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-POSTIVE 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 GSE9891).

Results We confirmed previous findings that high density of CD8+ cells in HGSC is associated with longer OS compared to low density (HR 0.55; 95% CI 0.33–0.85; 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 GSE9891 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 CxCa.

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-taken 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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