A Phase II, Double-Blind, Randomised, Placebo-Controlled Study to Assess the Efficacy and Safety of Selumetinib (AZD6244; ARRY-142886) (Hyd-Sulfate) in Combination with Docetaxel, Compared with Placebo in Combination with Docetaxel, in Patients receiving second line treatment for Locally Advanced or Metastatic Non Small Cell Lung Cancer (Stage IIIB-IV)

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To assess the efficacy, measured as progression free survival, and safety of Selumetinib in combination with docetaxel, compared to docetaxel alone, in patients receiving second line treatment for KRAS mutation negative locally advanced or...

Ethical review	Approved WMO
Status	Pending
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON40353

Source
ToetsingOnline

Brief title
SELECT-2

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lung cancer, Non small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Opdrachtgever/sponsor AstraZeneca

Intervention

Keyword: Docetaxel, KRAS, Non Small Cell Lung Cancer, Selumetinib

Outcome measures

Primary outcome

Progression Free Survival (PFS)

Secondary outcome

- Overall survival (OS)

- Objective Response Rate (ORR)

- Duration of Response (DoR)

- Change in tumor size

- Safety

- Tolerability

- To explore whether KRAS mutation is predictive of efficacy of selumetinib in

combination with docetaxel, compared to docetaxel alone

- To assess the effect on non small cell lung cancer symptoms

- To assess the effect on health-related quality of life

- To investigate the pharmacokinetics of Selumetinib and N-desmethyl

Selumetinib when administered in combination with docetaxel.

Study description

Background summary

Patients with advanced non-small cell lung cancer (NSCLC) have a very poor prognosis. Therefore, there is a strong medical need for medicines that have more benefit for the patient than the current standard treatment.
Selumetinib works by blocking the action of a protein, that controls cell growth. This protein (MEK) is activated by another protein called KRAS.
Blocking MEK may lead to an improvement in response to treatment with docetaxel when givenb with selumetinib, compared to when docetaxel is given alone. Rcent published research showed that drugs that are blocking MEK appears to increase the activity if combined with other anticancer medicines compared to when chemotherapy is given alone, in both tumours with and without KRAS mutation. This study will include patients that will not have a KRAS mutation seen in tumour samples.
Further studies are necessary to assess the efficacy and safety of Selumitinib in combination with docetaxel in patients with KRAS mutation- negative NSCLC.

Study objective

To assess the efficacy, measured as progression free survival, and safety of Selumetinib in combination with docetaxel, compared to docetaxel alone, in patients receiving second line treatment for KRAS mutation negative locally advanced or metastatic non small cell lung cancer.

Study design

Phase II, double-blind, randomised, placebo-controlled study
Randomised in a ratio of 2:2:1
- Selumetinib (75 mg dd on every day of a cycle of 21 days) in combination with 75 mg/m2 docetaxel (given on day 1 of every 21 day cycle)
- Selumetinib (75 mg dd on every day of a cycle of 21 days) in combination with 60 mg/m2 docetaxel (given on day 1 of every 21 day cycle)
- Placebo in combination with 75 mg/m2 docetaxel (given on day 1 of every 21 day cycle)

Intervention

Patient will be dosed twicedaily with a oral dose (capsules) of Selumetinib or

placebo in combination with 75 mg/m2 of 60 mg/m2 docetaxel iv, administered on day 1 of each 21 day cycle.

