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 is efficacy, side effects, tolerance en costs in patients with early RA in treatment with COBRA-light compared with COBRA according to BeSt?

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	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

Secundary 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 is efficacy, side effects, tolerance en 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. 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

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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

Uncontrolable non-insuline dependent diabetes mellitus
Decompensatio cordis class 3-4
Uncontrolable hypertension
ALAT/ASAT > 3 times normal values
Reduced renal function (serum creat > 15mcmol)
Contra-indications for methotrexate, sulfasalzine 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

Review commission: METC Amsterdam UMC

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