(MLH1PHM). Women with MLH1PHM tumors are considered at low risk for Lynch Syndrome and forgo referral to cancer genetic clinics. Regardless of MLH1PHM status, MLH1-d IHC helps to classify EC according to TCGA-based molecular classification and for consideration of immunotherapy. This study sought to examine the proportion of MLH1PHM in MLH1-d cases.

Methods
Retrospective audit of pathology reports (2018–2021) in a major community laboratory in Ontario, Canada (Life Labs) identified EC samplings that were evaluated by IHC for MMR proteins (MLH1, MSH2, MSH6, and PMS2) followed by MLH1PHM test, when appropriate.

Results
Among 1229 consecutive EC samples tested by MMR-IHC, 14 could not be classified due to insufficient tumor cells or ambiguous staining. The remaining 1215 ECs were classified into MMR-d (n=324, 26.7%) or proficient (n=891, 73.3%). Among MMR-d cases, 274 showed loss of MLH1 and 206 had available MLH1 methylation testing data. MLH1PHM was detected in 201/206 (97.6%), designated as most likely sporadic whereas 5/206 cases (2.4%) were not hypermethylated raising the possibility for Lynch syndrome.

Conclusions
Our audit confirms the feasibility of testing endometrial samplings for MMR-IHC and promoter hypermethylation testing. MLH1PHM accounts for vast majority of MLH1/PMS2-deficient cancers in a universally screened EC population. The very high proportion of MLH1PHM challenges the practice algorithm and raises the need to explore practice revision.
Abstracts

Objective: 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 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

Pamela Peters*, Regina Whittaker, Felicia Lim, Shonagh Russell, Justin Pollara, Elizabeth Bloom, Kyle Strickland, Amer Beg, Andrew Berchuck, Scott Antonia, Rebecca Previs. Duke University, Obstetrics and Gynecology, Durham, USA; Duke University, Pharmacology and Cancer Biology, Durham, USA; Duke University, Obstetrics and Gynecology, Durham, USA; Duke University, Surgery, Durham, USA; Duke University School of Medicine, Pathology, Durham, USA; Memgen, Inc, Chief Scientific Officer, Houston, USA; Moffitt Cancer Center, Immunology, Tampa, USA; Duke University, Medicine, Durham, USA

Objective: 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.

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

Junsik Park*, Jung Chul Kim, Mi-Ran Lee, Joohyang Lee, Sunghoon Kim, Wun Kim, Jung-Yun Lee. Yonsei University, Severance Biomedical Science Institute, Seoul, Korea, Republic of; Yonsei University College of Medicine, Department of Obstetrics and Gynecology, Seoul, Korea, Republic of

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