Treating Early-stage Non-Small Cell Lung Cancer With Durvalumab and Radiation Therapy

ClinicalTrials.gov Identifier: NCT04716946

Recruitment Status ! : Recruiting
First Posted ! : January 20, 2021
Last Update Posted ! : January 20, 2023

See **Contacts and Locations**

View this study on Beta.ClinicalTrials.gov

Sponsor:
Memorial Sloan Kettering Cancer Center

Collaborator:
AstraZeneca

Information provided by (Responsible Party):

Memorial Sloan Kettering Cancer Center

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

Study Description

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Brief Summary:

The purpose of this study is to find out whether treatment with the study drug durvalumab combined with a type of radiation therapy called stereotactic body radiation (SBRT) is a more effective treatment for early-stage non-small cell lung cancer (NSCLC) than SBRT alone.

Condition or disease !	Intervention/treatment !	Phase !
NSCLC Non-small Cell Lung Cancer Lung Cancer Non-small Cell Lung Cancer Stage I Non-small Cell Lung Cancer Stage II Non-small Cell Lung Cancer Stage III Non-small Cell Lung Cancer Stage IIIA PD-L1 Gene Mutation	Drug: Durvalumab Radiation: Stereotactic Body Radiation Therapy	Phase 2

Study Design

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Study Type ! :	Interventional (Clinical Trial)
Estimated Enrollment ! :	40 participants
Allocation:	N/A
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment

Official Title: Stereotactic Body Radiation Therapy With Consolidation Durvalumab in High-Risk Early-Stage Non-Small Cell Lung Cancer - A Phase II Single-Arm Trial

Actual Study Start Date ! : January 27, 2021
Estimated Primary Completion Date ! : February 2024
Estimated Study Completion Date ! : February 2024

Resource links provided by the National Library of Medicine

MedlinePlus Genetics related topics: Lung cancer

MedlinePlus related topics: Lung Cancer

Drug Information available for: Durvalumab

U.S. FDA Resources

Arms and Interventions

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Arm !	Intervention/treatment !
Experimental: Participants with Early-stage Non-Small Cell Lung Cancer Participants will be diagnosed with Stage IIIIA NSCLC and will be ineligible for surgery and will have any level of PD-L1	Drug: Durvalumab Patients will receive durvalumab 1500mg durvalumab via IV infusion over 1 hour, once every 4 weeks (Q4W) for up to a maximum of 6 months (up to 6 doses/cycles) unless there is unacceptable toxicity, withdrawal of consent, or another discontinuation criterion is met. Radiation: Stereotactic Body Radiation Therapy Radiation therapy will be performed with external beam ionizing radiation in accordance with institutional standard practice. 3D conformal radiation therapy (3D-CRT), intensity-modulated radiation

	therapy (IMRT) or volumetric arc therapy (VMAT) will be used at the discretion of the treating radiation oncologist. Other Name: SBRT

Outcome Measures

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Primary Outcome Measures ! :

1. Progression Free Survival [Time Frame: 2 years]

   The primary objective of the study is to evaluate 2- year progression-free survival (PFS) per RECIST 1.1 with durvalumab combined with stereotactic body radiation therapy (SBRT) compared to historical controls with SBRT alone.

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:

- Capable of giving signed informed consent which includes compliance with the requirements

and restrictions listed in the informed consent form (ICF) and in this protocol. Written informed consent and any locally required authorization obtained from the patient/legal representative prior to performing any protocol- related procedures.

- Patient age ≥ 18 at time of consent
- Early stage NSCLC (Stage I to IIIA; T1-4 excluding patients with satellite nodules in the same or ipsilateral lobes, N0; AJCC 8th edition)
- Ineligible for or unwilling to undergo surgical resection. Reasons for surgical ineligibility include: medically inoperable or surgically unresectable (due to tumor size, location etc.), as assessed by MSKCC thoracic surgeon or multi-disciplinary tumor board consensus. Reasons for ineligibility or patient's unwillingness to undergo surgical resection must be clearly documented.
- Histological and/or cytological confirmation of NSCLC as per standard of care biopsy; no additional research protocol-specific biopsy is needed.
- ECOG/WHO PS 0-1 (KPS 70-100)
- Candidates for definitive SBRT

  ° If, after candidates have been planned for RT, they are unable to be treated with the institutional dose constraints as listed in the appendix, they will be labeled ineligible and removed from the study. Ineligible patients will be replaced.
- A predicted 2-year PFS of <80% (≥20% risk for disease progression) based on an MSKCCdeveloped radiomics risk prediction model (see section 9.0).
- Body weight > 30kg
- Adequate normal organ and marrow function as defined below:
  - Hemoglobin ≥9.0 g/dL
  - Absolute neutrophil count (ANC) 1.5 x (> 1500 per mm^3)
  - Platelet count ≥75 x 10^9/L (>75,000 per mm^3)
  - Serum bilirubin ≤1.5 x institutional upper limit of normal (ULN). This will not apply to patients with confirmed Gilbert's syndrome (persistent or recurrent hyperbilirubinemia that is predominantly unconjugated in the absence of hemolysis or hepatic pathology), who will be allowed only in consultation with their physician.
  - AST (SGOT)/ALT (SGPT) ≤2.5 x institutional upper limit of normal
- Evidence of post-menopausal status or negative urinary or serum pregnancy test for female pre-menopausal patients. Women will be considered postmenopausal if they have been amenorrheic for 12 months without an alternative medical cause. The following age- specific requirements apply:

- Women <50 years of age would be considered post-menopausal if they have been amenorrheic for 12 months or more following cessation of exogenous hormonal treatments and if they have luteinizing hormone and follicle-stimulating hormone levels in the postmenopausal range for the institution or underwent surgical sterilization (bilateral oophorectomy or hysterectomy).
- Women ≥50 years of age would be considered post-menopausal if they have been amenorrheic for 12 months or more following cessation of all exogenous hormonal treatments, had radiation-induced menopause with last menses >1 year ago, had chemotherapy-induced menopause with last menses >1 year ago, or underwent surgical sterilization (bilateral oophorectomy, bilateral salpingectomy or hysterectomy).

- Must have a life expectancy of at least 12 weeks Exclusion Criteria:

- Participation in another clinical study with an investigational product during the last 4 weeks.
- Previous thoracic radiation precluding definitive SBRT to the current tumor.
- Active or prior documented autoimmune or inflammatory disorders (including inflammatory bowel disease [e.g., colitis or Crohn's disease], diverticulitis [with the exception of diverticulosis], systemic lupus erythematosus, Sarcoidosis syndrome, or Wegener syndrome [granulomatosis with polyangiitis, Graves' disease, rheumatoid arthritis, hypophysitis, uveitis, etc]). The following are exceptions to this criterion:
    1. Patients with vitiligo or alopecia
    2. Patients with hypothyroidism (e.g., following Hashimoto syndrome) stable on hormone replacement
    3. Any chronic skin condition that does not require systemic therapy
    4. Patients without active disease in the last 5 years may be included but only after consultation with the PI
    5. Patients with celiac disease controlled by diet alone
- Any unresolved toxicity NCI CTCAE Grade ≥2 from previous anticancer therapy with the exception of alopecia, vitiligo, and the laboratory values defined in the inclusion criteria
    1. Patients with Grade ≥2 neuropathy will be evaluated on a case-by-case basis after consultation with the PI.
    2. Patients with irreversible toxicity not reasonably expected to be exacerbated by treatment with durvalumab may be included only after consultation with the PI.
- Prior/Current Therapies:

1. Treatment with a monoclonal antibody within 4 weeks prior to study Day 1 or has not recovered (i.e., ≥ Grade 1 at baseline) from adverse events due to agents administered > 4 weeks earlier (intraocular bevacizumab is acceptable).
2. Prior chemotherapy or targeted small molecule therapy, within 3 weeks prior to study Day 1 or has not recovered (i.e., ≥ Grade 1 at baseline) from adverse events due to a previously administered agent).
3. Prior therapy with an anti-PD-1, anti-PD-L1, including durvalumab, anti-PDL2, antiCD137, anti-Cytotoxic T- lymphocyte-associated antigen-4 (CTLA-4) antibody, or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways.
4. Current or prior use of immunosuppressive medication within 14 days before the first dose of durvalumab. The following are exceptions to this criterion:

i. Intranasal, inhaled, topical steroids, or local steroid injections (e.g., intra articular injection) ii. Systemic corticosteroids at physiologic doses not to exceed <<10 mg/day>> of prednisone or its equivalent iii. Steroids as premedication for hypersensitivity reactions (e.g., CT scan premedication) e. Any concurrent chemotherapy, IP, biologic, or hormonal therapy for cancer treatment. Concurrent use of hormonal therapy for non-cancer-related conditions (e.g., hormone replacement therapy) is acceptable. f. Prior chemotherapy for this diagnosis of lung cancer

- Major surgical procedure (as defined by the Investigator) within 28 days prior to the first dose of IP. Note: Local surgery of isolated lesions for palliative intent is acceptable.
- History of allogenic organ transplantation.
- Severe concurrent illness:

1. Known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial.
2. Known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or in situ cervical cancer that has undergone potentially curative therapy.
3. Active infection including tuberculosis (clinical evaluation that includes clinical history, physical examination and radiographic findings, and TB testing in line with local practice), hepatitis B (known positive HBV surface antigen (HBsAg) result), hepatitis C, or human immunodeficiency virus (positive HIV 1/2 antibodies). Patients with a past or resolved HBV infection (defined as the presence of hepatitis B core antibody [anti-HBc] and absence of HBsAg) are eligible. Patients positive for hepatitis C (HCV) antibody are eligible only if polymerase chain reaction is negative for HCV RNA.

4. Active infection requiring systemic therapy.
5. Evidence of interstitial lung disease or active, non-infectious pneumonitis.
6. Clinically significant (i.e., active) cardiovascular disease: symptomatic cerebral vascular accident/stroke (< 6 months prior to enrollment), myocardial infarction (< 6 months prior to enrollment), unstable angina, congestive heart failure (≥ New York Heart Association Classification Class II), or serious cardiac arrhythmia requiring medication.

