A phase III, randomized, double-blind, placebo-controlled multi-center study of ASA404 in combination with docetaxel in second-line treatment of patients with advanced or metastatic (stage IIIb/IV) non-small cell lung cancer (NSCLC).

Published: 10-02-2009
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Primary Objective:The primary objective of the study is to compare overall survival between the ASA404 plus docetaxel group and the placebo plus docetaxel group Key Secondary Objectives:To compare Progression-Free Survival (PFS) and the Overall...

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

Summary

ID

NL-OMON33036

Source
ToetsingOnline

Brief title
ATTRACT-2

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
advanced lung cancer, locally advanced or metastatic non-small cell lung cancer

Research involving

Human

Sponsors and support

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

Intervention

Keyword: ASA404, non-small cell lung cancer, second-line therapy, tumour Vascular Disrupting Agent

Outcome measures

Primary outcome

The primary efficacy endpoint will be overall survival

Secondary outcome

The key secondary efficacy endpoints (PFS,ORR) will be based on documentation

of response or progression per RECIST assessed by the investigators criteria.

Study description

Background summary

Lung cancer is the leading cause of cancer death in the world, accounting for 32% of cancer deaths in males and 25% in females, 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.
Patients are often diagnosed at an already 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, and radiation therapy is primarily used as palliative treatment in advanced stages of NSCLC.
Since the late 1990s, three drugs have been approved for the second line therapy of NSCLC: docetaxel, pemetrexed and erlotinib.
Despite the recent progress with additional treatment options in second-line NSCLC, additional therapies with better efficacy and safety profiles are needed to improve the overall survival, response to treatment and QoL for patient*s with second-line NSCLC.

Study objective

Primary Objective:
The primary objective of the study is to compare overall survival between the ASA404 plus docetaxel group and the placebo plus docetaxel group

Key Secondary Objectives:
To compare Progression-Free Survival (PFS) and the Overall Response Rate (ORR) per RECIST assessed by the investigators between patients receiving ASA404 or placebo in combination with docetaxel

Other Objectives:
* To assess Time to Response (CR or PR for responders only) and Duration of Response (CR or PR for responders only) per RECIST assessed by the investigators between patients receiving ASA404 or placebo in combination with docetaxel
* To assess safety of ASA404 in combination with docetaxel
* To determine population pharmacokinetics and factors influencing systemic exposure to ASA404
* To assess the Quality of Life (QoL) of patients receiving ASA404 or placebo in combination with docetaxel

Exploratory Objectives:
* To explore the effect of ASA404 on pharmacodynamic biomarkers in plasma
* To explore whether tumor biomarkers predictive for ASA404 response can be defined
* To explore ASA404 mechanism of action through measuring circulating endothelial cells and gene expression (US sites ONLY)
* To explore genetic polymorphisms that may affect ASA404 metabolism and response

Study design

This is a prospective, global, multi-center, double-blind, placebo-controlled, randomized Phase III trial.

Patients will be randomized into one of the following two treatment arms:
1. ASA404 1800 mg/m2 plus docetaxel 75 mg/m2
OR
2. placebo plus docetaxel 75 mg/m2

Randomization will be stratified by:
* WHO PS 0-1 vs 2
* Histology (squamous vs non-squamous)
* Prior treatment with vs without a paclitaxel-based regimen in the first-line setting

Nine-hundred patients will be enrolled into the study.
All patients must begin study treatment within 7 days from randomization. A treatment cycle is 21 days. Study treatment with docetaxel will be administered for a maximum of 6 cycles. However, once 6 cycles of study treatment with docetaxel are completed the patient may continue to receive study drug (ASA404 or placebo) as maintenance treatment until disease progression, unacceptable toxicity or withdrawal of consent. If study treatment is stopped due to toxicity attributed specifically to docetaxel prior to completing the maximum 6 cycles of docetaxel chemotherapy, the patient may continue to receive study drug as maintenance treatment until documented disease progression, unacceptable toxicity occurs or consent is withdrawn. Maintenance treatment with study drug can commence once docetaxel related toxicities have resolved at the next scheduled cycle visit.
Tumor assessments will be performed every 6 weeks or more frequently if there are signs suggesting disease progression. Following treatment discontinuation or documented disease progression, patients will be followed every 6 weeks for survival.

Intervention

Addition of ASA404 to the standard treatment.

