Comparing Methotrexate monotherapy with methotrexate Plus LEflunomide combination ThErapy in Psoriatic Arthritis: A pragmatic randomized placebo-controlled double-blind clinical trial.

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

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

Summary

ID

NL-OMON46222

Source
ToetsingOnline

Brief title
COMPLETE-PsA

Condition

- Autoimmune disorders
- Joint disorders
- Epidermal and dermal conditions

Synonym
psoriasis and joint inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Sint Maartenskliniek
Source(s) of monetary or material Support: St Maartenskliniek en voor een klein deel uit een gemeenschappelijke junior research grant van de St Maartenskliniek en het Radboudumc

Intervention

Keyword: clinical trial, leflunomide, methotrexate, psoriatic arthritis

Outcome measures

Primary outcome

Primary endpoint is the difference in efficacy between monotherapy MTX and combination therapy MTX plus LEF on 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.

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

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 disease-modifying antirheumatic 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.

Study 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).

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.

Study burden and risks

-Venapuncture (4x), low risk. This will be done according to our local toxicity protocol and is part of usual care when patients start with cDMARD therapy. Only if patients participate in the additional blood sampling for the explorative immunoprofiling objective, an extra venapuncture at baseline will be performed (if it is not possible to combine this with regular blood drawing).

-Clinical examinations and questionnaires (two assessment points), low burden. The intervention will be embedded in daily clinical care. The study visits will be planned in combination with the regular clinical visit. Filling out of

questionnaires will take 15-30 minutes.

-Therapeutic intervention with either monotherapy MTX (first line treatment in usual care) or combination therapy MTX and LEF(used as second line treatment regimen in usual care) in PsA patients in the St Maartenskliniek, low risk .
The cDMARDs that will be administered in this trial are common and registered treatments for patients with PsA.

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

-Adult male or female;-Age *18 years;-Clinical diagnoses of PsA;-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;-Oral or injected corticosteroids (intramuscular, intravenous and intra-articular) have to be discontinued 8 weeks prior to first dose of study drug

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:;oActive human immunodeficiency virus (HIV);oActive TB;-History of an allergic reaction or significant sensitivity to constituents of the study drugs (MTX/LEF);-Current or history of liver insufficiency;-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. Prior history of fibromyalgia is permitted if documentation of change in diagnosis to PsA or documentation that the diagnosis of fibromyalgia was made incorrectly.;-Abnormal laboratory values within 1 month prior to baseline visit: ;oSerum alanine transaminase (ALT) > 1.5 × ULN;;oEstimated glomerular filtration rate (GFR) by simplified 4-variable Modification of Diet in Renal Disease (MDRD) formula < 40 mL/min/1.73m2;;oTotal white blood cell count (WBC) < 3,000/*L;;oPlatelet count < 100,000/*L;;oHemoglobin < 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 phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-02-2019
Enrollment:	78
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Arava
Generic name:	Leflunomide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Methotrexate
Generic name:	Methotrexate
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	09-07-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	19-11-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	14-05-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	14-11-2019

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-02-2020
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
EudraCT	EUCTR2018-002362-39-NL
CCMO	NL66544.091.18