A Ranomized, Double Blinded, Multi-Center, Phase 2 Study to Estimate the Efficacy and Evaluate the Safety and Tolerability of Cisplatin & Capecitabine (CX) in Combination with AMG 386 or Placebo in Subjects with Metastatic Gastric, Gastroesophageal Junction, or Distal Esophageal Adenocarcinoma

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To estimate the treatment effect as measured by progression free survival(PFS) of subjects receiving AMG 386 (at 2 doses) in combination with cisplatin + capecitabinerelative to cisplatin + capecitabine + placebo

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

Summary

ID

NL-OMON32061

Source
ToetsingOnline

Brief title
AMG 386 in subjects with Metastatic Gastric or Esophageal Adenocarcinoma

Condition

- Other condition

Synonym
distal esophageal carcinoma, gastroesophageal junction, metastatic gastric

Health condition

Maag- en slokdarmkanker

Research involving
Human

Sponsors and support

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

Intervention

Keyword: AMG386, Esophageal ca, First-line treatment, Metastatic Gastric-, Phase II

Outcome measures

Primary outcome

Progression-free survival (PFS).

Secondary outcome

-Objective response Rate (ORR): the incidence of either a confirmed complete

response (CR) or partial response (PR) per modified RECIST criteria.

-Duration of response (DOR): (calculated only for those subjects with a

confirmed objective response) time from first confirmed objective response to

disease progression (per the modified RECIST criteria)

-Overall survival (OS): time from randomization date to date of death

-Incidence of AEs and significant laboratory changes from baseline

-Incidence of anti-AMG 386 antibody formation

-Time to progression (TTP): time from randomization to date of disease

progression per the modified RECIST criteria

-Time to response: time from randomization date to date of first objective response for confirmed responders

-Change in tumor burden as measured by percentage change from baseline in the sum of the longest diameters of target lesions

- Relative dose intensity of CX for the entire treatment period and over the first 18 weeks of the treatment period.

- AMG 386 pharmacokinetic parameters when used in combination with capecitabine and cisplatin

- Change in cancer-related symptoms as assessed with the QLQ-STO22

Exploratory:

-Baseline values and changes from baseline in pharmacodynamic markers as assessed by blood levels of angiogenic cytokines (eg VEGF, bFGF, PIGF, Ang-1, Ang-2)

-To evaluate the pharmacokinetics (PK) of capecitabine, its metabolite 5-FU and cisplatin when used in combination with AMG386 in a sub-group of subjects at selected sites

-Association of tumor apoptosis and other markers with response to treatment

-Baseline values and changes from baseline in immunologic, biochemical, pharmacogenomic, and angiogenic markers in tumor biopsies or serum samples

-Change from baseline in cancer-related and treatment related symptoms and health-related quality of life assessed with QLQ-STO22 and QLQ-C30

Change from baseline in the EuroQol EQ-5D summary score

Study description

Background summary

In this study, the study medication AMG 386 is evaluated for the treatment of patients with metastatic gastric or esophageal cancer. AMG 386 is a man-made medication that is designed to stop the development of blood vessels in cancer tissues. Cancer tissues rely on the development of new blood vessels, a process called angiogenesis, to obtain a supply of oxygen and nutrients to grow. AMG 386 is considered experimental (or investigational). AMG 386 is not approved by any regulatory organization (such as the Food and Drug Administration, FDA) to treat any type of cancer. AMG 386 will be evaluated in this study in combination with cisplatin and capecitabine. Cisplatin in combination with capecitabine is the standard treatment for patients with Metastatic Gastric, Gastroesophageal Junction, and Distal Esophageal Adenocarcinoma. About 165 patients from 40 centers will participate in this study from regions including the Unites States and Europe. Amgen Inc. a for-profit drug company, is funding this clinical study.

Study objective

To estimate the treatment effect as measured by progression free survival (PFS) of subjects receiving AMG 386 (at 2 doses) in combination with cisplatin + capecitabine
relative to cisplatin + capecitabine + placebo

Study design

This is a multicentre, randomized, phase 2 study. The study consists of 3 of parts. The first part is the screening. If the patient is eligible for the study, he/she will go into the treatment phase and this phase lasts until the patients* cancer worsens, is unable to tolerate the investigational drug, or decides to withdraw consent. After completion of the treatment, the patient will be followed by the study staff by telephone or at routine clinic visits approximately every 3 months for up to 4 years after the last subject starts the study treatment (long term follow up). Each subject participating in this clinical research study will receive 1 of the following treatments:
Arm A: - Cisplatin 80 mg/m² IV Q3W
- Capecitabine 1000 mg/m² PO BID x 14 days Q3W
- AMG 386 10 mg/kg IV QW.
Arm B: - Cisplatin 80 mg/m² IV Q3W
- Capecitabine 1000 mg/m² PO BID x 14 days Q3W
- AMG 386 3 mg/kg IV QW.
Arm C: - Cisplatin 80 mg/m² IV Q3W
- Capecitabine 1000 mg/m² PO BID x 14 days Q3W

- Placebo QW.

Intervention

Subjects will receive cisplatin/ capecitabine (Arms A, B, and C) in addition to either blinded AMG 386 or placebo until they develop disease progression per modified RECIST criteria, clinical progression, unacceptable toxicity, withdraw consent, or death.

Study burden and risks

Estimated median length of subject treatment is 6 months for subjects on cisplatin/ capecitabine plus placebo (Arm C), 8 months for subjects on cisplatin/ capecitabine plus AMG 386 (Arms A and B). Safety follow up assessments for each individual subject will be conducted 30 (+7) days after discontinuation of all study drug (AMG 386 or placebo, cisplatin and capecitabine). Subjects need to visit the clinic weekly during the treatment phase, study visits with the subject receiving studymedication will last 4-6 hours.

Contacts

Public
Amgen

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Histologically or cytologically confirmed adenocarcinoma of the stomach, gastroesophageal junction or distal esophagus with metastatic disease.
- 18 years of age or older at the time the written informed consent is obtained
- Subjects of child-bearing potential and sexually active must use an accepted and effective non-hormonal method of contraception (ie, double barrier method [eg, condom plus diaphragm]) from signing the informed consent through 6 months following last administration of study drug
- Able to tolerate intravenous infusions
- Able to swallow oral medication
- ECOG of 0 or 1 (within 14 days prior to randomization)
- Adequate organ and hematological function as evidenced by laboratory studies within 14 days prior to randomization.
For a complete list of all inclusion criteria please see protocol page 41 and 42.

Exclusion criteria

- Prior chemotherapy for metastatic disease (1st line)
- Less than 12 months have elapsed from completion of previous adjuvant or neoadjuvant chemotherapy or chemoradiotherapy
- Patients with persistant gastric outlet obstruction, complete dysphagia or feeding jejunostomy.
For a complete list of all exclusion criteria please see protocol page 42 and 43.

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):	18-03-2008
Enrollment:	9
Type:	Actual

Ethics review

Approved WMO Date:	28-12-2007
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	18-02-2008
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	14-05-2008
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	04-07-2008
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	08-07-2008
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	22-08-2008

Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	26-08-2008
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	12-05-2009
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	30-12-2009
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	17-03-2010
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	14-10-2010
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	09-12-2010
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	10-10-2011
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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	EUCTR2007-003573-50-NL
CCMO	NL20002.096.07
Other	Nog niet bekend