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.

Abstract 8/#234 Figure 1

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

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.