**Abstracts**

**1032 STRONG ASSOCIATION BETWEEN PATHOLOGICAL RESPONSE TO NEOADJUVANT CHEMOTHERAPY, TILS AND MODELED CA125 KELIM IN OVARIAN CARCINOMAS: CHIVA TRIAL, GINECO**

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Conclusion** High consistency was found between the modeled CA125 KELIM calculated during the first 100 days of neo-adjuvant chemotherapy and the pathological response, consistent with their values as indicators of the tumor chemosensitivity in first-line setting. Moreover, TILs changes were strongly associated with chemosensitivity, opening hypotheses about the mechanisms of chemosensitivity, and immunotherapy opportunity.

**1057 DEVELOPMENT AND VALIDATION OF A MACHINE-LEARNING-DERIVED RNASEQ PROGNOSTIC SIGNATURE IN ENDOMETRIAL CANCER**

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Introduction/Background** Because of inter-tumor heterogeneity of endometrial carcinoma (EC), prognostication remains challenging. We aimed to develop a RNAseq signature to stratify EC patient prognosis beyond molecular subtyping.

Methodology** A prognostic signature was identified using a LASSO-penalized Cox regression model on TCGA (N=543 patients). A polyA-RNAseq-based method was developed for validation of the signature in a cohort of stage I-IV EC patients treated in two Paris Hospitals between 2010 and 2017. Model performances were evaluated using time-dependent ROC curves (prediction of disease-specific-survival (DSS)). The additional value of the RNAseq signature was evaluated using uni/multivariable Cox models (hazard ratio (HR) with [95% confidence interval]) and Kaplan-Meier analysis.

Result(s)** Among 209 patients included in the randomized phase II trial CHIVA (NCT01583322, neo-adjuvant carboplatin-paclitaxel +/- nintedanib, +/- IDS, n=188 patients). The 30 patients with the highest KELIM (very chemosensitive) or the lowest KELIM (poorly chemosensitive) were selected. HE-stained sections from available tissue blocks at baseline and after chemotherapy were analyzed for stromal TILs (sTILs, surface of the tumor stroma occupied by lymphocytes) and intra-epithelial TILs (iTILs, brisk or non-brisk). The pathological response (pR) was assessed on the most tumoral available tissue block obtained after chemotherapy (good response if extensive fibrous changes with no or isolated tumor cells, or <2 mm cell clusters). Descriptive statistics assessed the relationships between KELIM, TIL changes, and pR.

Result(s)** No relationships between KELIM and iTILs infiltrates on baseline tumor samples were found. However, strong associations were found between KELIM and iTILs infiltrates after neo-adjuvant chemotherapy for sTILs (median KELIM for sTILs 0-5% vs >5%: 0.28 versus 1.32, P < 0.001) and for iTILs (median KELIM for iTILs non-brisk versus brisk: 0.31 versus 1.31, P = 0.04). Similarly, an association was found between KELIM and the quality of pR (median KELIM for patients with poor vs good pR: 0.31 versus 1.32, P = 0.05).
CLINICAL IMPACT OF MESOTHELIN EXPRESSION IN OVARIAN CANCER: A TISSUE MICROARRAY STUDY ON 113 PATIENTS

Introduction/Background

Mesothelin (MSLN) is a CA125 binding protein that mediates cell adhesion. This interaction was suggested to play a role in the peritoneal metastasis development. In preclinical models, MSLN overexpression activates the PI3K/Akt, NFκB, and MAPK/ERK pathways, to promote cell proliferation, migration and metastasis. For these reasons, MSLN represents an attractive molecule for targeted ovarian cancer (OC) therapies.

Methodology

Paraffin-embedded tumor tissue samples from 113 primary OC patients were selected from TOC biobank (www.toc-network.de) and assessed for the immunohistochemical expression of MSLN on Tissue Microarray. For 51 included HGSOC patients, also paired recurrent samples were available and selected for MSLN evaluation.

