unable to complete the study or comply with study procedures. - Previous immunosuppressive treatment for sarcoidosis - Use of systemic immunosuppressive therapy within the preceding three months for another disease than sarcoidosis - Pregnant, breastfeeding, or planning to become pregnant or breastfeed during the study treatment or within 90 days after the last dose in the randomized study phase. For males; planning to pro-create during the study or within 90 days after the last dose of the

randomized study phase. - Primary systemic treatment indication being an extra pulmonary location of sarcoidosis (e.g. cardiac of neurological) - Contra-indication for methotrexate or corticosteroids: • severely impaired renal function (creatinine clearance <30 ml/min) • impaired hepatic function (serum bilirubin-value >5 mg/dl or 85,5 micromole/l) • bone marrow insufficiency with severe leukopenia, thrombocytopenia, or anaemia • severe acute or chronic infections, such as tuberculosis, HIV, parasitic infections or other immunodeficiency syndromes • mouth, stomach or duodenal ulcers

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-07-2020
Enrollment:	138
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Methotrexate
Generic name:	Methotrexate
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Prednisone

Generic name:	Prednisone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-11-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-02-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-12-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-01-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-10-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-10-2024
Application type:	Amendment
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
EU-CTR	CTIS2024-514055-15-00
EudraCT	EUCTR2019-004148-31-NL
CCMO	NL71782.078.19