Randomized, Multicenter, Double-Blind, Phase 3 Trial Comparing the Efficacy of Ipilimumab in Addition to Paclitaxel and Carboplatin versus Placebo in Addition to Paclitaxel and Carboplatin in subjects with Stage IV/Recurrent Non-Small Cell Lung Cancer (NSCLC).

Published: 21-03-2011
Last updated: 27-04-2024

Primary Objective: To compare Overall Survival (OS) of subjects with Stage IV/recurrent NSCLC of squamous histology who have been randomized to ipilimumab in addition to paclitaxel and carboplatin versus placebo in addition to paclitaxel and...

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

Summary

ID

NL-OMON39194

Source
ToetsingOnline

Brief title
IDEATE (078/306)

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Non-small cell lung Cancer (NSCLC)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Combination therapy, Ipilimumab, Non-small cell lung cancer, Overall survival

Outcome measures

Primary outcome

Primary objective:

To compare Overall Survival (OS) of subjects with Stage IV/recurrent NSCLC of squamous histology who have been randomized to ipilimumab in addition to paclitaxel and carboplatin versus placebo in addition to paclitaxel and carboplatin

Secondary outcome

Secondary objectives:

- Compare overall survival in all randomized subjects who received at least one dose of blinded study therapy (OS2)

- Compare Progression-free survival (PFS) per mWHO between the two treatment arms

- Compare Best Overall Response Rate (BORR) per mWHO between 2 treatment arms

Study description

Background summary

The dose and schedule of ipilimumab (4 induction doses every 3 weeks and maintenance dosing every 12 weeks) that subjects will receive up to the time they experience irPD have been established in 3 Phase 2 studies performed in subjects with metastatic melanoma. Re-induction was explored in the MDX10-20 and the CA184025 studies and results were mentioned previously [in the protocol]. Among the 3 dose levels, 10 mg/kg provided the best benefit/risk ratio.
Re-induction may have value for subjects who have experienced clinical benefit and an acceptable tolerability during their first administration of ipilimumab. They might still experience clinical benefit upon re-induction with a safety profile similar to that reported during induction.
The efficacy and safety profile of ipilimumab combined with carboplatin and paclitaxel versus subjects treated with carboplatin and paclitaxel alone have been explored in CA184041. Two (2) administration schedules were explored. The phased schedule resulted in the best efficacy and safety profile.
Based on the above, this Phase 3 study is designed to demonstrate that paclitaxel/carboplatin/ipilimumab will demonstrate superiority over paclitaxel/ carboplatin/placebo.

Study objective

Primary Objective: To compare Overall Survival (OS) of subjects with Stage IV/recurrent NSCLC of squamous histology who have been randomized to ipilimumab in addition to paclitaxel and carboplatin versus placebo in addition to paclitaxel and carboplatin.
Secondary Objectives: To compare Overall Survival in all randomized subjects who received at least 1 dose of blinded study therapy (OS2), Progression-Free Survival (PFS) per mWHO and Best Overall Response Rate (BORR) per mWHO between the two treatment arms.

Study design

Study Design: This is a randomized, multicenter, double-blind Phase 3 study in chemotherapy naive subjects with Stage IV or recurrent NSCLC of squamous histology. The study will randomize approximately 920 eligible NSCLC subjects at a 1:1 ratio to 1 of 2 treatment arms, stratified by ECOG performance status, smoking status, gender, and region.
Subjects will receive 1 of 2 treatment regimens:
• Arm A: Paclitaxel 175 mg/m2 IV q 3 weeks for up to 6 doses starting at randomization. Carboplatin AUC = 6 IV q 3 weeks for up to 6 doses starting at randomization. Ipilimumab 10 mg/kg IV, Induction: q 3 weeks for up to 4 doses starting at cycle 3, ipilimumab maintenance: q 12 weeks for eligible subjects beginning 9 weeks after last ipilimumab dose.
• Arm B: Paclitaxel 175 mg/m2 IV q 3 weeks for up to 6 doses starting at randomization. Carboplatin AUC = 6 IV q 3 weeks for up to 6 doses starting at randomization. Placebo, Induction: q 3 weeks for up to 4 doses starting at

cycle 3, and placebo maintenance: q 12 weeks for eligible subjects beginning 9 weeks after last placebo induction dose.

This study is divided into 4 phases: Screening, Induction, Maintenance and Follow up (Toxicity/Progression Follow-up and Overall Survival Follow-up).

Intervention

Combination chemotherapy paclitaxel/carboplatin/ipilimumab versus paclitaxel/carboplatin/placebo

Study burden and risks

An extensive list of side effects is provided in Appendix 2 (pages 8-17) of the patient information.
Common side effects related to paclitaxel include:
- Burns (if paclitaxel leaks outside of the vein or under the skin)
- Hair loss
- Neuropathy
- Neutropenia, thrombocytopenia, anemia
Common side effects related to carboplatin include:
- Burns (if carboplatin leaks outside the vein or under the skin)
- Nausea, vomiting
- Neutropenia, thrombocytopenia, anemia
- Stomach pain, diarrhea, changes in taste, loss of appetite or weight, changes in vision, hair loss
- Common side effects related to ipilimumab: infusion reaction

-Side Effects considered to be Related to Ipilimumab and advanced melanoma: diarrhea, skin rash, skin itchiness, fatique, nausea, fever, decreased appetite, vomiting, inflammation of the colon, abdominal pain, weight loss, headache, dehydration.

