
ClinicalTrials.gov Identifier: NCT03631784

Recruitment Status: Recruiting
First Posted: August 15, 2018
Last Update Posted: July 19, 2019

See Contacts and Locations

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

Study Description

Brief Summary:
This is a trial in adult participants with unresectable, locally advanced, Stage III non-small cell lung cancer (NSCLC) treated with pembrolizumab in combination with platinum doublet chemotherapy and standard thoracic radiotherapy followed by pembrolizumab monotherapy. The primary hypothesis of the trial is that within each platinum doublet
A Trial of Pembrolizumab in Combination With Chemotherapy and Radiotherapy in Stage III NSCLC (KEYNOTE-799, MK-3475-799). - Full Text View - Cli...

Chemotherapy cohort, the percentage of participants who develop Grade 3 or higher pneumonitis is ≤10%.

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<thead>
<tr>
<th>Condition or disease</th>
<th>Intervention/treatment</th>
<th>Phase</th>
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<tbody>
<tr>
<td>Non-small Cell Lung Cancer</td>
<td>Drug: Pembrolizumab 200 mg&lt;br&gt;Drug: Paclitaxel 45 mg/m²&lt;br&gt;Drug: Carboplatin AUC6&lt;br&gt;Drug: Cisplatin 75 mg/m²&lt;br&gt;Drug: Pemetrexed 500 mg/m²&lt;br&gt;Radiation: Thoracic Radiation Therapy (TRT)&lt;br&gt;Drug: Paclitaxel 200 mg/m²&lt;br&gt;Drug: Carboplatin AUC2</td>
<td>Phase 2</td>
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Study Design

Study Type: Interventional (Clinical Trial)
Estimated Enrollment: 216 participants
Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: Double (Participant, Investigator)
Primary Purpose: Treatment
Official Title: A Phase 2 Trial of Pembrolizumab (MK-3475) in Combination With Platinum Doublet Chemotherapy and Radiotherapy for Participants With Unresectable, Locally Advanced Stage III Non-Small Cell Lung Cancer (NSCLC) (KEYNOTE-799).

Actual Study Start Date: October 19, 2018
Estimated Primary Completion Date: December 15, 2020
Estimated Study Completion Date: March 14, 2022

Resource links provided by the National Library of Medicine

Genetics Home Reference related topics: Lung cancer
Drug Information available for: Pembrolizumab
U.S. FDA Resources

Arms and Interventions

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<th>Arm</th>
<th>Intervention/treatment</th>
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Experimental: Cohort A

Participants will receive 1 cycle of pembrolizumab 200 mg on Day 1 with paclitaxel 200 mg/m², and carboplatin area under the curve (AUC) AUC6. Approximately 3 weeks later, participants will receive 2 cycles of pembrolizumab 200 mg administered every 3 weeks (Q3W) and carboplatin AUC2 with paclitaxel 45 mg/m² administered weekly for 6 weeks in conjunction with standard thoracic radiotherapy (60 Gray [Gy]). To conclude the study treatments, participants will receive 14 additional cycles of pembrolizumab 200 mg administered Q3W.

Drug: Pembrolizumab 200 mg
Pembrolizumab 200 mg intravenous (IV) infusion on Days 1 of each 3-week cycle for up to 17 cycles
Other Name: MK-3475

Drug: Paclitaxel 45 mg/m²
Paclitaxel 45 mg/m² IV infusion on Days 1, 8, 15 of each 3-week cycle for Cycles 2, and 3 during radiation therapy.

Drug: Carboplatin AUC6
Carboplatin AUC6 IV infusion on Day 1 of the 21-day cycle for Cycle 1.

Radiation: Thoracic Radiation Therapy (TRT)
The target total dose of TRT will be 60 Gy in 30 daily fractions of 2 Gy, prescribed to the planning target volume.

Drug: Paclitaxel 200
Paclitaxel 200 mg/m^2 IV infusion on Day 1 of the 21-day cycle of Cycle 1.

