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A controlled randomised double-blind multicentre study comparing two therapy strategies in disease modifying anti-rheumatic drug-naive early rheumatoid arthritis patients over 48 weeks: induction therapy with adalimumab and methotrexate over 24 weeks followed by methotrexate monotherapy up to week 48 versus methotrexate monotherapy

Submission date
03/07/2006

Registration date
11/08/2006

Last Edited
16/07/2013

Recruitment status
No longer recruiting

Overall study status
Completed

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

Contact name
Prof Gerd-Rüdiger Burmester

Contact details
Charité - Universitätsmedizin Berlin
Department of Rheumatology and Clinical Immunology
Berlin
Germany
10117

Additional identifiers

EudraCT/CTIS number
2006-003146-41

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
50021031-2

Study information

Scientific Title

Acronym
HIT HARD

Study objectives
To compare the efficacy of an induction therapy over 24 weeks with subsequent methotrexate (MTX) therapy to MTX alone over 48 weeks in subjects with active early rheumatoid arthritis (RA).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the Landesamt für Gesundheit und Soziales, Ethikkommission des Landes Berlin on the 8th March 2007 (ref: EK 7 500/06).

Study design
A controlled randomised double-blind multicentre study.

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet

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

Interventions

Patients will be randomised into one of following groups to receive:
1. Adalimumab (ADA) and MTX over 24 weeks followed by MTX monotherapy up to week 48
2. MTX monotherapy and placebo

All subjects will receive MTX subcutaneously (15 mg/week). In the case of an insufficient effect of MTX the dose can be increased to 20 mg/week within the first 12 weeks. The dose of ADA will be given as one injection of 40 mg at the end of the week. The dose of placebo drug (PB) will be given as one injection at the end of the week.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Methotrexate, adalimumab

Primary outcome measure
Efficacy is primary measured with the Disease Activity Score 28 (DAS 28) at week 48.

Secondary outcome measures
1. To evaluate DAS 28 at week 24
2. The partial-remission (DAS 28 less than 2.6) at week 24 and 48
3. The duration of clinical remission during the trial
4. The variables of the World Health Organization (WHO)/International League of Associations for Rheumatology (ILAR) core set for clinical trials (DAS 28, Health Assessment Questionnaire [HAQ])
5. To evaluate ACR 20, ACR 50 and ACR 70 values from baseline to week 24
6. To evaluate ACR 20, ACR 50 and ACR 70 values from baseline to week 48
7. The change in ACR 20, ACR 50 and ACR 70 values response between week 24 to week 48
8. The radiographic change (X-ray of hands and feet in two dimensions) from baseline to week 48 by central assessment by the modifyed Sharp-Score and Ratingen Score
9. Descriptive analysis of change glucocorticoid, NSAIDs/Coxib dosage
10. Report on adverse events and serious adverse events (referring to International Conference on Harmonisation guidelines on Good Clinical Practice [ICH GCP]/Committee for Proprietary Medicinal Products International Conference on Harmonisation guidelines on E2: Clinical Safety [CPMP ICH E2]).

Overall study start date
01/08/2006

Completion date
31/07/2009

Eligibility

Key inclusion criteria
Each patient must meet all of the following inclusion criteria to be enrolled into this study:
1. Patients with definite RA referring to the American College of Rheumatology (ACR)

Classification Criteria of 1987 up to one year after first RA symptoms
2. Aged 18 to 70 years
3. Has active disease at the time of randomisation as indicated by: six from 68 tender and six from 66 swollen joints and at least one of the following two criteria:
3.1. Westergren erythrocyte sedimentation rate (ESR) of 28 mm/hour
3.2. C-reactive protein (CRP) levels more than 1.0 mg/dl
4. Has morning stiffness for longer than 30 minutes
5. No current or prior therapy with Disease Modifying Anti-Rheumatic Drugs (DMARDs) or biologics
6. Non steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids treatment has to be stable two weeks prior to screening and during the trial with maximal less than or equal to 10 mg /d prednisolone equivalent
7. Is capable of understanding and signing an informed consent form
8. Is able and willing to self-inject study drug or have a designee who can do so
9. Is able and willing to take oral medication
10. Is able to store injectable test article at 2°C to 8°C
11. Sexually active women participating in the study must use a medically acceptable form of contraception for women. This includes oral contraception, injectable or implantable methods, intrauterine devices, or properly used barrier contraception

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
180

Key exclusion criteria
Patients meeting any following exclusion criteria are not to be enrolled in this study:
1. Has significant concurrent medical diseases including cancer or a history of cancer (other than resected cutaneous basal and squamous cell carcinoma, in situ cervical cancer) in the last five years
2. Has 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 syndrome, other rheumatologic diseases than RA, or central nervous systems demyelinating events suggestive or multiple sclerosis
3. Received anti-CD4, diphtheria interleukin-2 fusion protein, anti-interleukin-6, rituximab or other immunsuppressive biologic before screening, and treatment with such agents if there are persistent signs of immunosuppression (with a subsequent abnormal absolute T-cell count) at

screening count
4. Received any live (attenuated) vaccines within four weeks of screening visit
5. Received intra-articular corticosteroid injection within four weeks of screening
6. Received bolus intramuscular/intravenous treatment with corticosteroids
(more than 10 mg prednisone or equivalent) within four weeks of screening visit
7. Is taking more than 10 mg/d prednisone or equivalent
8. Has a history of confirmed blood dyscrasias
9. Has a significant active infection or any underlying diseases that could predispose subjects to infections (e.g. history of recurring infections,
leg ulcers, advanced or poorly controlled diabetes)
10. Has active infection with Hepatitis A, B or C virus, tuberculosis, chronic infections, latent tuberculosis (has to be excluded by Chest X-ray and Purified Protein Derivative [PPD] Test according to Mendel-Mantoux), in case of latent tuberculosis
isoniazid 300 mg for ten months, starting one month prior to treatment is obligatory
11. Has renal disease (creatine level more than 175 µmol/L) or a history of known liver cirrhosis, fibrosis
12. Has an abnormal liver function (aspartate aminotransferase [AST], gamma-glutamyl transpeptidase [GGT], alanine aminotransferase [ALT] two times the upper limit of normal [ULN])
13. Has a history of psychiatric disease that would interfere with the ability to comply with the study protocol
14. Is pregnant or breast-feeding

Date of first enrolment
01/08/2006

Date of final enrolment
31/07/2009

Locations

Countries of recruitment
Germany

Study participating centre
Charité - Universitätsmedizin Berlin
Berlin
Germany
10117

Sponsor information

Organisation
Charité - University Medicine Berlin (Germany)

Sponsor details

Charité - Universitätsmedizin Berlin
Department of Rheumatology and Clinical Immunology
Berlin
Germany
10117

Sponsor type
University/education

ROR
https://ror.org/001w7jn25

Funder(s)

Funder type
Government

Funder Name
German Federal Ministry of Education and Research (BMBF) (Germany)

Funder Name
German Research Foundation (Deutsche Forschungsgemeinsschaft [DFG]) (Germany)

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	01/06/2013		Yes	No