Pembrolizumab (MK-3475) Versus Standard Treatment for Recurrent or Metastatic Head and Neck Cancer (MK-3475-040/KEYNOTE-040)

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

**Purpose**

This is a study of pembrolizumab versus standard treatment (methotrexate, docetaxel, or cetuximab) for the treatment of recurrent or metastatic head and neck squamous cell cancer (HNSCC). Participants will be randomly assigned to receive either pembrolizumab or investigator's choice of standard treatment. The primary study hypothesis is that pembrolizumab treatment prolongs progression-free survival and overall survival when compared to standard treatment.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
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</table>
| Head and Neck Squamous Cell Cancer | Biological: pembrolizumab
Drug: methotrexate
Drug: docetaxel
Biological: cetuximab | Phase 3 |

**Study Details**

- **Study Type:** Interventional
- **Study Design:** Allocation: Randomized
  - Endpoint Classification: Safety/Efficacy Study
  - Intervention Model: Parallel Assignment
  - Masking: Open Label
  - Primary Purpose: Treatment

**Official Title:** A Phase III Randomized Trial of MK-3475 (Pembrolizumab) Versus Standard Treatment in Subjects With Recurrent or Metastatic Head and Neck Cancer

**Resource links provided by NLM:**

- MedlinePlus related topics: Cancer
- Drug Information available for: Methotrexate, Cetuximab, Pembrolizumab
- Genetic and Rare Diseases Information Center resources: Squamous Cell Carcinoma of the Head and Neck
- U.S. FDA Resources

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

**Primary Outcome Measures:**
Progression-free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) for All Participants  
[ Time Frame: Up to 2 years ]  [ Designated as safety issue: No ]

Overall Survival (OS) for All Participants  [ Time Frame: Up to 2 years ]  [ Designated as safety issue: No ]

Secondary Outcome Measures:

- PFS per Modified RECIST 1.1 for All Participants  [ Time Frame: Up to 2 years ]  [ Designated as safety issue: No ]
- Objective Response Rate (ORR) per RECIST 1.1 for All Participants  [ Time Frame: Up to 2 years ]  [ Designated as safety issue: No ]
- ORR per Modified RECIST 1.1 for All Participants  [ Time Frame: Up to 2 years ]  [ Designated as safety issue: No ]
- PFS per RECIST 1.1 in Programmed Cell Death Ligand 1 (PD-L1)-Positive Participants  [ Time Frame: Up to 2 years ]  [ Designated as safety issue: No ]
- OS in PD-L1-Positive Participants  [ Time Frame: Up to 2 years ]  [ Designated as safety issue: No ]
- ORR in PD-L1-Positive Participants  [ Time Frame: Up to 2 years ]  [ Designated as safety issue: No ]
- Time to First Grade 3-5 Adverse Event (AE)  [ Time Frame: Up to 2 years ]  [ Designated as safety issue: Yes ]
- Percentage of Participants Experiencing Grade 3-5 AEs  [ Time Frame: Up to 2 years ]  [ Designated as safety issue: Yes ]

Estimated Enrollment: 466
Study Start Date: November 2014
Estimated Study Completion Date: March 2017
Estimated Primary Completion Date: March 2017 (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</td>
<td>Biological: pembrolizumab</td>
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<tr>
<td>Participants receive pembrolizumab 200 mg intravenous (IV) on Day 1 of each 3-week cycle</td>
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<tr>
<td>Active Comparator: Active Comparator</td>
<td>Drug: methotrexate Drug: docetaxel Biological: cetuximab</td>
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<tr>
<td>Participants receive methotrexate 40 mg/m² IV (may be escalated to 60 mg/m² maximum dose) on Days 1, 8, and 15 of each 3-week cycle; or docetaxel 75 mg/m² IV on Day 1 of each 3-week cycle; or cetuximab 400 mg/m² IV loading dose on Day 1 and 250 mg/m² IV on Days 8 and 15 of Cycle 1, followed by cetuximab 250 mg/m² on Days 1, 8, and 15 of each subsequent 3-week cycle</td>
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</tr>
</tbody>
</table>