Carboplatin AUC2
Carboplatin AUC2 IV infusion on Day 1, 8, 15 for Cycles 2 and 3 during radiation therapy.

**Experimental: Cohort B**

Participants will receive 3 cycles of pembrolizumab 200 mg on Day 1 of each 3-week cycle and 3 cycles of pemetrexed 500 mg/m^2 and cisplatin 75 mg/m^2. Treatment will be given in conjunction with standard thoracic radiotherapy (60 Gy) in Cycles 2 and 3. To conclude the study treatments, participants will receive 14 additional cycles of pembrolizumab 200 mg administered Q3W.

Pembrolizumab 200 mg intravenous (IV) infusion on Days 1 of each 3-week cycle for up to 17 cycles
Other Name: MK-3475

Cisplatin 75 mg/m^2
Cisplatin 75 mg/m^2 IV infusion on Day 1 of each 21-day cycle for Cycles 1, 2, 3.

Pemetrexed 500 mg/m^2
Pemetrexed 500 mg/m^2 IV infusion on Day 1 of each 21-day cycle for Cycles 1,
Outcome Measures

**Primary Outcome Measures**:  
1. Percentage of Participants Who Develop Grade 3 or Higher Pneumonitis [ Time Frame: Up to approximately 1 year ]
   
   Pneumonitis is an immune-mediated adverse event which is of interest in light of the mechanism of action of pembrolizumab.

2. Percentage of Participants with a Complete or Partial Response [ Time Frame: Up to approximately 1 year ]
   
   **Complete Response (CR):**
   Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.

   **Partial Response (PR):**
   At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

**Secondary Outcome Measures**:  
1. Progression Free Survival (PFS) [ Time Frame: Up to approximately 1 year ]
   
   PFS defined as the time from enrollment to the first documented disease progression of local recurrence or distant metastasis or death due to any cause, whichever occurs first, as assessed by blinded independent central review (BICR) according to Response Evaluation Criteria in Solid Tumors (RECIST 1.1) modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ.
2. Overall Survival (OS) [ Time Frame: Up to approximately 1 year ]
   OS is defined as the time from enrollment to death due to any cause.

3. Adverse Events (AEs) [ Time Frame: Up to approximately 1 1/4 years ]
   Percentage of participants who experienced one or more AEs.

4. Discontinuations due to AEs [ Time Frame: Up to approximately 1 year ]
   Percentage of participants discontinuing study treatment(s) due to an AE.

Eligibility Criteria

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

Criteria

Inclusion Criteria:

- Male/female participants, who are at least 18 years of age on the day of signing informed consent with previously untreated, unresectable, pathologically confirmed NSCLC and Stage IIIA, IIIB or IIIC NSCLC by American Joint Committee on Cancer Version 8.
- No evidence of metastatic disease by whole body positron emission tomography/computed tomography (PET/CT) scan, diagnostic quality CT scan, and brain imaging.
- Have measurable disease per RECIST 1.1 as assessed by the local site investigator/radiology.
- Have provided tumor tissue sample (core, incisional, or excisional biopsy).
- Have an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1.
- Have adequate pulmonary function test (PFT)
- Have adequate organ function
- A male participant must agree to use contraception through the end of treatment and refrain from...
• A female participant is eligible to participate if she is not pregnant, not breastfeeding, and if participant is a woman of childbearing potential (WOCBP), agrees to follow the contraceptive guidance as provided in the protocol through the end of treatment.

