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The effects of SCH 351125 on mononuclear cell trafficking to joints, synovial inflammation and expression of chemokines in subjects with rheumatoid arthritis

Submission date
23/08/2007

Recruitment status
No longer recruiting

Registration date
23/08/2007

Overall study status
Completed

Last Edited
29/08/2007

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
P03653

Study information

Scientific Title

Study objectives
SCH 351125 50 mg twice daily (BID) 2/days is an effective treatment for Rheumatoid Arthritis (RA).

Primary objectives of the study are to determine the effects of SCH 351125 on mononuclear cell migration into synovial tissue in subjects with rheumatoid arthritis, and to evaluate the safety and tolerability of multiple-dose administration of SCH 351125 50 mg BID in subjects with rheumatoid arthritis when administered for 28 days.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the Medical Ethics Committee of the Academic Medical Centre (University of Amsterdam) on the 21st January 2004 (ref: 03/267).

Study design
Randomised, double-blind, placebo controlled, parallel group trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Rheumatoid arthritis

Interventions
Subjects with active Rheumatoid Arthritis (RA) were enrolled in a randomised double-blind, placebo-controlled, parallel-group study exposed to either SCH 351125 50 mg BID or matched placebo, in a 2:1 ratio, for 28 days.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
SCH 351125

Primary outcome(s)
1. To determine the effects of SCH 351125, a CCR5 receptor antagonist, on mononuclear cell migration into synovial tissue in subjects with rheumatoid arthritis
2. To evaluate the safety and tolerability of multiple-dose administration of SCH 351125 50 mg twice-daily in subjects with rheumatoid arthritis when administered for 28 days

Key secondary outcome(s))
1. To explore the effects of SCH 351125 on:
1.1. Synovial inflammation via MRI
1.2. Chemokine expression and concentrations in the plasma, synovial tissue and synovial fluid (messenger Ribonucleic Acid [mRNA] expression only)
1.3. Mononuclear cell concentrations in the peripheral blood
1.4. Clinical signs and symptoms of rheumatoid arthritis
1.5. To determine the single-dose and multiple dose pharmacokinetic profile of SCH 351125 in subjects with rheumatoid arthritis

Completion date
01/05/2005

Eligibility

Key inclusion criteria
1. Subjects 18 to 70 years of age, of either sex, and of any race
2. Diagnosis of RA according to the American College of Rheumatology (ACR) criteria, for at least six weeks prior to entry in the study
3. Active RA defined as:
3.1. Three or more tender joints
3.2. Three or more swollen joints, and
3.3. At least one of the following three:
3.3.1. Duration of morning stiffness equal to or greater than 45 minutes
3.3.2. Erythrocyte sedimentation rate equal to or greater than 28 mm/hour
3.3.3. C-reactive protein equal to or greater than 10 mg/L
4. Functional class I, II or III
5. Subjects must be free of any clinically significant disease (other than rheumatoid arthritis) that would interfere with the study evaluations and/or safety
6. Subjects must be willing to give written informed consent and able to adhere to dose and visit schedules
7. Females must not be breast-feeding, and either be of non-childbearing potential (i.e., sterilised via hysterectomy or bilateral tubal ligation or at least one year postmenopausal) or if of child bearing potential, must be practicing effective double barrier contraceptive methods from at least two weeks prior to day 1 and until 30 days following cessation of dosing
8. Female subjects of childbearing potential must have a negative serum pregnancy test (beta human Chorionic Gonadotropin [beta-hCG]) at screening
9. Males must practice an effective barrier method of contraception from day 1 until 30 days following cessation of dosing
10. A physical examination must be without clinically significant findings with exception of those finding related to rheumatoid arthritis
11. At screening, Electrocardiogram (ECG) conduction intervals must be within the gender specific normal range (i.e., QTc for males less than 430 msec and females less than 450 msec)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Individuals with a history of any significant medical disorder which require a physician's care (excluding rheumatoid arthritis) and would interfere with the study evaluations or compromise subject safety
2. Individuals who have a history of any clinically significant local or systemic infectious disease within four weeks prior to drug administration
3. Any subject with an allergy to gadolinium
4. Any subject with a pacemaker, metal object implanted their body or any other device or condition which may interfere with a subject's safety during the Magnetic Resonance Imaging (MRI) procedure
5. Any subject who has received Disease Modifying Anti-Rheumatic Drug (DMARD) treatment within 30 days prior to enrolment (leflunomide requires a charcoal or cholestyramine washout)
6. Any subject who has received anti-Tumour Necrotising Factor (anti-TNF) therapy (except enteracept) or any biologic therapy within the previous 90 days
7. Any subject whose baseline Disease Activity Score (DAS-28) has significantly changed since screening to indicate unstable disease
8. Any individual who does not comply with the requirement that he should not have used:
8.1. Any drugs (including herbal and mineral supplements or vitamins), other than acetaminophen or an approved stable regimen of low dose prednisone (10 mg/day) and/or Non-Steroidal Anti-Inflammatory Drugs (NSAIDS), for at least two weeks prior to study drug administration
8.2. Alcohol in amounts of greater than 50 grams a day throughout the study
9. Subjects that have been diagnosed with Juvenile RA
10. A history of systemic lupus erythematosus, or signs and symptoms suggesting systemic lupus erythematosus
11. Subjects who are positive for hepatitis B surface antigen, hepatitis C Ribonucleic Acid (RNA) or for Human Immunodeficiency Virus (HIV) antibodies
12. Individuals who have participated in a clinical trial of an investigational drug within 90 days prior to the start of study drug administration, or have received prior treatment with a CCR5 receptor antagonist
13. Individuals with a positive screen for drugs of abuse
14. Individuals who have donated blood (greater than 300 mL) within the preceding 90 days
15. Males who are unwilling to use/practice an effective method of contraception (i.e., condom in conjunction with spermicide from study start until 30 days after the last study treatment
16. Females who are unwilling to use/practice an effective method of contraception (i.e., condom in conjunction with spermicide from two weeks prior to study start until 30 days after the last study treatment
17. Individuals who have received any vaccinations within 30 days prior to screening
18. Individuals with any clinically significant history of food or drug allergy or allergy to any component of SCH 351125
19. Subjects who are not willing to follow the study restrictions or procedures

Date of first enrolment

01/03/2004

Date of final enrolment
01/05/2005

Locations

Countries of recruitment
Netherlands

Study participating centre
Academic Medical Centre (AMC)
Amsterdam
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Sponsor information

Organisation
Schering Plough Research Institute (USA)

ROR
https://ror.org/02891sr49

Funder(s)

Funder type
Industry

Funder Name
Schering Plough Research Institute (USA)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration