LUX-Lung 8: A randomized, open-label Phase III trial of afatinib versus erlotinib in patients with advanced squamous cell carcinoma of the lung as second-line therapy following first-line platinum-based chemotherapy

Published: 16-04-2012
Last updated: 29-04-2024

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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-OMON38119

Source
ToetsingOnline

Brief title
LUX-Lung 8

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lung cancer, Non-small cell lung cancer

Research involving

Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim BV.

Intervention

Keyword: afatinib, erlotinib, NSCLC, squamous cel carcinoma

Outcome measures

Primary outcome

Progression free Survial (PFS)

Secondary outcome

- Overall Survival (OS)

- Objective response

- Disease control

- Tumour shrinkage

- Health related quality of life (QoL)

- Safety

Study description

Background summary

Treatment options for patients with advanced squamous cell carcinoma of the lung are limited following first line chemotherapy with most patients recurring and eventually succumbing to their disease. For patients eligible to tolerate, chemotherapy has been an option and docetaxel is indicated in the second line setting for patients with advanced NSCLC with associated chemotherapy related morbidity. The EGFR pathway has been shown to play a significant role in propagation of human epithelial malignancies including NSCLC. Erlotinib inhibits the TK domain of the EGFR and is indicated in the treatment of NSCLC following failure of one prior chemotherapy regimen or in patients not progressing after receiving four cycles of platinum based chemotherapy. Patients with adenocarcinoma tend to derive higher response rates than other histologies of NSCLC in erlotinib trials. There remains thus a significant void for patients with squamous cell carcinoma of the lung whose therapeutic options are limited in the second line and maintenance setting.
Afatinib is an irreversible EGFR inhibitor with a favourable risk benefit ratio that is currently in Phase 3 clinical trials in lung cancer, breast cancer and squamous cancer of head and neck (SCCHN). The clinical experience of afatnib includes over 2000 patients. Afatinib is relatively well tolerated, with most common adverse events being diarrhhea, rash and stomatitis as expected for this class of agents.
Afatinib has shown evidence of clinical activity in patients with Squamous cancer of the head and neck in a randomized clinical Phase 2 trial and early evidence of clinical activity in patients with squamous carcinoma of the lung in ongoing clinical trials.

Study objective

This randomized, open label phase III trial will be performed in patients with squamous carcinoma of the lung. The objectives of the trial are to compare the efficacy of afatinib with erlotinib as maintenance and second-line treatment for this group of patients.

Study design

A randomized phase III open-label trial

Intervention

Patients will be randomized to receive a 2nd line cancer treatment of either afatinib or erlotinib.

Study burden and risks

Patients will be screened for elegibility for the trial (Full physical exam, Limited physical exam, ECOG Performance Score, ECG, echo or MUGA scans, blood samples and CT/MRI voor tumor assessment. Treatment follows with an oral tablet intake for 28 days per cycle.
During the first treatment cycle the patients will visit the clinic twice (day 1 and day 8), thereafter only once every 28 days.
CT scans (or MRI) will be performed at week 8, 12, 16 , and every 8 weeks thereafter.

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. Diagnosis of advanced stage NSCLC squamous histology , including mixed histology.;2. Completion of at least 4 cycles of platinum-based doublet chemotherapy, with or without additional [non-EGFR] targeted agents, as 1st line treatment of Stage IIIB/IV NSCLC. Note the below scenarios are also considered to meet this requirement:;A) Patients relapsing within 6 months of receiving adjuvant-intent/neo-advjuvant/curative-intent chemoradiotherapy/chemoradiotherapy(Note: these patients are still to have had the equivalent of 4 cycles of platinum-based doublet chemotherapy exept in setting below).;OR;B) Patients intending to recieve four cycles of platinum-based doublet chemotherapy but due to toxicity, and not PD, discontinue just the platinum agent after at least two cycles of platinum doublet had been administered.;3. Eligible to receive 2nd line therapy in the opinion of the investigator.;4. Measurable disease according to RECIST 1.1 (R09-0262). ;5. Eastern Cooperative Oncology Group (ECOG) score of 0 or 1 (R01-0787). ;6. Availability of tumour tissue material for correlative studies. Archived tumour tissue is acceptable.;7. Adequate organ function.

Exclusion criteria

1. Prior treatment with EGFR directed small molecules or antibodies.;2. Curative intent chemoradiotherapy as the only treatment for stage IIIB NSCLC unless relapse occurs within 6 months of completion of treatment, and in the opinion of the investigator the patient has received an equivalent of 4 cycles of platinum-based doublet therapy.;3. Radiotherapy within 4 weeks prior to randomization.;4. Active brain metastases (stable for <4 weeks, symptomatic, or leptomeningeal disease). Dexamethasone therapy will be allowed if administered as a stable dose for at least 4 weeks before randomization.;5. Patients without Progressive Disease

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):	30-07-2012
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nog nietbekend
Generic name:	Afatinib
Product type:	Medicine
Brand name:	Tarceva
Generic name:	Erlotinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	16-04-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-05-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-07-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-08-2012

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-09-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-10-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-01-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-03-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-04-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-07-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-11-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-11-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-11-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-11-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-01-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-03-2014
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-10-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-10-2015
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	EUCTR2011-002380-24-NL
ClinicalTrials.gov	NCT01523587
CCMO	NL37158.060.11