Exclusion Criteria:

• A WOCBP who has a positive urine pregnancy test within 72 hours prior to treatment allocation
• Has small cell lung cancer.
• Has had documented weight loss >10% in the preceding 3 months.
• Participants whose radiation treatment plans are likely to encompass a volume of whole lung receiving >20 Gy in total (V20) of more than 31% of lung volume.
• Has received prior radiotherapy to the thorax, including radiotherapy to the esophagus or for breast cancer.
• Has received prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent (programmed cell death protein 1 [PD-1] and its ligands, programmed cell death ligand 1 [PD-L1] and programmed cell death ligand 2 [PD-L2]) or with an agent directed to another stimulatory or co-inhibitory T-cell receptor (eg, CTLA-4, OX-40, CD137).
• Has received a live vaccine within 30 days prior to the first dose of study drug.
• Has had an allogenic tissue/solid organ transplant.
• Is currently participating in or has participated in a study of an investigational agent or has used an investigational device within 4 weeks prior to the first dose of study treatment.
• Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (in dosing exceeding 10 mg prednisone daily or equivalent) or any other form of immunosuppressive therapy within 7 days prior the first dose of study drug.
• Has a known additional malignancy that is progressing or has required active treatment within the past 5 years.
• Has severe hypersensitivity (Grade 3 or higher) to pembrolizumab and/or any of its excipients.
• Has a known severe hypersensitivity (Grade 3 or higher) to any of the study chemotherapy agents and/or to any of their excipients.
• Has an active autoimmune disease that has required systemic treatment in past 2 years (ie, with use of disease modifying agents, corticosteroids or immunosuppressive drugs).
• Has a history of (non-infectious) pneumonitis/interstitial lung disease that required steroids or has current pneumonitis/interstitial lung disease that requires steroids.
• Has an active infection requiring systemic therapy.
• Has a known history of human immunodeficiency virus (HIV) infection. HIV testing is not required unless mandated by local health authority.
• Has a known history of hepatitis B (defined as hepatitis B surface antigen [HBsAg] reactive) or known active hepatitis C virus (defined as HCV RNA [qualitative] is detected) infection.
• Has a known history of active tuberculosis (TB; Bacillus tuberculosis).
Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the study, interfere with the participant's participation for the full duration of the study, or is not in the best interest of the participant to participate, in the opinion of the treating investigator.

- Has a known psychiatric or substance abuse disorder that would interfere with cooperating with the requirements of the study.
- Is pregnant or breastfeeding or expecting to conceive or father children within the projected duration of the study through the end of treatment.

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):

NCT03631784

Contacts and Locations

Contacts

Contact: Toll Free Number  1-888-577-8839  Trialsites@merck.com

Show 56 Study Locations

Sponsors and Collaborators

Merck Sharp & Dohme Corp.

Investigators

Study Director:  Medical Director  Merck Sharp & Dohme Corp.

More Information

Responsible Party:  Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:  NCT03631784  History of Changes

Other Study ID Numbers: 3475-799

MK-3475-799 (Other Identifier: Merck Protocol Number)

First Posted:  August 15, 2018  Key Record Dates

Last Update Posted:  July 19, 2019

Last Verified:  July 2019
Individual Participant Data (IPD) Sharing Statement:
Plan to Share IPD: Yes
Plan Description: http://engagezone.msd.com/doc/ProcedureAccessClinicalTrialData.pdf
URL: http://engagezone.msd.com/ds_documentation.php

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

Keywords provided by Merck Sharp & Dohme Corp.:
PD1
PD-1
PDL1
PD-L1

Additional relevant MeSH terms:
Lung Neoplasms
Carcinoma, Non-Small-Cell Lung
Respiratory Tract Neoplasms
Thoracic Neoplasms
Neoplasms by Site
Lung Diseases
Respiratory Tract Diseases
Carcinoma, Bronchogenic
Bronchial Neoplasms
Paclitaxel
Albumin-Bound Paclitaxel
Cisplatin
Carboplatin
Pembrolizumab
Pemetrexed
Antineoplastic Agents, Phytogenic
Antineoplastic Agents
Tubulin Modulators
Antimitotic Agents
Mitosis Modulators
Molecular Mechanisms of Pharmacological Action
Antineoplastic Agents, Immunological
Enzyme Inhibitors
Folic Acid Antagonists
Nucleic Acid Synthesis Inhibitors