

**Conclusion** These observations add to the collective body of evidence regarding the changing treatment landscape in aOC.

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### HOMOLOGOUS RECOMBINATION DEFICIENCY (HRD): A NEW OVARIAN CANCER BIOMARKER – VALIDATION OF DECENTRALIZED GENOMIC PROFILING, WITH A FOCUS ON GENOMIC LARGE REARRANGEMENTS (LRS)

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**Introduction/Background** The diagnostic evaluation of HRD is central to define targeted therapy strategies for patients with ovarian carcinoma, so advances in decentralized genomic profiling are mandatory to allow for broader testing. We show the feasibility of implementing HRD assays in academic setting laboratories, and evaluate prevalence of genomic large rearrangements (LRs) in real life cohorts of high-grade ovarian cancer patients.

**Methodology** We evaluated HRD in 514 ovarian carcinoma samples by a hybrid capture next-generation sequencing assay using the standardized Myriad Mychoice cdx HRD test. Each patient's HRD status was evaluated by measuring the BRCA1/2 mutational status and the Genomic Instability Score (GIS). All samples were measured twice, in the central Myriad laboratory and in an academic molecular pathology laboratory, and the concordance was analyzed. Afterwards, the cohort was extended to 1163 ovarian cancer samples to determine real world prevalence of LRs in HRR genes.

**Results** Combining GIS and BRCA-mutations, a total of 200 (38.9%) of 514 tumors were HRD-positive. High-grade serous histology ( $p < 0.000001$ ), grade 3 tumors ( $p = 0.001$ ) and patient age  $< 60$  years ( $p = 0.0003$ ) were significantly associated with a positive GIS. Concordance between both laboratories for the HRD-status was 97.1% (499/514 tumors) with a sensitivity of 94.6% and a specificity of 98.4%.

LRs were found in 88/1163 (7.5%) of ovarian cancer samples. Interestingly, RAD51B, CDK12, BRCA1, ATM and BRCA2 were found to constitute 74% of all observed LRs.

**Conclusion** The percentage of HRD-positive tumors found was similar to that observed in the PAOLA-1 trial, with a high concordance between central and local laboratories. These results support introduction of standardized HRD assay in academic molecular pathology laboratories, to allow for broad access to personalized oncology strategies for patients with ovarian cancer. Genomic LRs are observed in a small portion of ovarian cancer samples, with a skewed occurrence towards 5/15 genes.

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### RECURRENCE IN OVARIAN CANCER AFTER CYTOREDUCTIVE SURGERY ACCORDING TO THE TYPE OF CHEMOTHERAPY

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**Introduction/Background** Ovarian cancer (OC) has a low incidence, but high mortality due to a habitual diagnosis in advanced cancer stages. Regardless of the histological subtype, the main route of spread is the peritoneal cavity. Therefore, intraperitoneal chemotherapy has an important role where the advantages are still unknown. To determine whether patients treated with intraperitoneal chemotherapy have later recurrences and a different pattern of recurrence in patients with advanced ovarian cancer.

**Methodology** Retrospective cohort and observational study enrolling stage III-IV OC patients who underwent primary surgery and complete cytoreduction, with a minimum of 6 year follow up from 2011 to 2019. We examine 2 groups: Group A (n=17) receiving intraperitoneal chemotherapy and Group B (n=22) receiving standard chemotherapy.

**Results** Following the FIGO 2021 histopathologic classification, most of our ovarian cancer cases were of epithelial origin. Serous carcinoma was the most common with 88% (n=15) in group A and 72% (n=16) in group B. All patients with recurrence had moderately or poorly differentiated histological grading. Regardless of the chemotherapy, after a median follow-up of 54 month the risk of disease progression or death was 50%. In group A the progression-free survival after 12 months was 86% increasing up to 45.7% after 5 years. In group B the progression free survival after 12 months was 90% increasing up to 52.8% after 5 years. No significant progression-free survival increase was observed with either both chemotherapy regimen (log-rank p-value 0.74)

**Conclusion** Chemotherapy does not seem to have a direct impact on the recurrence time in advanced ovarian cancer patients. However, there is little evidence that needs to be confirmed with more studies.

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### DIFFERENTIAL METABOLISM OF ESTROGENS IN MODEL CELL LINES AND TISSUES OF HGSO SUBTYPES

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**Introduction/Background** Ovarian cancer is highly lethal and heterogeneous. Several hormones are involved in its etiology, including estrogens. After menopause, when ovarian cancer usually develops, estrogens are formed primarily in the local tissues from the circulating steroid precursors dehydroepiandrosterone sulfate (DHEA-S) or estrone-sulfate (E1-S). Despite the known tumor-promoting role of estrogens in ovarian cancer, the expression of E1-S or DHEA-S transporters, estrogen biosynthetic or metabolic enzymes, estrogen receptors, and the metabolism of estrogens has not yet been systematically evaluated in this disease.