A Phase III, multi-center, placebo-controlled trial of Sorafenib (BAY 43-9006) in patients with relapsed or refractory advanced predominantly non squamous Non-Small Cell Lung Cancer (NSCLC) after 2 or 3 previous treatment regimens

Published: 09-03-2009
Last updated: 06-05-2024

The objective of this phase III study is to compare the efficacy and safety of sorafenib monotherapy plus best supportive care (BSC) versus placebo plus BSC for the treatment of patients with relapsed or refractory advanced predominantly non...

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

Summary

ID

NL-OMON37229

Source
ToetsingOnline

Brief title
Bayer 13266 - MISSION

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym

Lung Cancer, Non Small Cell Lung Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Bayer B.V.

Intervention

Keyword: Non-Small Cell Lung Cancer (NSCLC), Safety and efficacy, Sorafenib

Outcome measures

Primary outcome

The primary efficacy variable is overall survival (OS).

Secondary outcome

Secondary efficacy variables are progression-free-survival (PFS), disease

control rate (DCR), best overall response rate (ORR), time to progression

(TTP), and patient reported outcomes (PRO) on health related quality of life

(HRQOL), lung cancer symptoms and utilities.

Study description

Background summary

See protocol page 8 -12.

Study objective

The objective of this phase III study is to compare the efficacy and safety of sorafenib monotherapy plus best supportive care (BSC) versus placebo plus BSC for the treatment of patients with relapsed or refractory advanced predominantly non squamous NSCLC after two or 3 prior treatment regimens.

Study design

A phase III randomized, double-blind, placebo-controlled study evaluating the combination of sorafenib and best supportive care (BSC) versus placebo and BSC for subjects with advanced relapsed or refractory, predominantly non squamous NSCLC.
Subjects are eligible if they have progressed or relapsed following at least two but not more than three prior treatment regimens.
All subjects who meet the entry criteria will be randomized in a 1:1 ratio to receive either sorafenib or matching placebo combined with BSC.
Randomization will be stratified for
• Number of prior lines of treatment (2 vs. 3)
• Presence of brain metastases vs. none
• Prior EGFr inhibitor treatment vs. no prior EGFr inhibitor treatment
• Geographic Region [Group 1 (consisting of North America, Northern/Western Europe and Australia) vs. Group 2 (consisting of South America, Eastern Europe and Asia-Pacific].

It is planned to randomize approximately 700 subjects (350 in each arm) in approximately 150-160 centers.
Overall survival (OS) will be measured from the date of randomization to the date of death for any cause.
Subjects will take 800 mg of sorafenib (two 200 mg tablets twice daily) or matching placebo twice daily orally. In addition, all subjects will receive best supportive care (BSC) in accordance with local center standards, as defined in the protocol.
Sorafenib will be taken on a continuous basis. For administrative reasons, 21 days (three weeks) of treatment will be considered one treatment cycle. There will be no dose interruptions between cycles.

During the treatment period, subjects will have study visits every three weeks.
Radiological assessments (CT/ MRI) will be performed every six weeks.
Radiological evaluations will be based on the Response Evaluation Criteria in Solid Tumors (RECIST).
Treatment will be continued until the occurrence of:
• Unequivocal evidence of disease progression
• intolerable toxicity
• patient's consent withdrawal
Treatment may also be discontinued at the investigator*s discretion.
At the end of the treatment period, an End of Treatment (EOT) visit will take place 7-14 days after stopping the study drug.
Regardless of the reason for stopping the study drug, all subjects will continue to be managed per local standard of care and followed for monthly updates and overall survival.
The expected study duration is 28 months.

Once the expected final number of events is reached and results are available, the study will be unblinded. The remaining patients on sorafenib treatment, who are considered by the Investigator to benefit from continued sorafenib

treatment, can be enrolled into a sorafenib long term extension program, or transferred to commercial medication supply
The end of the study for regulatory purposes will be considered to be when the last subject has had their end of study visit.

Intervention

See protocol page 67 (flowchart)

Study burden and risks

Blood collection or venipuncture risks:
-Frequent blood samples will be collected during this study. Patient may experience pain, bleeding from
the puncture site or in tissues surrounding the puncture site, blood clot formation, or local infection and
inflammation in the vicinity of the puncture site (very rare).

