Phase 2 Trial of Enoblimizumab Plus Retifanlimab or Tebotelimab in First-Line Treatment of Patients with Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma

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Study Background

Monoclonal Antibodies

- Enoblimizumab (MGA271) is an investigational, humanized immunoglobulin G (IgG) 1κ monoclonal antibody (mAb) that binds the B7-H3 (CD274) antigen and triggers tumor cell lysis by activating Fc gamma receptors (CD16A, CD16B, CD32A, CD32B), particularly the low-affinity allele CD16A-158F (Figure 1).

- Tebotelimab (MGA335) is an investigational humanized, hinge-stabilized, IgG1 mAb that targets programmed death-ligand 1 (PD-L1) (Figure 1). Widespread PD-L1 expression in head and neck squamous cell carcinoma (SCCHN) tumors has been associated with antitumor activity in patients treated with checkpoint inhibitors (CP-MGA271-03). The PD-L1 expression level that is either:
  - 9% or more in the Squamous Cohort
  - 16% or more in the Retifanlimab Cohort (PD-L1+ CPS ≥1; N=50)

- Retifanlimab is licensed to Incyte with an indication for the treatment of metastatic melanoma and non–small cell lung cancer (NSCLC) with a PD-L1+ CPS ≥1.

- Nivolumab is licensed to Bristol Myers Squibb with an indication for the treatment of metastatic melanoma and NSCLC with a PD-L1+ CPS ≥1.


Specific Targets

- B7-H3, B7-homolog 3
- B7-H3–expressing tumor cells
- Cytotoxic T lymphocytes
- Natural killer cells
- Tumor cells

- Anti-programmed (PD)-protein 1 (PD-1) mAb blocking binding of PD-ligand 1 (PD-L1) or PD-L2, programmed death-ligand 2

- Relationships between PK, PD, and clinical efficacy

- Correlation with clinical response

- Immunogenicity of treatment

- Antitumor activity

Table 1. Summary of Efficacy Data With Anti-B7-H3 Antibody Plus Anti-PD-1 Blockade in the Context of Anti-PD-1 Blockade Monotherapy in Patients With SCCHN or NSCLC

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<td>Anti-PD-1 only</td>
<td>- Investigate MGA271, MGA335, in combination with pembrolizumab or nivolumab</td>
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Table 2. Study Objectives

- Study design: multi-center, open-label, non-randomized, dose-escalation trial (NCT04634825)

- Key Inclusion Criteria:
  - Patients ≥18 years of age with histologically proven recurrent or metastatic SCCHN not curable by local therapy with no prior systemic therapy for SCCHN (CPS <1)
  - Patients who completed systemic therapy within the last 12 months before the first dose of study drug

- Key Exclusion Criteria:
  - Presence of an active malignancy other than SCCHN or NSCLC
  - History of any significant medical condition that, in the investigator's judgment, may preclude participation or interfere with the completion of the study

- Study Endpoints:
  - RECIST v1.1-assessed PFS, DCR, and ORR
  - Correlation of treatment with clinical response
  - Immunogenicity of treatment
  - Antitumor activity

- Rationales for Study:
  - The simultaneous targeting of either PD-1 and B7-H3, or PD-1 and LAG-3 is supported by the complementary biology of these 3 molecules in mediating the immune response against tumor cells.

Rationale for PK Study:

- Investigators suggest that both retifanlimab and tebotelimab have potential to enhance enoblimizumab-mediated immune activation and antitumor activity.

- Combination of enoblimizumab with retifanlimab or tebotelimab has the ability to natural killer cells and CD8+ T cells from peripheral blood mononuclear cells cultured with tumor cells to produce interferon-gamma upon re-stimulation (Figure 3).

- Both retifanlimab and tebotelimab enhanced enoblimizumab-dependent cytotoxicity targeting CD8+ T cells (Figure 4).

- Retifanlimab in combination with enoblimizumab has the ability to enhance the antitumor activity of enoblimizumab (Figure 3).

- Relationship between PK, PD, and clinical efficacy

- Correlation with clinical response

- Immunogenicity of treatment

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References


Disclosures

G. Obara has no conflict of interest to declare.