Abstracts

Objectives Dostarlimab is an approved programmed death 1 (PD-1) inhibitor. PD-1 therapy can lead to immune-related adverse events (irAEs). Here we report on the management of irAEs across multiple tumor types evaluated in GARNET.

Methods GARNET is a multicenter, open-label, single-arm phase 1 study with dose expansion in multiple tumor types: dMMR solid tumors, mismatch repair proficient EC, non-small cell lung cancer, and platinum-resistant ovarian cancer. Patients received 500 mg of dostarlimab intravenously Q3W for 4 cycles, then 1000 mg Q6W until disease progression, discontinuation, or withdrawal.

Results At this third interim analysis of GARNET, the safety population included 605 patients. irAEs were experienced by 32.2%, with 10.1% of patients experiencing grade ≥3 irAEs (Table 1). Few, 5.5%, discontinued treatment because of an irAE. No irAEs led to death. Of patients experiencing irAEs, 64.6% were treated with immune modulatory medications (IMMs; referring to steroids, immune suppressant, and/or thyroid therapy); 58.7% of these patients experienced resolution. Average time to resolution was 69 days. For the 35.4% of patients not treated with IMMs, 56.5% experienced a resolution. Average time to resolution was 67 days. The most common irAEs were hypothyroidism (7.6%; 45 of 46 [97.8%] patients treated with thyroid therapy) and arthralgia (5.6%; 8 of 34 [23.5%] patients treated with steroids).

Conclusions Across all tumor types evaluated in GARNET, 32.2% of patients experienced irAEs, 68.7% of whom experienced grade 2 events. 58.7% of patients experienced resolution of irAEs upon treatment with an IMM. Overall discontinuation due to irAEs was low.

Poster rounds with the professors: Group C1

7/#178 ONCOLYTIC ADENOVIRUS MEM-288 ENCODING MEMBRANE-STABLE CD40L AND IFN BETA INDUCES AN ANTI-TUMOR IMMUNE RESPONSE IN A HIGH GRADE SEROUS OVARIAN CANCER MOUSE MODEL

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Objectives This study investigates a novel approach for immune recruitment to the ovarian cancer microenvironment using an oncolytic adenovirus, MEM-288, encoding a modified membrane-stable CD40L (MEM40) and IFNβ.

Methods Mouse ovarian cancer cells (STOSE-luc) were injected intraperitoneally into 7-week FVB mice and randomized to treatment with saline (n=8), GFP-expressing adenovirus (Adv-GFP, n=9) or MEM-288 (n=9) on days 12 and 15 with euthanasia on day 27. Tumors were dissociated and evaluated via flow cytometry. Splenocytes were dissociated and incubated with STOSE-luc target cells for IFN-γ enzyme-linked immunospot (ELISPOT) assay. Statistical tests of significance were calculated by one-way ANOVA.

Abstract 7/#178 Figure 1 (A) Tumor burden was decreased after MEM-288 treatment as measured by ascites volume, (B) number of metastatic sites, and (C) decreased tumor weights compared to saline-treated mice. (D) Enzyme-linked immunospot (ELISPOT) assay demonstrated higher number of tumor-reactive splenocytes for saline, Adv-GFP, and MEM-288 treated mice. Number of spots per well represents number of splenocytes secreting IFN-γ in after exposure to irradiated STOSE-luc target cells.

Results MEM-288-treated mice demonstrated improved tumor control compared to Adv-GFP and saline across multiple parameters (mean ± SD), including ascites volume (0.02 ± 0.04 mL vs. 1.1 ± 1.5 mL vs. 1.6 ± 0.95 mL; p=0.01); metastatic sites (3.1 ± 0.8 vs. 4.4 ± 2.2 vs. 5.4 ± 1.4; p=0.03); and tumor weight (0.41 ± 0.21 g vs. 0.91 ± 1.1 g vs. 1.1 ± 0.66 g; p=0.20). These anti-tumor effects directly correlated with T cell-associated immune responses in the tumor microenvironment through expansion of tumor-infiltrating CD8+ T-cells (p = 0.0005). MEM-288 induced a systemic immune response with increased number of tumor-reactive T-cells in splenocytes via IFN-γ ELISPOT assay (p=0.004) compared to other groups. CD8+ T-cell inhibitory markers CTLA4+/PD1- (p = 0.002) and CTLA4+/PD1+ (p=0.01) were decreased with MEM-288 treatment.

Conclusions MEM-288 has potent anti-tumor activity in an immune competent ovarian cancer mouse model, likely through recruitment of cytotoxic T-cells and promotion of a systemic anti-tumor T-cell response.

8/#234 IMMUNE PROPERTIES OF TUMOR-INFILTRATING LYMPHOCYTES IN OVARIAN CLEAR CELL CARCINOMA RELATIVE TO OVARIAN HIGH-GRADE SEROUS CARCINOMA

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Objectives A recent series of clinical trials have demonstrated the potential efficacy of immune checkpoint inhibitors (ICIs)