Purpose

The purpose of this study is to determine the efficacy and safety of investigational medical products (MEDI4736 monotherapy, tremelimumab monotherapy, and MEDI4736 + tremelimumab combination therapy) in the treatment of patients with recurrent or metastatic carcinoma of the head and neck who have progressed during or after treatment with a platinum containing regimen for recurrent/metastatic disease.

Condition

<table>
<thead>
<tr>
<th>Recurrent/Metastatic Squamous Cell Carcinoma of Head &amp; Neck</th>
</tr>
</thead>
</table>

Intervention

| Drug: MEDI4736 |
| Drug: Tremelimumab |
| Drug: MEDI4736 + Tremelimumab |

Phase

Phase 2

Primary Outcome Measures:

- Objective Response Rate (ORR) [ Time Frame: Up to 2 years ] [ Designated as safety issue: Yes ]
  to assess the efficacy of MEDI4736 monotherapy, tremelimumab monotherapy, and MEDI4736 + tremelimumab combination therapy in terms of ORR

Secondary Outcome Measures:

- Duration of response (DoR) [ Time Frame: Up to 2 years ] [ Designated as safety issue: Yes ]
  to assess the efficacy of MEDI4736 monotherapy, tremelimumab monotherapy, and MEDI4736 + tremelimumab combination therapy in terms of DoR

- Disease control rate (DCR) [ Time Frame: Up to 2 years ] [ Designated as safety issue: Yes ]
  to assess the efficacy of MEDI4736 monotherapy, tremelimumab monotherapy, and MEDI4736 + tremelimumab combination therapy in terms of DCR

- Progression-free survival (PFS) [ Time Frame: Up to 2 years ] [ Designated as safety issue: Yes ]
  to assess the efficacy of MEDI4736 monotherapy, tremelimumab monotherapy, and MEDI4736 + tremelimumab combination therapy in terms of PFS

- Overall survival (OS) [ Time Frame: Up to 2 years ] [ Designated as safety issue: Yes ]
  to assess the efficacy of MEDI4736 monotherapy, tremelimumab monotherapy, and MEDI4736 + tremelimumab combination therapy in terms of OS

- Best objective response (BoR) [ Time Frame: Up to 2 years ] [ Designated as safety issue: Yes ]

Resource links provided by NLM:

- Genetics Home Reference related topics: head and neck squamous cell carcinoma
- 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 AstraZeneca:
to assess the efficacy of MEDI4736 monotherapy, tremelimumab monotherapy, and MEDI4736 + tremelimumab combination therapy in terms of BoR

Other Outcome Measures:

- AEs, physical examinations, laboratory findings (including clinical chemistry, hematology, and urinalysis), vital signs (including blood pressure, pulse, and oxygen saturation), and ECGs [ Time Frame: Up to 2 years | Designated as safety issue: Yes ]

- to assess the safety and tolerability profile

Estimated Enrollment: 240
Study Start Date: April 2015
Estimated Study Completion Date: December 2017
Estimated Primary Completion Date: December 2017 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental: MEDI4736</td>
<td>Drug: MEDI4736</td>
</tr>
<tr>
<td>MEDI4736 monotherapy</td>
<td>MEDI4736 monotherapy</td>
</tr>
<tr>
<td>Experimental: Tremelimumab</td>
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<td>Experimental: MEDI4736 + Tremelimumab</td>
<td>Drug: MEDI4736 + Tremelimumab</td>
</tr>
<tr>
<td>MEDI4736 + Tremelimumab combination therapy</td>
<td>MEDI4736 + Tremelimumab combination therapy</td>
</tr>
</tbody>
</table>

Detailed Description:

This is a randomized, open-label, multi-center, global, Phase II study to determine the efficacy and safety of MEDI4736 monotherapy, tremelimumab monotherapy, and MEDI4736 + tremelimumab combination therapy in the treatment of patients with recurrent or metastatic PD-L1-negative squamous cell carcinoma of the head and neck (SCCHN) who have progressed during or after treatment with a platinum-containing regimen for recurrent or metastatic disease.

Patients will be randomized in a stratified manner according to prognostic factors, including human papillomavirus (HPV) status and smoking status to achieve a balance between treatments for each of the factors. Patients will be randomized in a 1:1:2 fashion to receive MEDI4736 monotherapy, tremelimumab monotherapy, or MEDI4736 + tremelimumab combination.

All treatments will be administered beginning on Day 0 for 12 months or until confirmed progression of disease; unless, in the Investigator's opinion, the patient continues to receive benefit from the treatment), initiation of alternative cancer therapy, unacceptable toxicity, withdrawal of consent, or another discontinuation criterion is met. Patients with confirmed progression of disease who, in the Investigator's opinion, continue to receive benefit from their assigned investigational product and who meet the criteria for treatment in the setting of progression of disease may continue to receive their assigned investigational product treatment for a maximum of 12 months after consultation with the Sponsor and at the Investigator's discretion. The monotherapy arms (tremelimumab and MEDI4736) should be discontinued if there is confirmed progression of disease following a previous response (complete response or partial response).

