A randomized phase III trial of erlotinib versus docetaxel in patients with advanced squamous cell non-small cell lung cancer who failed first line platinum based doublet chemotherapy stratified by VeriStrat Good vs VeriStrat Poor (EMPHASIS, NVALT13, ETOP 3-12)

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Primary: Explore the predictive ability of the VeriStrat signature, by testing for interaction between treatment arms (Arm A: erlotinib vs Arm B: docetaxel) and VeriStrat status (VSG vs VSP) using as outcome progression free survival. Secondary...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract neoplasms
Study type	Interventional

Summary

ID

NL-OMON38457

Source
ToetsingOnline

Brief title
NVALT13

Condition

- Respiratory tract neoplasms

Synonym
non-small cell lung cancer; lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: European Thoracic Oncology Platform (ETOP)
Source(s) of monetary or material Support: Biodesix, Inc.,ETOP

Intervention

Keyword: docetaxel, erlotinib, NSCLC, VeriStrat

Outcome measures

Primary outcome

Progression free survival.

Secondary outcome

Objective response rate and disease control rate, overall survival, safety.

Study description

Background summary

Standard treatment of non-small cell lung cancer (NSCLC) is platinum-containing chemotherapy. After failure of this treatment docetaxel en erlotinib are used as monotherapy, because of the favorable results in comparison with best supportive care.
Currently there are no accepted baseline criteria to allow choosing between docetaxel or erlotinib, except for the presence of an activating epidermal growth factor receptor (EGFR) mutation, provided patients did not receive an EGFR-tyrosine kinase inhibitor (TKI) as first line therapy. In fact, the INTEREST trial that randomized NSCLC patients with all histologies between gefitinib and docetaxel in the second line setting, showed no difference in PFS and OS in the EGFR wild-type (WT) population. In a subgroup analysis, patients with squamous cell carcinomas did not present any difference in PFS or OS between both treatment groups.
Recently, a blood-based proteomic test, VeriStrat®, that appears to be both predictive and prognostic for outcome in patients with NSCLC, has become available. VeriStrat assigns each sample a *good* (VSG) or *poor* (VSP) label. In approximately 2% of cases, an unequivocal label cannot be assigned and an indeterminate classification is reported. The test has been validated in a

study with De gefitinib and erlotinib. These studies confirmed that patients classified as VSG had better PFS and OS outcome than patients classified as VSP. VeriStrat demonstrated outstanding reproducibility. Retrospective analysis of VeriStrat performed on available serum samples of patients from a trial of erlotinib versus placebo confirmed the above results for the treatment arms. De resultaten van de VeriStrat test bij het gevorderde plaveiselcelcarcinoom in de populatie met een uitslag *goed* waren onverwacht positief na behandeling gefitinib. In the initial evaluation of VeriStrat it was found that patients with relapsed squamous cell lung carcinoma and designated to the VSG population had an unexpectedly favorable outcome following treatment with gefitinib. The test does not seem to discriminate between patients who receive cytotoxic chemotherapy, including docetaxel.
Thus, one rational approach for using the VeriStrat test is a trial design where patients with relapsed squamous cell lung cancer in both strata (VSG and VSP) are randomized between an EGFR-TKI and chemotherapy. As both erlotinib and docetaxel are currently approved for this indication, these drugs will be used in the proposed trial.

Study objective

Primary: Explore the predictive ability of the VeriStrat signature, by testing for interaction between treatment arms (Arm A: erlotinib vs Arm B: docetaxel) and VeriStrat status (VSG vs VSP) using as outcome progression free survival.
Secondary Objectives: Objective response rate (ORR) and disease control rate (DCR), Duration of response, OS, Safety.
Secondary: Explore whether treatment with erlotinib provides progression free survival benefit as compared to docetaxel in the VSG group. Compare progression free survival in the two treatment arms (Arm A: erlotinib vs Arm B: docetaxel) in the VSP group. Explore the prognostic ability of the VeriStrat signature by testing for an overall difference in progression free survival between the two VeriStrat groups (in case of no significant interaction). Effects on OS, response rate and disease control rate. Assess the safety and the tolerability of the two treatments separately in each VeriStrat group and overall.

Study design

Multicenter randomized open phase III parallel group study.
Testing of VeriStrat status (good/poor). Only patients with a definite VeriStrat status will be included.
Patient will be randomly allocated to either:
* Docetaxel IV infusions every 3 weeks, 75 mg/m2.
* Erlotinib tablets 150 mg daily.
Stratification for VeriStrat status.
Study duration: till disease progression.
Approx. 500 patients.

Intervention

Treatment with docetaxel or erlotinib.

Study burden and risks

Risk: Adverse events of study treatment.
Burden: The study follows the standard treatment for medication (docetaxel or erlotinib), hospital visits, safety blood tests and imaging.
Extra test:
Blood test VeriStrat 3,5 ml blood once.

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

* Histologically/cytologically proven stage III or IV squamous NSCLC.
* Progressive disease upon or after previous chemotherapy including at least one line of platinum-based chemotherapy.
* Measurable or evaluable disease.
* Age * 18 years.
* ECOG Performance Status of 0 * 2.
* Life expectancy of at least 12 weeks.
* Adequate contraception for females of childbearing potential during the study and in the 12 months thereafter.
* Adequate contraception for male participants during the study.

Exclusion criteria

* Previous treatment with EGFR-TKI or docetaxel.
* Documented brain metastasis. Exceptions: see protocol page 10.
* Documented presence of activating EGFR mutations, if the patient was tested for EGFR mutations.
* Pregnancy or lactation.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-05-2013

Enrollment:	160
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tarceva
Generic name:	erlotinib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxotere
Generic name:	docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	13-12-2012
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	12-03-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	19-03-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	10-04-2013

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 19-04-2013

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 06-06-2013

Application type: Amendment

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Approved WMO
Date: 13-06-2013

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 19-07-2013

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 23-07-2013

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 03-06-2014

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
Other	clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2012-001896-35-NL
CCMO	NL42928.098.12