

# COBRA-light study, an open randomised trial comparing a modified COBRA therapy with the COBRA therapy according to BeSt in early rheumatoid arthritis.

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Are there differences in efficacy, side effects, tolerance and costs in patients with early RA in treatment with COBRA-light compared with COBRA according to BeSt?

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruiting
<b>Health condition type</b>	Autoimmune disorders
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON37036

### Source

ToetsingOnline

### Brief title

COBRA-light study.

### Condition

- Autoimmune disorders
- Joint disorders

### Synonym

Rheumatoid Arthritis

### Research involving

Human

## Sponsors and support

**Primary sponsor:** Vrije Universiteit Medisch Centrum

**Source(s) of monetary or material Support:** Farmaceutische industrie

## Intervention

**Keyword:** COBRA, DAS-guided treatment, early rheumatoid arthritis, Prednisone

## Outcome measures

### Primary outcome

Difference in delta DAS compared at baseline between the both treatment strategies after 6 months.

### Secondary outcome

Secondary parameters:

- Difference in delta DAS compared with baseline between the treatmentstrategies after 12 months
- % patients with ACR 20, 50, 70 response
- Low disease status (DAS 44 <2,4)
- HAQ
- delta Sharp van der Heijde score
- % patients with radiologic remission
- number of patients started with anti-TNF
- patients in clinical remission after six or twelve months will be tested for subclinical synovitis with a PET-scan, echography and MRI.

Tertiary parameters:

- Bone and cartilage

- Cardiovascular
- Gastro-intestinal
- Infections
- Proteomics
- Costs
- Hemostasis
- Glucocorticoid receptor

## Study description

### Background summary

Early treatment of rheumatoid arthritis is important to lower disease activity and suppress radiologic progression. (\*window of opportunity\*)  
 Combination therapy is proven to be superior to monotherapy in the treatment of early RA. The COBRA therapy is effective in several trials, and the positive effect on radiologic progression sustained over time.  
 In a recent trial (BeSt) comparing different treatment strategies the COBRA therapy and initial therapy with Infliximab (a TNF-blocker) were equally effective in improving functional ability and preventing radiographic damage. Apparently most rheumatologists and or patients have resistance in prescribing this therapy. This is because of the possible side effects, the combination of MTX and sulfasalazine, the low dose MTX and the complexity of the medication. For this reason several rheumatologists treat their patients with different combinations of prednisone (usually lower then the 60mg used in the original COBRA-schedule) and different dosages of MTX.  
 It is obvious that it is a step forward if we could demonstrate that the proposed COBRA-light is as effective as the original COBRA-schedule according to BeSt.

### Study objective

Are there differences in efficacy, side effects, tolerance and costs in patients with early RA in treatment with COBRA-light compared with COBRA according to BeSt?

### Study design

Open, randomised trial comparing the efficacy, side effects, tolerance en costs of COBRA-light in patients with early RA in treatment with COBRA according to BeSt.

In the first year patients will be seen frequently in order to follow disease-activity, side effects and cardiovascular parameters. In the first year patients will be seen at 2, 4, 8, 13, 26, 39 en 52 weeks. In the follow-up period of the second year patients will be seen every six months.

## **Intervention**

COBRA light:

Week 1: Pred 30mg  
Week 2: Pred 20mg MTX 10mg  
Week 3: Pred 15mg MTX 10mg  
Week 4: Pred 10mg MTX 10mg  
Week 5: Pred 10mg MTX 17,5mg  
Week 6: Pred 10mg MTX 17,5mg  
Week 7: Pred 10mg MTX 17,5mg  
Week 8: Pred 10mg MTX 17,5mg  
Va wk 9: Pred 7,5mg MTX 25mg

COBRA BeSt:

Week 1: Pred 60mg  
Week 2: Pred 40mg MTX 7.5mg SSZ 500  
Week 3: Pred 25mg MTX 7.5mg SSZ 1000  
Week 4: Pred 20mg MTX 7.5mg SSZ 1500  
Week 5: Pred 15mg MTX 7.5mg SSZ 2000  
Week 6: Pred 10mg MTX 7.5mg SSZ 2000  
Va wk 7: Pred 7,5mg MTX 7.5mg SSZ 2000

At 13, 26, 39, 52, 78 en 104 weeks the disease activity will be measured. If the disease activity measured by DAS(44) is  $> 1,6$  the medication needs to be adjusted.  $\text{DAS}(44) < 1,6$  is regarded al clinical remission: no change of therapy. All patients will receive folic acid 5 mg/day.

## **Study burden and risks**

Normal risks.

The total radiation of the X-rays meets the requirements as obtained in The Netherlands.

## Contacts

### Public

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### Scientific

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adults (18-64 years)

Elderly (65 years and older)

### Inclusion criteria

Active RA according to ACR criteria  
>6 swollen joints or >6 painful joints  
Disease duration < 2jr  
ESR > 28mm  
VAS > 20  
Age > 18 years

### Exclusion criteria

Prior treatment DMARDs (except hydroxychloroquine)  
Insulin-dependent Diabetes mellitus

Uncontrollable non-insuline dependent diabetes mellitus  
Decompensatio cordis class 3-4  
Uncontrollable hypertension  
ALAT/ASAT > 3 times normal values  
Reduced renal function (serum creat > 15mcmol)  
Contra-indications for methotrexate, sulfasalazine or prednisolone  
Indications of probable tuberculosis

## Study design

### Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

### Recruitment

NL	
Recruitment status:	Recruiting
Start date (anticipated):	17-03-2008
Enrollment:	160
Type:	Actual

### Medical products/devices used

Product type:	Medicine
Brand name:	Methotrexate
Generic name:	Methotrexate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Prednisone
Generic name:	glucocorticoid

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Sulphasalazine
Generic name:	Salazopyrine
Registration:	Yes - NL intended use

## Ethics review

Approved WMO	
Date:	08-08-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	06-09-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	12-11-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	20-01-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	16-12-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	12-09-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	28-10-2011
Application type:	Amendment

## 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	EUCTR2007-002976-32-NL
ISRCTN	ISRCTN55552928
CCMO	NL17260.029.07