Phase IIIB randomized trial of BIBW 2992 plus weekly paclitaxel versus Investigator's choise of chemotherapy following BIBW 2992 monotherapy in non-small cell lung cancer patients failing previous erlotinib or gefitinib treatment

Published: 02-07-2010
Last updated: 02-05-2024

The primairy objective of the trial is to determine the efficacy of BIBW 2992 plus weekly paclitaxel compared to the investigators choise of chemotherapy alone in patients with NSCLC stage IIIb or IV progressing after experiencing a benefit from...

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

Summary

ID

NL-OMON36544

Source
ToetsingOnline

Brief title
LuxLung 5

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
non-small-cell lungcancer/ lungcancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: BIBW 2992, Non small cell lung cancer, Paclitaxel

Outcome measures

Primary outcome

Primary endpoint:

Overall survival time from the day of randomization until death for patients randomized to either BIBW 2992/ paclitaxel combination therapy or comparator chemotherapy.

Secondary outcome

Secondary endpoints:

1: progression free survival as determined by RECIST1.1(response evaluation criteria in solid tumours), separately for Part A and Part B

2: Clinical benefit rate at 3 month defined as the progression free survival rate at 3 month, separately for Part A and Part B

3: Objective response rate (CR {complete response} PR {partial response}) of BIBW 2992 monotherapy according to RECIST 1.1

4: Objective response rate (CR or PR) of BIBW 2992/ Paclitaxel combination therapy and comparator therapy in Part B after progression in Part A according to RECIST 1.1

5: Time to objective response, separately for Part A and Part B

6: HRQOL defined as time to deterioration fro the three symptoms cough,

dyspnoe, and pain, measured using the European Organization for Research and

Treatment of Cancer questionaires (QLO-LC13 and QLQ C30)

Study description

Background summary

Non-small cell lung cancer (NSCLC) is the leading cause of cancer death globally, with an estimated one million new cases diagnosed and 880.000 death each year. The prognosis for advanced stage disease has not changed significantly in the past 20 years. With n overall 5-years survival rate of only 15%, the treatment of this disease remains a major clinical challenge.
In patients with advanced NSCLC (stage IIIb pleural effusion or stage IV metastatic disease)systemic chemotherapy is considered the first treatment of choise, prolonging the median survival and palliating tumor-related symptoms.
Despite the high levels of epidermal growth factor receptor(EGFR) overexpression in the tumoours for the majority pf patients with NSCLC, recent clinical experiences with specific EGFR-tyrosine kinase inhibitors (TKI's) have demonstrated tumour regression in only 10% to 15% of unselevted NSCLC patients.
Further investigations in patients who responded to TKI therapy have indicated that the sensitivity to therapy may be correlated with the presence of EGFR activating mutations.
BIBW 2992 is a second generation TKI which binds irreversable to EGFR and HER2 and is thought to have potential benefit over the first generation TKI's such as erlotinib and gefitinib.
One of the reasons for the potential benefit is that BIBW2992 may have activity against EGFR-tyrosine kinases with mutations which are resistant to the first generation TKI's. Additionally, the irriversible binding may confer more prolonged activity, further delaying tumour progression when compared to reversible TKI's.

Study objective

The primairy objective of the trial is to determine the efficacy of BIBW 2992 plus weekly paclitaxel compared to the investigators choise of chemotherapy alone in patients with NSCLC stage IIIb or IV progressing after experiencing a benefit from BIBW 2992 monotherapy.
Additional information on safety and the health related quality of life (HRQOL) will be collected. Patients on both arms will receive the best supportive care

in addition to study treatment.
Randomized patients in the trial will be treated and followed until death, study termination or are lost to follow up.

Study design

Phase III, randomized, open label study

Intervention

Part A:
BIBW 2992 monotherapy

Part B:
arm 1: BIBW 2992 plus Paclitaxel
arm 2: investigators choise of chemotherapy

Study burden and risks

During screening the participating patients will have a complete physical examination, an ECG, an echo or Muga scan(to check the ejection fraction), blood will be drawn(haematology and biochemistry) and a CT or MRI will be done for tumour evaluation.
During the following cycli of the visits 1, 2,and 3 (every 28 days) the patient will come twice per cycle to the clinic.
From cycle 4, the vsits will occur every 28 days.
Every 6 weeks the CT or MRI to establish the tumour response will be done

Contacts

Public
Boehringer Ingelheim

Comeniusstraat 6
1817 MS
NL
Scientific
Boehringer Ingelheim

Comeniusstraat 6
1817 MS
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In study part A:
1: Patients with confirmed diagnosis of NSCLC stage IIIb or stage IV who have failed treatment with erlotinib or gefitinib.
2: patients should have received and failed at least one line of cytotoxic chemotherapy, including a platinum-based regimen in patients eligible for platinum-based therapy for advanced or metastatic disease, however the following patients are exempted:
a) patients with known EGFR mutation shown by accepted methods after therapy with reversible TKI's are eligible without prior chemotherapy, OR
b) patients with clinical benefit to erlotinib or gefitinib for 6 month or more and than experience progression of the disease are eligible without prior chemotherapy
3: Eastern Cooperative Oncology Group (ECOG, R01-0787) score 0,1,or 2.
4: Patients with at least one tumour lesion measured by MRI or CT scan in at least one dimension with the longest diameter to be recorded equal or larger than 20 mm using conventional techniques or equal or larger than 10 mm using spiral CT scan to RECIST 1.1 (R09-0262)
5: Male and female patients of 18 years or older
6: life expectancy of at least 12 weeks;In study part B:
Clinical benefit (stable disease) for at least 12 weeks in part A of the trial, and than shown progression of the disease according to RECIST 1.1 criteria.

Exclusion criteria

1.previous treatment with BIBW
2. active brain metastasis
3. history or presence of clinically relevant cardiovasculair abnormalities
4. chemo-, hormone-, or immunotherapy within the past 4 weeks. For pre-treatment with reversible TKI's 2 weeks only.

5. significant or recent acute gastrointestinal disorder with diarrhea as a major symptom at baseline
6. other life-threatening illness or organ dysfunction, or other malignancies that either might compromise the patients safety or requiers therapy
7. radiotherapy within the past 2 weeks prior to treatment with the trial drug
8. history or presence of clinically relevant cardiovasculair abnormalities as defined in the exclusion criteria.
9. prior treatment with antracyclines with a cumulative dose of >= 400mg/m².
10. clinically significant abnormal lab functions as defined in the protocol
11. pregnant women, breastfeeding women or women of childbearing potential unwilling to use a medically acceptable method of contraception

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):	19-11-2010
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	geen
Generic name:	geen
Product type:	Medicine

Brand name:	Paclitaxel
Generic name:	Paclitaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	02-07-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-07-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-07-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-07-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-11-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-12-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	28-02-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-10-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-11-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-01-2013
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	EUCTR2009-014563-39-NL
CCMO	NL30914.100.10