A Randomized, Double-blind, Placebo-controlled Phase 2 Study to Determine the Safety and Efficacy of AMG 827 in Subjects with Inadequately Controlled Asthma

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Primary Objective: The primary objective is to determine if AMG 827 is effective compared to placebo as measured by change in Asthma Control Questionnaire (ACQ) composite scores from baseline to week 12. Secondary Objectives: Evaluate the efficacy...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON34185

Source
ToetsingOnline

Brief title
Phase 2 with AMG 827 with Inadequately Controlled Asthma

Condition

- Bronchial disorders (excl neoplasms)

Synonym
CARA, Chronic infection airways

Research involving
Human

Sponsors and support

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

Intervention

Keyword: AMG 827, Inadequately Controlled Asthma, Phase 2

Outcome measures

Primary outcome

• Change in ACQ composite scores from baseline to week 12.

Secondary outcome

• Change in FEV1 pre- and post-bronchodilator treatment from baseline to week 12

• Change in am and pm peak expiratory flow (PEFR) from baseline to week 12

• Change in frequency of rescue short-acting β-agonist (SABA) use from baseline

to week 12

• Change in daily total asthma symptoms (aggregate/night and individual) from

baseline to week 12

• Change in AQLQ score from baseline to week 12

• Proportion of symptom-free days from baseline to week 12

• Pharmacokinetic measures

Study description

Background summary

1.4 AMG 827 Background
AMG 827 is a fully human anti-interleukin-17 receptor (IL-17R) monoclonal antibody that selectively targets human IL-17R and antagonizes the IL-17 pathway. It binds with high affinity to human IL-17R and blocks the biological activity of IL-17 (IL-17A), IL-17F and IL-25 (IL-17E).

1.5 Clinical Hypotheses
AMG 827 is effective in improving asthma control (measured by the ACQ composite score) as assessed by a dose response relationship after 12 weeks of treatment in subjects with asthma who are inadequately controlled despite current therapies.
2. EXPERIMENTAL PLAN
2.1 Study Design
This is a randomized, placebo-controlled, double blind, dose-ranging study in subjects with inadequately controlled asthma. The study is designed to evaluate the safety, tolerability and clinical effect of AMG 827 with every other week (QOW) dosing for 12 weeks.
Approximately 300 subjects (75 subjects per treatment arm) will be randomized in a 1:1:1:1 ratio to receive
• 140 mg QOW (+ additional dose at week 1) SC AMG 827
• 210 mg QOW (+ additional dose at week 1) SC AMG 827
• 280 mg QOW (+ additional dose at week 1) SC AMG 827
• Placebo
Randomization will be stratified based on atopy status and ICS dose (< 500 µg and >= 500 µg fluticasone or equivalent) at baseline. Subjects will be defined as atopic if they are positive to skin prick (wheal diameter >= 3 mm and documented negative control) or RadioAllergoSorbent Test (RAST) to any allergen during the screening period or within the last 12 months before screening.
Subjects will undergo screening, followed by a 4-week run-in period. Subjects who require a washout of certain specified asthma medications (see exclusion criteria in Section 4.2 of the protocol) will wash-out, after the informed consent has been obtained and all screening procedures have been performed (see Section 7.2.1 of the protocol) but before the run-in period. All subjects must be receiving a total daily ICS dose of 200-1000 µg/day of fluticasone (or equivalent) and must be on a stable dose for >= 30 days before screening. The dose of ICS will remain the same from screening through the end of study (EOS). Subjects who wash out from a LABA will remain on the equivalent dose of ICS that was contained in the combination product. The run-in period will ensure stable baseline values and accustom subjects to the assessments before study start. The primary endpoint will be obtained after 12 weeks of treatment. Durability of effect and safety will be monitored during a 4-week follow-up period after treatment cessation.

Study objective

Primary Objective:
The primary objective is to determine if AMG 827 is effective compared to placebo as measured by change in Asthma Control Questionnaire (ACQ) composite scores from baseline to week 12.

