

# OPTimising Treatment with Tumour necrosis factor (TNF) Inhibitors in Rheumatoid Arthritis: is dose tapering practical in good responders?

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|----------------------------------------|-------------------------------------------------------|------------------------------------------------------|
| <b>Submission date</b><br>24/11/2010   | <b>Recruitment status</b><br>No longer recruiting     | <input type="checkbox"/> Prospectively registered    |
| <b>Registration date</b><br>25/05/2011 | <b>Overall study status</b><br>Completed              | <input type="checkbox"/> Protocol                    |
| <b>Last Edited</b><br>06/06/2018       | <b>Condition category</b><br>Musculoskeletal Diseases | <input type="checkbox"/> Statistical analysis plan   |
|                                        |                                                       | <input checked="" type="checkbox"/> Results          |
|                                        |                                                       | <input type="checkbox"/> Individual participant data |

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2010-020738-24

### Protocol serial number

## Study information

### Scientific Title

OPTimising Treatment with Tumour necrosis factor (TNF) Inhibitors in Rheumatoid Arthritis: is dose tapering practical in good responders? A 'proof of principle' and exploratory trial

### Acronym

OPTTIRA

### Study objectives

Our hypothesis is that tapering TNF inhibitors (to a minimum of one third of the initial induction doses) will not adversely affect disease control in established RA patients who have achieved a good response to standard doses of TNF inhibitors and are also receiving disease modifying anti-rheumatic drugs (DMARDs). We consider an increase of disease activity score (DAS28) at least 0.6 represents a clinically important change.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

North West London REC 2, 12/10/2010, ref: 10/H0720/69

### Primary study design

Interventional

### Study design

Randomised controlled open-label multicentre proof of principle trial followed by an open exploratory phase trial

### Study type(s)

Treatment

### Health condition(s) or problem(s) studied

Rheumatoid arthritis

### Interventions

Patients will be randomised to one of three tapering groups:

1. Experimental group 1: patients have their TNF inhibitor tapered to 66% of initial dose by reducing frequency of dosing
2. Experimental group 2: patients have their TNF inhibitor tapered to 33% of initial dose by reducing frequency of dosing
3. Control group: patients continue on standard doses

If the proof of principle phase supports TNF inhibitor tapering, patients will enter an exploratory extension study.

Progression to the Exploratory phase for Experimental groups 1 and 2 will be based on the patient level eligibility criteria to ensure that it is appropriate for the patient to continue

tapering. The Proof of Principle Control Group will have their TNF inhibitors tapered over 6 months to either 66% or 33% by reducing the frequency of their injections. Patients originally in the tapering groups will have their TNF inhibitors reduced further over 6 months by increasing the time between injections on each occasion until they are stopped completely.

## **Intervention Type**

Drug

## **Phase**

Not Applicable

## **Primary outcome(s)**

The development of flares, defined as an increase in DAS28 scores at least 0.6. To ensure such changes in DAS28 represent a genuine flare in RA and are not due to unrelated events (e.g. an inter-current illness like influenza) additional criteria required for a flare are:

1. It must include an increase in the swollen joint count
2. It must be present on two occasions at least one week apart
3. It results in DAS28 scores greater than 3.2

Large increases in DAS28 scores (1.2 or more) which result in DAS28 greater than 3.2 will not require any additional criteria. DAS28 measurements at baseline, 3, 6, 9 and 12 monthly assessments. The participants will also be telephoned every month to check whether their RA symptoms have increased. If it is suspected a patient is experiencing a flare, they should come in for a flare assessment within 2 weeks.

## **Key secondary outcome(s)**

1. DAS28 [tender and swollen joint counts, patient global Visual Analogue Scale (VAS), erythrocyte sedimentation rate (ESR)] and Extended Joint Count 68/66, monitored at baseline, 3, 6, 9 and 12 months
2. Simple disease activity score (SDAI) and clinical disease activity score (CDAI), at baseline, 3, 6, 9 and 12 months
3. Health Assessment Questionnaire (HAQ) scores, at baseline, 3, 6, and 12 months
4. Adverse events, at baseline, 3, 6, 9 and 12 months
5. EuroQol scores, at baseline, 3, 6, and 12 months
6. SF-36, at baseline, 3, 6, and 12 months
7. Plain x-rays of the hands and feet scored by Larsens and Van Der Heijdi Sharpe Modified Scores (to provide preliminary data), at baseline, 6, and 12 months
8. Analysis of serum, immunological and gene expression profiles; biomarker blood taken at baseline for the experimental groups and at 6 months for the control group

## **Completion date**

31/08/2013

# **Eligibility**

## **Key inclusion criteria**

1. RA by American College of Rheumatology and EULAR criteria
2. Etanercept or adalimumab treatment for at least 6 months (a break of up to 4 consecutive weeks is permitted)
3. Taking at least one DMARD
4. Stable clinical response for at least 3 months (one DAS28 score of 3.2 or less; no increase in

DAS28 greater than 0.6)

5. Patient considers he or she has achieved a suitable response to TNF inhibitors

6. Supervising rheumatologist considers further improvements are unlikely on the patients current treatment regimen

7. At least 18 years of age, either sex

8. Willing and able to give informed consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

All

**Key exclusion criteria**

1. Serious concurrent illness (e.g. terminal cancer)

2. Prednisolone at more than 10mg daily (for doses > 10mg daily, a 4 week washout period is required)

3. Recently received intramuscular (IM)/intra-arterial (IA) steroids (12 weeks washout required)

4. Pregnancy, breast-feeding or women of child-bearing potential not using adequate contraception

**Date of first enrolment**

14/12/2010

**Date of final enrolment**

31/08/2013

**Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

King's College London

London

United Kingdom

SE5 9RJ

# Sponsor information

## Organisation

King's College London (KCL) (UK)

## ROR

<https://ror.org/0220mzb33>

# Funder(s)

## Funder type

Charity

## Funder Name

Arthritis Research UK (UK)

## Alternative Name(s)

## Funding Body Type

Private sector organisation

## Funding Body Subtype

Other non-profit organizations

## Location

United Kingdom

# Results and Publications

## Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

| Output type                          | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|--------------------------------------|---------|--------------|------------|----------------|-----------------|
| <a href="#">Results article</a>      | results | 01/11/2017   |            | Yes            | No              |
| <a href="#">Results article</a>      | results | 17/05/2018   |            | Yes            | No              |
| <a href="#">HRA research summary</a> |         |              | 28/06/2023 | No             | No              |