ARCHIPELAGO OF OVARIAN CANCER RESEARCH: A DUTCH NATIONWIDE, INTERDISCIPLINARY OVARIAN CANCER RESEARCH INFRASTRUCTURE

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Objectives High-impact fundamental and translational research is urgently needed to improve survival of ovarian cancer patients. Therefore, we established the Dutch nationwide Archipelago of Ovarian Cancer Research (AOCR). This multi-center, interdisciplinary infrastructure and biobank is a collaboration between all 19 Dutch hospitals in which ovarian cancer surgery takes place, and is aimed at facilitating large-scale, high-quality fundamental and translational ovarian cancer research.

Methods Adult patients with (suspected) ovarian cancer are eligible for inclusion in the AOCR. Preoperative and follow-up blood samples, ascites, biopsies, and tissue from primary and metastatic tumor sites are collected and stored in a uniform matter for future (genetic) research. One representative histological hematoxylin and eosin stained slide per participant is digitized and reassessed by a gynecological pathologist. From these 273 patients, 775 blood samples, 572 tissue samples and 162 digital slides were collected.

Conclusions The AOCR ensures a large collection of samples to be used for research. It enhances interdisciplinary and multicenter collaboration at a national, and, hopefully in the future, international level. The AOCR facilitates large-scale, high-quality fundamental and translational ovarian cancer research with the ultimate aim to improve diagnostics, treatment and survival of ovarian cancer patients.

EP310/#1033 SOLUBLE HLA-E AND TNF-αPHASE EXPRESSION ASSOCIATION IN EPITHELIAL OVARIAN CARCINOMA ASCITES

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Objectives Most patients with ovarian carcinoma are diagnosed at an advanced stage, and therapeutic options for these patients still limited. The present study aims to investigate soluble Human leukocyte antigen-E (sHLA-E) and TNF-α inflammatory cytokine expression in ascites of patients with epithelial ovarian carcinoma (EOC).

Methods Thirty ascites specimens from EOC patients were collected. We optimized a direct sandwich enzyme-linked immunosorbent assay (ELISA) method to simultaneously determine the total antibody levels of sHLA-E and TNF-α.

Results Ascites from EOC patients showed increased sHLA-E levels (Mean: 1403pg/ml) and TNF-α levels (Mean: 40,4pg/ml). Interestingly, sHLA-E was positively correlated to TNF-α expression (Spearman r = 0.27, p < 0.05). Both soluble molecules were decreased in ascites of EOC patients with high CA-125 without significance (CA-125 < 35U vs CA125 ≥ 33U): sHLA-E: 1914 pg/ml vs 1307pg/ml and TNF-a: 154.2pg/ml vs 24.85pg/ml.

Conclusions Our preliminary data demonstrated that sHLA-E and TNF-α are increased in EOC patients’ ascites but decreased in those with high CA-125 tumor marker. sHLA-E might be highly secreted to decrease local inflammation and inhibit tumor progression. Further studies could shed light on the potential immune tolerance role of HLA-E in EOC.

EP311/#1038 SECRETED HLA-G PROFILING IN EPITHELIAL OVARIAN CARCINOMA ASCITES

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Objectives Human leukocyte antigen (HLA)-G expression has been correlated with disease status and cancer patients’ outcome. In this study, we aimed to investigate the expression levels of both free soluble molecules (sHLA-G) and via extracellular vesicles as a membrane anchored molecule (HLA-G_EV) in ascites from epithelial ovarian carcinoma (EOC) patients. We also explored their correlation with CA-125 tumor marker levels and histological subtypes.

Methods sHLA-G and HLA-G_EV levels were measured using Enzyme-Linked Immunosorbent Assay (ELISA) method in 30 ascites from EOC patients.

Results Secreted HLA-G was detected in most of the ascites of EOC patients (sHLA-G 93%; HLA-G_EV 70%) with increased
levels (sHLA-G: 6.46 ng/ml and HLA-G_EV: 3.62 ng/ml). Secreted HLA-G levels were highly increased in patients with serous ovarian carcinoma versus other subtypes (sHLA-G: 6.94 ng/ml vs 4.62 ng/ml, and HLA-G_EV: 4.20 ng/ml vs 1.45 ng/ml, respectively). Interestingly, sHLA-G level was increased in EOC patients with high CA-125 tumor marker levels (CA125 >35U/ml: 7.20 ng/ml vs CA-125 <35U/ml: 3.51 ng/ml). Similarly, HLA-G_EV level was increased in EOC patients with high CA-125 tumor marker levels (CA125 >35U/ml: 4.16 ng/ml vs CA-125 <35U/ml: 1.89 ng/ml).

**Conclusions**
Our preliminary data established that both sHLA-G and HLA-G_EV may provide an interesting new opportunity as tumor markers to evaluate patients with suspected ovarian cancer. Further studies still needed to consolidate our finding and clearly establish secreted HLA-G as new biomarkers for monitoring the disease.

**EP312/#486**

**COMPARISON OF HRD STATUS BEFORE AND AFTER NEOADJUVANT CHEMOTHERAPY IN PATIENTS WITH ADVANCED EPITHELIAL OVARIAN CANCER**

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Objectives Neoadjuvant chemotherapy (NACT) has been regarded as a standard treatment for those advanced epithelial ovarian cancer patients with massively disseminated tumors. The homologous recombination deficiency (HRD) status has guiding significance for the therapeutic selection of poly(ADP-ribose) polymerase (PARP) inhibitors. However, platinum may be mutagenic as a DNA cross-linker. So, the HRD status may change. Therefore, we analyze some clinical data to detect the change in HRD status before and after platinum-based NACT.

Methods A total of 41 patients with advanced epithelial ovarian cancer for which biopsies were obtained before receiving NACT were enrolled. The BRCA mutation, HRD score, and HRD status of the paired samples of biopsy and surgery were tested by the AmoyDx® HRD-Focus panel.

**Results**
HRD status was defined as HRD positive for tumors with BRCA1/2 mutation or HRD scores ≥41. Before NACT, 10 patients were BRCA mutation-positive and 22 were HRD positive. While 9 patients were BRCA mutation-positive, 21 were HRD positive and 1 was not detected after NACT. There were 3 paired samples changed in BRCA mutation, and 2 of them were BRCA mutation-positive changed into BRCA mutation-negative. The other pair showed the opposite change. Among 10 paired samples of HRD status changed, HRD positive to negative accounts for half.

Conclusions The HRD status of advanced epithelial ovarian cancer patients may be influenced by platinum-based chemotherapy. So, it should be detected by surgical sample after NACT.

**EP313/#490**

**VALIDATION OF MUTATION ANALYSIS OF OVARIAN CANCER PREDISPOSITION GENES IN TUMOR TISSUE**

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Objectives Almost 10% of ovarian cancer (OC) patients carry a somatic pathogenic variant (PV) in one of the ovarian cancer (OC) predisposition genes (e.g. BRCA1/2) and might respond to PARP inhibition. Without somatic testing these patients are denied effective treatment.

Methods To implement tumor testing of ovarian cancer predisposition genes the 523 gene panel (TSO500, Illumina) was validated in a cohort of 48 formalin-fixed paraffin-embedded archival samples with known mutation status. Blind data analysis was performed for mutational status using Franklin Genoox software (Franklin) and an in-house built Copy Number Variation (CNV) analysis. BRCA1 MLPA analysis was performed for all mutational negative samples.

Results The validation cohort consisted of ovarian (n=40), breast (n=6) and pancreas (n=2) samples of which 44 were known to contain a germline mutation and 3 a somatic mutation.