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ABLE Trial Afatinib Before Lung surgEry: a study investigating the effect of giving a course of a targeted tablet treatment called afatinib to patients with potentially curable non-small cell lung cancer during the short interval between their diagnosis and the removal of their cancer by surgery

Submission date
15/08/2013

Recruitment status
No longer recruiting

Registration date
16/08/2013

Overall study status
Completed

Last Edited
28/05/2020

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-afatinib-people-non-small-cell-lung-cancer-able

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2012-004537-16

Protocol serial number
14691

Study information

Scientific Title
An open label multi-centre preoperative window of opportunity study of afatinib in stage Ia to IIb non-small cell lung cancer

Acronym
ABLE

Study objectives
The anticancer effect of afatinib can be observed within fifteen days of starting treatment by Positron Emission Tomography (18F-FDG PET) imaging.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Yorkshire and the Humber - Leeds East, 08/01/2013, ref: 12/YH/0539

Study design
Open label non randomised interventional phase II clinical study; Design type: Treatment

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Lung Cancer; Disease: Lung (non-small cell)

Interventions
After giving informed consent patients will undergo a range of screening investigations including blood tests, ECG and a heart scan to ensure that they are eligible to take part.

Some patients will also be asked to undergo another optional biopsy in order to obtain cancer tissue for the research.

All eligible participants will be asked to take a single 50mg tablet of afatinib by mouth once each day until the date of their pre-planned surgery.

After participants have been taking the afatinib tablets for two weeks they will undergo another PET/CT scan to study what effect the afatinib has had upon their cancer. They will also have a chest X-ray and give a blood sample on this date.

The total duration of treatment with afatinib tablets will be at least fifteen days but no longer than 30 days from when each participant starts taking them. They will give another blood sample on the morning of their surgery.

The participants contribution to this study will end after they have been reviewed four weeks following their surgery. On this occasion they will give a final related blood sample.

The study team will also collect information about each participant by reviewing notes made at their routine lung cancer related outpatient appointments over the next five years.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Afatinib

Primary outcome(s)
The primary endpoint will assess whether a mean reduction in maximal Standardised Uptake Value (SUVmax) of 10% can be observed in the patient group enrolled in the study by 18F-FDG PET imaging after they have received fifteen days of therapy with oral afatinib

Key secondary outcome(s))
1. The CT volumetric secondary endpoint will assess whether a reduction of > 30% in tumour volume can be observed in the patient group enrolled in the study using the CT component of 18F-FDG PET/CT imaging after they have received fifteen days of therapy with oral afatinib.
2. Toxicity and safety data for each patient will be assessed. Toxicity analyses will be preformed after 10 and 30 consecutive patients have completed afatinib therapy and at the end the study.
3. Feasibility of conducting further Window of Opportunity trials in this setting in the UK for the NSCLC cancer population will be assessed through the ability to appropriately identify, approach, consent the target study population in compliance with the study protocol.

Completion date
16/09/2015

Eligibility

Key inclusion criteria
1. Able to give written informed consent and willing to follow the study protocol
2. Age >= 18 years
3. Histologically confirmed resectable non-small cell lung cancer, meeting one of the following clinical staging criteria:
a. Stage 1A or 1B (T12, N0)
b. Stage II (T12, N1 or T3, N0)
The number of participants with predominantly squamous histology eligible to enter the study

will be capped at twenty.
4. Measurable disease by contrast-enhanced CT scan:
4.1. The primary tumour must have a diameter on CT imaging of at least 8mm
4.2. The primary tumour must have an SUVmax on FDGPET of at least 3.0
5. Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0 1
6. Eligible for complete surgical resection, defined as the appropriate pulmonary parenchymal resection including lobectomy, bilobectomy, sleeve lobectomy, or pneumonectomy.
7. Adequate baseline haematopoietic, hepatic and renal function, defined as follows:
7.1. Absolute neutrophil count (ANC) ≥ 1.5 x 109/L
7.2. Platelet count ≥100 x 109/L
7.3. Bilirubin ≤ 1.5 x ULN
7.4. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≤ 3 x ULN
7.5. Creatinine ≤ 1.5 x ULN
8. Ability to take and absorb oral medications
9. Female patients of childbearing potential (i.e. premenopausal females, females who have been menopausal for < 1 year and not surgically sterilized, or males not surgically sterilized) must provide a negative pregnancy test (urine or serum) ≤ 7 days before study treatment begins and must agree to practice effective contraceptive measures for the duration of study drug therapy and for at least 30 days after completion of study drug therapy
10. Male participants must agree to use a barrier method of contraception for the duration of the study if sexually active with a female of childbearing potential and must continue to do so for 30 days after the end of treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
7

Key exclusion criteria
1. Tumours of mixed histology (combined small cell and non small cell carcinoma), pulmonary carcinoid tumours, or large cell carcinoma with evidence of neuroendocrine features. However non-small cell tumours with mixed adenocarcinoma and squamous cell carcinoma histology are eligible
2. Patients with preoperative radiological evidence of N2 disease by either PET/CT or CT scan (i.e. radiological evidence of metastasis to ipsilateral mediastinal and subcarinal lymph nodes) that is confirmed as N2 disease histologically/cytologically
3. Any prior or concurrent systemic chemotherapy for Non-small-cell lung carcinoma (NSCLC)
4. Any prior or concurrent radiotherapy for NSCLC

5. Any prior treatment with any epidermal growth factor receptor (EGFR) inhibitor
6. Current treatment with potent P-glycoprotein inhibitors or inducers
7. Any other concurrent malignancy with the exception of non-melanoma skin cancers
8. Known pre-existing interstitial lung disease
9. Significant or recent (within 6 months) acute gastrointestinal disorders with diarrhoea as a major symptom e.g. Crohns disease, malabsorption or CTC grade ≥ 2 diarrhoea of any aetiology
10. History or presence of clinically relevant cardiovascular abnormalities such as:
10.1. Uncontrolled hypertension
10.2. Congestive heart disease New York Heart Association (NYHA) Classification Grade 3
10.3. Unstable angina or poorly controlled arrhythmia
11. Congestive Cardiac failure, with left ventricular ejection fraction of < 50% as measured by echocardiography/Gated SPECT/MUGA imaging
12. Uncontrolled infection, or any serious illness or organ system dysfunction which in the opinion of the investigator would either compromise participant safety or interfere with the evaluation of the safety of the test drug
13. Pregnant (positive pregnancy test) or breast feeding women
14. History of a poorly controlled neurologic or psychiatric condition that, in the Investigators opinion, is likely to interfere with the participants ability to participate and / or to comply with the requirements of the study
15. Active hepatitis B infection, active hepatitis C infection or known HIV carrier
16. Ocular inflammatory or chronic infectious conditions
17. Poorly controlled diabetes mellitus
18. Known or suspected active drug or alcohol abuse
19. Participation in another investigational drug trial whilst on study
20. Known hypersensitivity to afatinib or to any of the excipients contained in the tablet preparation
21. Superior vena cava syndrome

Date of first enrolment
16/09/2013

Date of final enrolment
16/09/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St James' University Hospital
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Sponsor information

Organisation
University of Leeds (UK)

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Industry

Funder Name
Boehringer Ingelheim

Alternative Name(s)
Boehringer Ingelheim Pharmaceuticals, Inc., Boehringer Ingelheim International GmbH, BI, BIPI

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			28/05/2020	No	No
HRA research summary			28/06/2023	No	No