Study of Pembrolizumab (MK-3475) Plus Chemotherapy vs. Placebo Plus Chemotherapy for Previously Untreated Locally Recurrent Inoperable or Metastatic Triple Negative Breast Cancer (MK-3475-355/KEYNOTE-355)

This study is currently recruiting participants. (see Contacts and Locations)

Verified November 2016 by Merck Sharp & Dohme Corp.

Sponsor:
Merck Sharp & Dohme Corp.

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

ClinicalTrials.gov Identifier:
NCT02819518

First received: June 28, 2016
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Last verified: November 2016
History of Changes

Purpose

The study will consist of two parts. In Part 1, the safety of pembrolizumab (MK-3475) in combination with one of three different chemotherapies will be assessed in the treatment of locally recurrent inoperable or metastatic triple negative breast cancer (TNBC), which has not been previously treated with chemotherapy. In Part 2, the safety and efficacy of pembrolizumab plus chemotherapy will be assessed compared to the safety and efficacy of placebo plus chemotherapy in the treatment of locally recurrent inoperable or metastatic TNBC, which has not been previously treated with chemotherapy.

The primary hypotheses are that the combination of pembrolizumab and chemotherapy prolongs Progression-Free Survival (PFS) compared to placebo and chemotherapy in all participants and in participants with programmed cell death ligand 1 (PD-L1) positive tumors, and prolongs Overall Survival (OS) compared to placebo and chemotherapy in all participants and in participants with PD-L1 positive tumors.

Condition	Intervention	Phase
Triple Negative Breast Cancer (TNBC)	Biological: Pembrolizumab Drug: Nab-paclitaxel Drug: Paclitaxel Drug: Gemcitabine Drug: Carboplatin Drug: Normale Saline Solution	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: A Randomized, Double-Blind, Phase III Study of Pembrolizumab (MK-3475) Plus Chemotherapy vs Placebo Plus Chemotherapy for Previously Untreated Locally Recurrent Inoperable or Metastatic Triple Negative Breast Cancer - (**KEYNOTE-355**)

Resource links provided by NLM:

Genetics Home Reference related topics: breast cancer

MedlinePlus related topics: Breast Cancer Cancer

Drug Information available for: Pembrolizumab

U.S. FDA Resources

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Part 1: Percentage of Participants Who Experience an Adverse Event (AE) [Time Frame: Up to 44 months] [Designated as safety issue: Yes]
- Part 1: Percentage of Participants Who Discontinue Study Drug Due to an AE [Time Frame: Up to 41 months] [Designated as safety issue: Yes]
- Part 2: Progression-Free Survival (PFS) - All Participants [Time Frame: Up to 41 months] [Designated as safety issue: No]
- Part 2: PFS - Participants With PD-L1 Positive Tumors [Time Frame: Up to 41 months] [Designated as safety issue: No]
- Part 2: Overall Survival (OS) - All Participants [Time Frame: Up to 41 months] [Designated as safety issue: No]
- Part 2: OS - Participants With PD-L1 Positive Tumors [Time Frame: Up to 41 months] [Designated as safety issue: No]

Secondary Outcome Measures:

- Part 2: Objective Response Rate (ORR) - All Participants [Time Frame: Up to 41 months] [Designated as safety issue: No]
- Part 2: ORR - Participants With PD-L1 Positive Tumors [Time Frame: Up to 41 months] [Designated as safety issue: No]
- Part 2: Duration of Response (DOR) - All Participants [Time Frame: Up to 41 months] [Designated as safety issue: No]
- Part 2: DOR - Participants With PD-L1 Positive Tumors [Time Frame: Up to 41 months] [Designated as safety issue: No]
- Part 2: Disease Control Rate (DCR) - All Participants [Time Frame: Up to 41 months] [Designated as safety issue: No]
- Part 2: DCR - Participants With PD-L1 Positive Tumors [Time Frame: Up to 41 months] [Designated as safety issue: No]
- Part 2: Percentage of Participants Who Experience an AE [Time Frame: Up to 44 months] [Designated as safety issue: Yes]
- Part 2: Percentage of Participants Who Discontinue Study Drug Due to an AE [Time Frame: Up to 41 months] [Designated as safety issue: Yes]

Estimated Enrollment:	858
Study Start Date:	July 2016
Estimated Study Completion Date:	December 2019
Estimated Primary Completion Date:	December 2019 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Part 1: Pembrolizumab + Nab-paclitaxel Participants receive pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle PLUS nab-paclitaxel 100 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle.	Biological: Pembrolizumab IV infusion Other Names: • MK-3475 • KEYTRUDA® Drug: Nab-paclitaxel IV infusion Other Name: ABRAXANE®
Experimental: Part 1: Pembrolizumab + Paclitaxel Participants receive pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS paclitaxel 90 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle.	Biological: Pembrolizumab IV infusion Other Names: • MK-3475 • KEYTRUDA® Drug: Paclitaxel IV infusion Other Name: TAXOL®
Experimental: Part 1: Pembrolizumab + Gemcitabine/Carboplatin Participants receive pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS gemcitabine/carboplatin 1000 mg/m^2 (gemcitabine) and an Area Under the Curve (AUC) 2 (carboplatin) on Days 1 and 8 of each 21-day cycle.	Biological: Pembrolizumab IV infusion Other Names: • MK-3475 • KEYTRUDA® Drug: Gemcitabine IV infusion Other Name: GEMZAR® Drug: Carboplatin IV infusion

	Other Name: PARAPLATIN®
Experimental: Part 2: Pembrolizumab + Chemotherapy Participants receive pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS one of three chemotherapy regimens: 1) nab-paclitaxel 100 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel 90 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, OR 3) gemcitabine/carboplatin 1000 mg/m^2 (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle.	Biological: Pembrolizumab IV infusion Other Names: • MK-3475 • KEYTRUDA® Drug: Nab-paclitaxel IV infusion Other Name: ABRAXANE® Drug: Paclitaxel IV infusion Other Name: TAXOL® Drug: Gemcitabine IV infusion Other Name: GEMZAR® Drug: Carboplatin IV infusion Other Name: PARAPLATIN®
Active Comparator: Part 2: Placebo + Chemotherapy Participants receive placebo (normal saline) IV on Day 1 of each 21-day cycle PLUS one of three chemotherapy regimens: 1) nab-paclitaxel 100 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel 90 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, OR 3) gemcitabine/carboplatin 1000 mg/m^2 (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle.	Drug: Nab-paclitaxel IV infusion Other Name: ABRAXANE® Drug: Paclitaxel IV infusion Other Name: TAXOL® Drug: Gemcitabine IV infusion Other Name: GEMZAR® Drug: Carboplatin IV infusion Other Name: PARAPLATIN® Drug: Normale Saline Solution IV infusion

Eligibility

Ages Eligible for Study: 18 Years and older (Adult, Senior)
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Has locally recurrent inoperable breast cancer not previously treated with chemotherapy and which cannot be treated with curative intent OR has metastatic breast cancer not previously treated with chemotherapy.
- Has centrally confirmed TNBC, as defined by the most recent American Society of Clinical Oncology/college of American Pathologists (ASCO/CAP) guidelines.
- Has completed treatment for Stage I-III breast cancer, if indicated, and ≥6 months elapsed between the completion of treatment with curative intent (e.g., date of primary breast tumor surgery or date of last adjuvant chemotherapy administration, whichever occurred last) and first documented local or distant disease recurrence.
- Has been treated with (neo)adjuvant anthracycline, if they received systemic treatment in the (neo)adjuvant setting, unless anthracycline was contraindicated or not considered the best treatment option for the participant in the opinion of the treating physician.

