

# Rheumatoid arthritis prevention with abatacept - long-term outcome study

<b>Submission date</b> 05/03/2020	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 09/04/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 05/12/2024	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## 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

**ORCID ID**

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**Contact details**

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## Additional identifiers

**Clinical Trials Information System (CTIS)**

2020-000108-12

**Integrated Research Application System (IRAS)**

270373

**ClinicalTrials.gov (NCT)**

Nil known

**Protocol serial number**

IM101-865, IRAS 270373

## 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

### Study design

Long-term follow-up of the APIPPRA study

### Primary study design

Observational

### 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  $\geq 3$  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  $\geq 18$  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  $\geq 18$  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

Adult

### Lower age limit

18 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

United Kingdom

SE1 1UL

### **Study participating centre**

**King's College Hospital NHS Foundation Trust**

Denmark Hill

London

United Kingdom

SE5 9RS

**Study participating centre**

**University College London Hospitals NHS Trust**

3rd Floor Central

250 Euston Road

London

United Kingdom

NW1 2PG

**Study participating centre**

**LUMC, Department of Rheumatology**

Postzone C1-R

Visiting address room D3-49

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Leiden

Netherlands

2333 ZA

**Study participating centre**

**Basildon and Thurrock University Hospitals NHS Foundation Trust**

Basildon and Thurrock University

Nethermayne

Basildon Hospital

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United Kingdom

SS16 5NL

**Study participating centre**

**Cambridge University Hospital NHS Foundation Trust**

Rheumatology Clinical Research Unit

Box 194, Unit E6

Addenbrooke's Hospital

Hills Road

Cambridge

United Kingdom

CB2 0QQ

**Study participating centre**

**Glasgow Royal Infirmary**

4 Castle Street

Glasgow

United Kingdom

G4 0SF

**Study participating centre**

**Newcastle upon Tyne NHS Foundation Trust**

Musculoskeletal Research Group  
Institute of Cellular Medicine  
Newcastle University  
4th floor, Catherine Cookson Building  
The Medical School  
Framlington Place  
Newcastle upon Tyne  
United Kingdom  
NE2 4HH

**Study participating centre**

**Great Western Hospitals NHS Foundation Trust**

Great Western Hospital  
Marlborough Road  
United Kingdom  
SN3 6BB

**Study participating centre**

**The Dudley Group Of Hospitals NHS Foundation Trust**

Department of Rheumatology  
Russells Hall Hospital  
Pensnett Road  
Dudley  
United Kingdom  
DY1 2HQ

**Study participating centre**

**The University of Birmingham and University Hospitals Birmingham NHS Foundation Trust**

New Queen Elizabeth Hospital UHB & City (Birmingham)  
Rheumatology Research Group  
3rd Floor  
Institute For Biomedical Research  
Medical School  
Edgbaston  
Birmingham  
United Kingdom  
B15 2TT

**Study participating centre**



**Sandwell and West Birmingham Hospitals NHS Trust**  
Birmingham City Hospital  
Birmingham  
United Kingdom  
B18 7QH

**Study participating centre**  
**The Royal Wolverhampton NHS Trust**  
Cannock Chase Hospital  
Rheumatology Department  
Brunswick Road  
Cannock  
United Kingdom  
WS11 5XY

**Study participating centre**  
**Midlands Partnership NHS Foundation Trust**  
Haywood Hospital  
High Lane  
Stoke on Trent  
United Kingdom  
ST6 7AG

**Study participating centre**  
**The Leeds Teaching Hospital NHS Trust**  
Leeds Institute of Rheumatic & Musculoskeletal Medicine  
Chapel Allerton Hospital  
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Leeds  
United Kingdom  
LS7 4SA

**Study participating centre**  
**Central Manchester University Hospitals NHS Foundation Trust**  
The Kellgren Centre for Rheumatology  
Oxford Road  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**

**Nottingham University Hospitals NHS Trust**

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Nottingham  
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NG5 1PB

**Study participating centre**

**Royal Berkshire NHS Foundation Trust**

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Reading  
United Kingdom  
RG1 5AN

**Study participating centre**

**Countess of Chester Hospital NHS Foundation Trust**

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**Study participating centre**

**Maidstone & Tunbridge Wells NHS Trust**

Maidstone Hospital  
Hermitage Lane  
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ME16 9QQ

**Study participating centre**

**The Royal Wolverhampton NHS Trust**

New Cross Hospital  
Wolverhampton  
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WV10 0QP

**Study participating centre**

**Homerton University Hospital NHS Foundation Trust**

Dept of Rheumatology  
Homerton Hospital

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**Study participating centre**

**Luton & Dunstable Hospital NHS Foundation Trust**

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**Study participating centre**

**Heart of England NHS Foundation Trust**

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**Study participating centre**

**Northampton General Hospital NHS Trust**

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NN1 5BD

**Study participating centre**

**Hull Royal Infirmary**

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Anlaby Road  
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**Study participating centre**

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Netherlands  
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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?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes