A Phase 2, randomized, open-label, multicenter study to assess safety and efficacy of nab®-paclitaxel (ABI-007) with epigenetic modifying therapy of CC-486, and nab®-paclitaxel monotherapy as second-line treatment in subjects with advanced nonsquamous non-small cell lung cancer (NSCLC): ABOUND.2L

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To assess the efficacy of nab-paclitaxel administered intravenously (IV) on Days 8and 15 with epigenetic modifying therapy of CC-486 once daily (QD) on Days 1 to14 every 21 days, and nab-paclitaxel monotherapy administered IV on Days 1 and 8every 21...

Ethical review	Not approved
Status	Will not start
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON41094

Source
ToetsingOnline

Brief title
ABI-007-NSCL-006

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
advanced nonsquamous non-small cell lung cancer (NSCLC)., lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Celgene Corporation
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: ABI-007, CC-486, nabpaclitaxel, NSCLC

Outcome measures

Primary outcome

Progression free survival

Secondary outcome

Amongst others; disease control rate, overall response rate and overall

survival and safety endpoints.

Study description

Background summary

There is limited data of monotherapy nab-paclitaxel in the second-line setting; hence, this study
will assess the efficacy and tolerability of weekly nab-paclitaxel, when administered on Days 1
and 8 of each 21-day cycle. The proposed
nab-paclitaxel schedule (2 weeks treatment, 1 week rest) could offer the option of maintaining
consistent dose-intensity for NSCLC patients in this setting.
This Phase 2 study will test the hypothesis that epigenetic modifying therapy

with CC-486 can
improve the anti-tumor activity of nab-paclitaxel in second-line NSCLC
patients. Please refer to the protocol rationale for more information.

Study objective

To assess the efficacy of nab-paclitaxel administered intravenously (IV) on
Days 8
and 15 with epigenetic modifying therapy of CC-486 once daily (QD) on Days 1 to
14 every 21 days, and nab-paclitaxel monotherapy administered IV on Days 1 and 8
every 21 days as second-line treatment for advanced nonsquamous NSCLC, and the
relative efficacy of these two treatment regimens.

Study design

This is a Phase 2, randomized, open-label, multicenter study to assess efficacy
and safety of
nab-paclitaxel in combination with epigenetic modifying therapy of CC-486, and
nab-paclitaxel
monotherapy as second-line treatment in subjects with advanced nonsquamous
NSCLC who
have received one platinum-containing chemotherapy regimen. Approximately 160
subjects with
advanced nonsquamous NSCLC will be randomized 1:1 into one of the two treatment
arms: nabpaclitaxel
/ CC-486 combination therapy or nab-paclitaxel monotherapy prior to receiving
first dose of investigational product (IP). Randomization will be centralized
and stratified by Eastern
Cooperative Oncology Group (ECOG) performance status (0 versus 1), gender
(males versus females), and smoker (yes versus no).

Intervention

Subjects will receive nab-paclitaxel in combination with CC-486 or
nab-paclitaxel monotherapy
during the study. The CC-486 and nab-paclitaxel for both arms are designated as
IP and will be
packaged and supplied by Celgene Corporation.

Study burden and risks

Please refer to 'table of events' in the protocol for a complete overview.

Questionnaires will be taken during each treatment cycle on Day 1, at end of
treatment visit and follow-up visit 28 days after latest dosage.

Patients will receive the following treatment:
• nab®-paclitaxel 100 mg/m2 given as an intravenous (IV) infusion over 30 minutes on Day 1 and 8 of each 21-day treatment cycle;
• nab®-paclitaxel 100 mg/m2 given as an IV infusion over 30 minutes on Days 8 and 15, and CC-486 200 mg given as oral tablets every day from Day 1 to Day 14 of each 21-day treatment cycle.

A mandatory biomarker and genetic research is attached to this study.

Possible risks:
- Anaemia
- Low number of white blood cells with or without fever
- Decline of number of blood platelets
- infections, including pneumonia or urinary tract infection
- nausea
- vomiting
- stomach pain
- diarrhea
- constipation
- feeling tired, unwell, or weak
- fever
- sore throat with swelling, or pain in the nasal membranes or nose
- decreased appetite
- pain (including muscle, joints and chest pain)
- dizziness
- headache
- bruising, including tiny red or purple spots under the skin or other tissue
- pain, swelling or sores on the inside of the mouth
- neuropathies
- tired or week feeling
- swelling
- change of taste
- decrease of weight
- sleep problems
- depression
- coughing
- shortness of breath
- loose of hair
- rash, possibly red, bumpy or generalized
- itchiness
- changes in nails
- abnormal liver function test results
- dehydration
- nose bleed

Contacts

Public
Celgene Corporation

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US
Scientific
Celgene Corporation

Morris Avenue 86
NJ 07901
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1.Age >= 18 years the time of signing the Informed Consent Form (ICF).
2.Understand and voluntarily provide written informed consent prior to the conduct of any study related assessments/procedures.
3.Able to adhere to the study visit schedule and other protocol requirements
4.Histologically or cytologically confirmed advanced nonsquamous NSCLC.
5.No other current active malignancy requiring anticancer therapy.
6.Radiographically documented measurable disease (defined by the presence of >= 1 radiographically documented measurable lesion).
7.One prior platinum-containing chemotherapy for the treatment of advanced disease.
8.Absolute neutrophil count (ANC) >= 1500 cells/mm3.

