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A multicentre randomised double-blind placebo-controlled study comparing two regimens of combination induction therapy in early disease-modifying anti-rheumatic drug naïve rheumatoid arthritis

Submission date	Recruitment status	[_] Prospectively registered
25/10/2006	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
30/04/2007	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
19/09/2016	Musculoskeletal Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
RR05/7092

Study information

Scientific Title
A multicentre randomised double-blind placebo-controlled study comparing two regimens of combination induction therapy in early disease-modifying anti-rheumatic drug naïve rheumatoid arthritis

Acronym
IDEA (Infliximab as inDuction therapy in Early rheumatoid Arthritis)

Study objectives
To compare the efficacy of biologic therapy (infliximab) as induction therapy against current best practice therapy: early introduction of methotrexate in combination with steroid induction therapy and dose modification according to pre-defined disease activity measures.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Northern and Yorkshire Multi-Centre Research Ethics Committee,06/04/2006, ref: 05/MRE03/85

Study design
Multicentre double-blind placebo-controlled randomised clinical trial for 6 months followed by open-label observation period of treatment strategy

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Early rheumatoid arthritis

Interventions
Infliximab arm:
1. Methotrexate (10 mg, increasing to 20 mg by six weeks) orally once a week for the treatment period of the trial (18 months)
2. Infliximab (3 mg/kg) intravenous (IV) infusion at baseline, week two, week six and then eight-weekly) for the treatment period of the trial (18 months)

Steroid/placebo arm:
1. Methotrexate (10 mg, increasing to 20 mg by six weeks) orally once a week for the treatment period of the trial (18 months)
2. Methylprednisolone (250 mg IV infusion at baseline)
3. Placebo (250 ml 9 mg/l NaCl at weeks two, six, 14 and 22)

N.B.: These regimens are subject to modification depending upon patient response.

Intervention Type

Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Infliximab, methotrexate, steroid

Primary outcome(s)
Change in Sharpe van Der Heijde score at 50 weeks.

Key secondary outcome(s))
Secondary outcomes in this study include changes in clinical response over 18 months as measured by:
1. The number of patients having a major clinical response (DAS less than 1.6 maintained for six months)
2. The change in Sharpe van Der Heijde scores between baseline and 26 and 78 weeks
3. The number of patients in clinical remission (DAS less than 1.6) at 78 weeks
4. The number of patients in clinical remission (DAS less than 1.6) at 78 weeks, no longer on infliximab/placebo infusions
5. The number of patients in clinical remission (DAS less than 1.6) at 26 weeks
6. Rheumatoid Arthritis Quality of Life Questionnaire (RA QoL)
7. Health Assessment Questionnaire
8. Immunogenetic studies to predict long-term immune response
9. Immune phenotyping (flow cytometry) and assessment of immune effector and regulatory functions
10. Assessment of serum and plasma markers to predict response to therapy and vascular function

Completion date
30/09/2007

Eligibility

Key inclusion criteria
1. Men and women 18 to 80 years of age
2. Fulfil 1987 American College of Rheumatology (ACR) Criteria for rheumatoid arthritis (RA)
3. Symptoms of more than three months and less than 12 months duration
4. Men and women must use adequate birth control measures (e.g., abstinence, oral contraceptives, intra-uterine device, barrier method with spermicide, or surgical sterilisation) for the duration of the study and should continue such precautions for six months after receiving the last infusion or dose of methotrexate
5. The patient must be able to adhere to the study visit schedule and other protocol requirements
6. The patient must be capable of giving informed consent and the consent must be obtained prior to any screening procedures
7. Must have a chest radiograph within three months prior to first treatment dose with no evidence of malignancy, infection or fibrosis
8. Are considered eligible according to the tuberculosis (TB) eligibility assessment, screening, and early detection of reactivation rules defined in the protocol
9. Active disease as defined by Disease Activity Score (DAS) more than 2.4

10. Tumour necrotising factor (TNF) therapy naïve
11. Disease-modifying anti-rheumatic drug (DMARD) therapy naïve
12. Negative hepatitis B and C screening tests within three months prior to screening visit

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Women who are pregnant, nursing, or men or women planning pregnancy within 24 months after screening (i.e., approximately six months following last study medications)
2. Use of any investigational (unlicensed) drug within one month prior to screening or within five half-lives of the investigational agent, whichever is longer
3. Previous or current treatment with any other therapeutic agent targeted at reducing TNF (e. g., pentoxifylline, thalidomide, etanercept, infliximab, adalimumab etc.)
4. Prior treatment with any DMARD
5. Serious infections (such as pneumonia or pyelonephritis) in the previous three months. Less serious infections (such as acute upper respiratory tract infection [colds] or simple urinary tract infection) need not be considered exclusions at the discretion of the investigator
6. Documented human immunodeficiency virus (HIV) infection
7. Hepatitis B or hepatitis C serology positive (must be checked within three months prior to screening)
8. Are considered ineligible according to the TB eligibility assessment, screening, and early detection of reactivation rules defined in the protocol
9. Have or have had an opportunistic infection (e.g., herpes zoster [shingles], cytomegalovirus, Pneumocystis carinii, aspergillosis, histoplasmosis, or mycobacteria other than TB) within six months prior to screening
10. Significant haematological or biochemical abnormality:
10.1. Haemoglobin less than or equal to 8.5 g/dL
10.2. White blood cells (WBC) less than or equal to 3.5 x 10^9/L
10.3. Neutrophils less than or equal to 1.5 x 10^9/L
10.4. Platelets less than or equal to 100 x 10^9/L
10.5. Alanine aminotransferase (ALT) more than two times upper limit of normal (ULN) for the laboratory conducting the test
10.6. Creatinine more than 1.5 times ULN for the laboratory conducting the test
11. Have current signs or symptoms of severe, progressive or uncontrolled renal, hepatic, haematologic, gastrointestinal, endocrine, pulmonary, cardiac, neurologic, or cerebral disease

(including demyelinating diseases such as multiple sclerosis)
12. Concomitant congestive heart failure, including medically controlled asymptomatic patients
13. Presence of a transplanted organ (with the exception of a corneal transplant more than three months prior to screening)
14. Malignancy within the past five years (except for squamous or basal cell carcinoma of the skin that has been treated with no evidence of recurrence)
15. History of lymphoproliferative disease including lymphoma, or signs and symptoms suggestive of possible lymphoproliferative disease, such as lymphadenopathy of unusual size or location (such as nodes in the posterior triangle of the neck, infra-clavicular, epitrochlear, or periaortic areas), or splenomegaly
16. Known recent substance abuse (drug or alcohol)
17. Poor tolerability of venipuncture or lack of adequate venous access for required blood sampling during the study period
18. Have a chest radiograph at screening that shows evidence of malignancy, infection, or any abnormalities suggestive of TB as described in the protocol
19. Have a positive Mantoux test or evidence of active TB infection, or recent close contact with an individual with active TB
20. Previous oral, intramuscular (IM), intra-arterial (IA) or intravenous (IV) corticosteroids within one month
21. Receiving treatment with anakinra
22. Contraindications to methotrexate, infliximab or steroids

Date of first enrolment
26/09/2006

Date of final enrolment
30/09/2007

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Chapel Allerton Hospital
Leeds
United Kingdom
LS7 4SA

Sponsor information

Organisation
University of Leeds (UK)

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Industry

Funder Name
Schering-Plough Ltd (UK) - Investigator-initiated study funding grant

Results and Publications

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	01/01/2014		Yes	No
Results article	results	01/12/2016		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes