A Phase III, randomized, double-blind, placebo-controlled multi-center study of ASA404 in combination with paclitaxel and carboplatin as first-line treatment for locally advanced or metastatic (stage IIIb/IV) non-small cell lung cancer (NSCLC)

Published: 21-04-2008
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The primary objective is to compare the overall survival (OS) of patients receiving ASA404 or placebo in combination with paclitaxel and carboplatin for first-line treatment of stage IIIb/IV NSCLC

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

Summary

ID

NL-OMON32300

Source
ToetsingOnline

Brief title
ASA404 combined with paclitaxel and carboplatin in NSCLC stage IIb/IV

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Non-small cell lungcancer

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Farmaceutische industrie: Novartis Pharma

Intervention

Keyword: ASA404, first-line therapy, non-small cell lung cancer

Outcome measures

Primary outcome

Overall survival (OS) of patients receiving ASA404 or placebo in combination

with paclitaxel and carboplatin for first-line treatment of stage IIIb/IV

NSCLC.

Secondary outcome

The Overall survival of patients with non-squamous NSCLC receiving ASA404 or

placebo in combination with paclitaxel and carboplatin

The Overall survival of patients with squamous NSCLC receiving ASA404 or

placebo in combination with paclitaxel and carboplatin

Also progression-free survival, overall response rate, time to overall response

(CR or PR) for responders only and duration of overall response (CR or PR) for

responders only.

Study description

Background summary

Lung cancer is the leading cause of cancer death in the world, affecting approximately 171,000 people annually in the US and more than 200,000 people in

Europe. Of all these patients, approximately 85% have non-small cell lung cancer.
Non-small cell lung cancer (NSCLC) is a heterogeneous aggregate of histologies. The most common histologies are squamous cell carcinoma.
Patients are often diagnosed with an advanced stage of disease, and approximately 85% of patients will die from their disease within one year with only 1% of patients surviving 5 years.
Patients having Stage IIIb/IV NSCLC are not considered to be candidates for curative resection surgery or radiation. Platinum and taxane based therapies are commonly administered to patients with NSCLC, however, previous studies indicate a response rate of only 19% and a median survival time of approximately 8 months. Therefore, the development of new treatments is needed for patients with NSCLC.

ASA404 is a novel Tumor-Vascular Disrupting Agent (VDA). These drugs selectively attack tumor blood vessels, giving them broad potential against solid cancers, which depend on their blood supply to survive and grow. ASA404 has shown synergistic qualities when combined with a carboplatin and paclitaxel chemotherapy regimen in patients with NSCLC.

Study objective

The primary objective is to compare the overall survival (OS) of patients receiving ASA404 or placebo in combination with paclitaxel and carboplatin for first-line treatment of stage IIIb/IV NSCLC

Study design

This is a double-blind, placebo-controlled, randomized Phase III trial.
Patients will be randomized in a 1:1 ratio into one of the following two treatment arms:
1. ASA404 1800 mg/m2 plus paclitaxel 200mg/m2 plus carboplatin AUC 6.0 OR
2. placebo plus paclitaxel 200mg/m2 plus carboplatin AUC 6.0

Randomization will be stratified by:
* Gender (male vs. female)
* NSCLC histology (Squamous NSCLC vs. Non-Squamous NSCLC)

A total of 1200 patients will be enrolled into the study. Tumor assessments will be performed every 6 weeks (every 2 cycles). Study treatment will be administered for a maximum of 6 treatment cycles.

Intervention

Patients will be randomized in a 1:1 ratio into one of the following two treatment arms:

1. ASA404 1800 mg/m2 plus paclitaxel 200mg/m2 plus carboplatin AUC 6.0 OR
2. placebo plus paclitaxel 200mg/m2 plus carboplatin AUC 6.0

Study burden and risks

Patients will receive 6 cycles. Patient will have 2 visits in one cycle. On day 1 of each cycle the patient receives the studymedication will be administered intravenously and the patient will stay in the hospital for approximately 6 hrs.
Prior to the infusion and one hour after the administration of ASA404, 6 bloodsamples will be taken (Pk and biomarkers) and 2 ECGs will be made. On day 12 of each cycle the patient returns to the hospital for a bloodtest (hematology). Every 6 weeks a CT-scan wil be performed for tumor evaluation. Also a bloodsample for optional biomarker study will be collected.
After discontinuation of the studymedication due to progression the patient will be followed every 6 weeks for survival. If the patient discontinued for other reasons than progression the patient will be followed by CT-scan every 6 weeks until progression, thereafter survival data will be collected every 6 weeks until death.

