A Three Cohort Phase II trial of BMS-275183 given orally on a twice weekly schedule in pretreated locally advanced or metastatic NSCLC patients

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

Summary

ID

NL-OMON29907

Source
ToetsingOnline

Brief title
CA165-026

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: BMS-275183, NSCLC, oral taxane, Phase II

Outcome measures

Primary outcome

The primary objective of the trial is to assess efficacy of BMS-275183 in

pretreated NSCLC patients as measured by tumor response rate according to the

SWOG criteria.

Secondary outcome

*Qualitative and quantitative toxicityies of BMS-275183

Response duration.

*Progression free survival time.

*Overall survival time.

*Plasma pharmacokinetics of BMS-275183 at the recommended dose of 100 mg/m²

given orally on a twice weekly schedule (Cmax, Tmax, AUC(INF), T-HALFCL/F).

Study description

Background summary

Lung Cancer is among the most common malignancies of the world. Non-Small Cell Lung Cancer (NSCLC) is the commonest type of lung cancer, accounting for 80% of cases.

Patients with stage III disease generally do not benefit form surgery alone, they are best managed by combined treatment which may include chemotherapy and/or radiation therapy in addition to surgery. Stage IV patients may be considered for chemotherapy if they have a good performance status. The current standard treatment for these patients is a platinum based therapy first-line followed by docetaxol second line. Although docetaxol has shown efficacy in patients with NSCLC who have received prior platinum based chemotherapy, more than 90% of these patients do not achieve an objective tumour response rate and

treatment is associated with significant toxicity. Erlotinib, a novel Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor (EGFR-TKI) has been shown to been effective in patient who have failed prior platinum and docetaxol regiments, however response rates are still low at less than 10%. There is therefore a growing population of patients who have failed all of their therapeutic options.

BMS-275183 is a novel tubulin polymerizing agent that can be administered orally. Phase I studies have demonstrated an acceptable safety profile together with promising activity seen in patients with heavily pre-treated NSCLC and other tumour types.

Study objective

The aim of this study is to assess the clinical activity of BMS-275183 in patients who have failed prior treatment.

Study design

An open label, non-randomised, multicenter, phase II study with an anticipated enrollment period of 18 months to enroll patients in 20 centers in Euope and the USA.

Intervention

All patients receive BMS-275183 on a twice weekly schedule at a dose of 100 mg/m2. BMS-275183 will be administered orally as a 25 mg capsule. Treatment duration will consist of a maximum of 8 cycles (a cycle consists of dose administration on Days 1, 4, 8, 11, 15, 18, 22 and 25).

Study burden and risks

Patienten zullen na uitgebreid vooronderzoek eens per kuur (4 weken) naar de polikliniek komen voor lichamelijk onderzoek, bloedafname, ECG (alleen tijdens de 1e kuur) en tumor meting (om de kuur). Ultgebreid farmacokinetisch onderzoek vindt plaats op dag 1 en 18 van kuur 1, waarvoor de patient 4 uur in het ziekenuis moet blijven. Na maximaal 8 cycli stopt de behandeling en worden patienten vervolgd tot overlijden. De te verwachten risico's zijn de aan de onderzoeksmedicatie gerelateerde risico's zoals vermeld in de patienteninformatie.

Aftera screening phase and enrollment, patients will come once every cycle (4 weeks) to the outpatient clinic to undergo physical exams, blood draws, ECG (at screening only) and tumor measurements (every other cycle). PK measurements will be done at days 1 and 18 of the first cycle, for which the patient has to

stay in the clinic for 4 hours. Total treatment is maximized at 8 cycles after which the patients will be followed for survival. The anticipated risks are related to the use of the study drug and are described in the patient information.

Contacts

Public
Bristol-Myers Squibb

Vijzelmolenlaan 9
3440 AM Woerden
Nederland
Scientific
Bristol-Myers Squibb

Vijzelmolenlaan 9
3440 AM Woerden
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1) Signed written informed consent 2) The subject population will consist of patients with histologically or cytologically confirmed locally advanced or metastatic NSCLC who failed only one prior chemotherapy regimen. 3) Prior chemotherapy with a minimum of two chemotherapy cycles given at a full dose. Prior chemo-radiation is not allowed unless the patient received a full dose of chemotherapy concomitantly with the radiation or the concomitant chemo-radiation was preceded or followed by a minimum of two cycles of the

