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

2022-RA-1492-ESGO 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.

2022-RA-1493-ESGO 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 examinate 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.

2022-RA-1495-ESGO DIFFERENTIAL METABOLISM OF ESTROGENS IN MODEL CELL LINES AND TISSUES OF HGSOC 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.

Methodology We performed targeted transcriptomics analysis of 50 genes using qPCR and estrogen metabolism analyses using LC-MS/MS. The model systems were high-grade serous ovarian cancer (HGSOC) cell lines OVSAHO, Kuramochi, COV632, and immortalized normal ovarian epithelial HIO-80 cells. The results in cell lines were compared with public transcriptome and proteome data for the HGSOC tissues.

Results In all model systems, HGSOC cell lines and tissues, high steroid sulfatase expression, and weak/undetected aromatase (*CYP19A1*) expression supported the formation of estrogens from the E1-S precursor. In ovarian cancer cells, the metabolism of E1-S to estradiol was the highest in OVSAHO, followed by Kuramochi and COV362 cells, and decreased with increasing chemoresistance. In addition, higher *HSD17B14* and *CYP1A2* expressions were observed in highly chemoresistant COV362 cells and platinum-resistant tissues compared to HIO-80 cells and platinum-sensitive tissues. The HGSOC cell models differed in *HSD17B10, CYP1B1*, and *NQO1* expression. Proteomic data also showed different levels of HSD17B10, CYP1B1, NQO1, and SULT1E1 between the four HGSOC subtypes: differentiated, immunoreactive, proliferative, and mesenchymal.

Conclusion The results of our study suggest that in HGSOCs, the metabolism of E1-S precursor into estrogens decreases with increasing chemoresistance and that HGSOC subtypes form different levels of estrogens and their metabolites. The estrogen-biosynthesis-associated targets identified in our research present a base for further studies leading to potential personalized treatment development.

2022-RA-1505-ESGO OVARIAN CANCER RETROSPECTIVE EUROPEAN (O'CARE) OBSERVATIONAL STUDY: ANALYSIS OF FIRST-LINE (1L) OUTCOMES IN PATIENTS WITH OVARIAN CANCER (OC) STRATIFIED BY NUMBER OF RISK FACTORS FOR PROGRESSION

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Introduction/Background The O'CaRE study assessed real-world burden of disease, treatment patterns, and outcomes in patients with OC in 5 European countries (UK, France, Germany, Spain, and Italy). The analysis presented provides real-world data on the cumulative impact of risk factors (RFs) on disease progression and survival following 1L treatment.

Methodology O'CaRE was a multicentre, noninterventional retrospective medical chart review study of patients aged ≥18 years diagnosed with epithelial ovarian, fallopian tube, or primary peritoneal cancer from 1 January 2014 to 31 December 2015. Patients were classified into moderate- or high-risk categories based on number of RFs for progression (Table). High-risk patients were further grouped by total number of RFs. Patients were followed from index date (date of diagnosis) until last activity or study end (maximum follow of 4 years). Kaplan-Meier methodology was used to estimate progression-free survival (PFS) and overall survival (OS).

Results The analysis included 412 patients: 7 (1.7%) had moderate risk of progression, whereas 405 (98%) had high risk of progression (table 1). For those with high risk, 84 (20.4%), 133 (32.3%), 139 (33.7%), and 49 (11.9%) had 1, 2, 3, and 4 RFs, respectively. Median PFS was 31.3 months for patients with 0 RFs and 12.6, 7.9, 5.9, and 3.5 months for patients with 1, 2, 3, or 4 RFs, respectively. Median OS was 41.9 months for patients with 0 RFs and not reached, 25.0, 18.0, and 7.4 months for patients with 1, 2, 3, or 4 RFs, respectively.

Abstract 2022-RA-1505-ESGO Table 1 Outcomes by risk factors

Risk Factor Classifications					
Moderate risk		High risk			
Stage III disease No VRD PDS *BRCA*m		Presence of ≥1 of the following: Stage IV disease VRD IDS or other surgery *BRCA*wt or *BRCA*unk			
	Moderate risk	High risk			
	0 Risk Factors	1 Risk Factor	2 Risk Factors	3 Risk Factors	4 Risk Factors
n (%)	7 (1.7)	84 (20.4)	133 (32.3)	139 (33.7)	49 (11.9)
mPFS (95% CI), months	31.3 (14.2–NR)	12.6 (10.8–19.6)	7.9 (6.3–11.1)	5.9 (4.5–8.2)	3.5 (1.9–5.0)
mOS (95% CI), months	41.9 (41.9–NR)	NR (34.4–NR)	25.0 (21.1–30.2)	18.0 (13.7–24.2)	7.4 (5.1–19.4)

*BRCA*m, *BRCA* mutant; *BRCA*unk, *BRCA* unknown; *BRCA*wt, *BRCA* wild-type; IDS, interval debulking surgery; mOS, median overall survival; mPFS, median progression-free survival; NR, not reached; PDS, primary debulking surgery; VRD, visible residual disease.

Conclusion This real-world analysis of patients with OC from 5 European countries demonstrated that higher numbers of RFs were associated with shorter median PFS and OS. This analysis provides real-world data relating to 1L treatment outcomes for patients with OC; if validated in clinical trials, the number of RFs could be a stratification factor for future 1L OC trials.

2022-RA-1515-ESGO IMPACT OF SURGICAL STAGING ON SURVIVAL OF LOW GRADE ENDOMETRIOID OVARIAN CANCER APPARENTLY CONFINED TO THE OVARY

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