A Randomized, Double-Blind, Placebo-Controlled, Multiple Dose Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Subcutaneous AMG 108 in Subjects with Rheumatoid Arthritis

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

Summary

ID

NL-OMON30331

Source
ToetsingOnline

Brief title
Clinical study with active RA patients to evaluate the effect of AMG 108

Condition

- Autoimmune disorders
- Joint disorders

Synonym
Rheumatoid Arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Amgen financiert het onderzoek volledig

Intervention

Keyword: Cytokines, Il-1beta antagonist, Rheumatoid Arthritis, Treatment

Outcome measures

Primary outcome

The primary efficacy endpoint is the ACR20 response at Week 16.

Secondary outcome

- ACR50 and ACR70 responses at Week 16

- DAS28 score and change in DAS28 score from baseline (EULAR28 response) at

week 16

- ACRn and AUC ACRn at week 16

Study description

Background summary

Rheumatoid Arthritis (RA) is a chronic, systemic, autoimmune, inflammatory arthropathy of unknown etiology. RA is characterized by progressive destruction of the affected joints, deformity, disability and premature death.
Current treatments for RA include palliative, nonspecific anti-inflammatory agents (eg, NSAIDs and corticosteroids) and DMARDs such as MTX.
Current anti-cytokine therapies show promising results, but some patients respond subs optimally develop intolerance to the drugs or become refractory to therapy. Because IL-I may not be sufficiently antagonized by ankinra, anti-Il1 therapy remains an incompletely explored treatment option for inflammatory diseases. Results for anakinra show clear indications of efficacy with an excellent safety profile, but higher levels of Il-1 blockage may result in

benefits over existing therapies.

Study objective

The primary objective for this study is to determine whether AMG 108 at a monthly dose of 250 mg SC or less in combination with MTX demonstrates a higher frequency in clinical response (ACR20) than that observed with placebo (MTX alone) in RA subjects at Week 16 of therapy.

Study design

The study will be a double-blind, placebo-controlled, and parallel dosing trial of AMG 108 at 3 doses (50, 125 and 250 mg sub coetaneous) administered Q4W X 4 in RA subjects with active disease continuing on stable MTX therapy 10 to 25 mg weekly, and of all other DMARDs prior to randomization. All subjects will be biologic-naïve meaning they cannot have ever been on a commercial or experimental biologic therapy for RA. Randomization will be equal across all 4-treatment arms.

Intervention

After completing all screening procedures and meeting all eligibility criteria, subjects will be randomized equally to receive either AMG 108 (50mg, 125 mg, or 250 mg) or placebo SC administration once every 4 weeks for a total of 4 doses. Randomization assignment to the treatment arms will be based on a computer-generated randomization schedule prepared by Amgen before the start of the study

Study burden and risks

AMG 108 is an antibody that inhibits Interleukin-one (IL-1), a naturally occurring substance in the body. In theory, a decrease in IL-1 levels may reduce the body*s inflammatory response. Since studies in humans with AMG108 began, approximately 417 subjects have been enrolled in Amgen sponsored trials, a limited number, and therefore the potential adverse effects are not completely known. In an AMG 108 clinical study, subjects with osteoarthritis have reported the following commonly (1% to 10%) occurring adverse events: arthralgia, headache, painful joints and back pain.
Lower than normal levels, or counts, of a certain type of white blood cells (neutrophils) have been observed in a subset of patients in AMG 108 studies. The significance of this decrease in neutrophils is currently unknown. Changes in neutrophil counts can be due to multiple causes. When neutrophil counts become very low the body*s ability to fight certain infections may be weakened. Infection leading to death could result. This decrease in neutrophils was temporary and subjects* levels returned to normal ranges, generally within a

few weeks.

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

Subjects must be diagnosed with RA as determined by meeting 1987 American College of Rheumatology ACR classification criteria.
Active RA defined as > 6 swollen joint and >6 tender / painful joints and at least one of the following: ESR . 28 mm/hr, CRP >2.0 mg / dl, or duration of morning stiffness > 45 minutes at time of screening
Sable use of MTX at 10-25 mg weekly
See also page 30-32

Exclusion criteria

Previous receipt of commercial or experimental biologic therapies.
Uncontrolled, clinically significant systemic disease other than RA such as diabetes mellitus, cadiovascular disease or hupertension
Presence of a serious infection, defined as requiring hospitalization or recurretn, acute or chronic infections within 8 weeks 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:	Pending
Start date (anticipated):	01-06-2006
Enrollment:	30
Type:	Anticipated

Ethics review

Approved WMO Date:	19-05-2006
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-10-2006

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-10-2007
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	EUCTR2005-003558-83-NL
CCMO	NL11287.018.06