

TYPE OF CANCER: LUNG CANCER
TYPE OF TRIAL: Phase II
TRIAL SPONSOR: Bristol Myers Squibb

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STUDY SUMMARY

A Randomized, Double-Blind, Parallel, Three Arm, Multicenter, Phase II Trial Evaluating the Efficacy and Safety of Ipilimumab (BMS-734016) in Combination with Taxol®/Paraplatin® (Paclitaxel/Carboplatin) Compared to Taxol®/Paraplatin® Alone in Previously Untreated Subjects with Lung Cancer.

TREATMENT OVERVIEW

This Phase II study will evaluate ipilimumab activity in Non-Small Cell Lung Carcinoma (NSCLC) and Small Cell Lung Carcinoma (SCLC). Two different dosing schedules of ipilimumab (concurrent and sequential) in combination with Taxol®/Paraplatin® will be explored and two related but distinct response criteria will be used, Immune related response criteria (irRC) and mWHO criteria. This study is divided into four phases: Screening, Treatment, Maintenance and Follow-Up.

PRETREATMENT ASSESMENT

- Informed consent
- Inclusion/exclusion criteria
- Medical history
- Physical Examination
- Vital signs (height, weight, ECOG)
- HIV, Hep B and Hep C
- Bone scan
- Radiographic Tumor Assessment [CT/MRI of chest, abdomen and pelvis and other applicable soft tissues]
- Brain CT/MRI
- 12 Lead EKG/ECG
- Pretreatment events
- Call IVRS at enrollment
- Hematology, Chemistry
- Urine analysis
- Urine Pregnancy test

ENTRANCE CRITERIA FOR PARTICIPATION IN TRIAL

Inclusion Criteria

1) Signed Written Informed Consent

- a) Willing and able to give informed consent;

2) Target Population

a) Subjects with histologically- or cytologically-documented NSCLC (squamous, adeno, large cell anaplastic, bronchioalveolar, and non-small cell carcinoma not otherwise specified) who present with Stage IIIB/Stage IV disease, or recurrent disease following radiation therapy or surgical resection. The cytological documentation of NSCLC may be from brushing, washing or needle aspiration of a defined lesion but not from sputum cytology alone.

OR

b) Subjects with histologically- or cytologically-documented SCLC who present with extensive stage disease (e.g. tumor that is too widespread to be included within the definition of limited-stage disease. Subjects with distant metastases (M1) are always considered to have extensive-stage SCLC). The cytological documentation of SCLC may be from brushing, washing or needle aspiration of a defined lesion but not from sputum cytology alone.

c) Measurable tumor lesion (as long as it is not located in a previously irradiated area) as defined by modified WHO criteria (mWHO).

d) Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1 at study entry.

e) Accessible for treatment and follow-up. Subjects enrolled in this trial must be treated at the participating center(s).

3) Age and Sex

a) Men and women, ≥ 18 years of age

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 last dose of study drug in such a manner that the risk of pregnancy is minimized. WOCBP include any female who has experienced menarche and who has not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation, or bilateral oophorectomy) or is not postmenopausal (defined as amenorrhea ≥ 12 consecutive months; or women on hormone replacement therapy [HRT] with documented serum follicle stimulating hormone [FSH] level > 35 mIU/mL). Even women who are using oral contraceptives, other hormonal contraceptives (vaginal products, skin patches, or implanted or injectable products), or mechanical products such as an intrauterine device or barrier methods (diaphragm, condoms, spermicides) to prevent pregnancy, or are practicing abstinence or where their partner is sterile (e.g., vasectomy) should be considered to be of childbearing potential.

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.

Exclusion Criteria

1) Sex and Reproductive Status

- a) WOCBP who are unwilling or unable to use an acceptable method to avoid pregnancy for the entire study period and for up to 8 weeks after the last dose of ipilimumab.
- b) Women who are pregnant or breastfeeding
- c) Women with a positive pregnancy test on enrollment or prior to investigational product administration.
- d) Sexually active fertile men not using effective birth control if their partners are WOCBP.

2) Target Disease Exceptions

- a) History of or current brain metastases
- b) Malignant pleural effusion that is recurrent despite appropriate supportive care

3) Medical History and Concurrent Diseases

- a) Autoimmune disease: subjects with a documented history of inflammatory bowel disease, including ulcerative colitis and Crohn's disease are excluded from this study as are subjects with a history of symptomatic disease (e.g., rheumatoid arthritis, systemic progressive sclerosis [scleroderma], Systemic Lupus Erythematosus, autoimmune vasculitis [e.g., Wegener's Granulomatosis]). Subjects with motor neuropathy considered of autoimmune origin (e.g., Guillain Barré Syndrome) are excluded from this study;
- b) History and/or concurrent paraneoplastic syndromes related to SCLC;
- c) Dementia, altered mental status, or any psychiatric condition that would prohibit the understanding or rendering of informed consent or completing questionnaires;
- d) A serious uncontrolled medical disorder that, in the opinion of the Investigator, would impair the ability of the subject to receive protocol therapy;
- e) Any concurrent malignancy other than non-melanoma skin cancer, or carcinoma in situ of the cervix, carcinoma in situ of the breast, or prostate cancer treated with systemic therapy (Subjects with a previous malignancy but without evidence of disease for 5 years will be allowed to enter the study);
- f) HIV or Hepatitis B or Hepatitis C infection;
- g) Subjects who received prior systemic therapy for lung cancer are excluded. Prior radiation therapy or loco-regional surgeries are allowed if performed at least 3 weeks prior to randomization date;
- h) Subjects with \geq Grade 2 peripheral neuropathy (motor or sensory).

4) Physical and Laboratory Test Findings

- a) Inadequate hematologic function defined by an absolute neutrophil count (ANC) < 1,500/mm³, a platelet count < 100,000/mm³, or a hemoglobin level < 9 g/dL;
- b) Inadequate hepatic function defined by a total bilirubin level > 2.0 times the upper limit of normal (ULN) or ≥ 2.5 times the upper limit of normal (ULN) if liver metastases are present, AST and ALT levels ≥ 2.5 times the ULN or ≥ 5 times the ULN if liver metastases are present;
- c) Inadequate renal function defined by a serum creatinine level ≥ 2.5 times the ULN;
- d) Inadequate creatinine clearance defined as less than 50 mL/min.

5) Prohibited Treatments and/or Therapies

- a) Chronic use of immunosuppressants and/or systemic corticosteroids (used in the management of cancer or non-cancer-related illnesses). However, use of corticosteroids are allowed if used as premedication for Taxol® infusion, treating irAEs, or adrenal insufficiencies;
- b) Any non-oncology vaccine therapy used for prevention of infectious diseases (for up to 4 weeks prior to or after any dose of ipilimumab);
- c) Prior treatment with a CD137 agonist or CTLA-4 inhibitor or agonist.

6) Other Exclusion Criteria

- a) Prisoners or subjects who are involuntarily incarcerated;
- b) Subjects who are compulsorily detained for treatment of either a psychiatric or physical (e.g. infectious disease) illness;
- c) Subjects should not participate in other clinical trials while in the treatment or maintenance phases of this study.