Switch maintenance treatment with gemcitabine for patients with malignant mesothelioma who do not progress after 1st line therapy with a pemetrexed-platinum combination. A randomised open label phase II study. ;NVALT 19

Published: 17-05-2013
Last updated: 07-02-2025

Primary objectives:1. Determine the potential improvement of the duration of progression-free survival by maintenance treatment with gemcitabine. Secondary objectives:1. To compare the objective radiological response (ORR) rate2. To compare overall...

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

Summary

ID

NL-OMON47831

Source
ToetsingOnline

Brief title
Maintenance treatment with gemcitabine for patients with MM

Condition

- Mesotheliomas

Synonym
pleural mesothelioma

Research involving

Human

Sponsors and support

Primary sponsor: Stichting NVALT studies
Source(s) of monetary or material Support: Stichting Mesotheliomen Werkgroep Nederland;KWF Kankerbestrijding (CKS)

Intervention

Keyword: best supportive care, maintenance Gemcitabine, malignant mesothelioma, non PD after first line chemo

Outcome measures

Primary outcome

The primary endpoint is progression free survival, defined as time from

randomisation to disease progression or death (in case no progression has been

documented)

Secondary outcome

- Adverse events

- Objective radiological response rate in patients with measurable disease

- Overall survival

- Changes in vital capacity and FEV1.

Exploratory endpoints include:

- biomarker analysis

- germline polymorphisms of relevant candidate genes

- new techniques to analyse standard imaging data

Study description

Background summary

Malignant mesothelioma (MM) is a nearly invariably lethal tumor of the pleura or peritoneum. Evidence from both mesothelioma studies and other solid malignancies indicates the potential to deliver real benefits to patients using a maintenance chemotherapy strategy.
The aim of this study is to perform a randomised phase II clinical trial to characterise the potential clinical benefit, toxicity, and biomarkers of outcome for maintenance chemotherapy with gemcitabine in patients with malignant pleural mesothelioma who have completed first line chemotherapy without progression. The choice of gemcitabine builds on previous work in mesothelioma and non-small cell lung cancer, which proposes a non-cross resistant *switch maintenance* agent.

Study objective

Primary objectives:
1. Determine the potential improvement of the duration of progression-free survival by maintenance treatment with gemcitabine.

Secondary objectives:
1. To compare the objective radiological response (ORR) rate
2. To compare overall survival (OS)
3. To assess and compare the lung function
4. To describe the toxicity
5. To identify potential biomarkers

Exploratory objectives:
1. To correlate tumour biomarkers and SNP*s with PFS and severe toxicity
2. To explore new techniques to analyse standard imaging data

Study design

This is a randomised, phase II multicentre trial of maintenance single agent gemcitabine or best supportive care in patients with malignant pleural mesothelioma who have completed first line chemotherapy without progression.

Intervention

Treatment with Gemcitabine or best supportive care.
Gemcitabine will be given intravenously at day 1 and day 8 of a 3-weeks cycle at a dose of 1250 mg/m2. Study treatment will continue until disease progression; unacceptable grade 3 or 4 treatment toxicity; serious intercurrent

illness; patient request for discontinuation; need or use for any other anti-cancer agent other than protocol treatment, except for palliative radiotherapy.

Study burden and risks

Risks: side effects of Gemcitabine
Burden: the extent of the burden for the patient is less. A lot of tests which the patient should have undergone are common practise, but more frequently done.
Additional investigations will be done for start of the study at all participants: extra bloodsampling for genotyping, biomarker and immunological research, lung function examination. On day 22, before second course and every 6 weeks on the same day as the response evaluation extra bloodsampling will be taken for immunological research at the participants in the pilot study. The extra blood tests will take place combined with the routine laboratory tests, so the patient doesn't have to be pricked extra. The CT scan is done by default. The standard CT-scan and a lung function examination will be done every 6 weeks on everyone and every 3 weeks a routine laboratory testing will be done. Only on patients who have randomized for the Gemcitabine arm, blood (haematology) will be taken off on day 8 to determine whether the patient is able to get the chemotherapy treatment.

Contacts

Public
Stichting NVALT studies

Luijbenstraat 15
's Hertogenbosch 5211 BR
NL
Scientific
Stichting NVALT studies

Luijbenstraat 15
's Hertogenbosch 5211 BR
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Patients with histologically or cytologically proven malignant mesothelioma • Age >= 18 years. • At the date of randomisation, the patients must have completed 4 cycles of first-line chemotherapy with a platinum (cisplatin or carboplatin) and pemetrexed combination at least 21 days but no more than 42 days prior to study entry, and have no evidence of progressive disease following first-line treatment. • Measurable or evaluable disease, according to modified RECIST criteria for pleural mesothelioma. • Ability to understand the study and give signed informed consent prior to beginning of protocol specific procedures. • WHO performance status <= 2 • Adequate organ function as evidenced by the following peripheral blood counts or serum chemistries at study entry: - Hematology: Neutrophil count >= 1.5 x 109/l, Platelets >= 100 x 109/l, Hemoglobin >= 6.2 mmol/l. - Hepatic function as defined by serum bilirubin <= 1.25 times the upper limit of normal (ULN), ALT and AST <= 2.5 times the ULN, except if liver metastases then ALAT and ASAT < 5 times the ULN. - Renal function as defined by serum creatinine <= 1.25 times ULN or creatinine clearance >= 50 ml/min (by Cockcroft-Gault formula).

Exclusion criteria

• Active uncontrolled infection or severe cardiac dysfunction (such as New York Heart Association Class III or IV cardiac disease, myocardial infarction within the last 6 months, unstable arrhythmias, or unstable angina).
• Presence of symptomatic CNS metastases.
• Radiotherapy within 2 weeks prior to study entry.
• Unstable peptic ulcer, unstable diabetes mellitus or other serious disabling condition.
• Concomitant administration of any other experimental drugs under investigation.

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:	Completed
Start date (anticipated):	20-03-2014
Enrollment:	124
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Gemcitabine
Generic name:	Gemcitabine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	17-05-2013
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-07-2013
Application type:	First submission

Review commission:	METC NedMec
Approved WMO Date:	29-11-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-12-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-02-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-01-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-11-2016
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	12-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-03-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-03-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-06-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-01-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-01-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-10-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-11-2018
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	26-04-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-05-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-01-2024
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

ID: 26963
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2012-005834-12-NL
CCMO	NL43041.031.13