Phase 1b multi-indication study of anetumab ravtansine (BAY 94-9343) in patients with mesothelin expressing advanced or recurrent malignancies

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

Summary

ID

NL-OMON48947

Source
ToetsingOnline

Brief title
ARCS-MT (Basket)

Condition

- Other condition

Synonym
mesothelin expressing advanced or recurrent malignancies, multi-indication

Health condition

neoplasmata maligne en niet-gespecificeerd van de borst, maagdarmstelsel, lever- en galwegen en endocriene organen

Research involving
Human

Sponsors and support

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

Intervention

Keyword: cancer, mesothelin overexpression, solid tumors

Outcome measures

Primary outcome

1) Maximum tolerated dose (MTD) of anetumab ravtansine in combination with cisplatin and in combination with gemcitabine in patients with mesothelin-expressing cholangiocarcinoma and pancreatic adenocarcinoma. Timeframe of Measurement: At least 3 weeks after the last patient starts treatment.

2) Objective response rate (ORR) of anetumab ravtansine for monotherapy and combination therapy in mesothelin expressing advanced solid tumors. Timeframe of measurement: 18 weeks after last patient starts treatment.
Durable Disease Control Rate (DDCR) as dual primary variables in pancreatic and gastric cancer.

Secondary outcome

1) Number of serious and non-serious adverse events (AEs) of the respective anetumab ravtansine monotherapy or combination treatments in the respective indications of mesothelin expressing advanced solid tumors. Timeframe of Measurement: 18 weeks after last patient starts treatment.

2) Disease control rate (DCR). Timeframe of Measurement: 18 weeks after last patient starts treatment.

3) Duration of response (DOR). Timeframe of Measurement: Approximately 24 months after last patient starts treatment.

4) Durable response rate (DRR). Timeframe of Measurement: Approximately 24 months after last patient starts treatment.

5) Progression free survival (PFS). Timeframe of Measurement: Approximately 24 months after last patient starts treatment.

Study description

Background summary

Anetumab ravtansine is an antibody-drug conjugate (ADC) targeting mesothelin which has demonstrated favorable safety profile and improvement in objective response rate in preclinical and phase I studies in solid tumors. The potential for anetumab ravtansine to impart clinical benefit in other advanced solid tumors, for which there is a high unmet medical need for effective treatment options.

Study objective

The key purpose of Safety lead in part of this study is to determine the maximum tolerable dose of anebumab ravtansine in combination with cisplatin for treatment of mesothelin-expressing cholangiocarcinoma, and similar for the combination with gemcitabin for the treatment of mesothelin-expressing adenocarcinoma of the pancreas.
The key purpose of Main study is to assess efficacy and safety of anetumab ravtansine in treatment of mesothelin-expressing advanced solid tumors.

Study design

This is a Phase 1b single arm, multi-indication study of anetumab ravtansine monotherapy in mesothelin positive tumors including NSCLC adenocarcinoma, TNBC, gastric adenocarcinoma including GEJ cancer, thymic carcinoma, and of anetumab ravtansine in combination with cisplatin in mesothelin positive cholangiocarcinoma, and in combination with gemcitabine in mesothelin positive pancreatic adenocarcinoma.

The study is composed of the following periods:
- Prescreening for mesothelin expression testing
- Full screening
- Treatment (for cholangiocarcinoma and pancreatic adenocarcinoma separate safety lead-in phases are included for determination of MTD for the combination treatments)
- Active follow-up (mandatory safety follow-up visit and efficacy follow-up visits, if applicable)
- Long-term follow-up

Intervention

Monotherapy indications: NSCLC adenocarcinoma, TNBC, gastric adenocarcinoma including GEJ cancer, thymic carcinoma
a) Anetumab ravtansine 6.5 mg/kg every 21 days (1 cycle)

Chemotherapy combination indication: cholangiocarcinoma
a) Safety lead-in for determination of MTD.
b) Main study: anetumab ravtansine at MTD followed by cisplatin 25 mg/m2.

Anetumab ravtansine will be given on Day 1 of a 21-day cycle.
Cisplatin will be given on Day 1 and Day 8 of a 21-day cycle.

Chemotherapy combination indication: pancreatic adenocarcinoma
a) Safety lead-in for determination of MTD.
b) Main study: anetumab ravtansine at MTD and gemcitabine 1000 mg/m2.

Anetumab ravtansine will be given on Day 1 of a 21-day cycle.
Gemcitabine will be given on Day 1 and Day 8 of a 21-day cycle.

Study burden and risks

Treatment with anetumab ravtansine may have therapeutic benefit but this cannot be guaranteed.
Most common risks for anetumab ravtansine are nausea, fatigue, vomiting, anorexia, diarrhea, peripheral neuropathy, increased ALT and AST, corneal epitheliopathy.
Most common risks for cisplatin are leukopenia, thrombocytopenia, anaemia, anorexia, nausea, vomiting, diarrhea, hearing impairment, renal failure,

nephrotoxicity, hyperuricaemia, fever
Most common risks for gemcitabin are leucopenia, thrombocytopenia, anaemia, dyspnoea vomiting, nausea, skin rash, alopecia , elevated AST, ALT and ALP, haematuria, proteinuria, fever, edema
Weekly visits with blood tests prior to drug administration and additional sampling at selected visits, and physical exams. Visits will continue until disease progresses, further follow up is done via 3 monthly telephone contacts.
Examination including eye examination, 2 patient questionnaires, ECG and radiological tumor assessments will be performed at specific visits.

Contacts

Public
Bayer

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Mijdrecht 3641 RT
NL
Scientific
Bayer

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Mijdrecht 3641 RT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Availability of tumor tissue for mesothelin expression testing

- Histologically-confirmed, mesothelin-expressing metastatic or advanced non-metastatic disease (tumour type specific inclusion criteria)
- At least one measurable lesion according to either RECIST 1.1 or ITMIG modified RECIST 1.1 as applicable
- Adequate bone marrow, liver, renal and coagulation function
- LVEF * 50% of the lower limit of normal (LLN) according to local institutional ranges
- ECOG 0 or 1
- Availability of additional tumor tissue for further biomarker analysis

Exclusion criteria

- More than one prior anti-tubulin/microtubule agent
- Corneal epitheliopathy or any eye disorder that may predispose the patients to this condition
- Symptomatic CNS metastases and/or carcinomatous meningitis
- Contraindication to both CT and MRI contrast agents
- Active hepatitis B or C infection
- Pregnant or breast-feeding patients
- Tumor type specific exclusion criteria

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-11-2017
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Gemzar
Generic name:	Gemcitabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	nvt
Generic name:	anetumab ravtansine
Product type:	Medicine
Brand name:	Platinol
Generic name:	Cisplatin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-05-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-08-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-11-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-12-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	31-01-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-02-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-02-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-03-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-04-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-05-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	09-10-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-11-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-04-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-05-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-07-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-09-2020

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2016-004002-33-NL
CCMO	NL61170.078.17

Study results

Results posted: 22-09-2022

First publication
01-01-1900

URL result
Type
ext
Naam
clinicaltrials.gov
URL