REDUCE PMR: Rituximab Effect on Decreasing glUcoCorticoid Exposition in newly diagnosed PolyMyalgia Rheumatica

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This study has been transitioned to CTIS with ID 2024-513544-28-00 check the CTIS register for the current data. The main objective is to study the efficacy of treatment with RTX in patients with newly diagnosed PMR compared to placebo.

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

Summary

ID

NL-OMON53492

Source
ToetsingOnline

Brief title
REDUCE PMR1

Condition

- Autoimmune disorders
- Joint disorders

Synonym
Polymyalgia rheumatica

Research involving
Human

Sponsors and support

Primary sponsor: Sint Maartenskliniek
Source(s) of monetary or material Support: ZonMW,ReumaNederland;RSMK

Intervention

Keyword: glucocorticoid sparing, Polymyalgia rheumatica, Randomized controlled trial, Rituximab

Outcome measures

Primary outcome

The primary outcome is the proportion of patients in GC free remission one year after RTX treatment compared to placebo. Remission will be defined as a polymyalgia rheumatica -activity score (PMR-AS) of <10.

Secondary outcome

Secondary study parameters include between group difference in proportion of patients in GC-free remission at week 21, the proportion of patients with low dose GC (<=5mg/day) remission at week 21 and 52, difference in PMR-AS, the number of disease relapses/recurrences at week 52, time to GC-free remission and to relapse, GC cumulative dose during the trial, and the proportion of patients with RTX/PCB retreatment, sex differences in frequencies of GC-remission and safety, change in Patient Reported Outcomes (PROMs), the frequency and types of GC- and RTX-related AE, change in the modified Glucocorticoid Toxicity Index (GTI) and cost-effectiveness.

Study description

Background summary

Polymyalgia rheumatica (PMR) is one of the most prevalent inflammatory rheumatic diseases among people older than 50 years. It is characterized by pain and stiffness of the neck, bilateral shoulder and hip girdle and is often associated with elevated inflammatory parameters. Untreated, it leads to a significant and long-term reduction in quality of life. Glucocorticoids (GC) are the cornerstone of treatment, but have several drawbacks. First, only a minority of patients achieves GC-free remission after one or two years. Second, GC-related adverse events (AE) occur in a large portion of patients, up to 65% depending on the GC dosage. When a patient experiences a relapse, intensification and longer duration of GC treatment is needed. This results in more GC related AE, and therefore, the search for GC-sparing agents is high on the research agenda. Although the exact pathogenesis of PMR is not known, there are several indications that B-cells have a role in PMR. This make Rituximab (RTX), a chimeric monoclonal antibody targeting B-cells via CD-20, a possible candidate for treatment of PMR. An exploratory proof of concept RCT demonstrated that a significantly higher proportion of PMR patients treated with RTX achieved GC-free remission at 21 and 52 weeks compared to placebo. The efficacy of RTX in patients with newly diagnosed PMR needs confirmation and should therefore be further investigated in a larger study with longer follow up.

Study objective

This study has been transitioned to CTIS with ID 2024-513544-28-00 check the CTIS register for the current data.

The main objective is to study the efficacy of treatment with RTX in patients with newly diagnosed PMR compared to placebo.

Study design

A total of 114 patients wil participate in this study. Patients will be randomized 1:1 to either RTX of placebo. At baseline treatment consists of 1000mg iv RTX with usual premedication, placebo group will receive 0mg iv RTX with similar oral pre-medication as the intervention group. Additionally at baseline all patients receive prednisolone 15mg/day in a 17-week accelerated tapering protocol with the possibility of increasing GC dose in case of non response or relapse.
Patients with a need for treatment intensification (based on relapse or increase of GC dose) will receive an extra dosage of 500mg iv RTX (or 0mg iv RTX in placebo group) after 24 weeks, unless adverse events occurred at infusion hampering the possibility of retreatment.

Study visits take place at 4, 12, 21, 32 and 52 weeks. Visits at week 4, 12 and 32 can be performed digitally or by telephone if preferred by patients and treating phycisian. Disease activity will be measured at every visit using

PMR-AS. PMR-AS is defined by CRP, duration of morning stiffness (minutes), elevation upper limb score (EUL) and the physicians and patients visual analogue scale (VAS). Remission is defined as PMR-AS < 10. At every study visit patients will be asked to fill in a few questionnaires regarding daily activities and quality of life.

Intervention

Patients will be randomized 1:1 to either RTX of placebo. At baseline treatment consists of 1000mg iv RTX with usual premedication, placebo group will receive 0mg iv RTX with similar oral pre-medication as the intervention group. Additionally at baseline all patients receive prednisolone 15mg/day in a 17-week accelerated tapering protocol with the possibility of increasing GC dose in case of non response or relapse.

Study burden and risks

In current practice, patients with PMR visit the outpatient clinic every two, three or six months, including measurement of disease activity and collecting blood samples. For this study patients will visit the clinic at baseline, 21 and 52 weeks. Other visits can be performed digitally of by phone if preferred by patients and treating physician. Blood sampling is done in accordance to regular practice. Questionnaires entailing a range of domains take a maximum of 30 minutes at every visit.
Possible risks when participating in this study include a chance of temporary increase of disease activity because of the accelerated GC tapering schema, especially in the placebo group. However, patients will be instructed to contact the research physician when this happens and they can immediately act upon this by increasing the GC dose if deemed necessary. Other possible adverse effects can be related to RTX treatment, including dose-dependent risk of infection (e.g. COVID-19) or infusion related side effects.
Based on our previous experience with RTX we expect a minimal risk for patients treated with RTX. We expect the risk for a severe COVID-19 infection (e.g. hospital admission required or lethal infection) to be minimal and the risk for mild COVID-19 comparable to the general population, because most patients will be vaccinated, RTX treatment initially consist of a one-time dosage and if retreatment is needed a lower dosage is given. Also patients can benefit from the reduced dose of GC and a lower chance of GC-related side effects, among which COVID-19 infections which are more prevalent at higher GC dose.

Contacts

Public
Sint Maartenskliniek

Hengstdal 3
Ubbergen 6574 NA
NL
Scientific
Sint Maartenskliniek

Hengstdal 3
Ubbergen 6574 NA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Newly diagnosed PMR (<12 weeks) according to the 2012 EULAR/ACR classification criteria. • Glucocorticoid treatment <= 8 weeks • Glucocorticoid dose equivalent of prednisolone <=30 mg/day.

Exclusion criteria

• Treatment with systemic immunosuppressants (other than GC, MTX, leflunomide and azathioprine) 3 months prior to inclusion
• (clinical) suspect concomitant giant cell arteritis or other rheumatic inflammatory disease
• Concomitant conditions that might significantly interfere with evaluation of PMR pain or movement as judged by the investigator
• Previous hypersensitivity for RTX of contra-indications to RTX
• Not being able to speak, read or write Dutch

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-02-2023
Enrollment:	114
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Rixathon, MabThera, Truxima, Ruxience
Generic name:	Rituximab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	19-12-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-01-2023
Application type:	First submission

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-03-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-04-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-05-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-05-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-06-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-02-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-04-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-05-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-08-2024
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-10-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	CTIS2024-513544-28-00
EudraCT	EUCTR2022-003127-18-NL
ClinicalTrials.gov	NCT05533125
CCMO	NL82627.091.22