PolyMyalgia Rheumatica treatment with Methotrexate in Optimal Dose in an Early disease phase

Published: 10-02-2020
Last updated: 15-05-2024

In patients with recently diagnosed PMR, MTX 25mg/week compared to placebo will lead to a higher proportion of patients in glucocorticoid free remission

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON22681

Source
NTR

Brief title
PMR MODE

Condition

- Autoimmune disorders

Synonym
Jylamvo, Methotrexate

Health condition

polymyalgia rheumatica (PMR) spierreuma

Research involving
Human

Sponsors and support

Primary sponsor: Sint Maartenskliniek Nijmegen
Source(s) of monetary or material Support: Dutch Arthritis Arhritis Society (ReumaNederland)

Intervention

Explanation

Outcome measures

Primary outcome

The between group difference in proportion of PMR patients in GC-free remission at week 52.

Secondary outcome

1. The proportion of GC-free remission at week 32; 2. The time to GC-free remission and first relapse; 3. The proportion of low-dose GC (≤ 5mg daily) remission at week 32 and 52; 4. The GC cumulative dose at week 32 and 52; 5. The number of relapses or recurrences during follow up at week 32 and 52; 6. The proportion of patients that relapsed or had a recurrence during follow up at week 32 and 52; 7. The change in PMR-AS; 8. The change with the core domain sets for outcome measures of PMR as proposed by the OMERACT, including: a. Systemic inflammation; b. Physical Function; c. Pain; d. Stiffness; 9. The change in Patient Reported Outcomes (PROs): transition and Patient Acceptable Symptom states (PASS) questions, Visual Analog Scales (VAS), the health related quality of life (EQ-5D-5L), Health Assessment Questionnaire (HAQ), and Patient Reported Outcome Measures Information System Physical-Function (PROMIS-PF); 10. The frequency and types of GC- and MTX-related adverse events; 11. The proportion of patients that require MTX/placebo (dose) adjustment. 12. Direct healthcare costs at week 52

Study description

Background summary

Rationale: Polymyalgia rheumatica (PMR) is an inflammatory rheumatic disease affecting about 1% of people older than 50, resulting in pain and stiffness of the neck, shoulder girdle, and pelvic girdle. Untreated, PMR can lead to a significant reduction in quality of life. The mainstay for treating PMR is glucocorticoids (GC). However, a large proportion of patients do not achieve GC-free remission within either the first (more than 70%) or second year of treatment (more than 50%). Furthermore, GC-related adverse events (AE) can be severe and occur in a large proportion of patients, ranging upwards of 65%. Some disease modifying antirheumatic drugs (DMARD) have been studied as possible GC-sparing treatments. Most

evidence, although limited, for a GC-sparing treatment exists for methotrexate (MTX) and the current EULAR/ACR guidelines for PMR recommend early introduction of MTX in patient groups at risk for prolonged therapy, relapse, or GC-related AE. However, the previously studied MTX dose was 7.5 – 10 mg, far below the 15 – 25 mg dose at which MTX is used as a DMARD for rheumatoid arthritis (RA), and no studies have been conducted investigating these higher dosages. Objective: The primary objective is to study the efficacy of treatment with optimally dosed MTX compared to placebo in patients recently diagnosed with PMR fulfilling the 2012 EULAR/ACR criteria. Study design: double blind, randomized, placebo-controlled superiority trial. Study population: 100 patients with recently diagnosed PMR according to the 2012 EULAR/ACR classification criteria will be recruited from the Sint Maartenskliniek. Exclusion criteria are not being able to speak, read or write Dutch, extensive previous GC exposure, exposure to other immunosuppressant drugs 3 months prior, other active inflammatory rheumatic diseases, conditions that might interfere with pain or movement evaluation, contra-indications for MTX, or a considerable risk of non-compliance. Intervention: Patients included will be randomly allocated in a 1:1 ratio to receive either MTX 25mg/week or placebo for a total of 52 weeks. All patients will receive folic acid 10mg/week, and prednisolone at an initial dose of 15mg/day, tapered through an accelerated protocol over the course of 24 weeks. In case of primary non-response or relapse, the prednisolone dose can be increased to up to 25mg/day. Patients will be assessed at baseline, 4, 12, 24, 32, and 52 weeks, with additional visits if necessary. Main study parameters/endpoints: The primary study outcome is the difference in proportion of PMR patients in GC-free remission at week 52. Secondary study parameters include proportion GC-free remission at week 32, The proportion of low-dose GC (≤ 5mg daily) remission at week 32 and 52, GC-cumulative dose at week 32 and 52, the time to first relapse and GC-free remission, the number and proportion of patients that had a relapse at week 32 and 52, the proportion of patients that get MTX/placebo dose adjustment, change in PMR-activity score (PMR-AS), change in Patient Reported Outcome Measures (PROMs), and the incidence density and types of AE, and cost-utility (based on EQ-5D and direct healthcare costs). Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Patients will be assessed at 6 visits over the course of 52 weeks. At baseline, demographics and patient and disease characteristics are assessed. Additionally, imaging and a several laboratory tests will be performed. At follow-up, data collection will take place to monitor disease activity and adverse events, consisting of blood samples, PROMs, and disease activity and adverse events assessment. Compared to routine care this means approximately 1 or 2 extra visits for the purpose of this study. The study questionnaires and measurements will take about an additional 15 minutes per visit. A potential risk associated with participation includes an increase in disease activity due to the accelerated GC tapering protocol. In case this happens, patients are instructed to contact their treating rheumatologist, who will increase GC dose accordingly. Potential side effects of MTX are mainly gastro-intestinal of nature, including nausea, abdominal pain, diarrhoea, liver enzyme abnormalities, as well as haematological abnormalities and non-basal-cell skin cancer. However, there is sufficient evidence that indicates that MTX has a relatively safe treatment profile, and it is registered for a number of indications. Therefore, we expect a minimal risk for patients treated with MTX. This research will be conducted according to the principles of the Declaration of Helsinki and all relevant Dutch legislation. METC approval will be requested and the trial will be submitted to the Dutch and EuropeanTrial Registries.

Study objective

In patients with recently diagnosed PMR, MTX 25mg/week compared to placebo will lead to a higher proportion of patients in glucocorticoid free remission

Study design

Assessments will be at week 0 (baseline), 4 weeks (v1), 12 weeks (v2), 24 weeks (v3), 32 weeks (v4), and 52 weeks (v5). Furthermore lab assessments for MTX related AE (without compulsory visit) is at week 8, week 16, and week 42. Total study duration per patient is 52 weeks.

Intervention

Methotrexate 25 mg/week

Contacts

Public
Sint Maartenskliniek Nijmegen
Noortje Kooijman

024 – 327 2948
Scientific
Sint Maartenskliniek Nijmegen
Noortje Kooijman

024 – 327 2948

Eligibility criteria

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

Inclusion criteria

- PMR according to the 2012 EULAR/ACR classification criteria - eligibility for treatment with MTX or placebo and show a willingness to follow the study protocol as judged by treating

rheumatologist - Signed written informed consent

Exclusion criteria

- Not being able to speak, read or write Dutch; - PMR-related GC treatment prior to inclusion consisting of either: GC exposure for > 8 weeks, GC treatment with > 30 mg/day, or No further information regarding GC treatment; - Exposure to other systemic immunosuppressant treatments other than GC 3 months prior to inclusion in the study; - Active concomitant GCA or other rheumatic diseases such as RA, spondylarthropathies, connective tissue diseases, or drug-induced myopathies; - Neuropathies or other conditions that might interfere with pain or movement evaluation of PMR, as judged by the treating rheumatologist; - Previous hypersensitivity for prednisolone or MTX.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-02-2020
Enrollment:	100
Type:	Actual

IPD sharing statement

Plan to share IPD: No

Ethics review

Approved WMO Date:	26-07-2021
Application type:	First submission
Review commission:	METC Oost-Nederland
	p/a Radboudumc, huispost 628,
	Postbus 9101
	6500 HB Nijmegen
	024 361 3154
	commissiemensgebondenonderzoek@radboudumc.nl

Study registrations

Followed up by the following (possibly more current) registration

ID: 54851
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL8366
EudraCT	2019-002413-18
CCMO	NL69979.091.19
OMON	NL-OMON54851

Study results