CT (Computerized Tomography) Scan:
-Patients may have claustrophobic feeling and will be exposed to radiation during this test. In addition,
there are the risks of veni-puncture (above) when the contrast medium is injected during the CT scan.
Patient may experience nausea, flushing, warmth, and a salty taste. Some patients might be allergic to
the contrast medium.

Contacts

Public
Bayer

Energieweg 1
3641 RT
NL
Scientific
Bayer

Energieweg 1
3641 RT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

•Ability to understand and willingness to sign a written Informed Consent. A signed Informed Consent must be obtained prior to performing any study specific procedures.
•Advanced relapsed or refractory predominantly non squamous NSCLC. The diagnosis must have been confirmed cyto-/ histologically (documentation of original cytology/ biopsy result is acceptable).
•Patients must have measurable or non-measurable disease as defined in Section 4.6.4.2. All sites of disease must be evaluated within 4 weeks prior to first dose of study medication.
•at least 2 but not more than 3 prior treatment regimens for advanced disease. (Adjuvant or neo-adjuvant anti-cancer treatments after which a relapse occurred within 1 year of therapy will be counted. Maintenance anti-cancer treament is counted as a separate regimen, if it was not administered as part of the immediate- past regimen).
o Prior therapy with bevacizumab (Avastin) permitted
o Prior therapy with standard EGFR inhibitors permitted. Every attempt should be made to enroll patient who have received an EGFR inhibitor in the geographic areas where this type of treatment is available.
•ECOG Performance Status of 0 or 1
•History of metastatic brain or meningeal tumors allowed, provided definitive therapy (surgery and/or radiation) has been administered before randomization , no further treatment of brain metastases is planned, and the subject is clinically and radiologically stable for at least 2 months prior to randomization. (Patients must be asymptomatic and off steroid treatment for at least 14 days prior to study entry (i.e. signature date of Study Informed Consent Form). Discontinuation of corticosteroid treatment must be done independent of study participation as per local standard of care and consent procedures).
•Male or female subjects >= 18 years of age (>= 20 for Japan) at the time of Informed Consent
•Life expectancy of at least 12 weeks
•Ability to swallow oral medication
•Women of childbearing potential must have a negative serum pregnancy test performed within 7 days prior to the start of treatment (assessed centrally)

•Both men and women enrolled in this trial must use adequate barrier birth control measures during the course of the trial and during the first 4 weeks after the completion of trial
•Adequate bone marrow, liver and renal function as assessed by the following laboratory requirements to be conducted within 7 days prior to start of the study drug:
o Haemoglobin > 9.0 g/dl
o Absolute neutrophil count (ANC) >1,500/mm3
o Platelet count * 100,000/µl
o Total bilirubin <= 1.5 x the upper limit of normal
o ALT < 2.5 x upper limit of normal (<= 5 x upper limit of normal in patients with liver metastases)
o AST < 2.5 x upper limit of normal (<= 5 x upper limit of normal in patients with liver metastases)
o Alkaline phosphatase < 4 x upper limit of normal (<= 5 x upper limit of normal in patients with liver metastases)
o PT-INR or PTT < 1.5 x upper limit of normal
o Serum creatinine < 1.5 x upper limit of normal
o Calculated creatinine clearance of >= 50 mL/min e.g.Cockroft-Gault, MDRD formula. (Measured creatinine clearance using EDTA, Inulin or 24 hours urine methods is recommended for patients with equivocal results or low body weight) NOTE: The central lab will use the Cockcroft-Gault calculation. Measured creatinine clearance will be done locally only if needed.

