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A multicentre randomised trial of etanercept and methotrexate to induce remission in early inflammatory arthritis

Submission date
25/10/2006

Recruitment status
No longer recruiting

Registration date
30/04/2007

Overall study status
Completed

Last Edited
10/09/2019

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] 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
2005-005467-29

IRAS number

ClinicalTrials.gov number
NCT01303874

Secondary identifying numbers
RR05/7150

Study information

Scientific Title
A multicentre randomised trial of etanercept and methotrexate to induce remission in early inflammatory arthritis

Acronym
The EMPIRE Trial (Etanercept and Methotrexate in Patients to Induce Remission in Early arthritis)

Study objectives
Induction therapy with Etanercept (ETN) in addition to Methotrexate (MTX) can induce sustained remission in patients with persistent early inflammatory arthritis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval received from the local Ethics Committee on the 30th March 2006 (ref: 06/Q1206/7).

Study design
Multicentre, double blind, placebo -controlled randomised clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Early Inflammatory Arthritis

Interventions
Etanercept and methotrexate versus placebo and methotrexate.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Etanercept, methotrexate

Primary outcome measure
To determine the number of patients in clinical remission at 12 months, as defined as the absence of symptoms and signs of inflammatory arthritis (i.e., Swollen Joint Count [SJC] zero; Tender Joint Count [TJC] zero).

Secondary outcome measures
1. The number of patients in clinical remission at 18 months (as defined as absence of symptoms and signs of clinical arthritis i.e., SJC zero; TJC zero)
2. Conventional disease activity measures (Visual Analogue Scale [VAS] pain/fatigue/global /physician, Early Morning Stiffness (EMS), TJC, SJC, C-Reactive Protein [CRP], Erythrocyte Sedimentation Rate [ESR])
3. Functional, work and quality of life assessments (Health Assessment Questionnaire [HAQ], WIS, WDA, EuroQoL [EQ-5d] instrument, Short Form health survey [SF-36])
4. Proportion of patients achieving 26 weeks of remission
5. Disease Activity Score (DAS) 28
6. The number of patients in drug-free remission at 12 and 18 months
7. The number of patients in etanercept-free remission at 12 and 18 months (ETN arm)
8. Remission by American College of Rheumatology (ACR) criteria
9. To compare the effects of the combination of ETN and MTX to MTX alone on radiographic change at 12 months and 18 months

Overall study start date
19/10/2006

Completion date
31/10/2008

Eligibility

Key inclusion criteria
Subject must fulfill all of the following conditions or characteristics in order to be considered for study enrolment or participation:
1. Aged 18 to 80 years
2. Patients have articular synovitis, within three months of diagnosis (synovitis is defined as the presence soft tissue swelling and at least one of the following two criteria: tenderness or decreased range of motion)
3. Either Rheumatoid Factor (RF) antibody (positive) or Anti-Cyclic Citrullinated Peptide (Anti-CCP) antibody (positive) or Shared Epitope (SE) (positive)
4. Demonstrates a negative serum pregnancy test at screening if female of childbearing potential. A woman of childbearing potential is defined as one who is biologically capable of becoming pregnant. This includes women who are using contraceptives or whose sexual

partners are either sterile or using contraceptives. Sexually active women participating in the study must use a medically acceptable form of contraception during the study and for three months after the last dose of study medications. Medically acceptable forms of contraception for women include oral contraception, injectable or implantable methods, intrauterine devices, or properly used barrier contraception
5. Agrees to use a medically accepted form of contraception during the study and for three months after the last dose of study drug, if sexually active male. Medically acceptable forms of contraception for males are a properly used barrier contraceptive or sterilisation
6. Is capable of understanding and signing an informed consent form
7. Is able and willing to self-inject study drug or have a designee who can do so
8. Is able and willing to take oral medication
9. Is able to store injectable test article at 2°C to 8°C
10. Demonstrates a negative tuberculosis screening test

