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Rituximab in Rheumatoid Arthritis in patients who failed therapy with tumour necrosis factor-blockers: a multi-centre clinical observational real-life study (phase IIIb)

Submission date
01/09/2006

Recruitment status
No longer recruiting

Registration date
21/12/2006

Overall study status
Completed

Last Edited
21/12/2006

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

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
3.1

Study information

Scientific Title

Acronym
RIRA

Study objectives
To investigate the efficacy of treatment in real life (routine clinical care) with rituximab (MabThera®) in patients with active Rheumatoid Arthritis (RA) whose current treatment with a Tumour Necrosis Factor (TNF)-blocker (Etanercept - Enbrel®, Infliximab Remicade® or Adalumimab - Humira®) in combination with Methotrexate (MTX) is insufficient.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethical committee and internal review board of the Medical University of Vienna (reference Number 049/2006), date of approval: 14/03/2006.

Primary study design
Observational

Study design
A clinical observational real-life study investigating the effect of Rituximab

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Rheumatoid Arthritis (RA)

Interventions
Infusion with rituximab (MabThera®)

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
Rituximab (MabThera®), Etanercept (Enbrel®), Infliximab (Remicade®), Adalumimab (Humira®) and Methotrexate (MTX)

Primary outcome(s)
Primary outcome measure will be the frequency of reaching low disease activity or remission as measured by the Clinical Disease Activity Index (CDAI) (less than or equal to ten).

Key secondary outcome(s)

1. Major CDAI response of -13.9
2. Moderate CDAI response of -6.7
3. Disease Activity Score based on 28 joints (DAS28)
4. Simplified Disease Activity Index (SDAI)
5. American College of Rheumatology (ACR) response criteria (20%, 50%, 70%)
6. Health Assessment Questionnaire (HAQ)
7. Short Form Health Sruvey (SF-36)

Completion date
01/09/2007

Eligibility

Key inclusion criteria
1. Women or men 18 years of age or older
2. Diagnosis of RA according to the revised 1987 criteria of the American Rheumtololgy Association (ARA) for at least three months prior to first administration of study medication
3. The current treatment with Etanercept, Infliximab or Adalimumab in combination with MTX is insufficient. The patients disease is considered to be active despite Disease Modifying Anti-Rheumatic Drug (DMARD) treatment
4. Active disease at the time of screening as defined by:
a. more than or equal to six swollen joints on a 66/68 joint count
b. more than or equal to six tender joints on a 66/68 joint count
c. and one out of the following three categories:
i. Erythrocyte Sedimentation Rate (ESR) more than or equal to 28 mm/h
ii. C-Reactive Protein (CRP) more than or equal to 1.5 mg/dl
iii. Morning stiffness more than or equal to 45 minutes
d. and one out of the following three categories:
i. bone erosion by x-ray prior to first administration of study medication
ii. Anti-Cyclic Citrullinated Peptide (Anti-CCP) antibody-positive
iii. Rheumatoid Factor (RF)-positive at screening
5. If using Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) or other analgesics for RA, must be on a stable dose for at least two weeks prior to the first administration of study agent
6. If using oral corticosteroids, must be on a stable dose equivalent to less than or equal to 10 mg of prednisone/day for at least two weeks prior to first administration of study agent. If currently not using corticosteroids, the subject must not have received oral corticosteroids for at least two weeks prior to first administration of study medication
7. Women of childbearing potential or men capable of fathering children must be using adequate birth control measures (e.g., abstinence, oral contraceptives, intrauterine device, barrier method with spermicide, surgical sterilisation) during the study and for six months after receiving the last administration of study agent
8. Female subjects of childbearing potential must test negative for pregnancy. A pregnancy test will be performed at the beginning and at the end of the study
9. The screening laboratory test must meet the following criteria:
a. haemoglobin more than or equal to 8.5 g/dl providing the low haemoglobin level is not due to other diseases than anemia of chronic inflammation
b. White Blood Cells (WBC) more than or equal to 3500/µl
c. neutrophils more than or equal to 1500/µl
d. platelets more than or equal to 100,000/µl
e. serum transaminase less than or equal to two times the Upper Limit of Normal (ULN)

f. serum creatinine less than or equal to 1.7 mg/dl
10. The patient must be able to adhere the study visit schedule and other protocol requirements and must have given informed consent prior to any screening procedures

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
Patients are excluded if they meet one of the following criteria:
1. Pregnant women, nursing mothers or a planned pregnancy within six months after last scheduled treatment
2. Patients with other inflammatory diseases that might interfere with the evaluation of the RA
3. Patients with fibromyalgia syndrome
4. Use of IntraMuscular (IM), IntraVenous (IV), IntraArterial (IA) corticosteroids within four weeks prior to screening
5. Treatment with any investigational drug within three months prior to screening
6. A history of known allergy to murine proteins, e.g. allergy to Infliximab
7. History of infected joint prothesis within the previous five years
8. Chronic infections
9. History of active tuberculosis requiring treatment within the previous three years, or history of opportunistic infections within two months, uncontrolled active infection or documented Human Immunodeficiency Virus (HIV) infection. Also excluded are patients with evidence of latent tuberculosis and patients with old tuberculosis (TB) without documented adequate therapy if they will not be treated according to the local TB guidelines
10. Current signs or symptoms of other severe uncontrolled disease which in the investigators opinion would put the patient at an unacceptable risk
11. History of lymphoproliferative disease, any current malignancies or history of malignancy within five years other than successfully treated basal cell carcinoma or squamous cell carcinoma of the skin
12. History of drug abuse

Date of first enrolment
01/09/2006

Date of final enrolment
01/09/2007

Locations

Countries of recruitment
Austria

Study participating centre
Medical University of Vienna
Vienna
Austria
1090

Sponsor information

Organisation
Medical University of Vienna (Austria)

ROR
https://ror.org/05n3x4p02

Funder(s)

Funder type
Other

Funder Name
The trial is an investigator driven study without any grant support, Roche provides the medication.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration