Treatment With Leflunomide in Patients With Polymyalgia Rheumatica

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21927

Source
NTR

Brief title
PMRLEFRCT

Health condition

Polymyalgia Rheumatica
PMR
Spierreuma

Sponsors and support

Primary sponsor: University Medical Center Groningen
Source(s) of monetary or material Support: Dutch Arthritis Foundation (Reumafonds)

Intervention

Outcome measures

Primary outcome

PMR relaps, timepoint: first 12 months of the study

Secondary outcome

Efectiveness concerning disease activity

a.Time till first relaps within first 24 months

b.Percentage of patients with at least 1 relaps in the first 12 or 24 months

c.Total relapses within the first 12 and 24 months

d.Time till gucocorticoid free remission

Gucocorticoid-sparing effect

a.Gucocorticoid dose after 6, 12, 18 and 24 months.

b.Cumulative glucocorticoid dose after 12, 18 and 24 months

Safety/side-effects

a.Amount of side effects

b.Amount of severe side effects

Study description

Background summary

Over the last decades outcome has greatly improved for RA and SpA. This is in sharp contrast to the situation for PMR (polymyalgia rheumatica), with a lifetime prevalence of 2.4% for women and 1.7% for men, PMR is the commonest auto-inflammatory musculoskeletal disease in adults aged ¡Ý50 years. Due to population ageing, the number of PMR patients will likely double in the decades to come (CBS).
Glucocorticoids are the mainstay of treatment [1] [2]. However, there is an unmet medical need of alternatives in the treatment of PMR as 50% of patients will relapse or have difficulties to reduce the corticosteroid doses [3]. Also, there is increasing awareness of steroid related toxicity and in addition, long-term toxicity is a well-known side-effect of glucocorticoids in PMR[3].

Low dose methotrexate (< 10 mg per week) has been tested in two blinded randomized control trials and 4 open label studies and has shown low to moderate efficacy as corticosteroid-sparing agent [4] [5] [6] [7] [8] [9]. Studies on TNF blockers yielded negative results [10-12]. The effectiveness of leflunomide has only been convincingly demonstrated in case series [13] [14].

The high rate of relapses and adverse events in steroid treated patients indicate that alternative adjuvant agents are needed.

There is evidence that leflunomide could serve as steroid sparing agent and that leflunomide can be used to prevent relapses in the clinical management of polymyalgia rheumatica.

We will perform a randomized placebo controlled trial. Eligible patients will be randomly assigned in a 1:1 ratio receiving either leflunomide 20 mg once daily + glucocorticoids , or placebo + glucocorticoids.

Study objective

Leflunomide is able to reduce the relapses, the glucocorticoid use and the adverse events associated with glucocorticoid s use in PMR patients.

Study design

Time Frame: 24 months of the study

Intervention

Leflunomide

Contacts

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Eligibility criteria

Inclusion criteria

1.Signed written informed consent

2.Female or male aged ¡Ý 50 years

3.PMR according to the ACR/EULAR 2012 PMR core (essential) classification criteria

4.Newly diagnosed PMR being on glucocorticoids for less than 4 weeks

Exclusion criteria

1.Presence of any other connective tissue disease, including vasculitis/giant-cell arteritis

2.PMR on glucocorticoids for >4 week or >25 mg/day

3.History of alcohol or drug abuse or current alcohol or drug abuse

4.Transplanted organ (except corneal transplant performed more than 3 months prior to screening)

5.Evidence (as assessed by the investigator) of active infection, presence of hepatitis B surface antigen or hepatitis C antibody in blood, HIV positivity.

6.Malignancy within 5 years prior to screening, except for non-melanoma skin cancer

7.Exposure to DMARD/biological in the last 5 years

8.Pain syndromes, e.g. fibromyalgia, drug-induced myalgia

9.Active thyroid disease

10.Neurological diseases, e.g. Parkinson's disease

11.Contraindications for Leflunomide (serious immunodeficiency, e.g. AIDS, cytopenia as defined under 12, moderate to severe kidney failure (as defined under 12), liver test abnormality (as defined under 12)

12.Laboratory abnormalities:

◦EGFR<50 ml/min

◦ALT or AST >1.5x upper limit of normal

◦Platelet count <100 x 109/L (100,000/mm3)

◦Hemoglobin <85 g/L (8.5 g/dL; 5.3 mmol/L)

◦White blood cells <3.0 x 109/L (3,000/mm3)Absolute neutrophil count <2.0 x 109/L (2,000/mm3)

◦Absolute lymphocyte count <0.5 x 109/L (500/mm3)

13.Uncontrolled or poorly controlled hypertension

14.Major surgery or hospitalization within 3 month prior to screening

15.Any medical condition that could interfere with the implementation or interpretation of the study or with the safety of the patient during the study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2018
Enrollment:	94
Type:	Anticipated

Ethics review

Positive opinion

Date:	10-04-2018
Application type:	First submission

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
NTR-new	NL6930
NTR-old	NTR7126
Other	UMCG : ABR57022

Study results

Summary results

1. Salvarani C, Cantini F, Hunder GG.
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17. Dasgupta B, Cimmino MA, Kremers HM, Schmidt WA, Schirmer M, Salvarani C, et al. 2012 Provisional classification criteria for PMR: a EULAR/ACR collaborative initiative. AR 2012 Apr;64(4):943-954.
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