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

Submission date
24/11/2010

Recruitment status
No longer recruiting

Registration date
25/05/2011

Overall study status
Completed

Last Edited
06/06/2018

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2010-020738-24

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
OPTTIRA Protocol - Version 1.1 - 14.09.10

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 clinical important change.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West London REC 2, 12/10/2010, ref: 10/H0720/69

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

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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 measure
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.

Secondary outcome measures
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

Overall study start date
14/12/2010

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
99

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-areterial (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
England

United Kingdom

Study participating centre
King's College London
London
United Kingdom
SE5 9RJ

Sponsor information

Organisation
King's College London (KCL) (UK)

Sponsor details
The Strand
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Sponsor type
University/education

Website
http://www.kcl.ac.uk/index.aspx

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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Results article	results	01/11/2017		Yes	No
Results article	results	17/05/2018		Yes	No
HRA research summary			28/06/2023	No	No