A multi-center, randomized, double-blind, placebo-controlled study to evaluate the safety, preliminary clinical activity and immunogenicity of multiple doses of MOR103 administered intravenously to patients with active rheumatoid arthritis.

Published: 27-08-2009
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Primary objective:To determine the safety and tolerability of multiple doses of MOR103 in patients with active rheumatoid arthritis, at ascending dose levels.Secondary objectives:- to evaluate signs of efficacy of MOR103 in patients with active...

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

Summary

ID

NL-OMON36374

Source
ToetsingOnline

Brief title
MOR103 Rheumatoid Arthritis PoC study

Condition

- Autoimmune disorders

Synonym
RA, rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: MorphoSys AG
Source(s) of monetary or material Support: MorphoSys AG

Intervention

Keyword: arthritis, intravenous, rheumatoid, safety

Outcome measures

Primary outcome

Safety and tolerability of MOR103 as assessed by the safety measures.

Secondary outcome

- Change in the DAS28 score from baseline to Day 29.

- Change in the DAS28 score from basline to Day 57.

- Proportion of patients achieving ACR20, ACR50 and ACR70 response on Day 29

and Day 57.

- EULAR28 responder index on Day 29 and Day 57 (compared to baseline).

- Change in individual components of the ACR core set of measures from baseline

to Day 29 and Day 57.

- Change from baseline to Day 29 and Day 57 of the joint scoring on MRI

according to the Rheumatoid Arthritis MRI scoring system (RAMRIS) for synovitis.

- Change from baseline to Day 29 and Day 57 of the joint scoring on MRI

according to the RAMRIS for bone edema.

- Immunogenicity of MO`R103 (anti-MOR193 antibodies).

- Pharmacokinetics (PK) endpoint: MOR103 serum concentrations and PK parameters

(through levels after each dose, exposure and terminal elimination after the

last dose, accumulation and dose proportionality based on estimated AUCtau).

- Health Assessment Questionnaire (HAQ).

- SF36 health survey.

- FACIT-Fatigue: Functional Assessment of Chronic Illness Trerapy-Fatigue.

Study description

Background summary

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease that affects 0.5% to 1% of the adult population world wide. RA primarily affects the joints and is characterized by chronic inflammation of the synovial tissue, which eventually leads to the destruction of cartilage, bone and ligaments and can cause joint deformity.

MOR103 is a recombinant human synthetic monoclonal antibody (mAb), IgG1 lambda, that specifically binds to human GM-CSF and neutralises the biological function of human GM-CSF by blocking its interaction with its cell surface receptors.

The purpose of this Phase Ib/IIa study is to evaluate the safety, preliminary clinical activity, pharmacokinetics and immunogenicity of multiple doses of MOR103 in patients with active RA, who are not expected to experience any benefit from a single dose of the study drug.

Study objective

Primary objective:
To determine the safety and tolerability of multiple doses of MOR103 in patients with active rheumatoid arthritis, at ascending dose levels.

Secondary objectives:
- to evaluate signs of efficacy of MOR103 in patients with active rheumatoid arthritis.
- to evaluate the pharmacokinetics of multiple doses of MOR103 in patients with active rheumatoid arthritis, at ascending dose levels, and
- to evaluate the potential immunogenicity of MOR103.

Study design

This is a multiple-dose, rising-dose study in three cohorts. Each cohort will be double-blind and randomized. Each patient will receive a total of 4 (four)

doses, one per week on Days 1, 8, 15 and 22. Screening may occur up to 35 days prior to dosing on Day 1 and the last visit is to be performed approximately 90 days after last dosing day (+/- 3 days). Maximum total duration for each individual: ~ 147 days.

Intervention

Selected patients will be randomized to a treatment on Day 1 (baseline). The study drug or placebo will be administered by slow intravenous infusion for one hour.

Other interventions that occur during the study are:
- filling out questionnaires
- physical examination and vital signs (a.o. blood pressure and heart rate)
- blood sampling
- urine sampling
- study medication infusion
- ECG
- MRI
- Pulmonary function testing

Study burden and risks

Each patient is expected to have 12 visits for a total duration of up to 5 months. During the visits, patients will have to undergo physical examination, blood and urine sampling, pulmonary function testing, ECG and MRI-scan. The patients are also asked to fill out questionnaires. Study medication will be administered by infusion, which takes about 1 hour.

