Phase 2/3 Open-label Trial of Enoblituzumab in Combination with MGA012, with and without Chemotherapy, in the Treatment of Patients with Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma

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Background

Squamous Cell Carcinoma of the Head and Neck (SCCHN)

- SCCHN accounts for >500,000 new cases and nearly 300,000 deaths annually in the United States.
- Patients with recurrent/metastatic (R/M) SCCHN have a poor prognosis with median overall survival (OS) of <1 year, requiring an unmet medical need.
- Pembrolizumab has shown efficacy in first-line treatment of R/M SCCHN.

SCCHN accounts for >500,000 new cases and nearly 300,000 deaths annually providing rationale for further development of this combination in patients with recurrent/metastatic SCCHN.

Rationale

- Pembrolizumab has shown efficacy in first-line treatment of R/M SCCHN.
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MGA012

- MGA012 also known as MCMA00272 is an investigational anti-PD-1 monoclonal antibody with a tolerable safety profile and activity signal consistent with other agents in its class demonstrated in early studies.

Rationale for Combination

- Hypothesis: Coordinate engagement of innate and adaptive immunity with enoblituzumab and anti-PD-1 may mediate greater antitumor activity than either alone.

Key Exclusion Criteria

- Adequate end organ function
- No prior systemic therapy for SCCHN in the recurrent or metastatic setting
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Key Objectives

- To select the preferred enoblituzumab + MGA012 regimen (with or without chemotherapy) for further evaluation in Phase 3. In comparison to pembrolizumab + chemotherapy, based primarily upon evaluation of Investigator-assessed overall response rate (ORR) and OS.

Secondary Objectives/Endpoints

- OS
- PK of enoblituzumab and MGA012, including PK and exposure-response analyses
- Immuno-phenotyping of enoblituzumab and MGA012

Exploratory Objectives/Endpoints

- Relationships between PD-L1, PD-L2, and PD-L3 expression and anti-PD-1 activity of the enoblituzumab + MGA012 combination with and without concurrent chemotherapy
- Relationships between PD-L1, PD-L2, and PD-L3 expression on tumor cells and response

Entry Criteria

- Key Inclusion Criteria
  - Histologically proven, recurrent or metastatic SCCHN not curable by local therapy
  - No prior systemic therapy for SCCHN in the recurrent or metastatic setting (with the exception of systemic therapy completed >6 months prior to given as part of multimodal treatment for locally advanced disease)
  - Primary tumor locations of oral pharynx, oral cavity, hypopharynx, or larynx
  - HPV test results available (positive and negative eligible)
  - ECOG performance status of 0 or 1
  - Adequate end organ function

- Key Exclusion Criteria
  - Progressive disease within 6 months of completion of curatively intended systemic treatment for locally advanced SCCHN
  - Radiation or other non-systemic treatment within 2 weeks of randomization
  - Diagnosis of immunodeficiency, or use of immunosuppressive therapy within 14 days of first dose of study drug

References