Eligibility

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

Criteria

Inclusion Criteria:
- Have histologically- or cytologically-confirmed recurrent or metastatic head and neck squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, and larynx that is considered incurable by local therapies
- Failure of prior platinum therapy
- Measurable disease based on RECIST 1.1
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Adequate organ function
- Female participants of childbearing potential must be willing to use 2 methods of birth control or abstain from heterosexual activity for the course of the study through 120 days after the last dose of study therapy
- Male participants must agree to use an adequate method of contraception starting with the first dose of study therapy through 120 days after the last dose of study therapy

Exclusion Criteria:
- Disease is suitable for local therapy administered with curative intent
- Currently participating in or has participated in a study of an investigational agent or using an investigational device within 4 weeks prior to the first dose of study therapy
- Previously treated with 3 or more systemic regimens given for recurrent and/or metastatic disease
- 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 therapy
• Not recovered from adverse events due to therapy more than 4 weeks earlier
• Prior chemotherapy, targeted small molecule therapy, or radiation therapy within 2 weeks prior to study Day 1
• Known additional malignancy that is progressing or requires active treatment (excepting basal cell carcinoma of the skin, squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cancer)
• Active central nervous system (CNS) metastases and/or carcinomatous meningitis
• 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 120 days after the last dose of trial therapy
• Prior therapy with an anti-PD-1 or anti-PD1-L1 or -L2 therapy
• Human immunodeficiency virus (HIV)
• Hepatitis B or C
• Live vaccine within 30 days of planned start of study therapy

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: NCT02252042

Contacts

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

Locations

United States, California

Call for Information (Investigational Site 0011)
La Jolla, California, United States, 92039
Recruiting

United States, Georgia

Call for Information (Investigational Site 0029)
Athens, Georgia, United States, 30607
Recruiting

United States, Missouri

Call for Information (Investigational Site 0001)
St. Louis, Missouri, United States, 63110
Recruiting

Belgium

MSD Belgium BVBA/SPRL
Brussels, Belgium
Contact: Marc Denayer 32 2 776 60 28
Recruiting

Canada, Quebec

Merck Canada
Kirkland, Quebec, Canada, H9H 3L1
Contact: Medical Information Centre / Centre de l'information medicale de Merck Canada 514-428-8600 / 1-800-567-2594
Recruiting

France

MSD France
Paris, France
Contact: Dominique Blazy 33 147548990
Recruiting

Ireland

MSD Ireland (Human Health) Ltd.
Dublin, Ireland
Contact: Colm Galligan 353 12998700
Recruiting

Italy
MSD Italia S.r.l.  
Rome, Italy  
Contact: Patrizia Nardini  39 06 361911

Korea, Republic of

MSD Korea LTD  
Seoul, Korea, Republic of  
Contact: Cem Ozesen  90 212 3361260

Lithuania

UAB "Merck Sharp & Dohme"  
Vilnius, Lithuania  
Contact: Andrius Bacevicius  370 52780243

Portugal

Merck Sharp & Dohme Lda.  
Paco D'arcos, Portugal  
Contact: Ana Maria Nogueira  351-21-4465890

Puerto Rico

Call for Information (Investigational Site 0096)  
Ponce, Puerto Rico, 00717

Call for Information (Investigational Site 0101)  
San Juan, Puerto Rico, 00927

Russian Federation

Merck Sharp & Dohme IDEA, Inc.  
Moscow, Russian Federation  
Contact: Tatiana Serebriakova  74959167100, EXT.366

Spain

Merck Sharp and Dohme de Espana S.A.  
Madrid, Spain  
Contact: Joaquin Mateos Chacon  34913210428

Switzerland

MSD International GmbH  
Lucerne 6, Switzerland  
Contact: Erik Mossdorf  41 58 618 33 79

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:  NCT02252042  History of Changes
Other Study ID Numbers:  3475-040, 2014-001749-26
Study First Received:  September 25, 2014
Last Updated:  February 25, 2015
Health Authority:  United States: Food and Drug Administration

Keywords provided by Merck Sharp & Dohme Corp.:  
Squamous cell carcinoma  
Head and neck carcinoma  
PD1

Additional relevant MeSH terms:
Carcinoma, Squamous Cell  Neoplasms by Histologic Type
Carcinoma
Neoplasms

ClinicalTrials.gov processed this record on March 03, 2015