LUME-Meso: Double blind, randomised, multicentre, phase II/III study of nintedanib in combination with pemetrexed / cisplatin followed by continuing nintedanib monotherapy versus placebo in combination with pemetrexed / cisplatin followed by continuing placebo monotherapy for the treatment of patients with unresectable malignant pleural mesothelioma

Published: 15-12-2015
Last updated: 20-04-2024

To evaluate the safety and efficacy in terms of progression-free survival (PFS) and overall survival (OS) of nintedanib + pemetrexed / cisplatin followed by nintedanib versus placebo + pemetrexed / cisplatin followed by placebo as first line...

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

Summary

ID

NL-OMON43431

Source
ToetsingOnline

Brief title
LUME-Meso: nintedanib in mesothelioma

Condition

- Mesotheliomas

Synonym
asbestos, pleural cancer

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim

Intervention

Keyword: chemotherapy, monotherapy, nintedanib, phase 3

Outcome measures

Primary outcome

The primary objective of this study is to evaluate whether treatment with nintedanib + pemetrexed / cisplatin followed by nintedanib monotherapy is more effective than treatment with placebo + pemetrexed / cisplatin followed by placebo monotherapy, as assessed by PFS.

Primary Endpoint: Progression free survival (PFS)

Secondary outcome

The key secondary objective is to evaluate whether treatment with nintednib p pemetrexed / cisplatin followed by nintedanib monotherapy is more effective than treatment with placebo + pemetrexed / cisplatin followed by placebo monotherapy, as assessed by OS.

Secondary Endpoints: Overall survival (OS) (key secondary endpoint), Objective tumour response according to modified RECIST criteria, Disease control

according to modified RECIST criteria.

Study description

Background summary

Most people who have unresectable mesothelioma die from their disease en new treatments are therefore necessary. Chemotherapy is standard therapy for mesothelioma, but interrupting the angiogenesis of tumors opens new possibilities for the improvement of the treatment.
Proteins involved in regulating the angiogenic process as vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) have been implicated in the prognosis of mesothelioma.
Nintedanib is a triple kinase inhibitor targeting VEGFR, PDGFR and FGFR (fibroblast growth factor receptor). Based on the available preclinical and clinical data, nintedanib displays a manageable safety profile and signal of efficacy in various tumour types.
Please refer also to section 1.1 of the clinical trial protocol

Study objective

To evaluate the safety and efficacy in terms of progression-free survival (PFS) and overall survival (OS) of nintedanib + pemetrexed / cisplatin followed by nintedanib versus placebo + pemetrexed / cisplatin followed by placebo as first line treatment for patients with unresectable malignant pleural mesothelioma (MPM). (also refer to section 2.1 and 2.2 of the clinical trial protocol)

Study design

This is a randomized, double-blind, placebo-controlled, multicenter phase 3 study. Globally 450 patients will be included and 15 in the Netherlands.
50% of the patients will be randomized and treated with nintedanib and 50% of the patients will be randomized and treated with nintedanib matching placebo (1:1 randomization)
(Please also refer to section 3.1 and 3.2 of the clnical trial protocol)

Intervention

Nintedanib or matching placebo will be administered in combination with standard pemetrexed and cisplatin for a maximum of 6 cycles of a 21-day cycle. For patients who have not progressed, nintedanib or matching placebo will continue to be administered orally on a daily basis until disease progression, unmanageable toxicity, withdrawal of consent or death.

Study burden and risks

Patients will spend approximately 40 hours at the hospital in a year time; consisting of 30 visits.

Patients will require somewhat more imaging than they receive regular care. Patients will be exposed to more radiation than standard of care and patients may experience side effects from nintedanib (and of pem/cis).

At every visit blood will be drawn and the patient will need to fill in 2 questionnaires.
Approximately 285 ml blood will be drawn in a year time. This includes the optional sampels.

Patients will receive a physical examination more often than usual.

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

- Histologically confirmed MPM (subtype: epithelioid);- Life expectancy of at least 3 months in the opinion of the investigator;- ECOG score of 0 or 1;- Measurable disease according to modified RECIST criteria

Exclusion criteria

- Previous systemic chemotherapy for MPM;- Prior treatment with nintedanib or any other prior line of therapy;- Patients with sarcomatoid or biphasic subtype MPM;- Radiotherapy (except extremities) within 3 months prior to baseline imaging;- Patients that may be eligible for or being considered for radical resection or elective surgery during the course of the study. ;- Radical surgery within 4 weeks prior to randomisation;- Active brain metastases (e.g. stable for < 4 weeks);- Therapeutic anticoagulation or anti-platelet therapy (except for low-dose therapy with acetylsalicylic acid < 325 mg per day);- Major injuries within the past 4 weeks prior to randomisation with incomplete wound healing;- Other malignancies within 3 years prior to screening other than basal cell skin cancer or carcinoma in situ of the cervix

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-07-2016

Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alimta
Generic name:	pemetrexed
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Cisplatine mayne, Platinol, Platistine, Platosin
Generic name:	Cisplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ovef
Generic name:	nintedanib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	15-12-2015
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	14-01-2016
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	15-08-2016
Application type:	Amendment
Review commission:	METC Atrium-Orbis-Zuyd
Approved WMO Date:	12-01-2017
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

Approved WMO Date:	27-06-2017
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	04-09-2017
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	05-09-2017
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	07-03-2018
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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	EUCTR2012-005201-48-NL
CCMO	NL55881.096.15
Other	NTC01907100