ISRCTN55552928 https://doi.org/10.1186/ISRCTN55552928

Combination therapy with rheumatoid arthritis (COBRA)-light study, an open randomised trial comparing a modified COBRA therapy with the COBRA therapy according to treatment strategies for rheumatoid arthritis (BeSt) in early rheumatoid arthritis

Submission date
14/03/2008

Recruitment status
No longer recruiting

Registration date
31/03/2008

Overall study status
Completed

Last Edited
21/09/2020

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

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
2007/150; NTR1213

Study information

Scientific Title
Combination therapy with rheumatoid arthritis (COBRA)-light study, an open randomised trial comparing a modified COBRA therapy with the COBRA therapy according to treatment strategies for rheumatoid arthritis (BeSt) in early rheumatoid arthritis

Acronym
COBRA-light

Study objectives
Early, aggressive treatment of rheumatoid arthritis (RA) with disease modifying anti-rheumatic drugs (DMARDs) has been proven to lower disease activity and suppress radiologic progression. Moreover, combination therapy is shown to be superior to monotherapy. The combination therapy with rheumatoid arthritis (COBRA) therapy is effective in several trials, and the positive effect on radiologic progression sustained over time. In a recent trial (BeSt [treatment strategies for Rheumatoid Arthritis] = see http://www.controlled-trials.com/ISRCTN32675862 for more details of this trial) comparing different treatment strategies the COBRA therapy and initial therapy with infliximab (a tumour necrotising factor [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.

Ethics approval required
Old ethics approval format

Ethics approval(s)
METC VUmc-Amsterdam (The Netherlands), 06/09/2007, ref: 2007/150

Study design
Open randomised active-controlled parallel-group multicentre 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
Participants will be randomly allocated to the two treatment strategies, i.e., COBRA or a modified COBRA schedule (COBRA-light):

COBRA:
Prednisone 60 mg/day, methotrexate 7.5 mg/wk and sulphasalazine (SSZ) 500 mg/day. Prednisone will be tapered to 7.5 mg/day in 7 weeks and in 28 weeks tapered to zero. SSZ will be increased to 2000 mg/day in 3 weeks.

COBRA-light:
Prednisone 30 mg/day, methotrexate 10 mg/wk. After 9 weeks prednisone will be tapered till 7.5 mg/day and methotrexate increased to 25 mg/week.

If patients have an active disease at week 26 or 39, anti-TNF therapy will be started in both treatment arms.

For both treatment arms the total treatment duration is one year with a second follow-up year. 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 and 52 weeks. Treatment will be adjusted according to the 44-item disease activity scale (DAS44) score. In the follow-up period of the second year patients will be seen every six months.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Methotrexate, sulphasalazine, prednisolone

Primary outcome measure
Difference in delta DAS compared at baseline between the both treatment strategies after six months.

Secondary outcome measures
1. Difference in delta DAS compared with baseline between the treatment strategies after 12 months
2. % patients with ACR 20, 50, 70 response
3. Low disease status (DAS 44 less than 2.4)
4. Health Assessment Questionnaire (HAQ) - delta Sharp van der Heijde score
5. % patients with radiological remission
6. Number of patients started with anti-TNF

7. Patients in clinical remission after six or twelve months will be tested for subclinical synovitis with a positron emission tomography (PET) scan, ultrasound and magnetic resonance imaging (MRI)

Tertiary outcome:
1. Bone and cartilage metabolism
2. Cardiovascular and endocrine parameters

Overall study start date
01/03/2008

Completion date
01/01/2012

Eligibility

Key inclusion criteria
1. Active RA according to American College of Rheumatology (ACR) criteria
2. Greater than six swollen joints or greater than six painful joints
3. Disease duration less than two years
4. Erythrocyte sedimentation rate (ESR) greater than 28 mm
5. Visual analogue scale (VAS) greater than 20
6. Age greater than 18 years, either sex

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
160

Key exclusion criteria
1. Prior treatment DMARDs (except hydroxychloroquine)
2. Insulin-dependent diabetes mellitus
3. Uncontrollable non-insulin dependent diabetes mellitus
4. Heart failure New York Heart Association (NYHA) class 3 - 4
5. Uncontrollable hypertension
6. Alanine aminotransferase (ALT)/aspartate aminotransferase (AST) greater than three times normal values
7. Reduced renal function (serum creatinine greater than 15 mcmol)
8. Contra-indications for methotrexate, sulphasalazine or prednisolone
9. Indications of probable tuberculosis

Date of first enrolment
01/03/2008

Date of final enrolment
01/01/2012

Locations

Countries of recruitment
Netherlands

Study participating centre
De Boelelaan 1117
Amsterdam
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Sponsor information

Organisation
Vrije University Medical Centre (VUMC) (The Netherlands)

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Sponsor type
Hospital/treatment centre

Website
http://www.vumc.nl

ROR
https://ror.org/00q6h8f30

Funder(s)

Funder type
Industry

Funder Name
Top Institute Pharma (TIPharma) (The Netherlands)

Alternative Name(s)
TI Pharma

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Netherlands

Funder Name
Wyeth Pharmaceuticals B.V. (The Netherlands)

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	01/06/2015		Yes	No
Results article	results	01/09/2016		Yes	No
Results article	results	02/03/2021	21/09/2020	Yes	No