A Global Phase 1 Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of the Half-life Extended Bispecific T-cell Engager AMG 910 in Subjects With Claudin 18.2-Positive Gastric and Gastroesophageal Junction Adenocarcinoma

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Primary• To evaluate the safety and tolerability of AMG 910 in adult subjects. • To determine the maximum tolerated dose (MTD) and/or recommended phase 2 dose (RP2D)Secondary• To characterize the PK of AMG 910• To evaluate preliminary anti-tumor…

Ethical review	Approved WMO
Status	Completed
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON55179

Source
ToetsingOnline

Brief title
20180292

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym

cancer of stomach, stomach cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: CLDN 18.2-postitive, First-in-human, Gastric Cancer, safety

Outcome measures

Primary outcome

• Dose-limiting toxicities (DLT)

• Treatment-emergent adverse events

• Treatment-related adverse events

• Changes in vital signs, electrocardiogram (ECG), and clinical laboratory tests

Secondary outcome

• PK parameters for AMG 910 following short-term intravenous (IV) and extended IV (eIV) administration including but not limited to maximum serum concentration (Cmax), minimum serum concentration (Cmin), area under the concentration-time curve (AUC) over the dosing interval, accumulation following multiple dosing, and, if feasible, half-life (t1/2) Objective response (OR) per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 and iRECIST Duration of response (DOR)

Study description

Background summary

AMG 910 is an HLE BiTE antibody construct designed to direct T cells (via CD3 binding) towards Claudin-18 isoform 2 (CLDN18.2)-expressing cells. In AMG 910, the binding arms for CLDN18.2 and CD3 are genetically fused to the N-terminus of a single chain IgG Fc (fragment crystallizable; scFc) region. The fusion to a Fc domain is a well-established strategy to prolong the half-life of protein therapeutics, such as cytokines, growth factors, and bispecific antibodies, with several approved for the treatment of cancer (Kontermann, 2011). The extended half-life of Fc fusion proteins is due to their interaction with the neonatal Fc receptor, which results in a protected intracellular protein reservoir that is recycled to the extracellular space (Rath, et al., 2015).

A detailed description of the chemistry, pharmacology, nonclinical pharmacokinetics, and toxicology of AMG 910 is provided in the AMG 910 Investigator*s Brochure.

Study objective

Primary
• To evaluate the safety and tolerability of AMG 910 in adult subjects.
• To determine the maximum tolerated dose (MTD) and/or recommended phase 2 dose (RP2D)
Secondary
• To characterize the PK of AMG 910
• To evaluate preliminary anti-tumor activity of AMG 910
Exploratory
• To evaluate immunogenicity of AMG 910
• To evaluate exploratory biomarkers including pharmacodynamic and potential patient selection biomarkers

Study design

This is an open-label, ascending, multiple dose, phase 1 study evaluating AMG 910 in subjects with CLDN18.2-positive gastric and GEJ adenocarcinoma. The study will consist of:
• Dose-exploration phase
• Dose-expansion phase
The dose-exploration phase of the study will estimate the MTD of AMG 910 using a Bayesian logistic regression model (BLRM). A RP2D may be identified based on emerging safety, efficacy, and pharmacodynamic data prior to reaching an MTD. Following the dose-exploration phase, a dose-expansion phase will be conducted

to confirm safety, PK, and pharmacodynamics at the MTD or RP2D and to obtain further safety and efficacy data and enable correlative biomarker analysis.

Intervention

Extended IV infusion over 96 hours in cycle 1 week 1 and as short-term IV infusions weekly (or twice weekly) starting cycle 1 day 8 onwards through cycle 6 of 28-day cycles.

Study burden and risks

The key safety risks for AMG 910:
• Cytokine Release Syndrome (CRS) /Infusion-Related Reactions
• Gastrointestinal Toxicity
• Neurologic Events
• Tumor Lysis Syndrome (TLS)
• Sucrose Toxicity:

Contacts

Public
Amgen

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NL
Scientific
Amgen

Minervum 7061
Breda 4817 ZK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Subjects with histologically or cytologically confirmed metastatic or locally advanced unresectable gastric or GEJ adenocarcinoma positive for CLDN18.2 as defined by the test described herein (Section 8.2.10.1). Prior treatment with any CLDN18.2-targeting product requires testing of a tissue sample obtained after the treatment with the CLDN18.2-targeting product (not applicable for re-treatment).
• Subjects should not be eligible for curative surgery and should have been refractory to or have relapsed after 2 or more prior lines of standard systemic therapy that included a platinum, a fluoropyrimidine, either a taxane or irinotecan, and an approved vascular endothelial growth factor receptor (VEGFR) antibody/tyrosine kinase inhibitor (TKI) and depending on country-specific standards and approvals.
• For subjects eligible for human epidermal growth factor receptor 2 (HER2) directed therapy, prior therapy should have included an approved HER2 targeting antibody.
• Subjects may also be included if the aforementioned therapeutic options were medically not appropriate for them. In these cases, the reason(s) why required prior therapies for gastric cancer were medically not appropriate should be documented in the subject*s electronic case report form (eCRF).
• For dose-expansion only: Subjects with at least 1 measurable lesion >= 10mm which has not undergone biopsy within 3 months of screening scan. This lesion cannot be biopsied at any time during the study.

For more inclusion criteria, please refer to section 5.1 of the protocol.

Exclusion criteria

• Any anticancer therapy or immunotherapy within 4 weeks of start of first dose (14 days for palliative radiation).
• Untreated or symptomatic central nervous system (CNS) metastases, leptomeningeal disease, or spinal cord compression.
• Autoimmune disorders requiring chronic systemic steroid therapy or any other form of immunosuppressive therapy while on study, eg, ulcerative colitis, Crohn*s disease, or any other gastrointestinal autoimmune disorder causing chronic nausea, vomiting, or diarrhea.
Recent or current use of inhaled steroids or physiological substitution in case

of adrenal insufficiency is not exclusionary.
• Evidence or history within last 3 months of gastrointestinal inflammatory conditions not associated with the underlying cancer disease including gastrinomas, duodenitis, proven gastric ulcer, duodenal ulcer, pancreatitis, or subjects with recent gastric bleeding. Subjects may be included if the symptomatic/immunosuppressive treatment is discontinued more than 4 weeks prior to the first dose of AMG 910, symptoms have resolved, and gastroscopy does not indicate signs of active disease.

For more inclusion criteria, please refer to section 5.2 of the protocol.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	30-06-2021
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AMG 910
Generic name:	AMG 910

Ethics review

Approved WMO

Date:	09-03-2020

Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-05-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-01-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2020-000312-30-NL
ClinicalTrials.gov	NCT04260191
CCMO	NL72431.056.20

Study results

Date completed: 01-04-2022

Results posted: 01-02-2023

First publication
02-12-2022