Open-label, multi-cohort, Phase 2 trial, evaluating the efficacy and safety of tusamitamab ravtansine (SAR408701) monotherapy and in combination in patients with CEACAM5-positive advanced solid tumors

Published: 21-12-2020
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The purpose of this multi-cohort study is to assess the safety and efficacy of tusamitamab ravtansine (SAR408701) in mBC and mPAC participants with CEACAM5 positive tumors which are known to be sensitive to taxanes.

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

Summary

ID

NL-OMON51893

Source
ToetsingOnline

Brief title
ACT16432 Carmen-BT01

Condition

- Metastases

Synonym
metastatic breast cancer, metastatic pancreatic adenocarcinoma

Research involving

Human

Sponsors and support

Primary sponsor: Genzyme Europe BV
Source(s) of monetary or material Support: Sanofi

Intervention

Keyword: Advanced solid tumors, CEACAM5-positive, Metastatic, tusamitamab ravtansine (SAR408701)

Outcome measures

Primary outcome

- Cohort A, B and C part 2: objective Response Rate (ORR) of tusamitamab ravtansine (SAR408701) of participants who have a confirmed complete response (CR) or partial response (PR).

- Cohort C part 1: Incidence of dose-limiting toxicites (DLTs) in the 28 Day DLT observation period (Cycle 1)

Secondary outcome

- Incidence of participants with treatment-emergent adverse events (TEAEs), serious adverse events (SAEs) and laboratory abnormalities according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v5.0.

- Progression-free survival (PFS).

- Disease control rate (DCR).

- Duration of response (DOR).

- Incidence of participants with anti-therapeutic antibodies (ATAs) against tusamitamab ravtansine (SAR408701).

- Pharmacokinetic parameters of tusamitamab ravtansine and gemcitabine

Study description

Background summary

A protein called CEACAM5 is expressed at the surface of some types of cancer. tusamitamab ravtansine (SAR408701) consists of a drug component called DM4. DM4 is linked to an antibody, this is a protein in the blood that protects the body against bacteria and viruses. It can recognize abnormal cells and binds to the surface of these cells. The antibody component of tusamitamab ravtansine (SAR408701) binds to the CEACAM5 antigen expressed at the surface of the tumor cell. Then tusamitamab ravtansine (SAR408701) enters the rumor cells and the drug DM4 kills the cell.

Study objective

The purpose of this multi-cohort study is to assess the safety and efficacy of tusamitamab ravtansine (SAR408701) in mBC and mPAC participants with CEACAM5 positive tumors which are known to be sensitive to taxanes.

Study design

Phase 2, non-randomized, parallel, open label.

Intervention

Cohort A&B: tusamitamab ravtansine (SAR408701), IV infusion, once every two weeks.
Cohort C: Treatment per cycles each consisitng of 28 days, with tusamitamab ravtansine (SAR408701) IV infusion followed by gemcitabine IV infusion on day 1 and day 14, and gemcitabine IV infusion on day 8.

Study burden and risks

Burden and risks are related to the blood sampling, CT or MRI scan (radiation burden), biopsy, and possible side effects of the study medication.

Contacts

Public

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Participant must be at least 18 years of age.
- Participants with at least one measurable lesion according to the RECIST 1.1 criteria that has not been irradiated (ie, newly arising lesions in previously irradiated areas are accepted).
- Participants with ECOG performance status 0 to 1.
- Evidence of metastatic disease.
- Expression of CEACAM5 by centrally assessed IHC assay.

Cohort A:
- Histological or cytologic diagnosis of breast cancer.
- Have received at least 2 prior cytotoxic chemotherapy regimens for non-TNBC tumor type or at least 1 for TNBC tumor type but not more than 4 in the locally recurrent or metastatic setting.

Cohort B:
- Have confirmed diagnosis of pancreatic ductal adenocarcinoma.

- Have documented radiographic progression or documented intolerance after at least 1 prior systemic chemotherapy line which included either gemcitabine (or relapsed within 6 months of completion of gemcitabine adjuvant therapy) or a 5-fluorouracil based regimen (including capecitabine) but no more than 2 prior chemotherapy lines for locally advanced/metastatic disease.

Cohort C:
- Have confirmed diagnosis of pancreatic ductal adenocarcinoma.
- Have documented radiographic progression or documented intolerance after 1st line
fluoropyrimidine-containing chemotherapy (or relapsed within 6 months of completion of
chemotherapy as adjuvant therapy) for locally advanced/metastatic disease.

- Contraceptive use by men or women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.
- Capable of giving signed informed consent.

Exclusion criteria

Medical Condition
- Medical condition requiring concomitant administration of a medication with a narrow therapeutic window, that is metabolized by cytochrome P450 (CYP450) and for which a dose reduction cannot be considered.
- Medical conditions requiring concomitant administration of strong CYP3A inhibitor, unless it can be discontinued at least 2 weeks before the first administration of study intervention.
- Life expectancy less than 3 months.
- Untreated brain metastases or history of leptomeningeal disease.
- Significant concomitant illness.
- History within the last 3 years of an invasive malignancy other than the one treated in this study, with the exception of resected/ablated basal or squamous-cell carcinoma of the skin or carcinoma in situ of the cervix, or other local tumors considered cured by local treatment.
- History of known acquired immunodeficiency syndrome (AIDS) related illnesses or known human immunodeficiency virus (HIV) disease requiring antiretroviral treatment, or active hepatitis A, B or C infection.
- Non-resolution of any prior treatment-related toxicity to to NCI CTCAE v5.0, with the exception of alopecia, vitiligo, or active
thyroiditis controlled with hormone replacement therapy (HRT).
- Unresolved corneal disorder or any previous corneal disorder considered by an ophthalmologist to predict higher risk of drug-induced keratopathy.
- Use of contact lenses. Participants using contact lenses who are not willing to stop wearing them for the duration of the study intervention are excluded.

Prior/Concomitant therapy
- Concurrent treatment with any other anti-cancer therapy.
- Washout period before the first administration of study intervention of less than 3 weeks of less than 5 times the half-life, whichever is shorter, for prior antitumor therapy (chemotherapy, targeted agents, immunotherapy and radiotherapy, or any investigational treatment).
- Any prior therapy targeting CEACAM5.
- Prior maytansinoid DM4 treatment (ADC).
- Any major surgery within the preceding 3 weeks of the first study intervention administration.
- Any previous systemic therapy with taxane or gemcitabine (for Cohort C only).

Prior/concurrent clinical study experience
- Previous enrollment in this study or current participation in any other clinical study involving an investigational study treatment or any other type of medical research.

Diagnostic assessments
- Poor renal function.
- Poor hepatic function.
- Poor bone marrow function.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-03-2021
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	gemcitabine
Generic name:	gemcitabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	niet van toepassing
Generic name:	tusamitamab ravtansine

Ethics review

Approved WMO Date:	21-12-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-02-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	04-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-09-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-01-2023
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO Date:	21-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-11-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-01-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-01-2024
Application type:	Amendment
Review commission:	METC NedMec

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	2020-003096-18

Register	ID
EudraCT	EUCTR2020-003096-18-NL
CCMO	NL75426.041.20