A Randomized, Double-Blind, Phase 3 Study Evaluating the Efficacy and Safety OF ABP 215 Compared with Bevacizumab in Subjects with Advanced Non-Small Cell Lung Cancer

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Primary Objective: The primary objective for this study is to compare the efficacy of ABP 215 with bevacizumab.Secondary Objective(s): The secondary objectives are to assess the safety and immunogenicity of ABP 215 compared with bevacizumab.

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

Summary

ID

NL-OMON40174

Source
ToetsingOnline

Brief title
Not Applicable

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
ADVANCED NON-SMALL CELL LUNG CANCER

Research involving
Human

Sponsors and support

Primary sponsor: Amgen Inc.
Source(s) of monetary or material Support: Amgen Inc.

Intervention

Keyword: Adults, Advanced Non-Small Cell Lung Cancer, BEVACIZUMAB, Biosimilars

Outcome measures

Primary outcome

Primary Efficacy Criterion:

* Risk ratio of the incidence of overall response rate (ORR)

Secondary outcome

Secondary Efficacy Criteria:

* Risk difference of the incidence of ORR

* Duration of response (DOR)

* Progression-free survival (PFS)

Safety Criteria:

* Treatment-emergent adverse events

* Treatment-emergent serious adverse events

* Incidence of anti-drug antibodies

* Overall survival (OS)

Study description

Background summary

Non-small cell lung cancer (NSCLC) is the leading cause of cancer death in both men and women in the US and the EU. In the US, there are an estimated 226,160 new cases of and 160,340 deaths due to NSCLC in 2012, and in the EU there were

an estimated 265,600 new cases and 236,000 deaths due to NSCLC in 2006 (American Cancer Society, 2012; Ferlay et al, 2007). NSCLC arises from the epithelial cells of the lung of the central bronchi to terminal alveoli. The histological type of NSCLC depends on the cells of origin, most commonly squamous cell carcinoma, large cell carcinoma, and adenocarcinoma. Cigarette smoking is the primary risk factor for NSCLC, and other risks include exposure to second hand smoke, family history, radon exposure, and exposure to air pollution (Hackshaw AK et al, 1997; Matakidou A et al, 2005; Lubin JH and Boice JD Jr, 1997; Vineis et al, 2004). For patients with metastatic (Stage IV) NSCLC or recurrent NSCLC following surgery and adjuvant chemotherapy, treatment usually consists of combination chemotherapy with a platinum-based regimen, such as cisplatin and gemcitabine or carboplatin and paclitaxel, in repeated 3-week cycles for up to 6 cycles. For patients without squamous cell histology or a recent history of hemoptysis, addition of the anti-vascular endothelial growth factor (VEGF) antibody bevacizumab to this regimen improved overall response rate (ORR) and prolongs progression-free survival (PFS)(Sandler A et al., 2006; Reck et al, 2009; Hurwitz H and Saini S, 2006).

Based on these and other data, bevacizumab has been approved in the US, EU, and elsewhere for first-line treatment in patients with advanced or recurrent nonsquamous NSCLC in combination with platinum-based chemotherapy.

Study objective

Primary Objective: The primary objective for this study is to compare the efficacy of ABP 215 with bevacizumab.
Secondary Objective(s): The secondary objectives are to assess the safety and immunogenicity of ABP 215 compared with bevacizumab.

Study design

This is a randomized, double-blind, active-controlled study in adult subjects with non-small cell lung cancer (NSCLC) receiving first-line chemotherapy with carboplatin and paclitaxel. Approximately 620 subjects (310 per treatment group) will be randomized (1:1) to receive investigational product (ABP 215 or bevacizumab) at a dose of 15 mg/kg administered as an IV infusion Q3W for 6 cycles. All subjects will receive carboplatin and paclitaxel chemotherapy Q3W for at least 4 and not more than 6 cycles. Subjects will be stratified by geographic region, Eastern Cooperative Oncology Group (ECOG) performance status (0 vs 1), and sex.
A subject will remain on the treatment phase until 21 days after the last dose of investigational product or study specified chemotherapy. Subjects will be followed for disease progression and overall survival (OS) after completing the end-of-treatment visit until the end of the clinical study, consent is withdrawn, they are lost to follow-up, die, or have proscribed therapy (eg, commercial bevacizumab, non-study anti-cancer treatment).

Intervention

STUDY TREATMENT(S):
Test Product, Dose and Mode of Administration:
ABP 215 administered at a dose of 15 mg/kg IV Q3W.
Reference Therapy, Dose and Mode of Administration:
Bevacizumab administered at a dose of 15 mg/kg IV Q3W.
Chemotherapy:
All subjects will receive carboplatin (target AUC 6) and paclitaxel (starting dose 200 mg/m2) Q3W after the ABP 215/bevacizumab infusion.

Study burden and risks

ABP 215 is being developed as a biosimilar to bevacizumab, which is currently marketed and used in the US, EU, and other regions. Bevacizumab is a recombinant immunoglobulin G1 (IgG1) monoclonal antibody that binds to VEGF and inhibits the interaction of VEGF with its receptors, VEGF receptor- (VEGFR-) 1 and VEGFR-2, thus inhibiting establishment of new blood vessels necessary for the maintenance and growth of solid tumors. Bevacizumab is approved in specific combinations in the US, EU, and other regions for the treatment of patients with unresectable, locally advanced, recurrent or metastatic nonsquamous NSCLC as well as metastatic carcinoma of the colon or rectum; metastatic renal cell carcinoma; and other region-specific indications.