Tumor assessments will be performed using computed tomography or magnetic resonance imaging. Efficacy for all patients will be assessed by objective partial response).

Following completion or discontinuation of treatment, patients will enter a follow-up period.

Eligibility:

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

Inclusion Criteria:

- Age ≥18 years;
- Written informed consent obtained from the patient/legal representative;
- Histologically confirmed recurrent or metastatic SCCHN; tumor progression or recurrence during or after treatment with 1 platinum-containing regimen for recurrent or metastatic disease; Patients who have only received chemo-radiation therapy for curative intent of locally advanced disease are not eligible. Patients who received chemo-radiation alone as part of treatment of their recurrent disease are also not eligible.
- Written consent to undergo a fresh tumor biopsy or to provide an available archival tumor sample (< 3 months ago)
- Confirmed PD-L1-negative SCCHN by a specified IHC assay;
- WHO performance status of 0 or 1;
- At least 1 lesion; No prior exposure to immune-mediated therapy;
- Adequate organ and marrow function; Evidence of post-menopausal status or negative urinary or serum pregnancy test.

Exclusion Criteria:

- Histologically confirmed squamous cell carcinoma of any other primary anatomic location in the head and neck;
- Received more than 1 regimen for recurrent or metastatic disease
- Any concurrent chemotherapy, investigational Product, biologic, or hormonal therapy for cancer treatment;
- Receipt of any investigational anticancer therapy within 28 days or 5 half-lives;
- Receipt of last dose of an approved (marketed) anticancer therapy (chemotherapy, targeted therapy, biologic therapy, mAbs, etc) within 21 days prior to the first dose of study treatment;
- Major surgical procedure within 28 days prior to the first dose of Investigational Product;
- 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 criterion;
- Current or prior use of immunosuppressive medication within 14 days before the first dose of their assigned Investigational Product;
- History of allogeneic organ transplantation;
- Active or prior documented autoimmune or inflammatory disorders;
- Uncontrolled intercurrent illness;
- another primary malignancy
- Patients with history of brain metastases, spinal cord compression, or a history of leptomeningeal carcinomatosis;
History of active primary immunodeficiency;
Known history of previous tuberculosis;
Active infection including hepatitis B, hepatitis C or human immunodeficiency virus (HIV);
Receipt of live, attenuated vaccine within 28 days prior to the first dose of Investigational Product;
Pregnant or breast-feeding female patients;
Mean QT interval corrected for heart rate (QTc) ≥470 ms calculated from 3 electrocardiograms (ECGs) using Friderica's Correction
Known allergy or hypersensitivity to Investigational Product.
Any condition that, in the opinion of the Investigator, would interfere with evaluation of the IP or interpretation of patient safety or study results

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: NCT02319044

Contacts
Contact: AstraZeneca Clinical Study Information Center 1-877-240-9479 information.center@astrazeneca.com
Contact: AstraZeneca Cancer Study Locator 1-877-400-4696 astraZeneca@emergingmed.com

Sponsors and Collaborators
AstraZeneca
PRA Health Sciences

Investigators
Study Director: Anthony Jarkowski III Medical Scientist AstraZeneca Anthony.Jarkowski@astrazeneca.com
Principal Investigator: Lillian Siu, MD Princess Margaret Hospital in Toronto, Ontario

More Information
No publications provided

ClinicalTrials.gov Identifier: NCT02319044
Other Study ID Numbers: D4193C00003
Study First Received: December 12, 2014
Last Updated: August 20, 2015
Health Authority:
Belgium: Federal Agency for Medicinal Products and Health Products
Canada: Health Canada
Czeck Republic: State Institute for Drug Control
France: National Agency for the Safety of Medicine and Health Products
Germany: Paul-Ehrlich-Institut
Hungary: National Institute of Pharmacy
Spain: Spanish Agency of Medicines
United Kingdom: Medicines and Healthcare Products Regulatory Agency
United States: Food and Drug Administration
United States: Institutional Review Board

Keywords provided by AstraZeneca:
Head and neck cancer; SCCHN

Additional relevant MeSH terms:
Carcinoma
Carcinoma, Squamous Cell
Head and Neck Neoplasms
Neoplasm
Neoplasms by Histologic Type
Neoplasms by Site
Neoplasms, Glandular and Epithelial
Neoplasms, Squamous Cell
Antibodies, Monoclonal
Tremelimumab
Antineoplastic Agents
Immunologic Factors
Pharmacologic Actions
Physiological Effects of Drugs
Therapeutic Uses

ClinicalTrials.gov processed this record on August 27, 2015

For Patients and Families | For Researchers | For Study Record Managers

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