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 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 treated with an IMM experienced resolution. No irAEs led to death. Of patients experiencing grade 2 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 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).

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 and IFNB.

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.

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)
for ovarian clear cell carcinoma (OCCC). However, little is known about the immune characteristics of OCCC. In this study, we investigated the immunologic properties of tumor-infiltrating lymphocytes (TILs) in patients with OCCC to elucidate therapeutic responses to ICIs.

**Methods** We analyzed peripheral blood mononuclear cells (PBMCs) and TILs from patients with ovarian cancer. CD8 and regulatory T (Treg) cells of treatment-naïve OCCC (n=22) and high-grade serous carcinoma (HGSC) patients (n=35) were compared using flow cytometry.

**Results** First, we explored the immune characteristics of OCCC-infiltrating T cells. The percentages of CD8 and FoxP3⁺CD4 T cells were higher in TILs than in PBMCs. Most CD8 TILs were CCR7⁻CD45RA-effector memory lymphocytes. CD8 TILs exhibited higher expression of PD-1, CD39, CD103, granzyme B, Ki-67 and TCF-1, compared with peripheral CD8 T cells. Tumor-infiltrating Treg cells were enriched with CD45RA⁻FoxP3high effector Treg cells and showed higher expression of PD-1, CTLA-4, 4-1BB, OX-40, CD39, and CCR8, compared with peripheral Treg cells. Second, we compared TILs from patients with OCCC and HGSC. The percentage of tumor-infiltrating Treg cells was significantly lower in OCCC than in HGSC. Furthermore, tumor-infiltrating Treg cells in OCCC showed lower TOX expression and less proliferative ability than those in HGSC.

**Conclusions** Overall, while the exhausted phenotypes of CD8 TILs in OCCC were similar to those in HGSC, OCCC showed less infiltration of highly suppressive Treg cells. Further research is warranted to investigate infiltrating Treg cell activity in OCCC.