

# Induction therapy with methotrexate and prednisone in rheumatoid or very early arthritic disease

<b>Submission date</b> 28/12/2006	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 28/12/2006	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 07/03/2018	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**EudraCT/CTIS number**  
2006-006186-16

**IRAS number**

**ClinicalTrials.gov number**

## Secondary identifying numbers

1

# Study information

## Scientific Title

IMPROVED: Induction therapy with Methotrexate and Prednisone in Rheumatoid Or Very Early arthritic Disease

## Acronym

IMPROVED

## Study objectives

There is a clinically and statistically significant difference in the percentage of patients who achieve and maintain clinical remission (defined as Disease Activity Score [DAS] less than 1.6) and in functional ability and progression of radiological joint damage after one year of follow-up in recent-onset arthritis patients (Rheumatoid Arthritis [RA] and Undifferentiated Arthritis [UA]) who, having failed to achieve remission on a combination of methotrexate and a tapered high dose of prednisone, receive extended medication in a combination of methotrexate, sulphasalazine, hydroxychloroquine and low dose prednisone, or who switch to a combination of methotrexate and adalimumab.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Not provided at time of registration

## Study design

Randomised controlled parallel-group single-blinded multicentre trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

Not available in web format, please use the contact details to request a patient information sheet

## Health condition(s) or problem(s) studied

Rheumatoid arthritis, undifferentiated arthritis

## Interventions

Four-monthly evaluations of Disease Activity Score and safety. Medication adjustments by protocol, based on DAS calculation, aimed at DAS less than 1.6 (remission).

Initial treatment with Methotrexate (MTX) and a tapered high dose of prednisone. If DAS more than 1.6, randomisation to either combination with MTX, Sulphasalazine (SSA), hydroxychloroquine and a tapered high dose of prednisone, or combination with MTX with adalimumab. In case of DAS less than 1.6: taper medication and discontinue if DAS remains less than 1.6.

## Intervention Type

Drug

## Phase

Not Applicable

## Drug/device/biological/vaccine name(s)

Methotrexate, prednisone, sulphasalazine, adalimumab, hydroxychloroquine

## Primary outcome measure

1. Percentage of patients in remission (DAS less than 1.6)
2. Functional ability as measured by Health Assessment Questionnaire (HAQ)
3. Radiological damage progression as measured by Sharp/van der Heijde score

## Secondary outcome measures

1. Quality of life, as measured with McMaster-Toronto Arthritis (MACTAR), Short Form health survey (SF-36), EuroQol questionnaire
2. Time-trade-off
3. Costs
4. ACR arthritis core-set

## Overall study start date

01/01/2007

## Completion date

01/07/2009

## Eligibility

### Key inclusion criteria

1. Patients more than or equal to 18 years of age with either RA according to the revised criteria of the American College of Rheumatology (ACR) of less than two years duration, or UA, suspected by the rheumatologist to have an early presentation of RA
2. All patients must have at least one (out of 66) swollen joint and at least one other (out of 68) painful joint, and a combined DAS of more than 1.6
3. All patients must be Disease Modifying Anti-Rheumatic Drugs (DMARDs) and corticosteroid naïve

## Participant type(s)

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

535

**Key exclusion criteria**

1. Previous therapy with DMARDs or with corticosteroids (exception: one dose of parenteral corticosteroids within the last six months, but not within the last two months, or an oral dose of prednisone of less than or equal to 10 mg/day for less than or equal to two weeks within the same period allowed)
2. Pregnancy or wish to become pregnant during the study, or childbearing potential without adequate contraception
3. Concomitant treatment with another experimental drug
4. History or presence of malignancy within the last five years
5. Bone marrow hypoplasia
6. Elevated hepatic enzyme levels (Aspartate Aminotransferase [AST], Alanine Aminotransferase [ALT] more than three times normal value)
7. Serum creatinine level more than 150 umol/l or estimated creatinin clearance of less than 75%
8. Uncontrolled diabetes mellitus (according to the rheumatologist)
9. Uncontrolled hypertension (according to the rheumatologist)
10. Heart failure (New York Heart Association [NYHA] functional class III or IV)
11. Alcohol or drug abuse
12. History of infected joint prosthesis within the previous three months
13. Serious infections, such as hepatitis, pneumonia, pyelonephritis in the previous three months
14. Chronic infectious disease such as chronic renal infection, chronic chest infection with bronchiectasis or sinusitis
15. History of active tuberculosis requiring treatment within previous three years, or signs and symptoms of latent infection with tuberculosis, based on medical history, physical examination, Purified Protein Derivative (PPD) skin test, X-thorax
16. History of opportunistic infections such as herpes zoster within previous two months
17. Evidence of active cytomegalovirus, active pneumocystis carinii, or drug resistant atypical mycobacterium infection etc
18. Evidence of hepatitis B infection
19. Documented Human Immunodeficiency Virus (HIV) infection, Acquired Immune Deficiency Syndrome (AIDS) or AIDS Related Complex (ARC)
20. History of lymphoproliferative disease including lymphoma or signs suggestive of possible lymphoproliferative disease
21. Multiple sclerosis or neurological symptoms suspect for demyelinating disease

**Date of first enrolment**

01/01/2007

**Date of final enrolment**

01/07/2009

# Locations

## Countries of recruitment

Netherlands

## Study participating centre

Leiden University Medical Center (LUMC)

Leiden

Netherlands

2300 RC

# Sponsor information

## Organisation

Leiden University Medical Center (LUMC) (The Netherlands)

## Sponsor details

Department of Rheumatology

PO Box 9600

Leiden

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2300 RC

## Sponsor type

Hospital/treatment centre

## Website

[http://www.lumc.nl/english/start\\_english.html#http://www.lumc.nl/english/start\\_english.html](http://www.lumc.nl/english/start_english.html#http://www.lumc.nl/english/start_english.html)

## ROR

<https://ror.org/05xvt9f17>

# Funder(s)

## Funder type

Industry

## Funder Name

Abbott (The Netherlands)

# Results and Publications

## Publication and dissemination plan

Not provided at time of registration

## Intention to publish date

## Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/09/2012		Yes	No
<a href="#">Results article</a>	results	01/12/2013		Yes	No
<a href="#">Results article</a>	results	01/07/2014		Yes	No
<a href="#">Results article</a>	results	15/02/2016		Yes	No
<a href="#">Results article</a>	results	30/09/2017		Yes	No
<a href="#">Results article</a>	results	26/02/2018		Yes	No