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 experiencing 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

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

Abstract 8/#234 Figure 1

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.

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**Abstracts**

**ROLE OF GENOME-WIDE METHYLATION PROFILING OF CIRCULATING CELL-FREE DNA BY METHYLATED DNA SEQUENCING (MED-SEQ) IN ADVANCED-STAGE OVARIAN CANCER**

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**Objectives**

Finding circulating DNA methylation markers in blood may help in the prediction of treatment response and prognosis of patients with advanced-stage ovarian cancer (ASOC). The aim of this study is to identify differentially methylated regions in cell-free DNA (cfDNA) of patients with ASOC at different time points and to correlate this to clinical parameters.

**Methods**

Liquid biopsies were collected pre- and post-surgery from patients with ASOC (FIGO-stage IIIB-IV). Plasma-derived cfDNA was isolated and analyzed by a new high-throughput genome wide DNA methylation sequencing technique: MeD-seq. A trainingset of pre-surgery samples were compared with healthy controls to define DNA methylation signatures (Chi-square test with Bonferroni correction for multiple testing).

**Results**

Nine pre-surgical samples of patients with ASOC showed a clear distinct DNA methylation signature from nine healthy controls (p-value <0.0001). 31 pre-operative samples significantly differed from 38 post-operative samples (p-value <0.0001). The day post-surgery and FIGO-stage influenced the methylation profile independently. When adjusted for these parameters complete CRS could be distinguished from incomplete CRS. Also, there was a trend towards less hypermethylation in women without a relapse within 12 months for patients with FIGO-stage IV and liquid biopsies taken on day 3 post-operatively.

**Conclusions**

The MeD-seq assay provides a promising new method for genome wide cfDNA methylation profiling. Patients with ASOC could clearly be distinguished from healthy controls. Moreover, cfDNA methylation differed pre- and postoperatively. A potential future application is to use this methylation profile by predicting response to treatment and to predict at baseline which women will relapse within 12 months.