Nivolumab, Cisplatin, and Pemetrexed Disodium or Gemcitabine Hydrochloride in Treating Patients With Stage I-IIIA Non-small Cell Lung Cancer That Can Be Removed by Surgery

ClinicalTrials.gov Identifier: NCT03366766

Recruitment Status ! : Active, not recruiting
First Posted ! : December 8, 2017
Last Update Posted ! : September 15, 2022

Sponsor:
Sidney Kimmel Cancer Center at Thomas Jefferson University

Collaborator:
Bristol-Myers Squibb

Information provided by (Responsible Party):
Thomas Jefferson University (Sidney Kimmel Cancer Center at Thomas Jefferson University)

Study Description

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Brief Summary:

This phase II trial studies how well Nivolumab, Cisplatin, and Pemetrexed Disodium or Gemcitabine Hydrochloride in treating patients with stage I-IIIA non-small cell lung cancer that can be removed by surgery. Monoclonal antibodies, such as Nivolumab, may interfere with the ability of tumor cells to grow and spread. Drugs used in chemotherapy, such as Cisplatin and Pemetrexed Disodium or Gemcitabine Hydrochloride, work in different ways to stop the growth of tumor cells, either by killing the cells, by stopping them from dividing, or by stopping them from spreading. Giving Nivolumab, Cisplatin, and Pemetrexed Disodium or Gemcitabine Hydrochloride may work better in treating patients with nonsmall cell lung cancer.

Condition or disease !	Intervention/treatment !	Phase !
Non-Squamous Non-Small Cell Lung Carcinoma Stage I Non-Small Cell Lung Cancer Stage IA Non-Small Cell Lung Carcinoma Stage IB Non-Small Cell Lung Carcinoma Stage II Non-Small Cell Lung Cancer Stage IIA Non-Small Cell Lung Carcinoma Stage IIB Non-Small Cell Lung Carcinoma Stage IIIA Non-Small Cell Lung Cancer	Biological: Nivolumab Drug: Cisplatin Drug: Pemetrexed Disodium Drug: Gemcitabine Hydrochloride	Phase 2

Detailed Description:

PRIMARY OBJECTIVES:

I. To estimate major pathologic response (mpCR) in patients with newly diagnosed and untreated non-small cell lung cancer (NSCLC) stage I-IIIA treated with three courses of induction nivolumab added to either cisplatin/pemetrexed or cisplatin/gemcitabine prior to surgery.

SECONDARY OBJECTIVES:

I. Safety. II. Complete pathologic response at all sites of disease. III. Major pathologic response rate at primary site. IV. Clinical complete response rate. V. 1 year progression free survival (PFS). VI. Overall survival.

TERTIARY OBJECTIVES:

I. To explore whether PDL1 expression is associated with treatment response. II. To explore whether there is a net change in the Th1/Th2 ratio (IFN-gamma, IL-4, IL10, etc.) or cell subset frequencies (M2 monocytes, myeloid-derived suppressor cells, etc.) within a patient's peripheral blood either at baseline or in response to treatment is associated with treatment response.

III. To explore whether exosomes or other immune related serum biomarkers change aftercombination therapy.

IV. To explore the predictive value of serial cell free deoxyribonucleic acid (DNA) levels andresponse.

V. PD-L1 assessment in tumor.

Study Design

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Study Type ! :	Interventional (Clinical Trial)
Actual Enrollment ! :	14 participants
Allocation:	Non-Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Nivolumab Plus Cisplatin/Pemetrexed or Cisplatin/Gemcitabine as Induction in Resectable Non-Small Cell Lung Cancer
Actual Study Start Date ! :	December 20, 2017
Actual Primary Completion Date ! :	December 6, 2020
Estimated Study Completion Date ! :	March 2023

Resource links provided by the National Library of Medicine

MedlinePlus Genetics related topics: Lung cancer

MedlinePlus related topics: Lung Cancer

Drug Information available for: Cisplatin Gemcitabine Gemcitabine hydrochloride Pemetrexed Pemetrexed disodium Nivolumab

U.S. FDA Resources

Arms and Interventions

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Arm !	Intervention/treatment !