Study burden and risks

Patients will receive up to 6 cycles of combination therapy. Patient will have 2 visits in one cycle. On day 1 of each cycle the patient the study medication will be administered intravenously and the patient will stay in the hospital for approximately 3 hrs.
Prior to the infusion and one hour after the administration of ASA404, bloodsamples will be taken (Pk and biomarkers) and 2 ECGs will be made. On day 10 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. One bloodsample for optional biomarker study will also be collected, after patient consent.
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 docetaxel or docetaxel alone.
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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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Histologically confirmed non-small cell carcinoma of the lung of all histologies.
2. Patients who have progressed while on or following a first-line chemotherapy regimen for Stage IIIb disease (malignant pleural effusion or pericardial effusion that have been confirmed cytologically) or Stage IV disease. Patients who have received bevacizumab and/or EGFR inhibitors in first-line will be eligible
3. Age * 18 years old
4. WHO Performance Status of 0-2
5. Measurable or non-measurable disease per RECIST criteria
6. Laboratory values within the range, as defined below, within 2 weeks of randomization:

* Absolute neutrophils count (ANC) * 2.0 x 109/L
* Platelets * 100 x109/L
* Hemoglobin * 10 g/dL
* Serum creatinine * 1.5 x ULN (* 120 micro mol/L)
* Serum bilirubin * 1.5 x ULN (* 25 micro mol/L)
* Alkaline phosphatase * 2.5 x ULN
* Aspartate transaminase (AST) and alanine transaminase (ALT) * 2.5 x ULN (* 5 x ULN if liver metastases)
* International Normalized Ratio (INR) or Prothrombin Time (PT) * 1.5 x ULN
* Electrolyte values (sodium, potassium, calcium, magnesium) within *1 x LLN and * 1 x ULN. Patients with corrected electrolyte values are eligible
* Females of child-bearing potential must have negative serum pregnancy test (confirmation of negative urine pregnancy test within 72 hours prior to initial dosing)
7. Life expectancy * 12 weeks
8. Written informed consent obtained according to local guidelines

Exclusion criteria

1. Patients having 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. Patients must have recovered from all radiotherapy-related toxicities.
4. Major surgery * 4 weeks prior to randomization (major surgery is defined by the use of general anesthesia). Endoscopic examinations with diagnostic intent are not considered major surgery. Minor surgery * 2 weeks prior to randomization. Insertion of a vascular access device is allowed. Insertion of a vascular access device is not considered major or minor surgery. Patients must have recovered from all surgery-related complications.
5. Treatment with first-line chemotherapy regimen * 3 weeks prior to randomization (* 6 weeks for bevacizumab, mitomycin and nitrosoureas)
6. Concurrent use of other investigational agents and patients who have received investigational agents * 4 weeks prior to randomization
7. Prior treatment with docetaxel for NSCLC in the first-line setting
8. Prior treatment with VDAs or tumor - VDAs for NSCLC in the firstline setting
9. Pleural effusion that causes * CTC grade 2 dyspnea
10. Patients with systolic BP > 160 mm Hg and/or diastolic BP > 90 mm Hg while on medication for hypertension
11. Patients with recent hemoptysis associated with NSCLC (> 1 teaspoon in a single episode within 4 weeks)
12. Patients with any one of the following:
* Patients with long QT syndrome
* Patients with a Baseline 12-lead ECG QTc of > 450 msec per central evaluation
* Congestive heart failure (NY Heart Association class III or IV)
* Patients with a myocardial infarction within 12 months of study entry or with implanted cardiac pacemaker

* Unstable or poorly controlled angina pectoris, including Prinzmetal variant angina pectoris
* History of labile hypertension or poor compliance with antihypertensive regimen
* History of a sustained ventricular tachycardia
* Any history of ventricular fibrillation or Torsades de Pointes
* Right bundle branch block and left anterior hemiblock (bifasicular block)
* Bradycardia defined as heart rate < 50 beats per minute
13. Concomitant use of drugs with a risk of causing Torsades de Pointes
14. Known allergy or hypersensitivity to docetaxel or drugs formulated with polysorbate 80
15. Peripheral sensory neuropathy with functional impairment (CTC grade 2 neuropathy, regardless of causality)
16. Pregnant or breast feeding females
17. Women of child bearing potential or sexually active males,
unwilling or unable to use the required highly effective method(s) of contraception for both sexes while receiving treatment and for at least 6 months after the discontinuation of study treatment.
18. Concurrent severe and/or uncontrolled medical disease
19. Significant neurologic or psychiatric disorder which could compromise participation in the study
20. Patient unwilling or unable to comply with the protocol

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):	04-06-2009
Enrollment:	18
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:	Taxotère
Generic name:	docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	10-02-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-04-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-05-2009
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-10-2009
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-02-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-08-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2008-002309-38-NL
ClinicalTrials.gov	NCT00738387
CCMO	NL26510.091.09