same chemotherapy administered at a full dose. That chemotherapy must be a taxane for cohort I, a platinum based but non taxane containing regimen for cohort II and any chemotherapy regimen and one EGFR-TKI inhibitor compound for cohort III patients. 4) Prior treatment with EGFR-TKI inhibitor is allowed only for patients in cohort 3. Prior treatment with a VEGFr inhibitor is allowed for all the patients. The VEGFr inhibitor cannot be in addition an EGFR inhibitor. 5) Prior chemotherapy may have been administered in adjuvant, neoadjuvant or advanced setting but only one prior chemotherapy regimen is allowed to which the patient must have failed treatment (i.e.: disease recurrence in adjuvant setting or tumor progression in advanced stages). 6) Patients must have at least one measurable lesion according to the SWOG criteria. 7) Prior anti cancer treatment must have been discontinued at least 3 weeks prior to study enrollment and the patient must have recovered from the acute toxicities of the prior treatment. 8) Prior radiation therapy must be completed at least 2 weeks prior to study enrollment and the patient must have recovered from its toxicities. 9) Prior curative surgery must have been completed at least 10 weeks, and prior palliative surgery must have been completed at least 2 weeks, prior to study enrollment. 10) Performance status of 0 or 1 on the ECOG scale or 90-100 on the Karnofsky scale (see Protocol Appendix 2). Adequate organ function is defined as: i) Adequate bone marrow function: absolute Neutrophil count of at least 1.5 x 10 9/L, platelets * 100 x 10 9 /L, and hemoglobin * 9 g/dl ii) Adequate hepatic function: Bilirubin less than or equal to the upper limit of normal (ULN), AST, ALT * 1.5 times ULN, and alkaline phosphatase * 2.5 ULN iii) Renal: Plasmatic creatinine < 1.5xULN 11) Estimate life*expectancy of a least 8 weeks 12) Men and women, age * 18 years 13) Women of childbearing potential (WOCBP) must be using an adequate method of contraception to avoid pregnancy throughout the study and for up to 8 weeks after the study in such a manner that the risk of pregnancy is minimized

Exclusion criteria

Sex and Reproductive Status 1) WOCBP who are unwilling or unable to use an acceptable method to avoid pregnancy for the entire study period and up to 8 weeks after the study. 2) Women who are pregnant or breastfeeding 3) Women with a positive pregnancy test on enrollment or prior to study drug administration. Target Disease Exceptions 4) Prior brain metastases, unless previously treated adequately, the patient is asymptomatic and no longer requires corticosteroids, and a minimum of 4 weeks has elapsed since the treatment of the brain lesions. Medical History and Concurrent Diseases 5) Second primary malignancy that is detectable at the time of consideration for study enrollment 6) Prior history of a major gastrointestinal surgery or malabsorption that could potentially influence the absorption of BMS-275183 7) Recent significant cardiovascular disease (i.e., myocardial infarction, unstable angina within 6 months, or any history of significant degree congestive heart failure with or without medical treatment, any history of clinically significant atrial or ventricular arrhythmias, any history of Grade 2 or 3 heart block). 8) QTc prolongation > 500 msec at the baseline 9) Serious concomitant systemic disorders that would compromise the safety of the patient or compromise the patient*s ability to complete the study 10) Prior treatment with BMS-275183 11) Active infection that, in the opinion of the investigator, is not compatible with the conduct of the study. Physical and Laboratory Test Findings 12) Inability or unwillingness to swallow the oral BMS-275183 13) NCI CTC AE Grade * 2 peripheral

neuropathy at study entry. 14) Significant weight loss, (i.e. * 10%, over the previous 6 weeks before study entry) Prohibited Therapies and/or Medications 15) Concomitant medication with efflux transporter PGP inhibitors such as Benzimidazoles (benzimidazoles includes PPIs such as omeprazole, esomeprazole, lansoprazole, pantoprazole) or prior medication with such drugs within seven days from study drug administration 16) Concomitant medication with a CYP 3A4 inhibitor or inducer (see Protocol Appendix 3). 17) Concomitant medication with Metoclopramide Other Exclusion Criteria 18) Prisoners or subjects who are compulsorily detained

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-10-2006
Enrollment:	12
Type:	Anticipated

Ethics review

Approved WMO

Date:	14-09-2006
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2005-005099-33-NL
ClinicalTrials.gov	NCT00359450
CCMO	NL13945.029.06