ISRCTN46017566 https://doi.org/10.1186/ISRCTN46017566

Arthritis Prevention In the Pre-clinical Phase of Rheumatoid Arthritis with Abatacept

Submission date
04/07/2014

Recruitment status
No longer recruiting

Registration date
04/07/2014

Overall study status
Completed

Last Edited
19/02/2024

Condition category
Musculoskeletal Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Rheumatoid arthritis (RA) is a common long-term inflammatory disease that causes pain, stiffness, swelling and limited motion of joints. RA can affect any joint (most commonly the small joints in the hands and feet) and can develop at any age. RA is thought to be an autoimmune disease, which means that something triggers the immune system to make an immune reaction (this includes the production of antibodies) that may cause damage to joint tissues. Over time, damage to the joint may lead to destruction of cartilage and bone. In some patients, the inflammation can affect other organs such as blood vessels, the eyes or lungs. If not well treated, the condition may lead to permanent damage to joints and disability, affecting quality of life. The purpose of this study is to find out whether RA can be prevented if treatment is given to people at high risk of developing the disease, as defined by the presence of autoantibodies in the blood, together with joint symptoms (pain but not joint swelling).

Who can participate?
Adults with joint pain and who have been found to have autoantibodies known to be associated with RA in their blood.

What does the study involve?
Participants will be randomly allocated to receive weekly injections of either abatacept (the drug licensed for use in established RA) or dummy (placebo) treatment over a 12-month period. This provides the best chance of establishing whether differences observed between the two groups are due to the treatment. The treatment will start at the first visit and participants will take weekly injections for 12 months and will be seen in the outpatient clinic every 3 months. Blood and urine tests will be done during these visits and some of the blood and urine will be used for routine monitoring of the effects of the study medication. Participants will also have an ultrasound scan of their joints at the first study visit and at 6, 12, 18 and 24 months, which may be performed on the same day. In addition to the three monthly visits, there will be brief telephone consultations to check that study subjects are administering their weekly injections, and to ask if there have been any changes in their symptoms. Once participants have completed the 12-month course of treatment, they will be seen in the outpatient clinic every 3 months to monitor the impact of the treatment. This follow-up period is especially important because if at any time participants develop new joint pains or swelling they will be assessed promptly and

treated appropriately, in a similar way that clinical staff would assess any new patient presenting with arthritis.

What are the possible benefits and risks of participating?
Participants receiving drug treatment could experience some of the following side effects: throat or chest infections, headache, blood pressure increase, changes in liver function, loose stool, nausea, sore throat, fever, rashes, reduced white blood cell and tiredness and risk of injection site reactions in the skin. In general these are mild, and previous studies of abatacept have shown that the medication is well tolerated in patients with early as well as established RA. Nevertheless, for these reasons participants will be monitored closely through regular clinical assessments and blood testing so that any infections or side effects can be treated promptly.

Where is the study run from?
The study will be run from up to 30 study sites across the UK and the Netherlands.

When is study starting and how long is it expected to run for?
It is expected that recruitment will start in July 2014. Participants will be enrolled in the study for a period of 12 months of treatment with a further 12 months of follow up.

Who is funding the study?
Bristol-Myers Squibb (UK).

Who is the main contact?
Professor Andrew P. Cope (Chief Investigator), apippra@kcl.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2013-003413-18

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
16221

Study information

Scientific Title
Arthritis Prevention In the Pre-clinical Phase of Rheumatoid Arthritis with Abatacept: a randomised controlled trial

Acronym
APIPPRA

Study objectives
This study will test the hypothesis that the onset of arthritis in an 'at risk' group can be prevented or delayed by weekly injections of abatacept for a period of 12 months.
The specific aims of this study are to:
1. Evaluate the feasibility, efficacy and acceptability of abatacept therapy in subjects at high risk of developing RA, and
2. Characterise immune and inflammatory responses associated with ACPA before, during and after therapy with abatacept.

On 13/01/2015 the following changes were made to the trial record:
1. Netherlands was added to the countries of recruitment (target number of participants: 20).
2. The overall trial start date was changed from 01/08/2014 to 12/12/2014.
3. The overall trial end date was changed from 31/07/2016 to 11/12/2018.
4. King’s College London was added as a sponsor.