- Has measurable disease based on Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) as determined by local radiology review.
- Has provided recently or newly obtained core or excisional biopsy from a locally recurrent inoperable or metastatic tumor lesion for central determination of TNBC status and PD-L1 expression, unless contraindicated due to site inaccessibility and/or participant safety concerns.
- Has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, as assessed within 10 days prior to the start of study drug.
- Has a life expectancy ≥12 weeks from randomization.
- Demonstrates adequate organ function, within 10 days prior to the start of study drug.
- Female participants of childbearing potential must be willing to use an adequate method of contraception for the course of the study through 120 days (or longer as specified by local institutional guidelines) after the last dose of study drug.
- Male participants of childbearing potential must agree to use an adequate method of contraception starting with the first dose of study drug through 120 days (or longer as specified by local institutional guidelines) after the last dose of study drug.

Exclusion Criteria:

- Is currently participating in a clinical study and receiving an investigational agent and/or using an investigational device, or has participated in a clinical study and received an investigational agent and/or used an investigational device within 4 weeks prior to randomization.
- Has not recovered (e.g., to ≤ Grade 1 or to baseline) from AEs due to a previously administered therapy.
- Has neuropathy ≥ Grade 2.
- Has an active autoimmune disease that has required systemic treatment in the past 2 years (e.g., with use of disease modifying agents, corticosteroids, or immunosuppressive drugs).
- Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to randomization.
- Has a known additional malignancy that progressed or required active treatment within the last 5 years. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin that has undergone potentially curative therapy, and in situ cervical cancer.
- Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis. Participants with previously treated brain metastases may participate provided they have stable brain metastases and did not receive chemotherapy for metastatic breast cancer.
- Has active, or a history of, pneumonitis requiring treatment with steroids.
- Has active, or a history of, interstitial lung disease.
- Has a known history of active tuberculosis (TB).
- Has an active infection requiring systemic therapy.
- Has a history of Class II-IV congestive heart failure or myocardial infarction within 6 months of randomization.
- Has a known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the study.
- Is pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of the study, starting with the screening visit through 120 days (or longer as specified by local institutional guidelines) after the last dose of study drug.
- Has received prior therapy with an anti-programmed cell death 1 (anti-PD-1), anti-PD-L1, or anti-PD-L2 agent or with an agent directed to another co-inhibitory T cell receptor (such as cytotoxic T-lymphocyte-associated protein 4 [CTLA-4], OX-40, CD137) or has previously participated in Merck pembrolizumab (MK-3475) clinical studies.
- Has a known history of human immunodeficiency virus (HIV).
- Has known active hepatitis B or hepatitis C.
- Has received a live vaccine within 30 days prior to randomization.
- Has a known history of hypersensitivity or allergy to pembrolizumab and any of its components and/or to any of the study chemotherapies (e.g., nab-paclitaxel, paclitaxel, gemcitabine, or carboplatin) and any of their components.
- Is receiving any medication prohibited in combination with study chemotherapies as described in the respective product labels, unless medication was stopped within 7 days prior to randomization.

Contacts and Locations

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, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02819518

Contacts

Contact: Toll Free Number 1-888-577-8839

Show 34 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.
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Keywords provided by Merck Sharp & Dohme Corp.:
PD1
PD-1
PDL1
PD-L1

Additional relevant MeSH terms:

Breast Neoplasms
Triple Negative Breast Neoplasms
Neoplasms by Site
Neoplasms
Breast Diseases
Skin Diseases
Paclitaxel
Gemcitabine
Pembrolizumab
Albumin-Bound Paclitaxel
Carboplatin
Antineoplastic Agents, Phytogenic
Antineoplastic Agents
Tubulin Modulators
Antimitotic Agents
Mitosis Modulators
Molecular Mechanisms of Pharmacological Action
Antimetabolites, Antineoplastic
Antimetabolites
Antiviral Agents
Anti-Infective Agents
Enzyme Inhibitors
Immunosuppressive Agents
Immunologic Factors
Physiological Effects of Drugs

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