A Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety, Tolerability, and Efficacy of AMG 827 in Subjects with Moderate to Severe Crohn's Disease

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Evaluate the Safety, Tolerability, and Efficacy of AMG 827 in Subjects with Moderate to Severe Crohn*s Disease.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON36256

Source
ToetsingOnline

Brief title
AMG 827 in Subjects with Moderate to Severe Crohn's Disease

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn□s disease, M. Crohn

Research involving
Human

Sponsors and support

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

Intervention

Keyword: AMG 827, Crohn's Disease

Outcome measures

Primary outcome

To evaluate the efficacy of AMG 827 compared with placebo as measured by the proportion of subjects achieving Crohn*s Disease Activity Index (CDAI) remission (* 150) at week 6.

Secondary outcome

* To evaluate the efficacy of AMG 827 as measured by the proportion of subjects with a CDAI response (reduction from baseline of * 100) at week 6

* To evaluate improvement from baseline in CDAI at week 6

* To evaluate the short term safety profile of AMG 827 in subjects with Crohn*s disease

* To characterize the pharmacokinetics (PK) of AMG 827 in subjects with Crohn*s disease

Study description

Background summary

Crohn*s disease is a chronic relapsing, remitting inflammatory disease of the gastrointestinal tract although some patients may have continuously active disease. The cause of Crohn*s disease remains unknown.
Crohn*s disease affects the gastrointestinal tract discontinuously from mouth to anus, but most commonly the disease is located both in the ileum and colon,

small bowel only, or colon only. Crohn*s occurs in all age groups with a higher incidence in the younger population; there is no marked sex difference. The incidence of Crohn*s disease in adults has been reported as up to approximately 8 per 100,000 person-years, with the highest reported adult-onset incidences in Spain (Saro Gismera et al, 2000), Sweden (Lapidus, 2006), and the United Kingdom (García Rodríguez et al, 2005).
Studies have found increased mortality in patients with Crohn*s disease (Duricova et al, 2009), as well as a negative impact to their daily life.
Medical therapy used in clinical practice includes aminosalicylates, corticosteroids, immunomodulators, antibiotics, and biologic therapies with nutritional support also having a role (Lichtenstein et al, 2009). When medical treatment is unsuccessful or with certain complications, surgery is indicated. Due to therapeutic failures and serious side effects of present therapies, alternatives are needed.

AMG 827 is a fully human IgG2 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).

Study objective

Evaluate the Safety, Tolerability, and Efficacy of AMG 827 in Subjects with Moderate to Severe Crohn*s Disease.

Study design

This is a randomized, double-blind, placebo-controlled study to evaluate the efficacy of AMG 827 (at intravenous [IV] infusion doses of 210, 350 or 700 mg) compared with placebo as measured by the proportion of subjects in remission (CDAI * 150) at week 6. After completing all screening assessments and meeting all eligibility criteria, subjects will be randomized in a 1:1:1:1 ratio to receive AMG 827 210 mg, 350 mg, or 700 mg, or placebo IV infusion at baseline and week 4. Randomization will be stratified to assure treatment balance in the PK substudy.
Subjects will be followed through week 12 for assessments of safety and sustainability of response.

Intervention

Subjects will receive AMG 827 210 mg, 350 mg or 700 mg, or a matching placebo, at day 1 and week 4 (randomized in a 1:1:1:1 ratio at the baseline visit). Investigational Product will be administered as an IV infusion over at least 30 minutes.

Study burden and risks

After screening, the patient should visit the hospital for another 6 times. The average estimated duration of every visit is 2 hours. Subjects participating in the PK sub study (60 from the 216 globally) will visit the site 3 times in addition (very short) visits for blood collections. If at week 2 ANC is <1500 cells uL, the subject does need to do an extra visit for an additional blood collection. The riscs for the participating patient are minimal. The infusion with AMG 827 or placebo and the blood collections may involve some risks. But, administration of medication and blood collections will only be done by trained and experienced personnel; the involved risks will there fore be minimized. If a subject is PPD positive and there is no thorax X-ray available witiin 3 months before first IP administration, a thorax X-ray does need to be done. However, the radiation exposure will be very minimal (0.1 mSv). AMG 827 is an experimental drug. The patient could may experience side effects as mentioned in the answer to question E9; in addition, the patient also may experience side effects which are unknow at this moment. The patients recieving AMG 827 may benefit from the treatment, which may result in a (earlier) remission.

