A phase II study of sorafenib and metformin in patients with locally advanced and/or metastatic non-smal cell lung cancer (NSCLC) with a K-Ras mutation

Published: 05-03-2012
Last updated: 07-02-2025

To assess the efficacy of combined treatment with sorafenib and metformin.

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

Summary

ID

NL-OMON37863

Source
ToetsingOnline

Brief title
Phase II study of combined treatment of sorafenib and metformin in NSCLC

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Non-small lung cancer; lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: K-Ras, metformin, NSCLC, sorafenib

Outcome measures

Primary outcome

Non Progressive Rate (NPR) after 6 weeks of treatment

Secondary outcome

Response Rate, duration of Response, Progression Free Survival and Overall

survival

Study description

Background summary

The overall survival in lung cancer patients is poor and chemotherapy treatment has reached a plateau to improve survival. Recently, metformin is discovered as an anti cancer agent. Metformin is known as a save drug, with minor toxicity and used in treatment of type II diabetes for more than 40 years. Preclinical studies have found that metformin has anti cancer properties by targeting mTOR, an effector in the PI3K pathway. Sorafenib is a multitarget tyrosine kinase inhibitor and is registered for second line treatment in renal cell and hepatocellular cancer. In non-small cell lung cancer (NSCLC), sorafenib is currently tested in phase III studies. Sorafenib targets Raf kinase, which is part of the Ras/Raf pathway. This pathway is overactive in patients harbouring a K-Ras mutation.The PI3K pathway and the Ras/Raf pathway have a close interaction and are both important stimulants for cell growth and proliferation. In this study we will treat patients with metformin and sorafenib. We hypothesize that metformin wil enhance the efficacy of sorafenib.

Study objective

To assess the efficacy of combined treatment with sorafenib and metformin.

Study design

An open label, multicenter, phase II study.

Intervention

treatment with sorafenib and metformin

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Sorafenib is previously tested in lung cancer patients and is found to be effective and tolerable. Metformin is a save and frequently prescribed drug used as first choice of treamtment for patients with type II diabetes mellitus. The frequency of tumor assessment using CT and blood samples is similar as by standard 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. Prior surgery and/or localized irradiation is permitted provided that the irradiated lesion is not the only measurable lesion. 4. Age > 18 years. 5. ECOG Performance Status of 0-2 6. Life expectancy of at least 12 weeks 7. 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): 5. Patients with seizure disorder requiring medication (such as steroids or anti-epileptics)

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-07-2012
Enrollment:	45
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	05-03-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-05-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-11-2012
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2011-004683-30-NL
CCMO	NL38229.029.11