tested cell lines. Table 1. IC50 values of agents sorted by cell lines. N/A indicating value not achieved at threshold of 10μm.

Conclusions Platinum-resistant ovarian cancer has a poor prognosis highlighting the need for new therapeutic modalities. Neither telaglenastat, savolitinib, nor AMG-232 exhibit any appreciable cytotoxicity; however, mithramycin demonstrates cytotoxicity in the low nanomolar range in several representative ovarian cancer cell lines, including two platinum-resistant lines. The potential therapeutic benefit of mithramycin warrants further preclinical evaluation.

**Abstract EPV001/#119 Table 1**

<table>
<thead>
<tr>
<th></th>
<th>CAOV3 (n=3)</th>
<th>UWB1.289 (n=3)</th>
<th>OVCAR3 (n=3)</th>
<th>UWB1.289-Platinum Resistant (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin (nm)</td>
<td>2733 ±208</td>
<td>2067 ±416</td>
<td>4733 ±1250</td>
<td>7267 ±2572</td>
</tr>
<tr>
<td>Mithramycin (nm)</td>
<td>42.4 ±8</td>
<td>57.9 ±46</td>
<td>65.5 ±38</td>
<td>62.2 ±54</td>
</tr>
<tr>
<td>Teleganestat</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Savolitinib</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>AMG-232</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Abstract EPV002/#308 Figure 1**

PCA of a. PEO1 vs PEO4, b. A2780 vs C200, c. MR182 vs R182; PLS-DA of d. PEO1 vs PEO4, e. A2780 vs C200, f. MR182 vs R182

**Abstract EPV002/#308 Figure 2**

Heat map of a. PEO1 vs PEO4, b. A2780 vs C200, c. MR182 vs R182; Volcano plot with FDR ≤ 5% and absolute fold-change ≥ 1.5 of d. PEO1 vs PEO4, e. A2780 vs C200, f. MR182 vs R182

Objectives Over 80% of ovarian cancer (OC) patients will experience relapse after an initial response to platinum-based chemotherapy. Acquisition of metabolomic adaptations is
thought to be an integral part of chemoresistance, but the relation of these adaptations to chemoresistance is poorly understood. Our aim was to identify the metabolic adaptations that are specifically associated with platinum-resistant (PR) cell lines and its platinum-sensitive (PS) derivatives across multiple OC cell lines.

**Methods** Targeted metabolic analysis evaluating 242 metabolites of the PS A2780, PEO1, and mR182 cell lines was performed along with their respective PR derivatives, C200, PEO4, R182. The group comparison was performed using unpaired t-tests followed by FDR correction. The differentially expressed metabolites were identified using two criteria: FDR ≤ 5% and absolute fold-change ≥ 1.5. The pathway analysis was performed using MetaboanalystTM with the metabolites that have unadjusted p-value ≤ 5%.

**Results** Many significantly impacted pathways were conserved among the PR cell lines. Compared to the PS counterparts, the PR PEO4, C200, and R182 lines had metabolite concentrations with FC≥1.5 in 29, 44, and 28 measured metabolites, respectively. The top pathways impacted were ‘nicotinate and nicotinamide metabolism’, ‘purine metabolism’, and ‘phenylalanine, tyrosine, tryptophan biosynthesis’. A global analysis of PS vs PR was performed. The top five significantly impacted pathways were: Arginine biosynthesis, Pyrimidine and Purine metabolism, Phenylalanine, tyrosine and tryptophan biosynthesis’ and ‘Starch and sucrose metabolism’.

**Abstract EPV002/#308 Figure 3** a) Volcano plot of sensitive cohort vs resistant cohort; b) Heat map of sensitive cohort vs resistant cohort

**Abstract EPV002/#308 Figure 4** Top impacted pathways of combined PR cohort compared to PS cohort

**Conclusions** We identified multiple shared metabolomic pathways among established PR OC cell lines that highlight conserved motifs of PR. These may represent targetable pathways to predict or reverse chemoresistance.

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**EPV003/#326** AN INTEGRATED GENOMIC, PROTEOMIC AND IMMUNOPEPTIDOMIC APPROACH TO DISCOVER NOVEL TUMOUR NEOANTIGENS IN AN IMMUNOLOGICALLY COLD OVARIAN CANCER FOR PERSONALISED T-CELL RECEPTOR THERAPY

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*10.1136/ijgc-2021-IGCS.70

**Objectives** Ovarian carcinosarcoma (OCS) are rare aggressive cancers with poor prognosis and limited effective treatments. The tumour mutation burden in OCS is often low. Therefore, these tumours are immunologically ‘cold’ and relatively insensitive to single agent immunotherapy. We explored tumour neoantigen discovery in an OCS using various genomic and proteomic platforms for personalised T-cell receptor (TCR) therapy.

**Methods** Whole genome sequencing (WGS) was performed on SFRCO1177 OCS tumour specimen taken at surgery. Fresh tumour specimens obtained at surgery and biopsy at recurrence were engrafted subcutaneously in NOD-scidIL2rgamma-knockout (NSG) to generate a paired patient derived xenograft (PDX) model. Whole exome sequencing and RNA sequencing (WES/RNAseq) together with nano-ultra-performance liquid chromatography coupled to high-resolution mass spectrometry were performed on the snap frozen tumours from the baseline and recurrent PDX for tumour neoantigen (TNA) discovery.

**Results** A total of 6,500 mutant TNA were predicted in silico from the baseline WGS data which were narrowed down to 65 and 33 respectively based on the baseline and recurrent PDX tumours WES/RNAseq data. The immunopeptidomic analysis revealed over 100 major histocompatibility complex bound antigens including mutant, spliced and cancer testis antigens. The PDX was re-established in NSG MHCnull (NSG) to generate a paired patient derived xenograft (PDX) model. Whole exome sequencing and RNA sequencing (WES/RNAseq) together with nano-ultra-performance liquid chromatography coupled to high-resolution mass spectrometry were performed on the snap frozen tumours from the baseline and recurrent PDX for tumour neoantigen (TNA) discovery.

**Conclusions** We have discovered multiple tumour specific neoantigens using the comprehensive TNA discovery platforms, which will direct our TCR engineering. In parallel, we have also established an OCS PDX model suitable for cell-based therapy testing.

**EPV004/#360** INHIBITION OF CANCER CELL-DEPENDENT GLYCOLYSIS THROUGH AVB-500, A SELECTIVE INHIBITOR OF G6PC-AXL, IN COMBINATION WITH PACLITAXEL IN HIGH-GRADE ENDOMETRIAL CANCER

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*10.1136/ijgc-2021-IGCS.71