Ethics approval required
Old ethics approval format

Ethics approval(s)
14/LO/0100; First MREC approval date 13/03/2014

Study design
Randomised; Interventional; Design type: Not specified

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Topic: Musculoskeletal disorders; Subtopic: Musculoskeletal (all Subtopics); Disease: Musculoskeletal

Interventions
Participants will be randomised into one of two arms:
1. Abatacept
2. Matching placebo

Participants will receive weekly injections of 125 mg/ml of abatacept or placebo, starting from baseline (week 0) for a period of 52 weeks. They will be trained to self-administer the study drug subcutaneously using the single-dose prefilled syringe according to local practices for the administration of biological therapy as part of standard care. They will be followed up for an additional period of 52 weeks. Participants will be seen at 3 monthly intervals throughout the duration of the study.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Abatacept

Primary outcome(s)
Time to development of clinical synovitis or RA

Key secondary outcome(s))
The development of RA according to the ACR/EULAR 2010 criteria

Completion date
13/01/2021

Eligibility

Key inclusion criteria
1. Male or female subjects, aged 18 years or over
2. Arthralgia, defined as non-traumatic joint pain localised to synovial joints including, but not necessarily confined to, hands, wrists or feet, and in the opinion of the supervising rheumatologist considered to be inflammatory in nature
3. Positive for serum rheumatoid factor (RF) and antibodies to citrullinated protein antigens (ACPA) as defined by local clinical laboratory testing. Subjects who are RF negative, but who carry high levels of serum ACPA (defined as being = 3 x upper limit of normal [ULN] for the assay) may be included
4. Able and willing to give written informed consent and comply with the requirements of the study protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
213

Key exclusion criteria
1. Previous diagnosis of RA or other form of inflammatory arthritis including, but not limited to, SLE, psoriatic arthritis, ankylosing spondylitis, gout or pyrophosphate arthopathy, and including current treatment with DMARDs or biological therapy
2. Arthralgia that, in the opinion of the supervising physician, is poorly localised, e.g., pelvic or shoulder girdle pain that is confined to the axial skeleton or entheses, or pain which the physician considers to be due to osteoarthritis or fibromyalgia, or related to other autoimmune conditions such as type I diabetes, coeliac or autoimmune thyroid disease
3. Clinically apparent arthritis, as assessed by a rheumatologist, characterised by soft tissue swelling of one or more synovial joints. Subclinical synovitis, as detected by imaging modalities such as ultrasonography or MRI, is NOT an exclusion criterion
4. A history of oral or parenteral use of corticosteroids within the last 12 weeks used to treat the current episode of musculoskeletal symptoms
5. Co-morbidities requiring chronic treatment with immunosuppressive or immune-modulating therapy
6. Subjects who have at any time received treatment with any investigational drug within 28 days
7. A history of acute allergic reactions to biological therapy or immunoglobulins
8. Subjects who are incapable of completing study-related assessments or give informed consent
9. Subjects with current symptoms of severe, progressive or uncontrolled renal, hepatic, hematologic, gastrointestinal, pulmonary, cardiac, neurologic or cerebral disease, whether or

not related to RA and which, in the opinion of the investigator, might place a subject at unacceptable risk for participation in the study
10. Subjects with a cancer history within the last 5 years
11. Subjects with tuberculosis (including those at high risk of tuberculosis), chronic viral infections, recent serious bacterial infections, or subjects receiving live vaccinations within 3 months of the anticipated first dose of study medication, or those with chronic illnesses that would, in the opinion of the investigator, put the patient at risk
12. Subjects who currently abuse drugs or alcohol
13. Subjects who are pregnant or who are breastfeeding
14. Male subjects or women of childbearing potential not willing to use adequate contraception during the period of IMP dosing and for up to 10 weeks after the last dose of study drug
15. Subjects with abnormal laboratory tests, as defined in the study protocol

Date of first enrolment
01/08/2014

Date of final enrolment
14/01/2019

Locations

Countries of recruitment
United Kingdom

England

Netherlands

Study participating centre
Wolfson Centre for Age Related Diseases
London
United Kingdom
SE1 1UL

Sponsor information

Organisation
Guy's and St Thomas' NHS Foundation Trust

ROR
https://ror.org/00j161312

Organisation

King’s College London

Funder(s)

Funder type
Industry

Funder Name
Bristol Myers Squibb (UK) Grant Codes: IM101-328

Alternative Name(s)
Bristol-Myers Squibb Company, Bristol Myers Squibb, Bristol-Myers Company, BMS

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available. Informed consent for sharing individual de-identified participant data was not obtained from the study participants.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		13/02/2024	19/02/2024	Yes	No
Protocol article	protocol	15/07/2019	05/06/2020	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes