predicted PD prior to imaging by an average of ~2.5 months (lead-time) and was significantly associated with worse progression-free survival (PFS) compared to patients with decreased ctDNA (HR = 0.14, 95% CI: 0.03–0.60; p < 0.01). TMB and MSI status (binary) were not predictive of response in univariate (p = 0.4, p = 0.4) analyses.

Conclusion ctDNA dynamics can accurately predict clinical benefit and allow for early prediction of PD in patients with advanced ovarian cancer receiving immunotherapy. Further study is warranted to evaluate the clinical utility of a personalized, tumor-informed ctDNA assay in patients with gynecologic malignancies undergoing systemic therapies.

**2022-RA-1007-ESGO**

**HIGH EXPRESSION OF FAP+ CANCER-ASSOCIATED FIBROBLASTS PREDICT POOR OUTCOME IN PATIENTS WITH HIGH-GRADE SEROUS OVARIAN CANCER WITH HIGH CD8-POSITIVE T-CELL INFILTRATION**

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**Introduction/Background** Tumor biology studies have implied that fibroblasts act as negative regulators of immune cell function in cancer. We investigated the impact of FAP-positive cells in high-grade serous ovarian cancer (HGSC) in relation to CD8 expression.

**Methodology** A discovery cohort (N = 113) of HGSC was subjected to immunohistochemistry (IHC) of FAP and CD8. Marker status was correlated with overall survival (OS) and progression-free survival (PFS). Findings were confirmed in a validation cohort (N = 121) and in public available datasets (TCGA and GSE8991).

**Results** We confirmed previous findings that high density of CD8+ cells in HGSC is associated with longer OS compared to low intensity of FAP (p = 0.007). In contrast, high intensity of FAP was associated with shorter OS compared to low intensity of FAP (p = 0.008). In the discovery cohort high intensity of FAP was associated with shorter median PFS in cases with high density of stromal CD8+ cells (11.4 versus 18.6 months) compared to low intensity of FAP (p = 0.007). In contrast, high intensity of FAP was not associated with PFS in cases with low density of CD8+ cells. In the validation cohort, high intensity of FAP in the patients with high density of stromal CD8+ cells was associated with shorter OS compared to low intensity of FAP (p = 0.01). This association was not seen in the cases with low density of CD8+ cells. The association between high FAP expression and poor outcome in the high density CD8+ group was confirmed in two independent gene-expression data sets, with a shorter PFS in the TCGA dataset and shorter PFS and OS in the GSE8981 dataset.

**Conclusion** The study shows a specific FAP positive fibroblast-subset of cases with poor prognosis restricted to a CD8 high density group of HGSC. Therapy targeting the immunosuppressive action of fibroblasts may be a tool to enhance the known positive prognostic effect of CD8-cells in ovarian cancer and may be explored in T-cell depended immune therapy.

**2022-RA-1093-ESGO**

**VALIDATION OF SELF-SAMPLING USE FOR A MULTIPLEXED BIOMARKER ASSAY FOR HPV AND DYSPLASIA DETECTION**

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**Introduction/Background** The use of self-sampling in cervical cancer (CxCa) screening increases the number of participants and enables the inclusion of prior underscreened women in rural areas. For PCR and DNA-based testing self-sampling is as sensitive as physician-sampling. We compared self- and physician-sampling for analysis by QuantiGene-Molecular-Profiling-Histology assay (QG-MPH) to detect and grade cervical dysplasia in a triage setting.

**Methodology** Women with an equivocal screening result were recruited and a cervical sample (Cervex broom) was taken into ThinPrep/PreservCyt. Participants were asked to take a self-sample (Evalyn-Brush) and fill a questionnaire. Crude lysates were used for the QG-MPH assay. This multiplexed Luminex bead-based technology platform (QuantiGene 2.0) detects and quantifies the mRNA abundance of 18 Human Papillomavirus (HPV) genotype-specific oncogenes, reference genes and cellular biomarkers characterizing dysplasia stages, simultaneously. Formerly developed biomarker-based risk scores predict CIN2+, CIN3+ or CxC.

**Results** Of 699 study participants, 601 performed self-sampling (85.9%). Invalid samples in QG-MPH was comparable between self- and physician-sampling with 16.1% and 14.9%, respectively. Of 132 histologically confirmed CIN3 lesions QG-MPH determined in the physician-taking sample 61.4% (n = 81) as CIN3 or higher, 25.8% (n = 34) as low-grade lesions, and 12.9% (n = 17) were not evaluable. Of 109 self-samplers from CIN3 positive women QG-MPH determined 17.4% (n = 19) as CIN3 or higher, 59.6% (n = 65) as low-grade and 22.9% (n = 25) were not evaluable. PCR-based HPV testing detected 78.2% of physician- and 74.9% of self-samples positive while QG-MPH 52.5% (n = 315) and 32.3% (n = 194), respectively. Concordance was 82.0% by PCR and 63.8% by QG-MPH.

**Conclusion** While cellularity of self-taken samples is sufficient for valid measurement by QG-MPH, less high-grade lesions and HPV-infections are detected. Optimization of cutoffs for the self-taken sample may improve the sensitivity. We hypothesize that ‘missed’ CIN3 by QG-MPH biomarker profiling may be non-progressor lesions. This will be investigated further.

**2022-RA-1126-ESGO**

**MESENCHYMAL PROGNOSTIC SIGNATURE IN OVARIAN CANCER**

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**Introduction/Background** The study shows a specific FAP positive fibroblast-subset of cases with poor prognosis restricted to a CD8 high density group of HGSC. Therapy targeting the immunosuppressive action of fibroblasts may be a tool to enhance the known positive prognostic effect of CD8-cells in ovarian cancer and may be explored in T-cell depended immune therapy.

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**Conclusion** While cellularity of self-taken samples is sufficient for valid measurement by QG-MPH, less high-grade lesions and HPV-infections are detected. Optimization of cutoffs for the self-taken sample may improve the sensitivity. We hypothesize that ‘missed’ CIN3 by QG-MPH biomarker profiling may be non-progressor lesions. This will be investigated further.
Abstracts

Introduction/Background In our previous microarray study we identified the 96-gene signature related to differential survival of patients with high-grade serous ovarian cancer (OC). Top differentially expressed genes were e.g. POSTN, COL11A1, SFRP2, MFAP5, ITGBL1, LOX. Similar mesenchymal signature has been observed also by others, but it has been ascribed to cancer associated fibroblasts, not epithelial cells. However, we postulate that these genes can be also expressed by cancer cells themselves.

Methodology For survival analysis we used Kaplan-Meier Plotter and Microarray Gene Expression Database of OC Subtype (CSIOVDB). Proteins expression was assessed by Heterogeneity_Analysis_Portal (lmdomics.org) [2]. Interaction networks were judged by STRING. Molecular cloning was performed using retroviral gene transfer; in vitro functional tests were done according to standard procedures; gene expression analyzed by PCR.

Results STRING algorithm applied to our prognostic signature showed interactions typical for proteins engaged in the function and structure of extracellular matrix. Our own qRT-PCR analysis, as well as Kaplan-Meier Plotter and CSIOVDB analysis confirmed that mRNA level of majority of genes from our negative prognostic signature is significantly related to survival of OC patients. Using Heterogeneity_Analysis_Portal we analyzed 24 out of these genes and found that they are strongly expressed by tumor stromal cells, while weakly by epithelial cells. We analyzed ten of these genes in several OC cell lines by semi-quantitative RT-PCR, and we found that they are expressed by epithelial cells as well. By functional in vitro assays we observed that overexpression of these genes (ITGBL1, MFAP5, SFRP2) may affect OC cells phenotype (migration, invasiveness, proliferation, chemosensitivity).

Conclusion Mesenchymal signature with negative prognostic significance in OC is expressed mostly by stromal, but also by epithelial cells, and may affect phenotype of the latter. Exact role of these genes in OC cells remains to be assessed.

Reference

2022-RA-1130-ESGO
EFFECT OF IMIQIUMOD TREATMENT ON HLA-G EXPRESSION IN HIGH-GRADE CERVICAL LESIONS

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Introduction/Background We showed that the topical application of the 5% imiquimod in treating cervical high-grade squamous intraepithelial lesions (HSIL) leads to a regression of about 50% of the lesions after 16 weeks of treatment (1). Tissue culture studies have attributed imiquimod’s antiviral and antitumor activity to the enhancement of the innate immune response. Knowing that the increase in soluble HLA-G (sHLA-G) expression is associated with disease progression and that the HLA-G molecule has an inhibitory effect on different immune cells, we further investigated whether imiquimod modulates the sHLA-G expression in the cervical lesions.

Methodology Cervical biopsies of 52 patients aged 18-40 with histological HSIL (CIN2p16+ and CIN3), who self-applied 250mg cream containing 5% of imiquimod three times a week for 16 weeks, were collected at admission and after completion of the treatment. Treatment success was defined as the absence of HSIL after treatment. For immunohistochemistry, we used the monoclonal anti-HLA-G antibody (Exbio, 5A6G7) (figure 1). The intensity of pixels obtained from the images of the slides, using the program Gimp 2.10.18, defined the protein levels (figure 2). We used the T-test to compare two groups, the ROC curve to define the cut-off point for risk-predicting sHLA-G expression, and the Fisher’s exact test to calculate the risk.

Results High tissue sHLA-G levels before treatment were associated with unsuccessful imiquimod treatment (p=0.0025). Imiquimod down-modulated sHLA-G in the lesion of those successfully treated (p=0.0467) or not (p<0.0001). According to the area under the curve of 0.72, 95%CI 0.61-0.84, p=0.0012, sHLA-G expression over 870847 pixels represented a 4-fold risk for unsuccessful imiquimod treatment (p=0.0088).

Abstract 2022-RA-1130-ESGO Figure 1 and 2

Conclusion We showed that imiquimod modulates HLA-G in cervical lesions and that treatment success depends on sHLA-G levels at admission.

2022-RA-1136-ESGO
A SINGLE-CELL MAP OF RARE OVARIAN CANCER

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10.1136/ijgc-2022-ESGO.884

Introduction/Background Non-epithelial ovarian tumours encompass a heterogeneous group of neoplasms that mainly include germ cell tumours (GCT) and sex-cord stromal tumours (SCST). These tumours are characterised by an extensive inter- and intratumoral heterogeneity. By applying single-cell RNA sequencing (scRNA-seq), we attempt to elucidate the complexity of the tumour microenvironment.

Methodology We performed scRNA-seq of 66 919 cells collected from 12 patients. Most fresh tissue samples were derived from SCST (n=9), including 7 adult granulosa cell