Exclusion criteria

•NSCLC patients with predominantly squamous cell carcinoma histology
Excluded medical conditions:
•History of cardiac disease:
o Congestive heart failure >New York Heart Association (NYHA) class 2
o Active coronary artery disease (CAD), i.e. angina with onset in last 3 months or with symptoms at rest [myocardial infarction more than 6 months prior to study entry is allowed]
o Cardiac arrhythmias (>Grade 2 NCI-CTCAE vers. 3.0) which are poorly controlled with anti-arrhythmic therapy
o Uncontrolled hypertension [systolic blood pressure >= 150 mmHg or diastolic blood pressure >= 90 mmHg despite two anti-hypertensive medications]
o Any of the following:
- History of HIV infection
- Current chronic active or acute hepatitis B or C
•History of organ allograft
•Active clinically serious infections (> grade 2 NCI-CTCAE vers. 3.0)
•Patients with seizure disorder requiring medication (Patients who experienced seizures due to brain metastases prior to radical treatment of these metastases are allowed if the inclusion criterion related to brain metastases is adhered to - see section 4.2.1, inclusion criteria, for details).
•Patients with evidence or history of bleeding diathesis or coagulopathy
•Patients undergoing renal dialysis

•Pulmonary hemorrhage/ bleeding event >= CTCAE grade 2 within four weeks prior to the first dose of the study drug
•Any other hemorrhage/ bleeding event >= CTCAE grade 3 within four weeks prior to the first dose of the study drug
•Non-healing wound, ulcer or bone fracture
•Thrombotic or embolic venous or arterial events such as cerebrovascular accident (including transient ischemic attacks), deep vein thrombosis or pulmonary embolism within the 6 months prior to the first dose of study drug
•Previously untreated or concurrent cancer that is distinct in primary site or histology from NSCLC, EXCEPT cervical carcinoma in situ, treated basal cell carcinoma, superficial bladder tumors (Ta, Tis, T1). Any cancer curatively treated >3 years prior to entry is permitted. All treatments must be completed at least 3 years prior to the study entry (i.e. signature date of Study Informed Consent).
•Substance abuse, medical, psychological or social conditions that may interfere with the subject*s participation in the study or evaluation of the study results
•Known or suspected allergy or any other contraindication for sorafenib administration
•Pregnant or breast-feeding women. [Both men and women enrolled in this trial must use adequate barrier birth control measures during the course of the trial and during the first four weeks after the completion of trial].
•Any disease which could affect the evaluation of the study drug
•Any condition that is unstable or could jeopardize the safety of the subject and their compliance in the study
•Any condition which could affect the absorption or pharmacokinetics of the study drug including any type of gastrointestinal resection or surgery;Excluded therapies and medications, previous and concomitant:
•All prior anti-cancer drugs or device therapy for NSCLC including outside of this trial should be completed at least 3 weeks prior to first dose of study drug (Day 1, Cycle 1 [D1C1]).•Prior treatment with other VEGFR inhibitors (i.e. sunitinib, thalidomide, vandetanib and other experimental agents of this class). Bevacizumab (Avastin) is permitted.
•Radiotherapy during study or 3 weeks prior to Day 1, Cycle 1 (first dose of study drug. [Palliative radiotherapy will be allowed as described in the Prior and Concomitant Therapy section. If radiotherapy to the target lesion(s) during study is required, this will be regarded as progressive disease]. No previous irradiation to the only site of measurable or evaluable disease, unless that site had subsequent evidence of progression.
•Major surgery within 4 weeks prior to start of study (Informed Consent signature). Minimal invasive biopsy is allowed.
•Use of biologic response modifiers, such as G-CSF, within 3 week prior to study entry. [Therapeutic G-CSF and other hematopoietic growth factors may be used in the management of acute toxicity such as febrile neutropenia when clinically indicated or at the discretion of the investigator, however they may not be substituted for a required dose reduction].
•Any agents which could affect the absorption or pharmacokinetics of the study drug
•Prior exposure to the study drug
•Therapeutic anticoagulation with vitamin K antagonists such as warfarin, or with heparins or heparinoids. Prophylactic low dose warfarin (1 mg po qd) is permitted if the INR (International normalized ratio) is <= 1.5. Low-dose aspirin is permitted (80-100 mg daily).

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):	21-08-2009
Enrollment:	13
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nexavar
Generic name:	Sorafenib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	09-03-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-04-2009
Application type:	First submission

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-05-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-05-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-06-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-06-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-06-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-06-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-07-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	16-09-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-09-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-03-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-03-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-03-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-04-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-05-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-05-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	29-06-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-07-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-07-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-07-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-12-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-12-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-06-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-06-2011

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2008-006914-62-NL
CCMO	NL27293.003.09