A randomized, open-label, active-controlled, Phase II study of intravenous anetumab ravtansine (BAY 94-9343) or vinorelbine in patients with advanced or metastatic malignant pleural mesothelioma overexpressing mesothelin and progressed on first line platinum/pemetrexed-based chemotherapy

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

Summary

ID

NL-OMON43748

Source
ToetsingOnline

Brief title
Mesothelioma.

Condition

- Mesotheliomas
- Pleural disorders

Synonym
asbestos cancer, carcinoma of the mesothelium lining lungs, Mesothelioma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Mesothelin overexpression, Pleural mesothelioma

Outcome measures

Primary outcome

To assess whether the study drug anetumab ravtansine is more effective than treatment with vinorelbine in patients with stage IV, mesothelin overexpressing malignant pleural mesothelioma measured by evaluating the progression free survival.

Secondary outcome

The secondary endpoints are overall survival, patient-reported outcomes, other efficacy parameters and safety. Other endpoints are evaluating the pharmacokinetics and biomarkers.

Study description

Background summary

Malignant pleural mesothelioma (MPM) is a locally invasive, usually fatal neoplasm arising from the mesothelial surfaces of the pleural cavity with a median life expectancy of approximately 1 year following diagnosis. Currently, there is no standard of care for second line therapy following a platinum based treatment. 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 advanced, unresectable or metastatic epithelial mesothelioma. Such responses would translate to the potential for anetumab ravtansine to impart clinical benefit as the 2nd line treatment for advanced mesothelioma which represents an indication of high unmet medical need for effective treatment options.

Study objective

The main purpose of this study is to assess whether the study drug anetumab ravtansine is more effective than treatment with vinorelbine in patients with stage IV, mesothelin overexpressing malignant pleural mesothelioma. Efficacy will be measured by evaluating the progression
free survival from randomization along with other indicators of tumor response. The safety of the study drug will also be investigated as well as overall survival. Further objectives are to evaluate the pharmacokinetics, anti-drug antibodies and biomarkers as well as Patient reported outcomes.

Study design

A randomized, open-label, active-controlled, two-arm, multicenter, phase II trial. patients will be randomly assigned in a 2:1 ratio to receive anetumab ravtansine or vinorelbine.

Intervention

Starting dose 6.5 mg / kg mg anetumab ravtansine intravenously once every three weeks compared with weekly intravenous infusion of 30 mg / m2 vinorelbine.

Study burden and risks

Each patient will undergo a pre-screening visit for testing mesothelin over-expression; in some cases, a new biopsy should be obtained for this purpose.
Examination including eye examination, 2 patient questionnaires, ECG and tumor assessments will be performed at specific visits.
Participation in the study will involve weekly or three weekly visits with blood tests (3-29 mL) and physical exams (full or brief).
Visits will continue until the disease progresses, further follow up will be done via 3 monthly telephone contacts

Anetumab ravtansine may have a therapeutic benefit, this can*t be guaranteed. Patients are at risk of side effects.
Most common anticipated risks associated with anetumab ravtansine are nausea, fatigue, vomiting, anorexia, diarrhea, peripheral neuropathy, increased Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) and eye toxicity.
Most common anticipated risks associated with vinorelbine are neutropenia, loss of some reflex reactions, constipation, nausea, vomiting, diarrhea, abnormal liver tests, alopecia, asthenia, fatigue, fever, erythema and local phlebitis.

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

1. Histological documentation of malignant pleural mesothelioma (MPM) overexpressing mesothelin

2. Unresectable locally advanced or metastatic MPM after a locally confirmed progression on 1st line treatment with platinum in combination with pemetrexed.
3. Patients must have measurable disease
4. Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 or 1
5. Life expectancy of at least 3 months
6. Adequate bone marrow, liver- and renal function
7. Left ventricular ejection fraction (LVEF) * 50% of the lower limit of normal (LLN) according to local institution ranges of normality.

Exclusion criteria

1. More than 1 previous systemic anti-cancer therapy line
2. Patients with corneal epitheliopathy or any eye disorder that may predispose the patients to this condition at the discretion of the ophtalmologist
3. Symptomatic brain metastases or meningeal tumors or other uncontrolled metastases in the central nervous system (CNS).
4. Evidence of history of bleeding diasthesis.
5. Ongoing or active infection (bacterial, fungal, or viral) of National Cancer Institute*s Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03 Grade > 2.
6. Pre-existing cardiac conditions

Study design

Design

Study phase:	2
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):	18-02-2016
Enrollment:	13

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Navelbine
Generic name:	Vinorelbine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	nvt
Generic name:	anetumab ravtansine

Ethics review

Approved WMO Date:	10-12-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-02-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-07-2016
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-09-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-10-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-12-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-12-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	08-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-01-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-06-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-07-2018
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	EUCTR2012-003650-88-NL
CCMO	NL55311.078.15