89Zr-AMG211 PET imaging in patients with relapsed/refractory gastrointestinal adenocarcinoma before and during treatment with AMG 211.

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Primary objective: To evaluate the in vivo biodistribution (measured in SUV) and quantitative radioactivity in organs of 89Zr-AMG211 in patients with relapse/refractory gastrointestinal adenocarcinoma as assessed by PET/CT. Secondary objectives: I)...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON43494

Source
ToetsingOnline

Brief title
89Zr-AMG211 PET imaging study

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
cholangio carcinoma, colon cancer, esophagus cancer, gastric cancer, pancreatic cancer, rectal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: AMGEN

Intervention

Keyword: 89Zr-AMG211, gastrointestinal adenocarcinoma

Outcome measures

Primary outcome

Quantitative uptake of 89Zr-AMG211 in tumor tissue, organs and blood by measuring standardized uptake value (SUV) on the 89Zr-AMG211 PET scans.

Secondary outcome

* Response to AMG 211 therapy will be analyzed in Study 20130354 according to the immune related response criteria (irRC). These results will be correlated to 89Zr-AMG211 tumor uptake data (measured in SUV).

* Number of patients with adverse events after 89Zr-AMG211 injection as a measure of safety and tolerability. Incidence, nature and severity of adverse events will be measured.

Study description

Background summary

AMG 211 is a potentially new targeted drug in the treatment of relapsed/refractory gastrointestinal adenocarcinoma, since those are CEA expressing tumors. AMG 211 is a bispecific single-chain antibody construct of the bispecific T-cell engager (BiTE®) class that targets human CEA antigen (CD66e) on (tumor) cells and the CD3 epsilon (*) subunit of the human T-cell receptor complex present on T-cells. A well-known challenge in current drug development using molecular targeted therapies is the high level of heterogeneity of target expression that is present in specific tumor types. Radio-labeling of AMG 211 with the positron emission tomography (PET)

radionuclide Zirconium-89 (89Zr) enables non-invasive imaging and quantification of AMG 211 distribution in cancer patients. By performing a 89Zr-AMG211 PET scan prior to treatment with AMG 211, the uptake of the tracer in the primary and metastatic tumor lesions and normal organ distribution can be evaluated. By performing a 89Zr-AMG211 PET scan during AMG 211 continuous intravenous (cIV) treatment we will be able to evaluate the impact of prolonged steady state exposure of AMG 211 on tumor and tissue uptake. Ultimately the 89Zr-AMG211 PET imaging study will be used to identify the optimal population to treat in the future.

Study objective

Primary objective: To evaluate the in vivo biodistribution (measured in SUV) and quantitative radioactivity in organs of 89Zr-AMG211 in patients with relapse/refractory gastrointestinal adenocarcinoma as assessed by PET/CT. Secondary objectives: I) To evaluate the correlation between 89Zr-AMG211 tumor uptake and response to therapy; II) To determine the number of patients with adverse events after 89Zr-AMG211 injection.

Study design

This is a multicenter investigator initiated trial designed to evaluate in vivo biodistribution and quantitative radioactivity in organs of 89Zr-AMG211 in patients with relapsed/refractory gastrointestinal adenocarcinoma. The study runs parallel to the separate phase 1 Study 20130354 with AMG 211 (EudraCT 2014-000201-12/NCT02291614). This imaging study will be performed before or during AMG 211 cIV treatment.

Intervention

In part A of the imaging trial, a dose finding imaging study will be performed to assess the optimal protein tracer dose of 89Zr-AMG211 and the optimal interval between tracer injection and scanning. Approximately 3 cohorts of about 2-3 patients each will undergo 89Zr-AMG211 PET imaging before start of cIV treatment with AMG 211. In part B, optimal protein tracer dose and schedule for imaging will be determined in approximately 6 AMG 211 pretreated patients. In part C, up to 20 additional patients will receive a 89Zr-AMG211 PET at the optimal protein tracer dose and schedule before start of treatment and immediately after completion of the second cIV treatment cycle. After and/or during participation within the imaging trial all patients must receive AMG 211 cIV therapy, provided they continue to meet the eligibility criteria to receive AMG 211.

Study burden and risks

For this imaging study patients have to make max. 3 extra visits to the clinic

for IV tracer administration and PET scanning at different time points. For study part A patients will be hospitalized for intravenous (IV) tracer injection and the first PET scan. For study parts B and C, hospitalization will be prolonged in order to administer the tracer IV and to perform the (first) PET scan. Before and during IV tracer administration vital signs will be measured regularly. Initially, in order to check for any side effects, patients will be hospitalized for 24 hours after tracer administration. When no side effects are observed in at least 3 patients, this hospitalization period may no longer be required. 89Zr-AMG211 implements a radiation burden of about 18 mSv and will be paired with a 1.5 mSv low-dose CT scan or with a 1.5 mSv low-dose CT scan and a 20 mSv diagnostic CT scan. Besides PET imaging patients will be asked to give in total maximum 3x2 blood samples (max. 3x 15 mL (10 mL + 5 mL tube), which will give minor discomfort. The risks associated with 89Zr-AMG211 seems minor and although patients do not directly benefit from this study, results of this study will be valuable for our understanding of tumor response and will guide further prospective research.

