Study of Pembrolizumab (MK-3475) as First-Line Monotherapy and Combination Therapy for Treatment of Advanced Gastric or Gastroesophageal Junction Adenocarcinoma (MK-3475-062/KEYNOTE-062)

Purpose

This is a study of pembrolizumab (MK-3475) as first-line treatment for participants with advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma. Participants will be randomly assigned to one of the 3 treatment arms of the study: pembrolizumab as monotherapy, or pembrolizumab + cisplatin + 5-fluorouracil (5-FU) or capecitabine, or placebo + cisplatin + 5-FU or capecitabine. The primary hypothesis is that pembrolizumab provides a clinically meaningful progression free and/or overall survival.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric Adenocarcinoma</td>
<td>Biological: pembrolizumab</td>
<td>Phase 3</td>
</tr>
<tr>
<td></td>
<td>Drug: cisplatin</td>
<td></td>
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<tr>
<td></td>
<td>Drug: 5-FU</td>
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<tr>
<td></td>
<td>Drug: capecitabine</td>
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</tbody>
</table>

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

Official Title: A Randomized, Active-Controlled, Partially Blinded, Biomarker Select, Phase III Clinical Trial of Pembrolizumab as Monotherapy and in Combination With Cisplatin+5-Fluorouracil Versus Placebo+Cisplatin+5-Fluorouracil as First-Line Treatment in Subjects With Advanced Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma

Resource links provided by NLM:

Drug Information available for: Fluorouracil  Cisplatin  Capecitabine  Pembrolizumab

Genetic and Rare Diseases Information Center resources: Stomach Carcinoma

U.S. FDA Resources

Further study details as provided by Merck Sharp & Dohme Corp.:
Primary Outcome Measures:
- Progression Free Survival (PFS) [Time Frame: Up to 44 months] [Designated as safety issue: No]
- Overall Survival (OS) [Time Frame: Up to 44 months] [Designated as safety issue: No]

Secondary Outcome Measures:
- Overall Response Rate (ORR) [Time Frame: Up to 44 months] [Designated as safety issue: No]

Estimated Enrollment: 750
Study Start Date: July 2015
Estimated Study Completion Date: April 2019
Estimated Primary Completion Date: April 2019 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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<tbody>
<tr>
<td>Experimental: Pembrolizumab monotherapy</td>
<td>Participants receive pembrolizumab 200 mg, intravenously (IV) on Day 1 of each 3 week cycle (Q3W)</td>
</tr>
<tr>
<td>Biological: pembrolizumab</td>
<td>Other Name: MK-3475</td>
</tr>
<tr>
<td>Drug: pembrolizumab</td>
<td></td>
</tr>
<tr>
<td>Other Name: MK-3475</td>
<td></td>
</tr>
<tr>
<td>Experimental: Pembrolizumab + cisplatin + 5-FU</td>
<td>Participants receive pembrolizumab 200 mg Q3W + cisplatin 80 mg/m^2 Q3W + 5-FU 800 mg/m^2/day IV infusion on Days 1-5 Q3W. Capecitabine 1000 mg/m^2 tw ice a day (BID) on Days 1-14 Q3W may be substituted for 5-FU per local guidelines.</td>
</tr>
<tr>
<td>Biological: pembrolizumab</td>
<td>Other Name: MK-3475</td>
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<tr>
<td>Drug: cisplatin</td>
<td>Drug: 5-FU</td>
</tr>
<tr>
<td>Drug: capecitabine</td>
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<tr>
<td>Active Comparator: Placebo + cisplatin + 5-FU</td>
<td>Participants receive placebo, IV, Q3W + cisplatin 80 mg/m^2 Q3W + 5-FU 800 mg/m^2/day IV infusion on Days 1-5 Q3W. Capecitabine 1000 mg/m^2 BID on Days 1-14 Q3W may be substituted for 5-FU per local guidelines.</td>
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<td>Drug: cisplatin</td>
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</table>

Eligibility
Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria
Inclusion Criteria:
- Performance status of 0 or 1 on the Eastern Cooperative Oncology Group (ECOG) Performance Scale
- Have histologically- or cytologically-confirmed diagnosis of locally advanced or metastatic gastric or GEJ adenocarcinoma
- HER2/neu protein negative and programmed cell death ligand 1 (PD-L1)-positive
- Have measurable disease
- Female participants of childbearing potential should be willing to use 2 methods of birth control or be surgically sterile, or abstain from heterosexual activity for the course of the trial through 180 days after the last dose of study medication
- Male participants should agree to use an adequate method of contraception starting with the first dose of study medication through 180 days after the last dose of study medication
- Adequate organ function

Exclusion Criteria:
- Squamous cell or undifferentiated gastric cancer
- Previous therapy for locally advanced or metastatic gastric/GEJ cancer. Participant may have received prior neoadjuvant or adjuvant therapy as long as it was completed at least 6 months prior to randomization
- Major surgery, open biopsy or significant traumatic injury within 28 days prior to randomization, or anticipation of the need for major surgery during the course of study treatment.
- Radiotherapy within 14 days of randomization
- Known additional malignancy that is progressing or requires active treatment with the exception of basal cell carcinoma of the skin, squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cervical cancer
- Known active central nervous system (CNS) metastases and/or carcinomatous meningitis
- Active autoimmune disease that has required systemic treatment in past 2 years
- Diagnosis of immunodeficiency or receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of study medication
- History or evidence of interstitial lung disease or active, non-infectious pneumonitis
Active infection requiring systemic therapy
Pregnant, breastfeeding, or expecting to conceive or father children within the projected duration of the trial, starting with the screening visit through 180 days after the last dose of study medication
Prior therapy with an anti-programmed cell death (PD)-1, anti-PD-L1, or anti-PD-L2 agent
Known history of human immunodeficiency virus (HIV)
Known active Hepatitis B or C
Currently participating in and receiving study therapy or has participated in a study of an investigational agent and received study therapy or used an investigational device within 4 weeks prior to the first dose of study medication
Received a live vaccine within 30 days of planned start of study medication

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: NCT02494583

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

Locations
United States, South Carolina
Call for Information (Investigational Site 0010) Recruiting
Greenville, South Carolina, United States, 29607

Sponsors and Collaborators
Merck Sharp & Dohme Corp.

Investigators
Study Director: Medical Director Merck Sharp & Dohme Corp.

More Information
No publications provided

Responsible Party: Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier: NCT02494583 History of Changes
Other Study ID Numbers: 3475-062, 2015-000972-88
Study First Received: July 8, 2015
Last Updated: August 28, 2015
Health Authority: United States: Food and Drug Administration

Keyw ords provided by Merck Sharp & Dohme Corp.:
Gastric carcinoma Gastroesophageal junction carcinoma
Gastric cancer PD1
Gastroesophageal junction cancer PDL1

Additional relevant MeSH terms:
Adenocarcinoma Antimetabolites, Antineoplastic
Carcinoma Antineoplastic Agents
Neoplasms Immunologic Factors
Neoplasms by Histologic Type Molecular Mechanisms of Pharmacological Action
Neoplasms, Glandular and Epithelial Pharmacologic Actions
Antibodies, Monoclonal Physiological Effects of Drugs
Capecitabine Radiation-Sensitizing Agents
Cisplatin Therapeutic Uses
Antimetabolites

ClinicalTrials.gov processed this record on September 03, 2015