Toxicity of ASA404 in combination with paclitaxel + carboplatine or combination with paclitaxel + carboplatine .
Radioation exposure of CT-scan and/or alleergic reaction on the contrast fluid.
The risk of taking blood may include fainting, pain, bleeding, puncture into the vein, and/or bruising.
The risk of having an intravenous catheter includes minor infection, bleeding, and slight discomfort or bruising at the site where the needle for the catheter is inserted.

Contacts

Public
Novartis

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Scientific
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Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Histological or cytological confirmed non-small cell carcinoma of the lung. (Sputum cytology is not acceptable.)
2. Newly diagnosed Stage IIIb disease or Stage IV disease
3. No prior systemic antineoplastic treatment for Stage IIIb/IV (Prior neoadjuvant or adjuvant chemotherapy for earlier stage I/II NSCLC is allowed)
4. WHO Performance Status of 0-1
5. Measurable or non-measurable disease per RECIST criteria
6. Lab values within the range, as defined below, within 2 weeks of randomization:
* Neutrophils count (ANC) > 2.0 x 109/L
* Platelets * 100 x109/L
* Hemoglobin * 6,28 mmol/l
* Serum creatinine * 1.5 x ULN (* 120 micro mol/L)
* Serum bilirubin * 1.5 x ULN (* 25 micro mol/L)
* Leverenzymen (AST and ALT) * 2.5x ULN (* 5x ULN if liver metatasis)
* INR or PTT * 1.5 x IULN
* Normal Electrolyte values (potassium, calcium, magnesium)
* Negative serum pregnancy test < 72 hours prior to initial dosing
7. Life expectancy * 12 weeks

Exclusion criteria

1. No present CNS metastases
2. Patients with a history of another primary malignancy * 5 years, with the exception of non-melanoma skin cancer or cervical cancer in situ.
3. Radiotherapy * 2 weeks prior to randomization.
4. Major surgery * 4 weeks prior to randomization
5. Concurrent use of other investigational agents * 4 weeks prior to randomization

6. Prior exposure to Tumor-VDAs or other vascular targeting agents
7. Pleural effusion that causes * CTC grade 2 dyspnea
8. Patients with systolic BP > 160 mm Hg and/or diastolic BP >90 mm Hg
9. Patients with recent hemoptysis associated with NSCLC
10. Patients with any significant impaired cardiac function or conduction of the heart:
* long QT syndrome, baseline 12-lead ECG QTc of >450 msec, congestive heart failure (NYHA class III or IV), myocardial infarction < 12 months of study entry, unstable or poorly controlled angina pectoris, history of labile hypertension or poor compliance with anti-hypertensive regimen, history of a sustained ventricular tachycardia, any history of ventricular fibrillation or Torsades de Pointes, right bundle branch block and left anterior hemiblock, bradycardia (heart rate <50 beats per min)
11. Concomitant use of drugs with a risk of causing Torsades de Pointes
12. Known allergy or hypersensitivity to platinum-containing drugs and/or taxanes, other drugs formulated in Cremophor EL (polyoxyethylated castor oil.
13. Peripheral sensory neuropathy grade 2 neuropathy
14. Concurrent severe and/or uncontrolled medical and significant neurologic or psychiatric disorder

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):	08-10-2008
Enrollment:	45
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	niet van toepassing, nog niet geregistreerd
Generic name:	nog geen
Product type:	Medicine
Brand name:	nvt
Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	nvt
Generic name:	paclitaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-04-2008
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-05-2008
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-12-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-05-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	19-03-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-03-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-06-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2007-006072-11-NL
CCMO	NL22600.060.08