ISRCTN11916566 https://doi.org/10.1186/ISRCTN11916566

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

Submission date	Recruitment status	[X] Prospectively registered
28/12/2006	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
28/12/2006	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
07/03/2018	Musculoskeletal Diseases	

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 prothesis 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) of 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 demyelinising 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
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Sponsor information

Organisation
Leiden University Medical Center (LUMC) (The Netherlands)

Sponsor details
Department of Rheumatology
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Sponsor type
Hospital/treatment centre

Website
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?
Results article	results	01/09/2012		Yes	No
Results article	results	01/12/2013		Yes	No
Results article	results	01/07/2014		Yes	No
Results article	results	15/02/2016		Yes	No
Results article	results	30/09/2017		Yes	No
Results article	results	26/02/2018		Yes	No