A comprehensive analytical characterization pre-evaluation has shown that beva cizumab drug product and ABP 215 drug product are comparable, notwithstanding minor differences that are not expected to affect the safety, efficacy, and quality of the product.

Adverse events that are reflected in warnings or precautions in the US and/or EU labeling information, and which may be serious or fatal, include gastrointestinal perforations, surgery and wound healing complications, hemorrhage (especially tumor-associated hemorrhage), nongastrointestinal fistula formation, arterial thromboembolic events, venous thromboembolic events, congestive heart failure (CHF), neutropenia and infections, severe hypertension, reversible posterior leukoencephalopathy syndrome (RPLS), proteinuria, infusion reactions, and ovarian failure (NCCN Clinical Practice Guidelines in Oncology: Non-small cell lung cancer, 2012; Kamba T and McDonald DM, 2007; Genentech, Inc. Prescriber*s Information for Avastin® (bevacizumab), 2012).

A large body of data from clinical studies and postmarketing use support the effectiveness and safety of bevacizumab in its approved indications. Based on the data available, it is anticipated that ABP 215 will perform similarly to bevacizumab in humans and provide similar benefits in patients.

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

Males and females * 18 and < 80 years of age;Histologically or cytologically confirmed non-squamous non-small cell lung cancer ;Stage 4 or recurrent metastatic NSCLC with measurable disease according to modified Response Evaluation Criteria in Solid Tumors (RECIST v1.1). For subjects with recurrent disease, at least 12 months must have elapsed since completing adjuvant chemotherapy. Subjects must have had a baseline scan (computed tomography [CT] or magnetic resonance imaging [MRI]) of the chest and abdomen to assess disease burden before enrolling in study and receiving first-line chemotherapy for NSCLC. If the scan was performed more than 28 days prior to randomization, an additional scan must be obtained;Subjects must be initiating first-line carboplatin/paclitaxel chemotherapy within 8 days after randomization and expected to receive at least 4 cycles of chemotherapy;ECOG performance status score 0 or 1 ;Normal bone marrow function as defined by:;*absolute neutrophil count (ANC) * 1.5 x 109 g/dL

(1,500/µL);*platelets * 100 x 109 g/dL (100,000/µL);*hemoglobin * 100 g/L (10.0 g/dL);Adequate hepatic function as defined by:;*total bilirubin < 1.5 × the upper limit of normal (ULN) ;*aspartate aminotransferase (AST) and alanine aminotransferase (ALT); < 3.0 × ULN; ;Adequate renal function as defined by creatinine < 1.5 × ULN;Subjects must sign an IRB/EC-approved informed consent form before any study specific procedures

Exclusion criteria

Small cell lung cancer (SCLC) or mixed SCLC and NSCLC;Mixed adenosquamous carcinomas with a predominantly squamous component;Central nervous system (CNS) metastases;Tumor invading or compressing major blood vessels or tumor cavitation;Malignancy other than NSCLC ;Palliative radiotherapy for bone lesions inside the thorax;Prior radiotherapy of bone marrow;Minor surgical procedure or core biopsy before randomization, or not yet recovered from prior minor surgery;Major surgery within 4 weeks before randomization or not yet recovered from prior surgery;Planned major surgical procedure during the treatment phase;Any of the following before randomization:;· Within 6 months: clinically significant cardiovascular disease; peripheral vascular disease, cerebrovascular accident or transient ischemic attack ;· within 3 months: history of hemoptysis;· at any time: history of thrombotic or hemorrhagic disorders;Proteinuria (with a urine dipstick value of 2+ or above or >100 mg/dl);Coagulation abnormalities or systemic anticoagulation or chronic aspirin therapy. Subjects may receive low dose anti-coagulation therapy for peripheral port patency;Medically uncontrolled hypertension or systolic blood pressure > 150 mmHg or diastolic blood pressure > 100 mmHg;Any serious, non-healing unhealed wound or bone fracture;Clinically significant peripheral neuropathy;Significant unplanned weight loss attributed to cancer during 6 months ;Any known co-morbid disease that would increase the risk of toxicity;Known to be positive for hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV), or human immunodeficiency virus (HIV);Recent infection requiring a course of systemic anti-infectives ;Life expectancy < 6 months;Woman of child-bearing potential who is pregnant or is breast feeding or who is not consenting to use highly effective methods of birth control during treatment and for an additional 6 months after the last administration of the protocol specified treatment;Man with a partner of childbearing potential who does not consent to use highly effective methods of birth control during treatment and for an additional 6 months after the last administration of the protocol specified treatment;Other investigational procedures while participating in this study ;Subject is currently enrolled in or has not yet completed at least 30 days since ending other investigational device or drug study(s), or subject is receiving other investigational agent(s);Subject has known sensitivity to any of the products to be administered during the study, including mammalian cell derived drug products;Subject has previously been randomized in this study;Subject likely to not be available to complete all protocol required study visits or procedures;History or evidence of any other clinically significant disorder, condition

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-11-2013
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ABP 215
Generic name:	ABP 215
Product type:	Medicine
Brand name:	Avastin
Generic name:	Bevacinumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-09-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-12-2013

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-12-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-01-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-05-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-05-2015
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	EUCTR2013-000738-36-NL
ClinicalTrials.gov	NCT01966003
CCMO	NL45408.060.13