# A PHASE II STUDY OF SORAFENIB IN PATIENTS WITH LOCALLY ADVANCED AND/OR METASTATIC (STAGE IIIB OR IV) NON-SMALL CELL LUNG CANCER (NSCLC) WITH A K-RAS MUTATION

Published: 21-01-2010
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Efficacy of sorafenib in NSCLC with a K-RAS mutation as determined by the Disease Control Rate at 6 weeks

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Respiratory and mediastinal neoplasms malignant and unspecified |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON32472

**Source**
ToetsingOnline

**Brief title**
Sorafenib in K-Ras mutated NSCLC

### Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

**Synonym**
non-small cell lung cancer

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Vrije Universiteit Medisch Centrum
**Source(s) of monetary or material Support:** Bayer

## Intervention

**Keyword:** K-Ras mutation, NSCLC, Sorafenib

## Outcome measures

### Primary outcome

Disease Control Rate

### Secondary outcome

objective response rate, duration of response, time to disease progression or

death, survival

# Study description

### Background summary

Lung cancer is the major cause of cancer related death in the Western World. In the year 2006 10357 cases of lung cancer were diagnosed in The Netherlands, 6667 in men and 3690 in women while 9889 patients died of lung cancer1. Non-small cell lung cancer (NSCLC) constitutes about 85% of all lung cancer and more than 50% of patients are not curable at presentation. The current standard of therapy for patients with advanced non small cell lung cancer is platinum based doublet chemotherapy. Therapeutic results are far from satisfactory: survival has reached a plateau at a median of 9-11 months in the recently published phase III trials. Therefore, clinical research of new treatment strategies is warranted. One way to improve on these results is to personalize treatment, amongst others based on tumor molecular characteristics. In NSCLC the most frequent occurring somatic mutations are located in 3 codons of the K-Ras gene. Constitutional activation of K-Ras, leads to signaling through the Raf-Mek-Erk pathway which is implicated in cellular growth and survival pathways. Treatment options for patients that have K-Ras mutated tumors are limited as these are believed to be poor responders to cytotoxic chemotherapy and refractory to EGFR TKI*s. Sorafenib, a multitargeted tyrosine kinase inhibitor, inhibits amongst others the Ras-Raf pathway. Sorafenib has been evaluated in unselected advanced NSCLC patients both as a single agent and in

conjuncture with platinum doublet chemotherapy as first line treatment. The results of these studies are not equivocal: while the single agent studies showed some activity of sorafenib in all lines of treatment, the ESCAPE phase III trial failed to improve survival when sorafenib was added to the commonly used paclitaxel-carboplatin doublet. Sorafenib is orally available and is labeled for all histologies of NSCLC. We hypothesized that selecting NSCLC patients with K-Ras mutated tumors will enhance the clinical efficacy of sorafenib

### Study objective

Efficacy of sorafenib in NSCLC with a K-RAS mutation as determined by the Disease Control Rate at 6 weeks

### Study design

Single arm open label phase II study.

### Intervention

Sorafenib 400 mg td po

### Study burden and risks

Usual risk associated with treatment with chemotherapy. Extra burden associated with participation is one additional tumor biopsy after 3 weeks of treatment (optional) and two additional venapunctures before and after 3 weeks of treatment.

## 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. Histologically advanced NSCLC stage IIIB or IV harbouring a K-RAS mutation
2. Disease progression after at least 1 prior chemotherapy regimen that should include a platinum doublet
3. Age > 18 years.
4. ECOG Performance Status of 0-2
5. Subjects with at least one uni-dimensional (for RECIST) measurable lesion. Lesions must be measured by CT-scan.
6. Adequate bone marrow, liver and renal function
9. Written informed consent

## Exclusion criteria

1. History of cardiac disease: congestive heart failure >NYHA class 2; active CAD (MI more than 6 mo prior to study entry is allowed); cardiac arythmias requiring anti-arythmic therapy( beta blockers or digoxin are permitted) or uncontrolled hypertension.
2. History of HIV infection or chronic hepatitis B or C.
3. Active clinically serious infections (> grade 2 NCI-CTC version 3.0)
4. Symptomatic metastatic brain or meningeal tumors (unless the patient is > 1 months from definitive radiotherapy and off steroids)

# Study design

## Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 01-05-2010 |
| Enrollment: | 48 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | nexavar |
| Generic name: | sorafenib |
| Registration: | Yes - NL outside intended use |

# Ethics review

Approved WMO

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|---|---|
| Date: | 21-01-2010 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |

Approved WMO

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|---|---|
| Date: | 16-02-2010 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |

Approved WMO

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|---|---|
| Date: | 08-04-2010 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# 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: 25401
Source: NTR
Title:

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2009-016632-12-NL |
| CCMO | NL30000.029.09 |
| OMON | NL-OMON25401 |