All patients were treated at Charité Medical University Berlin, Germany, through primary cytoreduction followed by platinum-based chemotherapy. MSLN expression profiles were correlated with patients’ clinic-pathological and survival data. MSLN expression was also compared between paired primary and recurrent HGSOC samples.

Results

164 samples were assessed for MSLN expression (113 primary OC and 51 recurrent OC).

Among the primary OC cohort, results showed that MSLN (+) samples were 85% of cases (96/113), whereas MSLN was negative in the remaining 15% of cases (17/113). MSLN expression did not differ among different OC histological subtypes (serous, clear cells and endometrioid), but MSLN(+) samples were diagnosed more frequent in the group of advanced FIGO stage (65/96 vs 31/96, p=0.022) and in platinum sensitive patients (85/96 vs 11/96, p=0.001).

Survival analysis showed that MSLN(+) was associated with a significant survival advantage at 5yOS (p=0.022) in HGSOC patients. No survival impact (5yPFS and/or 5yOS) of MSLN expression could be detected for other OC histologies.

Pairwise analysis on paired primary and recurrent HGSOC, also revealed that MSLN(+) tumors were more frequent among primary rather than recurrent HGSOC (46/51 vs 38/51, p=0.012); Furthermore, Spearman test showed a significant correlation among primary and recurrent samples in terms of MSLN expression decrease at recurrence (p=0.003).

Conclusion

Overexpression of MSLN was observed in FIGO advanced stage and in platinum sensitive primary OC patients. MSLN expression was equally distributed among different OC histologies, but in HGSOC conferred survival advantage. Moreover, its expression significantly decreased from primary to recurrent OC.


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CONTRIBUTION OF NETOSIS IN ADVANCED STAGES OF HIGH-GRAD SEROUS OVARIAN CANCER: DIAGNOSTIC IMPLICATIONS

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Introduction/Background

NETosis has recently been described as a new form of neutrophils’ immune response, by which they release extracellular networks (NETs) of DNA, histones and proteins. In the tumor environment, NETs participate in immunothrombosis, tumor progression, metastasis, and evasion of the immune system. Recent studies show that NETosis is involved in the initial metastasis of high-grade serous ovarian cancer (HGSOC), although its contribution in advanced stages or as a diagnostic biomarker is unknown, which is the objective of this study.

Methodology

We analyzed paired plasma and ascites fluid samples from women with HGSOC (n=28) and controls (n=16). As NETosis markers, we quantified cell-free circulating DNA (cfDNA, Quant-iT PicoGreen dsDNA kit), nucleosomes (Cell Death Detection ELISA PLUS kit), calprotectin (Human Calprotectin ELISA kit) and myeloperoxidase (MPO) (Human MPO ELISA kit) and we evaluated their differences with the SPSS program (v.21).

Results

Patients with HGSOC presented a higher concentration of cfDNA in plasma (median 1785.9 ng/mL; Q1-Q3, 5021.7-1610.9) vs controls (2128.9; 1477.8-2814.5), p<0.001. In addition, we observed an increase in the 4 NETosis markers evaluated in patients’ ascites: cfDNA [(2128.9; 1477.8-2814.5) vs (1148.1; 990.8-1235.3), p<0.001], nucleosomes [(2,58 AU; 1,27-3,16) vs (0,09; 0,003-0,55), p<0.001], calprotectin [(2606.8 ng/mL; 1028,3-5021.7) vs (353,5; 195,5-722,3), p<0.001] and MPO [(73,3 ng/mL; 48,8-141,4) vs (25,3; 22,6-29,4), p<0.001] (figure 1).

The levels of the 4 markers were positively correlated with each other in both biofluids (p<0.032) and with the levels of neutrophils in plasma (p<0.001). We also observed that cfDNA in plasma was able to distinguish patients from controls (AUC=0.842). Furthermore, the levels of cfDNA,