Experimental: Cohort I (nivolumab, cisplatin, pemetrexed disodium) Patients with non-squamous lung cancer receive nivolumab IV over 30 minutes, cisplatin IV over 60-120 minutes, and pemetrexed disodium IV over 10 minutes on day 1. Courses repeat every 3 weeks for up to 9 weeks in the absence of disease progression or unacceptable toxicity	Biological: Nivolumab Given IV Other Names: • BMS-936558 • NIVO • Opdivo • ONO-4538 Drug: Cisplatin Given IV Other Names: • (SP-4-2)-Diamminedichloroplatinum • Abiplatin • Blastolem • Briplatin • (CDDP) Cis-diammine-dichloroplatinum • Cis-dichloroammine Platinum (II) • Metaplatin • Plastistil • Platinol • Platinex • Platinol-AQ VHA Plus Peyrone's Salt

	Drug: Pemetrexed Disodium Given IV Other Names: • Alimta • N-[4-[2-(2-Amino-4,7-dihydro-4-oxo1H-pyrrolo[2,3-d]pyrimidin-5yl)ethyl]benzoyl]-L-glutamic Acid Disodium Salt
Experimental: Cohort I (nivolumab, cisplatin, gemcitabine hydrochloride) Patients with squamous lung cancer receive nivolumab IV over 30 minutes on day 1, cisplatin IV over 60-120 minutes on day 1, and gemcitabine hydrochloride IV over 1 hour on days 1 and 8. Courses repeat every 3 weeks for up to 9 weeks in the absence of disease progression or unacceptable toxicity.	Biological: Nivolumab Given IV Other Names: • BMS-936558 • NIVO • Opdivo • ONO-4538 Drug: Gemcitabine Hydrochloride Given IV Other Names: • Hydrochloride • Difluorodeoxycytidine Hydrochloride • Gemzar

Outcome Measures

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Primary Outcome Measures ! :

1. Major pathologic response (mpCR) defined as < 10% viable tumor [Time Frame: Up to 63 days]

   A minimax Simon two-stage design will be used. The mpCR rate and its associated score 95% confidence interval will be estimated using the methods

Secondary Outcome Measures ! :

1. Incidence of adverse events according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 [Time Frame: Up to 6 months] Safety data will be summarized descriptively.

2. Progression free survival [Time Frame: At 1 year]

   The distribution of progression-free survival will be estimated using the Kaplan-Meier method.

3. Overall survival [Time Frame: Up to 6 months]

   The distribution of overall survival will be estimated using the Kaplan-Meier method.

4. Overall clinical response [Time Frame: Up to 6 months]

   Will be summarized by presence of baseline measurable disease.

Eligibility Criteria

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Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Pathologically confirmed non small cell lung cancer (NSCLC), not previously treated, with a plan to undergo surgery

- Stage I-IIIA (stage I tumors must be >= 4 cm) per AJCC 8th edition
- Tumor sample must be available for PD-L1 testing; archival tissue within 3 months of study enrollment will be used; if archival tissue is unavailable, a fresh biopsy will be taken
- Eastern Cooperative Oncology Group (ECOG) performance status 0-1
- While blood cells 2000/ul or more
- Absolute neutrophil count 1500/ul or more
- Platelets 100,000/ul or more
- Hemoglobin 9 g/dl or more; (transfusion permitted)
- Bilirubin less than or equal to 1.5 x the upper limit of normal (except subjects with Gilbert syndrome, who can have total bilirubin < 3 mg/dl)
- Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) less than or equal to 3 x the upper limit of normal
- Glomerular filtration rate (GFR) greater than or equal to 40 ml/min using the Cockcroft-Gault formula or serum creatinine less than or equal to 1.5 x (ULN) upper limit of normal
- Women of reproductive potential should have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of human chorionic gonadotropin [HCG]) within 21 days of the study enrollment
- Women of reproductive potential must use highly effective contraception methods to avoid pregnancy for 23 weeks after the last dose of study drugs; "women of reproductive potential" is defined as any female who has experienced menarche and who has not undergone surgical sterilization (hysterectomy or bilateral oophorectomy) or who is not postmenopausal; menopause is defined clinically as 12 months of amenorrhea in a woman over 45 in the absence of other biological or physiological causes; in addition, women under the age of 55 must have a documented serum follicle stimulating hormone (FSH) level more than 40 mIU/mL
- Men of reproductive potential who are sexually active with women of reproductive potential must use any contraceptive method with a failure rate of less than 1% per year; men who are receiving the study medications will be instructed to adhere to contraception for 31 weeks after the last dose of study drugs; men who are azoospermic do not require contraception
- All subjects must be able to comprehend and sign a written informed consent document