-Side Effects considered to be Related to Ipilimumab + chemo therapy and advanced melanoma:
Nausea, Fatigue, Diarrhea, Fever, Increase in liver enzyme ALT, Increase in liver enzyme AST, Skin itchiness, Vomiting, Skin rash, Decreased appetite, Constipation, Chills

-Side Effects considered to be Related to Ipilimumab and advanced lung cancer:
Hair loss, Joint Pain, Nausea, Decreased red blood cells, Diarrhea, Fatigue, Numbness or muscle , weakness, Weakness, Vomiting, Tingling in hands and feet, Decreased white blood cells, Decreased platelets

Serious Side Effects:
Diarrhea, Inflammation of the colon, Increase in liver enzymes, Vomiting,

Dehydration, Abdominal pain, Fever, Decrease in hormones of pituitary gland, Inflammation of the liver, Inflammation of the pituitary gland, Decreased red blood cells

Furthermore, there are risks and discomforts associated with study procedures, including:
- Injection site reactions sich as bruising, bleeding, infection, fainting
- Rare occurences of allergic reactions to contrast dyes used in imaging, dependent on the type of scan a small amount of radiation (which would be a part of regular treatment / standard of care for this indication as well).

Contacts

Public
Bristol-Myers Squibb

Chaussee de la Hulpe 185
Brussels 1170
BE
Scientific
Bristol-Myers Squibb

Chaussee de la Hulpe 185
Brussels 1170
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1a) Willing and able to provide informed consent
2a) Subjects with NSCLC of predominantly squamous histology documented by histology or cytology from brushing, washing or needle aspiration of a defined lesion but not from sputum cytology alone.
2b) Subjects must present with Stage IV or Recurrent NSCLC (per the 7th International Association for the Study of Lung Cancer (IASLC) classification)
2c) At least 1 measurable tumor lesion, as defined by mWHO criteria, that is not located in a previously irradiated area
2d) Eastern Cooperative Oncology Group (ECOG) performance status less or equal than 1 at study entry
2e) Accessible for treatment and follow-up. Subjects enrolled in this trial must be treated at the participating centers
3a) Men and Women older than or equal to 18 years of age
3b) Women of childbearing potential (WOCBP) must be using an acceptable method of contraception to avoid pregnancy throughout the study and for up to 12 weeks after the last dose of ipilimumab in such a manner that the risk of pregnancy is minimized. See Section 3.3.3 for the definition of WOCBP
3c) WOCBP must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) within 72 hours prior to the start of investigational product
3d) Women must not be breastfeeding

Exclusion criteria

1a) Brain metastases present during screening
1b) Malignant pleural effusion that is recurrent despite appropriate supportive care
1c) Subjects who are known to have activating EGFR mutation
2a) Documented history of severe autoimmune or immune mediated symptomatic disease that required prolonged (more than 2 months) systemic immunosuppresant treatment such as: Ulcerative colitis and Crohn*s disease, Rheumatoid arthritis, systemic progressive sclerosis (scleroderma), Systemic Lupus Erythematosus, Autoimmune vasculitis (eg, Wegener*s Granulomatosis)
2b) Subjects with history of motor neuropathy considered of autoimmune origin (eg, Guillain Barré Syndrome)
2c) Subjects with a history of toxic epidermal necrolysis (TEN)
2d) Dementia, altered mental status, or any psychiatric condition that would prohibit the understanding or rendering of informed consent or completing questionnaires
2e) Serious uncontrolled medical disorder that, in the opinion of the investigator, would impair the ability of the subject to receive protocol therapy
2f) Prior malignancy, active within 5 years, except for locally curable cancers that have been apparently cured and need no subsequent therapy, such as basal or squamous cell skin cancer, superficial bladder cancer or carcinoma in situ of the cervix or breast
2g) HIV positive or active Hepatitis B or active Hepatitis C infection

2h) Prior systemic therapy for lung cancer including vaccines and other targeted therapies - Prior radiation therapy or loco-regional surgeries are allowed if performed at least 3 weeks prior to the date of randomization
2i) Subjects with equal or more than Grade 2 peripheral neuropathy
2j) History of allergy or hypersensitivity to any component of the treatment
3a) Inadequate hematologic function defined by: Absolute neutrophil count (ANC) < 1,500/mm3, or
Platelet count < 100,000/mm3; or Hemoglobin level < 9 g/dL
3b) Inadequate hepatic function as defined by either Total bilirubin level > 2.5 times the upper limit of normal (ULN), AST and ALT levels more than 2.5 times the ULN or * 5 times the ULN if liver metastases are present
3c) Inadequate renal function defined as calculated creatinine clearance < 50 ml/min based on the standard Cockroft and Gault formula
4a) Chronic use of immunosuppresants and/or systemic corticosteroids (used in the management of cancer or non-cancer related illnesses). Use of corticosteroids are allowed if used as premedication for chemotherapy administration or on study management of an irAE
4b) Any non-oncology vaccine therapy used for prevention of infectious disease (for up to 4 weeks prior to or after any dose of blinded study drug)
4c) Any immunotherapy for the treatment of cancer
4d) Prior treatment with any inhibitor or agonist of T-cell co-stimulation
5a) Sexually active fertile men not using effective birth control if their partners are WOCBP.
6a) Prisoners or subjects who are involuntarily incarcerated
6b) Subjects who are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease) illness

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):	22-08-2011
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MDX010
Generic name:	ipilimumab
Product type:	Medicine
Brand name:	Paraplatin
Generic name:	carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxol
Generic name:	paclitaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-03-2011
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-04-2011
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-06-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-07-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Approved WMO Date:	08-09-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	12-09-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-12-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-01-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-05-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-05-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-09-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	28-09-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-12-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO	

Date:	21-12-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-06-2013
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-08-2013
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-09-2013
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-09-2013
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-06-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	24-06-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	24-07-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	21-08-2014
Application type:	Amendment

Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	14-11-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	20-05-2015
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-06-2015
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	EUCTR2009-017396-19-NL
CCMO	NL35840.028.11