A Global Phase 1 Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of the Half-life Extended Bispecific T-cell Engager AMG 199 in Subjects With MUC17-Positive Solid Tumors Including Gastric, Gastroesophageal Junction, Colorectal, and Pancreatic Cancers

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Primary• To evaluate the safety and tolerability of AMG 199 in adult subjects• To determine the maximum tolerated dose (MTD) and/or recommended phase 2 dose (RP2D) Secondary• To characterize the PK of AMG 199 • To evaluate preliminary anti-tumor...

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56431

Source
ToetsingOnline

Brief title
20180290

Condition

- Other condition
- Malignant and unspecified neoplasms gastrointestinal NEC

- Gastrointestinal neoplasms malignant and unspecified

Synonym
cancer of stomach, stomach cancer

Health condition

maagkanker, kanker van de maag-slokdarmovergang, darm- en pancreaskanker

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Gastric Cancer, MUC17-postitive, pharmacokinetics, tolerability

Outcome measures

Primary outcome

Primary study parameters/outcome of the study:

• Dose-limiting toxicities (DLT)

• Treatment-emergent adverse events

• Treatment-related adverse events

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

tests

Secondary outcome

Secondary study parameters/outcome of the study:

• PK parameters for AMG 199 following

• intravenous (IV) 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.and iRECIST

• Duration of response (DOR)

• Time to progression

• Progression-free survival (PFS), 6-month and 1-year PFS

• Overall survival (OS), 1 and 2-year OS

Study description

Background summary

Bispecific T cell engager (BiTEs) are designed to direct T cells towards target cells. The proximity induced by the BiTE triggers target cell specific cytotoxicity which closely resembles standard cytotoxic T lymphocyte activation. Blinatumomab (BLINCYTO*), a CD19 BiTE*, is approved for the treatment of acute lymphoblastic leukemia (ALL). AMG 199 is an HLE BiTE * antibody construct designed to direct T cells towards MUC17-expressing cells. In AMG 199 the binding arms for MUC17 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 and pharmacology of AMG 199 is provided in the AMG 199 Investigator*s Brochure.

Study objective

Primary
• To evaluate the safety and tolerability of AMG 199 in adult subjects
• To determine the maximum tolerated dose (MTD) and/or recommended phase 2 dose (RP2D)

Secondary
• To characterize the PK of AMG 199
• To evaluate preliminary anti-tumor activity of AMG 199

Study design

This is an open-label, ascending, multiple dose, phase 1 study evaluating AMG 199 in subjects with MUC17-positive solid tumors. The study will consist of:
• Dose-exploration phase
• Dose-expansion phase
The dose-exploration phase of the study will estimate the MTD of AMG 199 using a Bayesian logistic regression model (BLRM). A RP2D may be identified based on emerging safety, efficacy, and PD data prior to reaching an MTD. Alternative dosing schedule(s) may be explored based on emerging PK and safety data. Following the dose-exploration phase, a dose-expansion phase will be conducted to confirm safety, PK, and PD at the MTD or RP2D and to obtain further safety and efficacy data and enable correlative biomarker analysis.

Intervention

AMG 199 will be administered as a short intravenous infusion given over approximately 60 minutes through a catheter (plastic needle) in a vein (for example, in your arm), or can be administered as extended intravenous infusion (continuous infusion).

Study burden and risks

Key Risks for AMG 199:
Cytokine Release Syndrome (CRS)/ Infusion-Related Reactions
Gastrointestinal Toxicity
Neurologic Events
Tumor Lysis Syndrome (TLS
Sucrose Toxicity
Embryofetal and Reproductive System

Contacts

Public
Amgen

Minervum 7061
Breda 4817 ZK
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

103 - Subjects with histologically or cytologically confirmed metastatic or locally advanced gastric adenocarcinoma or GEJ adenocarcinoma positive for MUC17 as defined by the test described herein. Subjects should have been refractory to or have relapsed after two or more prior lines of standard systemic therapy that included a platinum, a fluoropyrimidine, nivolumab (in combination with a platinum and a fluoropyrimidine), either a taxane or irinotecan, and an approved vascular endothelial growth factor receptor (VEGFR) antibody/tyrosine kinase inhibitor (TKI).
OR Subjects with histologically or cytologically confirmed metastatic or locally advanced unresectable CRC positive for MUC17 as defined by the test described herein. Subjects should have been refractory to or have relapsed after at least two and up to five prior lines of standard systemic therapy. Therapy should have included an approved vascular endothelial growth factor (VEGF) antibody (if clinically appropriate) and epidermal growth factor receptor (EGFR) antibody (if kirsten rat sarcoma (KRAS)/ neuroblastoma RAS viral oncogene homolog (NRAS)/ v-Raf murine sarcoma viral oncogene homolog B1 (BRAF) wild type tumor).
OR Subjects with histologically or cytologically confirmed unresectable or

metastatic pancreatic ductal adenocarcinoma positive for MUC17 as defined by the test described herein. Subjects should have been refractory to or have relapsed after at least one and up to three prior lines of standard systemic therapy.
104 - Gastric adenocarcinoma and GEJ adenocarcinoma: Subjects eligible for human epidermal growth factor receptor 2 (HER2) directed therapy, prior systemic therapy should have included a HER2 targeting antibody approved for treatment of gastric cancer. For Subjects with microsatellite instability high (MSI H) or mismatch repair deficient (dMMR) tumors a prior line of treatment should have included an approved PD-1-blocking antibody.
105 - Subjects may also be included if the aforementioned therapeutic options were medically not appropriate for them.
106 - For dose-expansion only: Subjects with at least one 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.

Refer to section 5.1 of the protocol.

Exclusion criteria

• Any anticancer therapy or immunotherapy within 4 weeks of start of first dose.
• Central nervous system (CNS) metastases, leptomeningeal, or spinal cord compression.
• Autoimmune disorders requiring chronic systemic steroid therapy or any other form of immunosuppressive therapy. Subjects may be included if the treatment is discontinued more than 3 months prior to the first dose of AMG 199, there is a low likelihood of relapse from the autoimmune disorder, AND there is agreement between the investigator and the Amgen Medical Monitor.

Refer to 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):	03-12-2020
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AMG199
Generic name:	AMG199

Ethics review

Approved WMO Date:	06-11-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-02-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-10-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-04-2021

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	16-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-03-2023
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
Other	NCT04117958
EudraCT	EUCTR2019-002708-42-NL
CCMO	NL71930.056.19

Study results

Date completed:	03-03-2023

Results posted: 17-01-2024

Summary results
Trial ended prematurely

First publication
01-12-2023