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Rheumatoid arthritis prevention with abatacept - long-term outcome study

Submission date
05/03/2020

Recruitment status
No longer recruiting

Registration date
09/04/2020

Overall study status
Completed

Last Edited
23/01/2026

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Rheumatoid arthritis (RA) is an autoimmune, long-term inflammatory disease that causes pain, stiffness, swelling and limited joint movement. RA can affect any joint (most commonly the small joints in the hands and feet) and can develop at any age. The condition can trigger and generate an immune response (e.g. this includes the production of antibodies) that may cause damage to joint tissues and over time may lead to the destruction of cartilage and bone. In some patients, the inflammation can affect other organs such as blood vessels, the eyes or lungs. If not effectively treated, the condition may lead to permanent damage to joints and functional disability in people, including limitations to the quality of life.
RA affects more than 500,000 people in the UK. If not treated effectively, the condition leads to joint damage and significant disability. RA is costly to individuals and their families; one third of patients with arthritis stop work within 2 years of onset because of their disease. RA is costly to the UK economy, estimated to be in the region of £5 billion per year, through direct costs to the NHS and associated healthcare providers, and indirect costs associated with early death and loss of productivity.
Disease-modifying anti-rheumatic drugs (DMARDs) have transformed the treatment of RA. Research has shown that this approach leads to higher proportions of patients becoming symptom-free for long periods. This means they have improved function and joint damage is slowed or even prevented. Intensive treatment of patients with very early RA can mean that some of them can be symptom-free without needing to take medicines. It is important to detect the early signs of RA and to predict which patients are likely to develop severe RA in order to reduce disability and inability to work. People who have mild joint pain can be tested for certain antibodies that are associated with the eventual development of RA.
A previous study called APIPPRA was started in 2013. This study tested whether treatment with a drug called abatacept (Orencia) could prevent the development of RA in people who had joint pain and were positive for the antibodies but did not have the inflammatory signs of RA. Results of this study are expected in early 2021. This study, called ALTO, is following the same participants in APIPPRA on a more long-term basis to investigate whether abatacept treatment prevents or delays additional joints being affected by pain or inflammation.

Who can participate?
Patients enrolled in the APIPPRA study who have completed at least one APIPPRA study visit

What does the study involve?
During the APIPPRA study, participants will have received abatacept or placebo (dummy) injections once weekly for a year and were then followed up without treatment for a further year. In ALTO, they will be assessed every 6 months for a further 3 years.

What are the possible benefits and risks of participating?
ALTO study participants will not receive any study drugs, so there are no risks of side effects as a result of participating. They might benefit from the regular assessment of their condition.

Where is the study run from?
Guy's and St Thomas's Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2020 to July 2024

Who is funding the study?
Bristol-Myers Squibb (USA), which sells abatacept

Who is the main contact?
Prof. Andrew Cope (Chief Investigator)
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Contact information

Type(s)
Scientific

Contact name
Prof Andrew Cope

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-000108-12

Integrated Research Application System (IRAS)
270373

Protocol serial number
IM101-865

Study information

Scientific Title
Arthritis prevention in the pre-clinical phase of rheumatoid arthritis with abatacept long-term outcome study

Acronym
ALTO

Study objectives
The purpose of this study is to capture long-term outcome data from the APIPPRA study to determine whether rheumatoid arthritis (RA) is prevented or delayed when targeted immunotherapy is given to participants in whom autoantibody screening, together with symptoms, indicates a high risk of developing the disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/03/2021, London -South East Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8085; londonsoutheast.rec@hra.nhs.uk), ref: 21/LO/0035

Primary study design
Observational

Study design
Long-term follow-up of the APIPPRA study

Study type(s)
Prevention

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

Interventions
Long-term observation of treatment with abatacept.

After consenting, patients are clinically checked and routine blood samples will be taken at each study visit for ESR and CRP to compute disease activity scores. Monitoring for drug toxicity for those study participants who are treated with conventional synthetic and/or biologic DMARDs will be left to the discretion of the supervising rheumatologist. Monitoring may be undertaken at the time of study visits, as part of standard care. There will be no additional blood taken for laboratory studies.

All participants (regardless of their disease status) will remain in the study and complete assessments (two questionnaires) on an approximately 6-monthly basis according to the

schedule of visits, including full documentation of treatment for their inflammatory arthritis, where relevant. The final visit will be completed by January 2023.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Current primary outcome measures as of 20/07/2021:
For those participants who met the APIPPRA primary endpoint during the APIPPRA study, this will be their primary endpoint in the ALTO study. For those study participants who did not meet the primary endpoint during the APIPPRA study, the primary endpoint in the ALTO study is the time from randomisation in the APIPPRA study to the development of clinical synovitis or RA defined by one of the following events, whichever is met first:
1. The development of clinically apparent synovitis in ≥3 joints, as determined by an assessor with experience in clinical assessment of RA
2. The development of RA according to the ACR/EULAR 2010 criteria, where joint involvement is defined as joint swelling
3. The prescription of first DMARD (e.g. methotrexate or equivalent) by a rheumatologist

Previous primary outcome measures:
1. Inflammation of the joints assessed by physical examination
2. RA medication (time of commencing DMARD therapy) taken from medical records
Timepoints: assessed at baseline and at every 6 monthly visit for max of 3 years (unless otherwise stated)

