Methotrexate and leflunomide combination therapy in psoriatic arthritis

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21424

Source
NTR

Brief title
COMPLETE-PsA

Health condition

Psoriatic arthritis

Artritis psoriatica

Sponsors and support

Primary sponsor: St Maartenskliniek, Nijmegen
Source(s) of monetary or material Support: Local research fund

Intervention

Outcome measures

Primary outcome

Primary endpoint is the difference in efficacy between monotherapy MTX and combination therapy MTX plus LEF on the Psoriatic Arthritis Disease Activity Score (PASDAS) at 16 weeks.

Secondary outcome

Key secondary parameters are: change in skin score, enthesitis score, dactylitis score and swollen/tender joint count. Furthermore, the difference in immunoprofile, treatment failure, and the percentage of (S)AE’s between the two groups will be assessed.

Study description

Background summary

Rationale:

Psoriatic arthritis (PsA) is a heterogeneous disease which involves at least five domains: peripheral joint disease, enthesitis, dactylitis, axial involvement, and skin and nail psoriasis. Once diagnosed PsA is notoriously difficult to treat. Monotherapy with first-line anti-rheumatic drugs (conventional (c)DMARDs: e.g. methotrexate, leflunomide) appears to lack efficacy in a substantial portion of patients. The effectiveness of cDMARDs on multiple domains in PsA is either inconsistent or not known. Furthermore, the effectiveness of combination cDMARD therapy in PsA has not been researched in representative studies. A combination of Methotrexate (MTX) and Leflunomide (LEF) has been proven effective in patients with rheumatoid arthritis. Therefore, we hypothesize that MTX and LEF combination therapy is superior to MTX monotherapy in patients with psoriatic arthritis.

Objective:

To compare the effectiveness of MTX monotherapy with MTX and LEF combination therapy in cDMARD-naïve psoriatic arthritis patients.

Study design:

Monocentre, pragmatic, double-blind, placebo-controlled, randomized clinical trial in cDMARD-naïve psoriatic arthritis patients. Patients will be randomised 1:1 to receive either MTX monotherapy (arm 1) or MTX and LEF combination therapy (arm 2). Treatment response will be assessed at 16 weeks and in case of treatment failure, further treatment decisions are based on shared decision making between patient and treating physician and according to local treatment protocol (usual care).

Study population:

A total of 78 cDMARD-naïve psoriatic arthritis patients, aged ≥16 years.

Intervention:

One group receives methotrexate 25 mg (oral or subcutaneous) once weekly plus 2 placebo tablets daily. The other group receives methotrexate 25 mg (oral or subcutaneous) once weekly plus 2 leflunomide 10 mg tablets daily.

Main study parameters/endpoints:

Primary endpoint is the difference in efficacy between monotherapy MTX and combination therapy MTX plus LEF on the Psoriatic Arthritis Disease Activity Score (PASDAS) at 16 weeks.

Key secondary parameters are: change in skin score, enthesitis score, dactylitis score and swollen/tender joint count. Furthermore, the difference in immunoprofile, treatment failure, and the percentage of (S)AE’s between the two groups will be assessed.

Study objective

We hypothesize that MTX and LEF combination therapy is superior to MTX monotherapy in patients with psoriatic arthritis

Study design

- Baseline

- 8 weeks

- 16 weeks

Intervention

Patients will be randomised 1:1 into two groups.

Arm 1: methotrexate monotherapy (methotrexate 25 mg once weekly plus 2 placebo tablets daily) Arm 2: methotrexate and leflunomide combination therapy (methotrexate 25 mg once weekly plus 2 leflunomide 10 mg tablets daily)

Contacts

Public
St Maartenskliniek
Michelle Mulder

024 365 92 76
Scientific
St Maartenskliniek
Michelle Mulder

024 365 92 76

Eligibility criteria

Inclusion criteria

-Adult male or female

-Age ≥16 years

-Clinical diagnoses of Psoriatic arthritis

-Evidence of active disease defined as ≥2 swollen joints, dactylitis counts as 1 swollen joint

-Subjects that have used cDMARDs and/or bDMARDs before, must have discontinued this treatment for at least 6 months prior to baseline visit

-Subjects who are already taking NSAIDs/COX-2 inhibitors may participate in the study but the dose has to be stable for at least one week prior to first dose of study drug

-Intramuscular and intra-articular corticosteroids have to be discontinued 8 weeks prior to first dose of study drug. With the exception of a failed intra-articular corticosteroid injection (defined as remaining swelling and (if previously present) tenderness of the injected joint 2 weeks after the injection). In the case of a failed injection, patients can participate in the study 2 weeks after the intra-articular injection

-Oral corticosteroids have to be discontinued 10 days prior to first dose of study drug

-If fumaric acid is used at baseline, this will be discontinued and switched to study medication (according to usual care)

Exclusion criteria

-Female subject who is pregnant, breastfeeding or is considering becoming pregnant during the study or for approximately 2 years after the last dose of study drug or up to 11 days after treatment when washout procedure is executed.

-Male subject who is considering fathering a child or donating sperm during the study or for approximately 2 years after the last dose of study drug or up to 11 days after treatment when washout procedure is executed.

-History of an inadequate response to MTX or LEF (prescribed by a rheumatologist for joint disease).

-Current severe infection including, but not limited to:

o Active human immunodeficiency virus (HIV)

o Active TB

-History of an allergic reaction or significant sensitivity to constituents of the study drugs

-Current or history of hepatic disease, including, but not limited to:

o Non-alcoholic Fatty Liver Disease (NAFLD)

o Non-alcoholic Steatohepatitis (NASH)

o Alcoholic cirrhosis

-History of clinically significant (per Investigator's judgment) drug or alcohol abuse within the last 6 months prior to baseline visit.

-Current or recent history of a severe, progressive, or uncontrolled renal, hepatic, hematological, gastrointestinal, metabolic, endocrine, pulmonary, cardiovascular or neurologic disease.

-History of any fibromyalgia or diagnosis of inflammatory rheumatic disease other than PsA. With the exception of an inflammatory rheumatic disease that has been in complete remission for at least 6 months, according to treating physician’s judgment. Prior history of fibromyalgia is permitted if documentation of change in diagnosis to PsA or documentation that the diagnosis of fibromyalgia was made incorrectly or if currently no active signs of fibromyalgia are present other than those which can be explained by PsA

-Abnormal laboratory values within 1 month prior to baseline visit:

o Serum alanine transaminase (ALT) > 1.5 × ULN;

o Estimated glomerular filtration rate (GFR) by simplified 4-variable Modification of Diet in Renal Disease (MDRD) formula < 40 mL/min/1.73m2;

o Total white blood cell count (WBC) < 3,000/µL;

o Platelet count < 100,000/µL;

o Hemoglobin < 10 g/dL (6.3 mmol/L).

-Current persistent hypertension requiring start or change of treatment regimen

-Malignancy in the past 5 years except for non-melanoma skin cancer

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2019
Enrollment:	78
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	23-11-2018
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	NL7407
NTR-old	NTR7632
CCMO	NL-nummer: NL66544.091.18

Study results