9.Platelets >= 100,000 cells/mm3.
10.Hemoglobin (Hgb) >= 9 g/dL.
11.Aspartate transaminase (AST/serum glutamic oxaloacetic transaminase [SGOT]) and alanine transaminase (ALT/serum glutamic pyruvic transaminase [SGPT]) <= 2.5 × upper limit of normal range (ULN) or <= 5.0 × ULN if liver metastases.
12.Total bilirubin <= 1.5 ULN (unless there is a known history of Gilberts Syndrome).
13.Serum creatinine <= 1.5 x ULN, or calculated creatinine clearance >= 60 mL/min (if renal impairment is suspected 24-hour urine collection for measurement is required).
14.Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1.
15.Females of childbearing potential [defined as a sexually mature woman who (1) have not undergone hysterectomy (the surgical removal of the uterus) or bilateral oophorectomy (the surgical removal of both ovaries) or (2) have not been naturally postmenopausal for at least 24 consecutive months (ie, has had menses at any time during the preceding 24 consecutive months)] must:
a.Have a negative pregnancy test (ß-hCG) as verified by the study doctor within 72 hours prior to starting study therapy. She must agree to ongoing pregnancy testing during the course of the study, and after end of study therapy. This applies even if the subject practices true abstinence* from heterosexual contact.
b.Either commit to true abstinence* from heterosexual contact or agree to use, and be able to comply with, effective contraception without interruption, 28 days prior to starting investigational product (IP), during the study therapy (including dose interruptions), and for 3 months after discontinuation of study therapy.
Male subjects must:
a.Practice true abstinence* or agree to use a condom during sexual contact with a pregnant female or a female of childbearing potential while participating in the study, during dose interruptions and for at least 6 months following IP discontinuation, even if he has undergone a successful vasectomy.
16.Females must abstain from breastfeeding during study participation and 3 months after IP discontinuation.

Exclusion criteria

1.Squamous cell NSCLC.
2.Prior taxane therapy.
3.Evidence of active brain metastases, including leptomeningeal involvement (prior evidence of brain metastasis are permitted only if asymptomatic and clinically stable for at least 8 weeks following

completion of therapy). MRI of the brain (or CT scan w/contrast) is preferred.
4.Only evidence of disease is non-measurable.
5.Known EGFR mutation.
6.Known EML4-ALK mutation.
7.Preexisting peripheral neuropathy of Grade > 2 (per NCI CTCAE v4.0).
8.Venous thromboembolism within 1 month prior to Cycle 1 Day 1.
9.Current congestive heart failure (New York Heart Association Class IIIV).
10.History of the following within 6 months prior to Cycle 1 Day 1: a myocardial infarction, severe/unstable angina pectoris, coronary/peripheral artery bypass graft, New York Heart Association (NYHA) Class III-IV heart failure, uncontrolled hypertension, clinically significant cardiac dysrhythmia or clinically significant electrocardiogram (ECG) abnormality, cerebrovascular accident, transient ischemic attack, or seizure disorder.
11.Known hepatitis B or C virus (HBV/HCV) infection, known history of human immunodeficiency virus (HIV) infection, or receiving immunosuppressive or myelosuppressive medications that would in the opinion of the investigator, increase the risk of serious neutropenic complications.
12.Active, uncontrolled bacterial, viral, or fungal infection(s) requiring systemic therapy, defined as ongoing signs/symptoms related to the infection without improvement despite appropriate antibiotics, antiviral therapy, and/or other treatment.
13.History of interstitial lung disease, sarcoidosis, silicosis, idiopathic pulmonary fibrosis, or pulmonary hypersensitivity pneumonitis.
14.Subject has a clinically significant malabsorption syndrome, persistent diarrhea, or known sub-acute bowel obstruction > NCI CTCAE Grade 2, despite medical management.
15.Treatment with any investigational product within 28 days prior to signing the ICF.
16.History of or suspected allergy to nab-paclitaxel, azacitidine, human albumin or mannitol.
17.Currently enrolled in any other clinical protocol or investigational trial that involves administration of experimental therapy and/or therapeutic devices.
18.Any other clinically significant medical condition, psychiatric illness, and/or organ dysfunction that will interfere with the administration of the therapy according to this protocol or which, in the views of investigator, preclude combination chemotherapy.
19.Any other malignancy within 5 years prior to randomization, or advanced malignant hepatic tumors, with the exception of adequately treated squamous cell carcinoma of the skin, in-situ carcinoma of the cervix, uteri, non-melanomatous skin cancer, carcinoma in situ of the breast, or incidental histological finding of prostate cancer (TNM Classification of Malignant Tumours (TNM) stage of T1a or T1b). (All treatment of which should have been completed 6 months prior to

signing ICF).
20.Any condition including the presence of laboratory abnormalities, which places the subject at unacceptable risk if he/she were to participate in the study.
21.Any medical condition that confounds the ability to interpret data from the study.
22.Pregnant or breastfeeding females.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	22
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	CC-486
Generic name:	Azacitidine
Product type:	Medicine
Brand name:	nab-Paclitaxel
Generic name:	Abraxane
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	31-10-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Not approved Date:	06-02-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2014-001105-41-NL
CCMO	NL50501.078.14