Secondary Objectives:
Evaluate the efficacy of AMG 827 as measured by:
• Pre- and post-bronchodilator FEV1 (forced expiratory volume in 1 second),

• AM and PM peak expiratory flow rate (PEFR),
• Use of rescue short-acting β-agonist,
• Daily symptoms (aggregate/night and individual symptoms; and symptom-free days),
• Asthma quality life of questionnaire (AQLQ).
Evaluate the pharmacokinetics of AMG 827

Study design

This is a randomized, double-blind, placebo controlled dose ranging study in subjects with inadequately controlled asthma where subjects will receive investigational product (IP) for 12 weeks. This study will be conducted in approximately 60 centers located globally.
Approximately 300 subjects (75 subjects per treatment arm) will be randomly assigned in a 1:1:1:1 ratio to receive 140, 210, 280 mg AMG 827 or placebo every other week (QOW) with an additional dose at week 1. Any medication washout will take place after informed consent and prior to the run-in period. All subjects must be receiving a total daily inhaled corticosteroid (ICS) dose of 200-1000 µg/day of fluticasone (or equivalent) and must be on a stable dose for >= 30 days before screening. The dose of ICS will remain the same from screening through the end of study (EOS).

Intervention

Amgen Investigational Product Dosage and Administration: Subjects will receive AMG 827 140 mg, 210 mg or 280 mg, or matching placebo at day 1, week 1, 2, 4, 6, 8, and 10. IP will be administered as 4 subcutaneous (SC) injections for each dose.
Control Group: Placebo

Study burden and risks

After screening, the subject will have to return to the clinic for 12 times. The estimated average duration of every visit is approximately 2 hours. Subjects participating in the PK sub study (60 globally), will have to return to the clinic 3 times (shorly) for blood collections (in total 5 additional blood colletions). Subjects in the biomarker sub-study will be have their blood drawn as part of the baseline, week 4 and week 12 or early termination visits. Approximately 100 subjects (globally) will be asked to participate in the sputum sub study. That is an inconvenient procedure. However, subjects are able to participate in the study, even if they are not willing to particpate in any of the 4 sub studies. For the PPD test, a seperate sc injection will be necessary. If a quantiferon test is necessary, one additional blood collection will be required.
In the event that a subject is found to have a positive test for neutralizing antibodies at the EOS time point, the treating physician will be notified by

Amgen. The physician should discuss with the subject to return to the clinic for follow-up seroreactivity sampling if deemed necessary. Suggested sampling is every 3 to 6 months until the subject is negative for neutralizing antibodies, or until the physician determines testing is no longer necessary. This will mean additional blood sample collection (approximately 5 mL per blood collection).
If the ANC from the prior visit was < 1500 cells/mm3 and the subject is at week 1 visit or the week 2 visit or beyond, the scheduled dose must be hold and the subject should return for a repeat CBC such that the data will be availble for repeat CBC to determine whether the subject can continue receive IP.
Sc administration of AMG 827 or placebo, blood collections and the sc injection for the PPD test, have some risks. However, these procedures will only be done by trained and experienced staff; risks will be maintained at a minimum.
The subject may experience side effects, mentioned in the answer of question E9; in addition, side effects may occur which are currenly unknown. Patients receiving AMG 827 may benefit the treatment. AMG 827 might increase astma control and other parameters like lung function.

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

4.1.1 Men or women 18 to 65 years of age at the time of screening
4.1.2 Percent of predicted FEV1 >= 50% and <= 80% at screening and baseline visits
4.1.3 At least 12% reversibility over pre-bronchodilator FEV1 with SABA inhalation (up to 8 puffs) or nebulized equivalent (up to 2 treatments with 2.5 mg albuterol), demonstrated in the office during screening
4.1.4 Inhaled corticosteroid (ICS) >= 200 and <= 1000 µg/day fluticasone or equivalent. Stable ICS dose for >= 30 days before screening and must have used ICS for at least the last 3 consecutive months before screening. The ICS dose is expected to remain the same from screening through the end of study.
4.1.5 Ongoing asthma symptoms with ACQ composite score >= 1.5 points at screening and baseline
4.1.6 If receiving allergen immunotherapy, a stable dose for > 3 months before screening and anticipated to remain stable for the duration of the study
4.1.7 Nonsmoker or ex-smoker with < 10 pack-years (eg, 1 pack per day for 10 years) who stopped >= 1 year ago
4.1.8 Subject has a negative purified protein derivative (tuberculin) skin test within 6 weeks prior to randomization and has not been exposed to a person with active tuberculosis within 6 months of screening. Subjects with a known positive tuberculin skin test are allowed if:
• They have completed treatment with appropriate chemoprophylaxis,
or
• They have a history of Bacillus Calmette-Guerin vaccination with a negative Quantiferon test
4.1.9 Subject or subject*s legally acceptable representative has provided informed consent, before any study specific procedure

