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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**Results** We confirmed previous findings that high density of CD8+ cells in HGSC is associated with longer OS compared to CD8- cells. In HGSC, high intensity of FAP in the patients with high density of stromal CD8+ cells was not associated with PFS in cases with low density of CD8+ cells. In the validation cohort, high intensity of FAP in CD8+ cells (11.4 versus 18.6 months) compared to low intensity of FAP (p=0.007). In contrast, high intensity of FAP (lead-time) was significantly associated with worse progression-free survival (PFS).

**Conclusion** 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, ITGB1, MFAP5, 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 (ITGB1, 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 IMIQIMOD 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 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 250 mg 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, S6G7) (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).

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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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 1 adult granulosa cell...