The risks of treatment with MOR103 are possibility of allergic reactions such as skin rash, swelling, breathing problems and lower blood pressure. Additionally, the drug may provoke an immune response, which may cause the patient to feel feverish or flu-like.

No adverse effects and no indications of the onset of an immune response were observed in animal tests involving doses equivalent to the ones which will be administered in this study. Theoretically. there is a possibility that the drug may cause transient lung abnormalities in persons who are susceptible to such conditions. In addition, there is a slight chance that the immune system may be (partially) suppressed, which may make the patient more prone to infections.

Different single doses of MOR103 up to 3 mg/kg were administered in a Phase I study with 63 human subjects. The most common unwanted side effects that were mostly mild were headache and nasopharyngitis (inflammation of the nose and the throat), dizziness and cough. Additionally, one subject experienced pneumonia and as a consequence of the pneumonia, a septic shock as a serious side effect.

Although a possible relationship to MOR103 administration cannot be excluded, this possibility was deemed to be low, because of other predisposing factors.

The MRI measurements in this study require the use of contrast agents that contain the substance gadolinium. Some of these gadolinium-containing contrast agents are suspected to be a risk for developing nephrogenic systemic fibrosis, a rare skin disease. If the patient has normally functioning kidneys, this possibility is very low.

For more details, see protocol page 29 and 30.

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 and female patients aged 18 years or older.
- Body Mass Index between 19.0 and 30.0 kg/m2 (extremes included)
- Diagnosis of rheumatoid arthritis (RA), according to the revised criteria of the American College of Rheumatology (ACR), 1987.
- Active disease defined as: 1. at least 3 swollen and 3 tender joints with at least 1 swollen joint involvement of the hand excluding the proximal interphalangeal (PIP) joint (using the DAS28 joint count); 2. Elevated CRP level (>= 10 mg/l); 3. Disease Activity Score "DAS28" <= 5.1.
- Functional status class I, II or III classified according to ACR 1991 revised criteria.
- Post-menopausal (for at lesat two years) or surgically sterile female patients.
- Male patients must be willing to use an effective contracteption method during the study and for at least 2 months following the completion/discontinuation of the study.
- Negative purified protein derivate (PPD) tuberculin skin test reaction or a negative tuberculosis enzyme-linked immuno sorbent assay (ELISA) test, according to the local standard practices.

Exclusion criteria

- If patients have been previously treated with anti-tumor necrosis factor alpha (TNF-α) or anti interleukin 1 (IL-1) therapy (or other biological therapy), immunosuppressive agents such as ciclosporin, mycophenolate mofetil or tacrolimus and do not comply with the following minimal washout periods prior to the first dosing of the study medication: 1. 1 month for etanercept, cilcosporin, mycophenolate mofetil, tacrolimus; 2. 2 months for adalimumab and; 3. 3 months for anakinra, infliximab and abatacept.
- Patients previously treated with rituximab.
- History of therapy with a cell depleting agent(s), including investigational agents (Campath, anti-CD3, anti-CD4, anti-CD5, anti-CD11a, anti-CD19, anti-CD22, anti-B Cell (Lymphocyte) Activating Factor antibodies [anti-Blys/BAFF]).
- Any therapy with human, chimeric or murine antibodies (other than above) or any experimental therapy within 3 months or 5 half-lives (whichever is longer) prior to screening.
- In case a patient has been discontinued from other DMARDs due to toxicity or for lack of efficacy, the time since last dose should be at least 1 month and the effects of that agent should have dissipated as indicated by the recognized duration of effect (e.g., hydroxychloroquine, sulfasalazine), or standard washout procedure (cholestyramine for leflunomide).
- Patients who received systemic steroids for other conditions (e.g. asthma), patients who received epidural steroid injections, patients who received intra-articular or systemic corticosteroid injections that were required for treatment of acute RA flare within 4 weeks before before baseline, and patients who received intra-articular injections for other conditions such as shoulder bursitis within 4 weeks.
- joint surgery within 2 months before screening.

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):	08-06-2010
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MOR103
Generic name:	MOR103

Ethics review

Approved WMO Date:	27-08-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	10-02-2010
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO	

Date:	26-04-2010
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	30-06-2010
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	14-10-2010
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	24-01-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	26-04-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	05-09-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	19-10-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	19-12-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	21-12-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO	

Date:	23-01-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2007-006129-29-NL
CCMO	NL28730.058.09