A Long-term Assessment of Safety and Physical Function with AMG 108 Subcutaneous Monthly Treatment in Subjects with Rheumatoid Arthritis

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Primary Objective: The primary objective of the study is to assess long-term safety of AMG 108 (125 mg, 250 mg) SC in subjects with RA previously enrolled in study 20050168.Secondary Objective(s): The secondary objectives of the study are:* To…

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

Summary

ID

NL-OMON30262

Source
ToetsingOnline

Brief title
AMG108 20060119

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 financieert het onderzoek volledig

Intervention

Keyword: AMG108, Longterm safety, Rheumatoid Arthritis

Outcome measures

Primary outcome

(S)AEs and (S)IEs (infectious events), reaction at injection site, safety

laboratory values, infections in patients with <1.5 x 103/µL neutrophils,

opportunistic infections, malignancies, antibodys against AMG 108.

Secondary outcome

Mental and physical sections of SF-36, HAQ-DI score, EQ-5D score, Work

Productivity and Activity Impairment (WPAI) questionnaire, ACR20 response:

changes compared to baseline. ACR20 response in patients with positive or

negative antibody testing against AMG 108. AMG 108 through concentrations.

Study description

Background summary

RA is a chronic, systemic, autoimmune, inflammatory arthropathy of unknown etiology. RA is characterized by progressive destruction of the affected joints, deformity, disability. Symptoms include joint stiffness, pain and swelling, fatigue, weakness, and psychologic depression. RA occurs worldwide in approximately 1% of adults of all races. Disease onset occurs most often between the ages 20 and 60 years, with peak occurrences at 35 to 40 years. RA has a higher prevalence in women than men. Current treatments for RA include NSAIDs and corticosteroids and DMARDs such as MTX. In addition, improved safety and efficacy profiles have been achieved with biologic response modifiers (BRMs) that selectively inhibit cytokines that are thought to be central to the pathogenesis of RA, including tumor necrosis factor (TNF) antagonists such as

etanercept and infliximab, and interleukin-1 (IL-1) antagonists such as anakinra. Current anti-cytokine therapies show promising results, but some patients respond suboptimally, develop intolerance to the drugs, or become refractory to therapy. Because IL-1 may not be sufficiently antagonized by anakinra, anti-IL-1 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.
AMG 108 is a fully human immunoglobulin type G2 (IgG2) monoclonal antibody and inhibits IL-1 signaling by targeting the IL-1 type I receptor (IL-1RI).
The primary aim of this study is longterm safety of AMG 108 in RA in the highest doses tested in the preceeding study 20050168. It is expected that these doses will give sufficient IL-1 suppression at the end of the 1 month dosage interval. AMG 108 was sofar well tolerated and seems to have a wide safety margin. All eligible patients have participated in the study 20050168.

Study objective

Primary Objective: The primary objective of the study is to assess long-term safety of AMG 108 (125 mg, 250 mg) SC in subjects with RA previously enrolled in study 20050168.

Secondary Objective(s): The secondary objectives of the study are:
* To assess impact of concomitant immunosuppressives on long-term safety profile of AMG 108
* To assess impact of comorbidity on adverse event (AE) profile of AMG 108
* To determine whether long-term use of AMG 108 improves function in subjects with RA
* To assess the change in mental and physical component summaries (MCS & PCS) and each of the 8 domain scores of SF-36 from baseline to weeks 24, 48, 96, 144 and EOS
* To determine effect of long- term use of AMG 108 on work productivity
* To evaluate long-term pharmacokinetics (trough levels) of AMG 108
* To assess the clinical effect of AMG 108 as determined by ACR20 response at week 24, 48, 96, 144 and EOS
* To determine whether immunogenicity of AMG 108 affects efficacy and safety as determined by frequency, subject incidence and time-to-onset of cardiovascular safety events and changes in biomarkers related to cardiovascular disease

Exploratory Objective(s):
* To assess the clinical effect of AMG 108 as determined by American College of
* Rheumatology (ACR) 50 and 70 response, ACRn and AUC ACRn, individual components of ACR response, morning stiffness and change in DAS28 from baseline (EULAR response) at weeks 24, 48, 96, 144 and EOS
* To assess cardiovascular outcomes in RA subjects treated with AMG 108 as determined by frequency, subject incidence and time-to-onset of cardiovascular

safety events and changes in biomarkers related to cardiovascular disease

Study design

This is a long-term extension study to evaluate the safety of AMG 108 at 125 mg and 250 mg SC monthly in subjects with RA who were eligible for and completed 24 weeks of participation in study 20050168. The study will be blinded to treatment doses until the study 20050168 is unblinded. An interim analysis for this study will be performed following the unblinding of study 20050168. All subjects will be on weekly MTX SC or PO at entry into this study unless discontinued for toxicity reasons in study 20050168. Subjects who met LOE criteria at or after week 12 in study 20050168 may be on additional therapies for RA at baseline in this study.
An external data monitoring committee (DMC) will monitor the safety of study participants throughout the study duration.

Intervention

Administration of AMG 108.

Study burden and risks

Written informed consent must be obtained from all subjects before screening. Upon completing all screening assessments and meeting all eligibility criteria, subjects will be enrolled and receive either 125mg or 250 mg AMG 108 Q4W for approximately 48 months or until an administrative decision is made to end the study.
The following procedures will be performed per the schedule outlined in Appendix A: pregnancy test (at screening only), physical exam, vital signs, blood draw for serum chemistry, hematology, PK, AMG 108 antibody assay, concomitant medication and AE recording, HAQ, EQ-5D, SF-36, SGA, Pain VAS, Morning Stiffness, WPAI questionnaires, CRP, ESR, PGA and joint assessments (tender and swollen joint counts). Once all procedures are completed, the subject will receive the dose of IP.

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 have met all inclusion criteria and none of the exclusion criteria for study 20050168, were randomized and completed 24 weeks of the study.
* Subjects must receive their first dose of IP within 18 days from their Week 24 visit in study 20050168.
* Signed informed consent

Exclusion criteria

* Uncontrolled or Significant concurrent medical events, in the opinion of the investigator, including:
- Asthma
- Malignancy
- Liver disease
- Renal disease
- Hematologic abnormality
- Diabetes mellitus
- Cardiovascular disease
- Hypertension
- Chronic inflammatory disease or connective disease other than RA or secondary Sjogren*s syndrome
- Infections (CTC grade 3) lasting > 2 consecutive weeks and/or not responding to treatment

in study 20050168
* Pregnant or nursing
* Sexually active subjects and their partners who are of childbearing potential (ie, neither surgically sterile nor postmenopausal) and not using adequate contraception
* Any physical and/or psychiatric condition that, in the opinion of the investigator, compromises the ability of the subject to give written informed consent
* Any condition or disorder that, in the opinion of the investigator, would interfere with compliance with study procedures
* Active substance abuse
* Requiring or having a condition that, in the opinion of the investigator, may be expected to require strong narcotic analgesics (except hydrocodone, codeine, dextropropoxyphene, propoxyphene, or oxycodone) or morphine derived medication for analgesic relief at screening
* Inability or unwillingness to self-administer (or by designated person) subcutaneous
* injections at home

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2006
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	AMG108

Generic name:	AMG108

Ethics review

Approved WMO Date:	02-10-2006
Application type:	First submission
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	EUCTR2006-003698-29-NL
CCMO	NL14618.018.06