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
80 Years

Sex
Not Specified

Target number of participants
110

Key exclusion criteria
Subjects with any of the following conditions or characteristics will be excluded from study enrolment:
1. Received previous treatment with any Disease Modifying Anti-Rheumatic Drugs (DMARDs)
2. Received previous treatment with ETN or other Tumour Necrosis Factor (TNF) antagonist (e.g. a TNF monoclonal antibody or a soluble TNF receptor)
3. Previous treatment with Interleukin-1 (IL-1) receptor antagonist
4. Chronic arthritis diagnosed before 16 years old
5. Received any investigational biological agent within three months of screening visit
6. Received treatment with any investigational drug of chemical nature within one month prior to study screening
7. Known Human Immunodeficiency Virus (HIV)
8. Presence of any contraindication to ETN or MTX
9. Has significant concurrent medical diseases including uncompensated congestive heart failure, myocardial infarction within 12 months, unstable angina pectoris, uncontrolled hypertension, severe pulmonary disease, or history of Human Immunodeficiency Virus (HIV) infection, immunodeficiency syndromes, Central Nervous System (CNS) demyelinating events suggestive of multiple sclerosis, renal or gastrointestinal conditions, which in the opinion of the investigator places the subject at an unacceptable risk for participation in the study

10. Has cancer or a history of cancer (other than resected cutaneous basal cell carcinoma, and in situ cervical cancer) within five years of entering the screening period
11. Current crystal or infective arthritis
12. Chronic infection of the upper respiratory tract (e.g., sinusitis), chest (e.g., bronchiectatic lung disease), urinary tract or skin (e.g., paronychia, chronic ulcers, open wounds)
13. Any ongoing or active infection or any major episode of infection requiring hospitalisation or treatment with intravenous (IV) antibiotics within the preceding 30 days and/or orally administered antibiotics in the preceding 15 days
14. Demonstrates liver function abnormality (Aspartate Transaminase [AST]/Alanine Transaminase [ALT] more than 2 x Upper Limit of Normal [ULN]) or bilirubin more than 51 µmol/L
15. Has renal disease (creatinine level more than 133 µmol/L)
16. Has leukopaenia (white blood cells less than 3000 x 10^6/L)
17. Has thrombocytopaenia (platelets less than 125 x 10^9/L)
18. Has a haemoglobin level of less than 9 g/L for males and less than 85 g/L for females
19. Is pregnant or breast-feeding
20. Joint surgery within preceding two months (at joints to be assessed within this study)
21. Received anti-CD4, diphtheria Interleukin-2 (IL-2) fusion protein, anti-Interleukin-6 (anti-IL-6), rituxamab or other immunosuppressive biologic during the last six months before screening, and treatment with such agents more than six months before screening if there are persistent signs of immunosuppression (with a subsequent abnormal absolute T-cell count) at screening visit
22. Received any live (attenuated) vaccines within four weeks of screening visit
23. Received cyclophosphamide within six months of screening visit
24. Any corticosteroids within 28 days prior to screening
25. Uses a dose of Non-Steroidal Anti-Inflammatory Drug (NSAID) greater than the maximum recommended dose in the product information at the screening visit
26. Has a history of confirmed blood dyscrasia
27. Has any condition judged by the physician to cause this study to be detrimental to the subject
28. Has a history of drug abuse or psychiatric disease that would interfere with the ability to comply with the study protocol
29. Has a history of alcohol abuse or excessive alcohol beverage consumption
30. Has a history of known liver cirrhosis, fibrosis, or fatty liver
31. Has a history of any viral hepatitis within one year of screening

Date of first enrolment
19/10/2006

Date of final enrolment
31/10/2008

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
c/o Anne-Maree Keenan
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Sponsor information

Organisation
University of Leeds (UK)

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Sponsor type
University/education

Website
http://www.leeds.ac.uk/

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Industry

Funder Name
Wyeth Pharmaceuticals Ltd (UK) - Investigator-initiated study funding grant

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	01/03/2010		Yes	No
Results article	results	01/06/2014		Yes	No