- Female patients who are pregnant or breastfeeding or male or female patients of reproductive potential who are not willing to employ a highly effective birth control from screening to 90 days after the last dose of durvalumab monotherapy.

  a. Highly effective methods of contraception, defined as one that results in a low failure rate (ie, less than 1% per year) when used consistently and correctly are described in Appendix B. Note that some contraception methods are not considered highly effective (e.g. male or female condom with or without spermicide; female cap, diaphragm, or sponge with or without spermicide; non-copper containing intrauterine device; progestogen-only oral hormonal contraceptive pills where inhibition of ovulation is not the primary mode of action [excluding Cerazette/desogestrel which is considered highly effective]; and triphasic combined oral contraceptive pills).

- Live vaccination within 4 weeks prior to the first dose of durvalumab and while on trial is prohibited except for administration of inactivated vaccines.
- Connective tissue disorders or idiopathic pulmonary fibrosis involving the lungs and/or esophagus
- Known actionable EGFR or ALK mutation
- Known contraindications to radiotherapy
- History of leptomeningeal carcinomatosis
- History of active primary immunodeficiency
- Known allergy or hypersensitivity to any of the study drugs or any of the study drug excipients.
- Prior randomization or treatment in a previous durvalumab clinical study regardless of treatment arm assignment.
- Participants must not donate blood while on durvalumab therapy.

Contacts and Locations

Go to

Information from the National Library of Medicine

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): ***NCT04716946***

Contacts

Contact: Andreas Rimner, MD 646-608-2449 Rimnera@MSKCC.ORG

Contact: Maria Thor, PhD, MS 646-888-8013 thorm@mskcc.org

Locations

United States, Connecticut

Hartford Healthcare (Data Collection) **Recruiting**

Hartford, Connecticut, United States, 06102

Contact: Helaine Bertsch, MD 860-545-2803

United States, Florida

Baptist Alliance - McI **Recruiting**

Miami, Florida, United States, 33143

Contact: Rupesh Kotecha, MD 786-596-2000

United States, New Jersey

Memorial Sloan Kettering Basking Ridge **Recruiting**

Basking Ridge, New Jersey, United States, 07920

Contact: Andreas Rimner, MD 646-608-2449

Memorial Sloan Kettering Monmouth **Recruiting**

Middletown, New Jersey, United States, 07748

Contact: Andreas Rimner, MD 646-608-2449

Memorial Sloan Kettering Bergen **Recruiting**

Montvale, New Jersey, United States, 07645

Contact: Andreas Rimner, MD 646-608-2449

United States, New York

Memorial Sloan Kettering Cancer Center @ Suffolk - Commack **Recruiting**

Commack, New York, United States, 11725

Contact: Andreas Rimner, MD 646-608-2449

Memorial Sloan Kettering Westchester **Recruiting**

Harrison, New York, United States, 10604

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Sponsors and Collaborators

Memorial Sloan Kettering Cancer Center

AstraZeneca

Investigators

Principal Investigator: Andreas Rimner, MD Memorial Sloan Kettering Cancer Center

More Information

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Additional Information:

Memorial Sloan Kettering Cancer Center EXIT

Responsible Party: Memorial Sloan Kettering Cancer Center
ClinicalTrials.gov Identifier: NCT04716946 History of Changes
Other Study ID Numbers: 20-415
First Posted: January 20, 2021 Key Record Dates
Last Update Posted: January 20, 2023 Last Verified: January 2023

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: Yes

Plan Description: Memorial Sloan Kettering Cancer Center supports the international committee of medical journal editors (ICMJE) and the ethical obligation of responsible sharing of data from clinical trials. The protocol summary, a statistical summary, and informed consent form will be made available on clinicaltrials.gov when required as a condition of Federal awards, other agreements supporting the research and/or as otherwise required. Requests for deidentified individual participant data can be made beginning 12 months after publication and for up to 36 months post publication. Deidentified individual participant data reported in the manuscript will be shared under the terms of a Data Use Agreement and may only be used for approved proposals. Requests may be made to: crdatashare@mskcc.org.

Studies a U.S. FDA-regulated Drug Product: Yes
Studies a U.S. FDA-regulated Device Product: No

Keywords provided by Memorial Sloan Kettering Cancer Center:

- Durvalumab
- NSCLC
- Non-small Cell Lung Cancer
- Non-small Cell Lung Cancer Stage I
- Non-small Cell Lung Cancer Stage II
- Non-small Cell Lung Cancer Stage III
- Non-small Cell Lung Cancer Stage IIIA
- Lung Cancer
- PD-L1 Gene Mutation
- Early stage NSCLC
- 20-145
- Memorial Sloan Kettering Cancer Center

Additional relevant MeSH terms:

- Lung Neoplasms
- Carcinoma, Non-Small-Cell Lung
- Respiratory Tract Neoplasms
- Thoracic Neoplasms
- Neoplasms by Site
- Neoplasms
- Lung Diseases
- Respiratory Tract Diseases
- Carcinoma, Bronchogenic
- Bronchial Neoplasms
- Durvalumab
- Antineoplastic Agents, Immunological
- Antineoplastic Agents