Key secondary outcome(s)
Current secondary outcome measures as of 20/07/2021:
1. The development of RA when imaging assessments are included, measured using tender and swollen joint counts and ultrasound, captured retrospectively then at baseline and every 6 months thereafter until 31/01/2023
2. Disease activity and progression over time, assessed using DAS28 (tender and swollen joint counts, patient global visual analogue score (VAS), CRP and ESR and Extended Joint Count 68 /66, Simple Disease Activity Score (SDAI) and Clinical Disease Activity Score (CDAI), Pain VAS, Health Assessment Questionnaire (HAQ), Euro-Quality of Life Questionnaire (EQ-5D-3L), captured retrospectively then at baseline and every 6 months thereafter until 31/01/2023
3. The proportion of participants requiring conventional synthetic DMARD (csDMARD) therapy, and the time to commencing oral or parenteral corticosteroids, measured using clinical visits and electronic health records, captured retrospectively then at baseline and every 6 months thereafter until 31/01/2023
4. The proportion of participants requiring biologic DMARD therapy, and the time to commencing biologic DMARD therapy, measured using clinical visits and electronic health records captured retrospectively then at baseline and every 6 months thereafter until 31/01 /2023
5. Radiographic changes in X-rays of the hands and feet from enrolment in APIPPRA to the end of ALTO, scored by van der Heijde Sharp Modified Scores at final visit by 31/01/2023

6. Safety, with emphasis on serious adverse events and events of special interest such as cardiovascular events, infection and cancer, assessed using clinical visits and electronic health records, captured retrospectively then at baseline and every 6 months thereafter until 31/01/2023

Previous secondary outcome measures:
1. Joint damage assessed by X-rays of hands and feet at the final visit
2. Quality of life assessed by Health Assessment Questionnaire (HAQ)
3. Quality of life assessed by Euro-Quality of Life Questionnaire (EQ-5D)
4. Joint damage/inflammation assessed by ultrasound of joints (only when they developed synovitis)
5. Concomitant medication use assessed by recording all concomitant medication
6. Adverse events: important medical events and events of special interest recorded following the participant's written consent to participate in the study
Timepoints: assessed at baseline and at every 6 monthly visit for max of 3 years (unless otherwise stated)

Completion date
30/07/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 20/07/2021:
1. Male or female participants, aged ≥18 years.
2. All participants deemed eligible and randomised to the APIPPRA study.
3. All participants who completed at least one APIPPRA study visit.
4. All participants who are willing to give written informed consent and comply with the requirements of the ALTO study protocol.

Previous inclusion criteria:
1. Male or female participants, aged ≥18 years
2. All participants deemed eligible and randomised to the APIPPRA study
3. All participants who completed at least one APIPPRA study visit
4. All participants who are willing to consent to the ALTO study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
143

Key exclusion criteria
1. Participants who are still participating in the APIPPRA study
2. Participants ineligible and randomised to the APIPPRA study in error
3. Participants deemed eligible and randomised to the APIPPRA study but who never received study drug
4. Those unable to give informed consent

Date of first enrolment
26/04/2021

Date of final enrolment
31/07/2023

Locations

Countries of recruitment
United Kingdom

England

Scotland

Netherlands

Study participating centre
Guy's & St Thomas's NHS Foundation Trust
Academic Department of Rheumatology
CMCBI, 1st floor, New Hunt's House
Guy's Hospital Campus
Great Maze Pond
London
England
SE1 1UL

Study participating centre
King's College Hospital NHS Foundation Trust
Denmark Hill
London
England
SE5 9RS

Study participating centre
University College London Hospitals NHS Trust
3rd Floor Central
250 Euston Road
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England
NW1 2PG

Study participating centre
Basildon and Thurrock University Hospitals NHS Foundation Trust
Basildon and Thurrock University
Nethermayne
Basildon Hospital
Basildon
England
SS16 5NL

Study participating centre
Cambridge University Hospital NHS Foundation Trust
Rheumatology Clinical Research Unit
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Addenbrooke's Hospital
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CB2 0QQ

Study participating centre
Glasgow Royal Infirmary
4 Castle Street
Glasgow
Scotland
G4 0SF

Study participating centre
Newcastle upon Tyne NHS Foundation Trust
Musculoskeletal Research Group
Institute of Cellular Medicine
Newcastle University
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Study participating centre
Great Western Hospitals NHS Foundation Trust
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Study participating centre
The Dudley Group Of Hospitals NHS Foundation Trust
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Study participating centre
The University of Birmingham and University Hospitals Birmingham NHS Foundation Trust
New Queen Elizabeth Hospital UHB & City (Birmingham)
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B15 2TT

Study participating centre
Sandwell and West Birmingham Hospitals NHS Trust
Birmingham City Hospital
Birmingham
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B18 7QH

Study participating centre
The Royal Wolverhampton NHS Trust
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WS11 5XY

Study participating centre
Midlands Partnership NHS Foundation Trust
Haywood Hospital
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ST6 7AG

Study participating centre
The Leeds Teaching Hospital NHS Trust
Leeds Institute of Rheumatic & Musculoskeletal Medicine
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LS7 4SA

Study participating centre
Central Manchester University Hospitals NHS Foundation Trust
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Study participating centre
Maidstone & Tunbridge Wells NHS Trust
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Study participating centre
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Study participating centre
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E9 6SR

Study participating centre

Luton & Dunstable Hospital NHS Foundation Trust
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Study participating centre
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Study participating centre

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Sponsor information

Organisation
Kings College London and Guy's and St Thomas' NHS Foundation Trust

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		20/01/2026	23/01/2026	Yes	No
HRA research summary			28/06/2023	No	No