Arthritis Prevention In the Pre-clinical Phase of RA with Abatacept.

Published: 28-09-2015
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The aim of this clinical trial is to evaluate the feasibility, efficacy and acceptability of abatacept therapy in subjects at high risk of developing RA.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON47610

Source
ToetsingOnline

Brief title
APIPPRA

Condition

- Other condition
- Autoimmune disorders

Synonym
Arthralgia, Reumatoid Arthritis

Health condition

gewrichsaandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Co sponsor King's College Londen UK,Bristol-Myers Squibb,Co-sponsor: King□s College London and Guy□s and St Thomas□ NHS Foundation Trust

Intervention

Keyword: Abatacept, Arthritis, Pre clinical RA, Prevention

Outcome measures

Primary outcome

The primary endpoint of this study is the time to development of clinical

synovitis or RA defined by one of the following methods, whichever is met first:

1) The time to development of clinically apparent synovitis in * 3 joints, as

determined by two independent assessors with experience in clinical assessment

of RA

2) The time to development of RA according to the ACR/EULAR 2010 criteria,

where joint involvement is defined as joint swelling.

In either case joint swelling will be confirmed by ultrasound.

Secondary outcome

The secondary efficacy parameters will include:

1. Assessments for the development of RA according to the ACR/EULAR 2010

criteria, where ultrasound assessments will be included.

2. Assessments of disease activity using DAS28 (tender and swollen joint

counts, patient global visual analogue score {VAS}, ESR).

3. Extended Joint Counts 68/66.

4. Simple Disease Activity Score (SDAI) and Clinical Disease Activity Score

(CDAI)

5. Health Assessment Questionnaire (HAQ) scores, EQ-5D scores and FACIT-F

scores. Analysis of

Pain VAS, Lifestyle Factors Questionnaire, modified Illness Perception

Questionnaire, Hospital

Anxiety and Depression scale and Work Instability Scale will also be included.

6. Progression of radiographic changes in X-rays of the hands and feet scored

by van der Heijde

Sharpe Modified Scores and/or by Larsen scores.

7. Changes in scores of synovitis and vascularity defined by high resolution

ultrasonography and power Doppler over time.

8. Adverse events.

9. Immune signatures derived from the analysis of biological samples.

Study description

Background summary

Rheumatoid arthritis is a common chronic inflammatory immune-mediated disease of joints. If not adequately treated the condition leads to destruction of synovial joints 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.

The introduction of therapeutic strategies that focus on early, intensive treatment with synthetic and biological disease modifying anti-rheumatic drugs (DMARDs) has transformed the treatment of RA. Clinical trials have demonstrated that this approach leads to higher proportions of patients achieving periods of sustained clinical remission. This is associated with improved function and slowing or even prevention of joint damage over time. Indeed, intensive *treat-to-target* strategies in patients with very early RA can subsequently lead to extended periods of drug free remission in a subset of

patients. If the pre-clinical phase of disease could be defined with accuracy, targeting therapy to those at highest risk of developing the more severe form of disease would have the potential to prevent or at the very least delay the onset of RA. Were such an approach to be successful, symptoms and signs of arthritis, disability and the potential risks of unemployment could be prevented, and the development of potentially life-threatening co-morbidities associated with chronic inflammatory diseases, such as cardiovascular disease and infection, substantially reduced.

The combination of the serum ACPA and joint pain (termed arthralgia), in the absence of clinically detectable synovitis, is considered to most accurately define subjects at high risk of progressing to RA. Data from longitudinal observational cohorts indicate that ~ 40% of such subjects progress to clinically apparent arthritis within 18 months. The combination of IgM rheumatoid factor (RF) and high serum ACPA levels define those at highest risk; recent unpublished data indicate that the risk of developing disease in subjects with high titre ACPA in the absence of RF may be comparable to ACPA+RF+ subjects. It follows from this that ACPA+RF+ or ACPA+RF-arthralgia individuals would provide a valid target population for therapeutic intervention aimed at prevention of the syndrome we recognise as RA.

Study objective

The aim of this clinical trial is to evaluate the feasibility, efficacy and acceptability of abatacept therapy in subjects at high risk of developing RA.

Study design

A randomised, placebo controlled clinical trial of abatacept in ACPA+ rheumatoid factor (RF)+ or ACPA+ subjects with arthralgia.
206 subjects will be recruited to the study. (181 in the UK and 25 in the Netherlands). If recruitment is going well it is poosible to recruit more patients. Recruitment is possible till 31-1-2018.

Intervention

Study subjects will be randomised 1:1 to receive weekly injections of abatacept (125mg) or placebo, administered by subcutaneous injection

Study burden and risks

Risk for the patient
* Blood sampling: pain during blood collection, bruising or bleeding after blood collection, minor dizziness and in rare cases infection can occur as a result of blood sampling.
* Medication use: possible side effects of the study medication (see page 27

and 28 of the protocol)

Burden for the patient
* 10 outpatient visits (1 screening, 1 baseline en 8 follow-up visits)
* 52 weeks weekly injection
* 3 x X-rays of hands and feet
* 5x ultrasonography of selected joints (wrists, hands and feet)*
* 1x chest X-ray
* 10x blood and urine collection
* Completion of patient diary
* Completion of 9 questionnaires (6 questionnaires 5x, 1 questionnaire 9x, 1 questionnaire 2x and 1 questionnaire 1x)

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Male or female subjects, aged * 18 years.
- Arthralgia that is considered to be inflammatory in nature.
- ACPA and RF positive, or high titre ACPA.
- Able and willing to give written informed consent and comply with the requirements of the study protocol.

Exclusion criteria

- Clinically apparent arthritis, as assessed by a rheumatologist.
- A history of inflammatory arthritis, as assessed by a rheumatologist.
- History or current use of DMARDs or biologics.
- History of oral or parenteral use of corticosteroids within the last 12 weeks.
- Co-morbidities requiring treatment with immunosuppressive or immune modulating therapy.
- Chronic illnesses that would, in the opinion of the investigator, put the subject at risk.
- Recipients of a live vaccine within 4 weeks of inclusion.
- Pregnant or breastfeeding
- Unable to give informed consent

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped

Start date (anticipated):	23-11-2017
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Orencia
Generic name:	Abatacept
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	28-09-2015
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	30-01-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	04-05-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	16-06-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	07-03-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	29-03-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	12-02-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	26-03-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	28-01-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-003413-18-NL
CCMO	NL53081.058.15
Other	NTR