Exclusion criteria

Disease specific criteria
4.2.1 Acute asthma exacerbation requiring emergency room treatment or hospitalization within 2 months of screening or any exacerbation between screening and baseline
4.2.2 Respiratory infection within 4 weeks of screening visit or 1 week of baseline visit
4.2.3 Any evidence of active infection at screening, during the run-in period or at the baseline visit requiring systemic antibiotics
4.2.4 History of endotracheal intubation for asthma-related exacerbation within 3 years of screening
4.2.5 History of chronic obstructive pulmonary disease or other chronic pulmonary condition

other than asthma
4.2.6 Current diagnosis of sleep apnea with ongoing symptoms or requiring continuous positive airway pressure
4.2.7 History of aspirin-sensitive asthma
Other medical conditions
4.2.8 Any uncontrolled or clinically significant systemic disease (eg, uncontrolled diabetes, liver disease)
4.2.9 Any finding on the screening ECG that in the opinion of the investigator requires further cardiovascular evaluation
4.2.10 Poorly controlled hypertension defined as resting blood pressure > 150/90 mmHg (assessed on 2 separate occasions during the screening period)
4.2.11 Malignancy (other than resected cutaneous basal or cutaneous squamous cell carcinoma, or treated in situ cervical cancer considered cured) within 5 years of screening visit (if a malignancy occurred > 5 years ago, subject is eligible with documentation of disease-free state since treatment)
4.2.12 Known to have tested positive for hepatitis B virus surface antigen, hepatitis C virus antibody or human immunodeficiency virus
Washouts and proscribed medications
4.2.13 Systemic corticosteroids within 6 weeks before screening visit
4.2.14 Received long-acting β-agonist (LABA), theophylline, inhaled anticholinergics, oral β-2 agonists, or cromolyn therapeutics within 1 week of first run-in visit
4.2.15 Leukotriene antagonists within 2 weeks before first run-in visit
4.2.16 5-lipoxygenase inhibitors for asthma (eg, Zyflo®) within 1 week before first run-in visit
4.2.17 Previous receipt of AMG 827
4.2.18 Current receipt of any experimental or commercial biologic agent at screening
4.2.19 Xolair® within 2 months before screening visit
4.2.20 Previous receipt of an experimental or commercially available biologic agent will require a washout period of 5 drug half-lives before screening
4.2.21 Received live attenuated vaccine within 4 weeks before screening
Laboratory abnormalities
4.2.22 Elevated aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >= 1.5 x the upper limit of normal at screening
4.2.23 Creatinine clearance < 60 mL/min (based on the Cockroft-Gault formula, calculated by the central laboratory)
4.2.24 Bilirubin >=1.5 x the upper limit of normal at screening
4.2.25 Hemoglobin < 11 g/dL
4.2.26 Platelet count < 125,000/mm3
4.2.27 White blood cell count < 3,000 cells/mm3
4.2.28 Absolute neutrophil count (ANC) < 2000 cells/mm3
4.2.29 Laboratory abnormality, which, in the opinion of the investigator, will prevent the subject from completing the study or will interfere with the interpretation of the study results
General
4.2.30 Female subject who is not willing to use highly effective birth control for the duration of the study including the follow-up period (except women >= 2 years post menopausal or surgically sterile).
4.2.31 Subject is pregnant or breast feeding, or planning to become pregnant while enrolled in the study, up to the subject*s last study visit including the follow-up period.

4.2.32 Subject currently is enrolled in or has not yet completed >= 30 days since ending other investigational device or drug study(s), or subject is receiving other investigational agent(s) 30 days before screening
4.2.33 Other investigational procedures are excluded
4.2.34 Any planned surgery (eg, elective cosmetic surgery) during the course of this study
4.2.35 Subject has known or suspected sensitivity to mammalian cell-derived (ie, from Chinese hamster ovary) products or any components of the study drug
4.2.36 Presence of any condition that could, in the opinion of the investigator, compromise the subject*s ability to participate in the study, such as history of substance abuse, alcoholism, or a psychiatric condition
4.2.37 Subject will not be available for protocol-required study visits, to the best of the subject and investigator*s knowledge.
4.2.38 Subject has any kind of disorder that, in the opinion of the investigator, may compromise the ability of the subject to give written informed consent and/or to comply with all required study procedures.

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):	19-08-2011
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Nog niet beschikbaar
Generic name:	Nog niet beschikbaar

Ethics review

Approved WMO Date:	29-10-2010
Application type:	First submission
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	19-01-2011
Application type:	First submission
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	20-04-2011
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	10-05-2011
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	11-05-2011
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	24-05-2011
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	30-05-2011
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	15-06-2011
Application type:	Amendment

Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	29-09-2011
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	10-10-2011
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)

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	EUCTR2010-019543-19-NL
ClinicalTrials.gov	NCT01199289
CCMO	NL34213.048.10