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

* Subject will be or is also participating in the ongoing phase 1 study 20130354 in which AMG 211 is administered via cIV. 89Zr-AMG211 PET imaging will be performed before and/or during treatment with AMG 211 cIV.
* Subject has provided informed consent to imaging study prior to initiation of any study-specific activities/procedures
* Male or Female * 18 years of age at the time of informed consent
* Pathologically documented, diagnosed GI adenocarcinoma (including but not limited to esophageal, gastric, small intestine, colorectal, or pancreatic cancers) that has failed standard treatments or for which standard curative or palliative measures do not exist or are no longer effective
* At least 1 measurable tumor lesion per modified irRC
o In case we do not find any uptake in metastatic liver lesions in the first set of patients on the 89Zr-AMG211 PET scan, than subsequent patients need to have at least 1 measurable tumor lesion outside the liver
* Archival tumor tissue available or is willing to undergo biopsy of a tumor lesion before the start of treatment
* Adequate hematological, renal, and liver function as follows:
o Absolute neutrophil count (ANC) > 1500/mm3 (1.5 × 109/L)
o Platelet count > 100,000 mm3 (100 × 109/L)
o White blood cell (WBC) count > 3 × 109/L
o Hemoglobin > 9.0 g/dL
o AST and ALT < 3.0 × the upper limit of normal (ULN)
o Alkaline phosphatase (ALP) * 2.5 × ULN
o Total bilirubin (TBL) < 1.5 × ULN (unless subject has suspected Gilbert*s syndrome or extrahepatic cause by increased indirect bilirubin fraction)
o Creatinine clearance > 50 mL/min calculated by Cockroft-Gault
o Lipase/amylase < 1.5 x ULN
o Prothrombin time, partial thromboplastin time, and international normalized ratio (INR) * 1.5 × ULN
* Life expectancy * 3 months, in the opinion of the investigator
* Karnofsky Performance Status * 70%
* Body weight * 45 kg

Exclusion criteria

* History of allergy or reaction to any component of the AMG 211 formulation
* Malignancy other than GI adenocarcinoma requiring current therapy
* Evidence of uncontrolled systemic disease (other than GI adenocarcinoma)

* Active infection or prior use of IV antibiotics for treatment of infection within 2 weeks prior to starting therapy with AMG 211
* Corrected QT interval (QTc) * 500 milliseconds at screening
* Hepatitis B and/or C based on the following results:
o Positive Hepatitis B Surface Antigen (HepBsAg) (indicative of chronic Hepatitis B or recent acute Hepatitis B)
o Negative HepBsAg and positive Hepatitis B core antibody: Hepatitis B virus DNA by polymerase chain reaction (PCR) is necessary. Detectable Hepatitis B virus DNA suggests occult Hepatitis B.
o Positive Hepatitis C virus antibody (HepCAb) Hepatitis C virus RNA by PCR is necessary. Detectable Hepatitis C virus RNA suggests chronic Hepatitis C
* Positive results for human immunodeficiency virus (HIV)
* Major surgery within 28 days of study day 1
* Prophylactic anti-infection vaccination within 1 month prior to starting therapy with AMG 211. Therapeutic vaccination for cancer or infection within 3 months prior to starting therapy with AMG 211.
* Currently receiving treatment in another investigational device or drug study, or less than 28 days since ending treatment in another investigational device or drug study. Other investigational procedures while participating in this study are excluded.
o Exception to this criterion is the participation in Study 20130354 and all procedures related to this study.
* Treatment with any chemotherapy, radiotherapy, immunotherapy, biologic, or hormonal therapy for cancer within 14 days prior to study entry or not recovered from treatment
* Unresolved toxicities from prior anti-tumor therapy, defined as not having resolved to Common Terminology Criteria for Adverse Events (CTCAE), version 4.0 grade 1 or to levels dictated in the eligibility criteria with the exception of alopecia or toxicities from anti-tumor therapy that are considered irreversible (defined as having been present and stable for > 6 months), may be allowed if they are not otherwise described in the exclusion criteria AND there is agreement to allow by both the investigator and the sponsor
* Recent history of cardiac disease, including myocardial infarction, unstable angina pectoris, or uncontrolled arrhythmia within 6 months; or evidence of severe congestive heart failure with New York Heart Association severity classification > Class I within 12 weeks prior to screening
* History or evidence of any other clinically significant disorder, condition or disease (with the exception of those outlined above), that in the opinion of the investigator or sponsor would pose a risk to subject*s safety or interfere with the study evaluation, procedures, or completion
* Clinical history of significant central nervous system (CNS) pathology (including but not limited to: history of brain metastasis, multiple occurrences of confusion, dementia, previous CNS infarctions, migraine headaches [within 6 months prior to starting therapy with AMG 211], seizure disorder, or major brain surgery)
* History of chronic autoimmune disease, e.g., rheumatoid arthritis, inflammatory bowel disease, systemic lupus erythematosus, or multiple sclerosis (with the exception of stable type 1 diabetes)
* Males or Females of reproductive potential and unwilling to practice an acceptable method of effective birth control while on study through 30 days after receiving the last dose of study drug. Acceptable methods of effective birth control include:

o sexual abstinence (males, females)
o use of a combination of 2 acceptable methods of effective birth control including: bilateral tubal ligation (females), vasectomy (males), oral, transdermal, injected, or implanted contraceptives, intrauterine device, female condom with spermicide, diaphragm with spermicide, contraceptive sponge with spermicide, cervical cap, or use of a condom with spermicide by the sexual partner)
* Females who are lactating/breastfeeding or who plan to breastfeed while on study through 30 days after receiving the last dose of study drug
* Females with a positive pregnancy test
* Females planning to become pregnant while on study through 30 days after receiving the last dose of investigational product
* Subject is likely to not be available to complete all protocol required study visits or procedures, and/or to comply with all required study procedures to the best of the subject and investigator*s knowledge

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-08-2016
Enrollment:	35
Type:	Actual

Ethics review

Approved WMO

Date:	20-06-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	07-07-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2015-004370-14-NL
CCMO	NL56345.042.16
Other	volgt