Study burden and risks

On several days during the study patients will undergo the following assessments:
- anamnesis (at screening also medical history)
- physical examination
- vital signs (blood pressure, pulse)
- length
- weight
- CT or MRI scan
- ECG
- eye assessment
- blood and urine assessments
- MUGA/echocardiogram
- questionnaires (LSCC (specific voor lung cancer symptoms) en SF-36v2)
- diary card
- pregnancy test
- tumor biopsy (optional)

Adverse events of Selumetinib (AZD6244), docetaxel or the combination:
Adverse events that may be caused by Selumetinib are: rash, dry skin, nail changes, fever, stomatitis, diarrhea, nausea, vomiting, swelling of the face or extremities, shortness of breath, fatigue, increase in blood pressure, blurring of vision, increase in phosphate level, increase in some liver proteins, low albumin level, decrease in the pumping performance of the heart,
Adverse events, that probably may be caused by selumetinib are: weakness of neck muscles, cough, eye problems, increase in blood level of CPK.
The most common side effects that may be caused by docetaxel are: decrease in number of white blood cells, rash, diarrhea, nausea, vomiting, hair loss, tiredness, burning or tingling sensation in hands or feet, muscle pain, elevated tear production, allergic reaction and nail changes.
When selumetinib was used in combination with docetaxel, the number of patients with side effects, and or the severity of side effects was increased.
Female patients cannot become pregnant during this study.

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

* Provision of informed consent
* Male and female patients
* Aged at least 18 years
* Histological or cytological confirmation of locally advanced or metastatic non small cell lung cancer
* Prospective confirmation of KRAS mutation negative status as determined using the cobas KRAS mutation Test via an AstraZeneca approved laboratory
* Failure of 1st line anti-cancer therapy due to radiological documentation of disease progression in advanced disease or subsequent relapse of disease following 1st line therapy
* WHO Performance status 0-1
* At least one evaluable lesion
* Serum creatinin clearance >50 mL/min
* Negative pregnancy test or postmenopausal
* Patients should be able to swallow capsules

Exclusion criteria

- Mixed small cell and non-small cell lung cancer histology;- Received >1 prior anti-cancer

drug regimen for advanced or metatstatic NSCLC;- Having received an investigational drug or any other systemic anti-cancer therapy within 30 days of starting treatment or within five half-lives of the compound;- Other concomitant anti-cancer therapy agents except steroids;- Prior treatment with a MEK inhibitor or any docetaxel-containing regimen;- Sympotomatic brain metastases or spinal cord compression. Patients with asymptomatic brain metastasis or treated and stable off steroids and anti-convulsants for at least 1 month prior to entry into the study are eligible;- Laboratory values as listed below:
* ANC <1.5 x 109/L (1500 per mm3)
* Platelets <100 x 109/L (100.000 per mm3)
* Haemoglobin < 9.0 g/dL
* Serum bilirubin > 1.5 x Upper Limit of Normal
* AST or ALT in patients with no liver metastasis: >2.5 x ULN
* AST or ALT in patients with liver metastasis: >5 x ULN
* AST or ALT > 3.5 x ULN and <5 x ULN in patients with liver metastasis and ALP > 6 x ULN;- Cardiac conditions as follows:
* Uncontrolled hypertension (BP >150/95 mmHg)
* Acute coronary syndrome within 6 months prior to starting treatment
* Angina Canadian Cardiovascular Society grade II-IV
* Symptomatic heart failure
* Prior or current cardiomyopathy
* Baseline LVEF < 55% by echocardiography or MUGA
* Several valvular heart disease
* Atrial fibrilation with a ventricular rate >100 bpm on ECG at rest;* Any evidence of severe uncontrolled systemic disease, active infection, active bleeding diatheses or renal transplant including hepatitis B, C and HIV;* Refractory nausea and vomiting, chronic gastrointestinal diseases or significant bowel resection that would preclude adequate absorption;- Ophthalmologic conditions:
* Current or past history of central serous retinopathy
* Current or past history of retinal vein occlusion
* Intraocular pressure > 21 mmHg or uncontrolled glaucoma

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2013
Enrollment:	19
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	Selumetinib

Ethics review

Approved WMO Date:	04-06-2013
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-10-2013
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-02-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-02-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	17-04-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-10-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	17-11-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-05-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	18-05-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-07-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-01-2016
Application type:	Amendment

Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-01-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-03-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-03-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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	EUCTR2012-003622-25-NL
ClinicalTrials.gov	NCT01750281
CCMO	NL44811.031.13