A Phase 1/2 Study Evaluating the Safety and Efficacy of ABT-751 in Combination with Pemetrexed Versus Pemetrexed Alone in Subjects with Advanced or Metastatic Non-Small Cell Lung Cancer

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The primary objective of the Phase 2 portion of the study is to assess if the addition of ABT-751 at the RPTD to standard pemetrexed can prolong PFS compared to pemetrexed alone in subjects with advanced or metastatic NSCLC.

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

Summary

ID

NL-OMON30442

Source
ToetsingOnline

Brief title
Safety and efficacy of ABT751 in subjects with NSCLC.

Condition

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

Synonym
Lungcancer, Non Small Cell Lung Carcinoma

Research involving

Human

Sponsors and support

Primary sponsor: Abbott
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: ABT-751, Non-small lungcancer, Pemetrexed, progressive disease

Outcome measures

Primary outcome

Primary: progression free surfival

Safety:

Adverse Events, laboratory values, ECGs, physical examinations and vital signs

will be examined during the study.

Secondary outcome

secundary: surfival, tumor respons ratio, respons time, time till progression,

quality of life.

Study description

Background summary

There are limited therapeutic options for subjects with advanced or metstatic NSCLC whose disease has progressed following one or more chemotherapy regimens. Drugs approved for NSCLC in this stage of disease are docetaxel, pemetrexed and erlotinib, but repons rates are only 5.5, 9.1 and 8.9 percent respectively with median survival of 7.9, 8.3 and 6.7 months, respectively.

ABT-751 is a novel cytotoxic agent which stops the celmitosis, which leads the cell to go into apoptosis.

This fase II study is designed to investigate if the combination of ABT-751 and pemetrxed can lead to a better anti-cancer effect then pemetrexed alone.

Study objective

The primary objective of the Phase 2 portion of the study is to assess if the addition of ABT-751 at the RPTD to standard pemetrexed can prolong PFS compared to pemetrexed alone in subjects with advanced or metastatic NSCLC.

Study design

The study is developed as a multicenter doubleblind phase II study.

Intervention

A cuclus is 21 days. The study consists of two arm in a 1:1 ratio.

50% of the subjects will receive pemetrexed (every 21 days 500mg/m2) and an oral placebo for the first 14 days.

50% of the subjects will receive pemetrexed (every 21 days 500mg/m2) and ABT-751 for the first 14 days.

The subject will continue with the cucli until the disease is progressive, the investigator decides for other reasons (e.g. toxicity) to withdraw the patient, or the patient itself decides to stop with the study.

Study burden and risks

Upon participation to this trial, patients may receive ABT-751 capsules. Some Adverse Events are known from phase I and II studies, however unexpected Adverse Events may occur. To monitor these Adverse Events outpatient clinic visits are neccesary, during which blood will be drawn (circa 15 ml each time). There is some burden and risk for each patient, but we try to minimalise this.

Because the end-points are not time-bound, it is unknown how often the patient needs to visit the hospital. If the patient is included at least 8 visits will be performed.

During the screening visit and after every 2 cycli, a CT- or MRI scan will be made and a 'Quality of life' questionaire needs to be completed. During the screening visit an ECG will be made.

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.Age minimum 18 years old.
2.The subject has pathologically (histologically and/or cytologically) documented NSCLC.
3.The subject has locally advanced (Stage III) NSCLC not amenable to curative surgery or radiotherapy or metastatic (Stage IV) NSCLC.
4.The subject has received only one prior anti-tumor treatment regimen in the advanced (Stage III non-curable disease or metastatic Stage IV) setting (i.e., study participation must be second line therapy in the advanced setting).
5.The subject may have received one additional anti-tumor treatment regimen in the neo-adjuvant or adjuvant setting.
6.The subject has experienced progressive disease either during or following the previous anti-tumor treatment regimen (Requirement for Phase 2 only).
7.The subject exhibits the presence of measurable disease by RECIST criteria (Requirement

for Phase 2 only).
8.Subjects with brain metastases must have had clinically controlled neurologic symptoms, defined as surgical excision and/or radiation therapy followed by 30 days of stable neurologic function and no evidence of CNS disease progression.
(Subjects with symptoms of CNS metastasis at Screening must have computed tomography [CT] or magnetic resonance imaging [MRI] scans of the brain prior to study entry that demonstrate no evidence of disease.)
9.The subject has an Eastern Cooperative Oncology Group (ECOG) performance score of 0-2.
10.All anti-tumor therapy has been discontinued at least 3 weeks prior to study start administration.
11.All adverse events from prior anti-tumor treatment are resolved or stable.
12.Adequate hematologic, renal and hepatic function
13.Female subjects must be surgically sterile, postmenopausal (for at least 1 year), or have negative results for a serum pregnancy test.
14.All female subjects not surgically sterile or postmenopausal (for at least 1 year) and non-vasectomized male subjects must practice at least one of the listed methods of birth control.
15.The subject's life expectancy is ³ 3 months.
16.The subject is amenable to completing the Quality of Life (QoL) questionnaire (Requirement for Phase 2 only).
17.Subject has voluntarily signed and dated an informed consent form, approved by an Independent Ethics Committee (IEC)/Institutional Review Board (IRB), prior to any study specific procedures.

Exclusion criteria

1.The subject has greater than Grade 1 NCI CTCAE (Version 3.07) neurology category findings (e.g., paresthesia, deep tendon reflexes, or weakness that is subjective and/or does not interfere with function).
2.The subject has a documented allergy to sulfa medications.
3.The subject has previously received ABT-751 or pemetrexed.
4.The subject has received more than one investigational agent for NSCLC as a single agent or part of a previous regimen. (An investigational agent is any drug not currently approved for use in humans. Please contact the Abbott medical monitor with questions regarding investigational agents.)
5.The subject exhibits significant weight loss (³ 10%) during the 6 weeks before study entry.
6.The subject has glucose-6-phosphate dehydrogenase deficiency and/or porphyria.
7.The subject has a significant history of cardiac, renal, neurologic, psychiatric, endocrinologic, metabolic, or hepatic disease that would adversely affect his/her participating in this study. Questions regarding inclusion of individual subjects should be directed to the Abbott Medical Monitor.
8.The subject has a current history of a Class 3-4 cardiovascular disability status in accordance with the New York Heart Association Functional Classification.
9.A female subject is pregnant or breastfeeding.
10.The subject has previous or current malignancies at other sites, with the exception of adequately treated in situ carcinoma of the cervix uteri, basal or squamous cell carcinoma of

the skin, previous nonpulmonary malignancy (e.g., localized prostate cancer) confined and surgically resected, treated with chemotherapy or radiation therapy, and is considered cured by the investigator.

Study design

Design

Study phase:	2
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):	27-03-2007
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alimta
Generic name:	pemetrexed
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	27-10-2006
Application type:	First submission

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-02-2007
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-03-2007
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-03-2007
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-06-2007
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-07-2007
Application type:	Amendment
Approved WMO Date:	08-08-2007
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-01-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-01-2008
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-03-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-04-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-06-2008
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	EUCTR2006-002830-38-NL
CCMO	NL14085.100.06