Exclusion Criteria:

- Patients who have participated in a study with an investigational agent or device within 2 weeks of enrollment

- Any prior radiotherapy to the lung
- Any prior treatment for NSCLC
- Epidermal growth factor receptor (EGFR) or alkaline phosphatase (ALK) activating alteration
- Any prior therapy with anti-PD-1, anti-PD-L2, anti-CTLA-4 antibody, or any other antibody or drug specifically targeting T-cell co-stimulation or immune checkpoint pathways
- Any history of a sever hypersensitivity reaction to any monoclonal antibody
- Any history of allergy to the study drug components
- Any concurrent malignancies- exceptions include- basal cell carcinoma of the skin, squamous cell carcinoma of the skin, superficial bladder cancer or in situ cervical cancer that has undergone potentially curative therapy; patients with a history of other prior malignancy must have been treated with curative intent and must have remained diseasefree for 3 years post-diagnosis
- Participants with an active autoimmune disease or any other condition requiring systemic treatment with either corticosteroids within 14 days (> 10 mg daily prednisone equivalent) or other immunosuppressive medications within 30 days of randomization. Inhaled or topical steroids, and adrenal replacement steroid doses > 10 mg daily prednisone equivalent, are permitted in the absence of active autoimmune disease.
- Participants with type I diabetes mellitus, hypothyroidism only requiring hormone replacement, skin disorders (such as vitiligo, psoriasis, or alopecia) not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enroll.• Patients with evidence of interstitial lung disease or active, noninfectious pneumonitis. Patients with a history of interstitial lung disease or non-infectious pneumonitis requiring treatment with steroids are also excluded.
- Patients with a known human immunodeficiency virus infection (HIV 1/2 antibodies) or acquired immunodeficiency syndrome (HIV/AIDS), active hepatitis B (e.g., hepatitis B surface antigen [HBsAg] reactive) or hepatitis C (e.g., hepatitis C virus [HCV] ribonucleic acid [RNA] [qualitative] is detected)
- Patients who have received a live vaccine within 30 days prior initiation of the systemic regimen
- Patients must not be receiving any other investigational agents
- Patients with uncontrolled intercurrent illnesses including, but not limited to an active infection requiring systemic therapy or a known psychiatric or substance abuse disorder(s) that would interfere with cooperation with the requirements of the trial
- Women must not be pregnant (as above) or breastfeeding

Contacts and Locations

Go to

Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03366766***

Locations

United States, Pennsylvania

Abington Hospital - Jefferson Health
Abington, Pennsylvania, United States, 19001

Sidney Kimmel Cancer Center at Thomas Jefferson University
Philadelphia, Pennsylvania, United States, 19107

Sponsors and Collaborators

Sidney Kimmel Cancer Center at Thomas Jefferson University Bristol-

Myers Squibb

Investigators

Principal Investigator: Rita Axelrod, MD Sidney Kimmel Cancer Center at Thomas Jefferson Un

More Information

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Additional Information:

Sidney Kimmel Cancer Center at Thomas Jefferson University EXIT

Thomas Jefferson University Hospital EXIT

Responsible Party:	Sidney Kimmel Cancer Center at Thomas Jefferson University
ClinicalTrials.gov Identifier:	NCT03366766 History of Changes
Other Study ID Numbers:	17P.556
First Posted:	December 8, 2017 Key Record Dates
Last Update Posted:	September 15, 2022
Last Verified:	September 2022
Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No

Additional relevant MeSH terms:

- Carcinoma
- Lung Neoplasms
- Carcinoma, Non-Small-Cell Lung
- Neoplasms, Glandular and Epithelial
- Neoplasms by Histologic Type
- Neoplasms
- Respiratory Tract Neoplasms
- Thoracic Neoplasms
- Neoplasms by Site
- Lung Diseases
- Respiratory Tract Diseases
- Carcinoma, Bronchogenic
- Bronchial Neoplasms
- Gemcitabine
- Cisplatin

Nivolumab

Pemetrexed

Antineoplastic Agents

Antimetabolites, Antineoplastic

Antimetabolites

Molecular Mechanisms of Pharmacological Action

Antiviral Agents

Anti-Infective Agents

Enzyme Inhibitors

Immunosuppressive Agents

Immunologic Factors

Physiological Effects of Drugs

Antineoplastic Agents, Immunological

Immune Checkpoint Inhibitors

Folic Acid Antagonists