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

4.1.2 Subject is * 18 and * 65 years of age at time of screening.
4.1.3 Subject has diagnosed ileal, ileo-colonic, or colonic Crohn*s disease for a minimum of 6 months prior to initiating IP.
4.1.4 Subject has moderately to severely active Crohn*s disease, as defined by a CDAI score * 250 and * 450 at baseline.
4.1.5 Subject has evidence of active inflammation, as demonstrated by at least one of the following:
* Endoscopic evidence of inflammation within 12 weeks prior to initiating IP
* Elevated C-Reactive Protein (CRP) at screening (> ULN as set by central laboratory)
* Fecal calprotectin assay indicative of active inflammation at screening (> ULN as set by central laboratory).
4.1.6 Subjects can be receiving the following treatments but the same dose must be maintained as specified below:
* 5-aminosalicylates, if stable dosage for * 2 weeks prior to initiating IP
* Prednisone or equivalent up to 20 mg/day, if stable dosage for * 2 weeks prior to initiating IP
* Budesonide (up to 6 mg/day), if stable dosage for * 2 weeks prior to initiating IP
* Azathioprine, if stable dosage for * 8 weeks prior to initiating IP
* 6-mercaptopurine, if stable dosages for * 8 weeks prior to initiating IP
* Methotrexate, if stable dosages for * 8 weeks prior to initiating IP
* Oral antibiotics for Crohn*s disease, if stable dosage for * 2 weeks prior to initiating IP.
4.1.7 Subject has a negative test at screening for hepatitis B surface antigen, hepatitis C antibody, and human immunodeficiency virus.
4.1.9 Subject has a negative purified protein derivative (PPD; tuberculin) test within 4 weeks before initiating IP. Tuberculin skin tests are considered positive when they have * 5 mm of induration at 48 to 72 hours after test is placed. Subjects with a positive tuberculin skin test (if * 14 mm of induration) are allowed if they meet all of the following criteria:
* a history of Bacillus Calmette-Guerin vaccination with a negative Quantiferon test in the past year
* no symptoms per tuberculosis worksheet
* a negative chest radiograph
Note: subjects with a history of a positive PPD may refuse a repeat PPD and be allowed to continue screening for tuberculosis as above, if there is a history of Bacillus Calmette-Guerin vaccination

Exclusion criteria

Disease-specific criteria

4.2.1 Subject has short bowel syndrome (defined as requiring oral or parenteral supplemental or total nutrition in order to maintain stable body weight, or more than 100 cm of small bowel resected).
4.2.2 Subject has had stricture with obstructive symptoms within 3 months prior to IP initiation.
4.2.3 Subject underwent bowel surgery within 12 weeks prior to IP initiation.
4.2.4 Subject has an ileostomy and/or colostomy.
4.2.5 Subject has any gastric or intestinal pouch
4.2.6 Subject has ulcerative colitis.
4.2.7 Subject has evidence of an infected abscess.
4.2.8 Subject has bowel perforation or evidence of noninflammatory obstruction during the 6 months prior to IP initiation.
4.2.9 Subject has stool positive for C. Difficile toxin at screening.
Other medical conditions.
4.2.14 Subject has one or more significant concurrent medical conditions, including:
* Diagnosis of type 1 diabetes
* Hemoglobin A1c > 8.0 in subjects with type 2 diabetes
* Moderate to severe heart failure (New York Heart Association class III or IV)
* Myocardial infarction or unstable angina pectoris within the past 12 months prior to IP initiation
* Uncontrolled hypertension as defined by a resting blood pressure * 150/90 mmHg prior to IP initiation (confirmed by a repeat assessment)
* Severe chronic pulmonary disease (eg, requiring oxygen therapy)
* Major chronic inflammatory disease or connective tissue disease (eg, rheumatoid arthritis, psoriasis, systemic lupus erythematosus)
* Active malignancy, including evidence of cutaneous basal or squamous cell carcinoma or melanoma, or history of cancer (except successfully treated in situ cervical cancer or squamous or basal cell carcinoma of the skin).
Laboratory abnormalities
* Serum direct bilirubin * 1.5x ULN
* Hemoglobin < 10 g/dL
* Platelet count < 125,000 cells/mm3
* White blood cell count < 3,000 cells/mm3
* Absolute neutrophil count < 2000 cells/mm3
* Creatinine clearance < 50 mL/min (Cockroft-Gault formula, calculated value to be provided to sites).
4.2.19 Subject has used Tysabri (natalizumab) within 1 year prior to IP initiation.
4.2.21 Subject received an anti-TNF agent within 8 weeks prior to IP initiation.
4.2.22 Subject received steroid enemas 2 weeks prior to IP initiation.
4.2.23 Subject received cyclosporine, mycophenolate mofetil, sirolimus (rapamycin), thalidomide or tacrolimus within 4 weeks prior to IP initiation.
4.2.24 Chronic narcotic use for reasons other than diarrhea.

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):	01-03-2011
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nog niet beschikbaar
Generic name:	Nog niet beschikbaar

Ethics review

Approved WMO Date:	20-09-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	06-01-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	24-03-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-08-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-08-2011
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	EUCTR2010-019544-39-NL
ClinicalTrials.gov	NCT01150890
CCMO	NL33509.029.10