

guidelines: non-endometrioid histology or stage III-IVA or TP53-mutated tumors), TP53-mutated molecular group was not significantly associated with poor prognosis ($p=0.18$). A The composite classifier identified three classes within this subgroup: RNAseq-good prognosis ($N=24$), non-TP53/RNAseq-poor prognosis ($N=16$), and TP53-mutated tumors ($N=41$), with 5-years DSS rates of 100%, 59%, and 71%, respectively ($p=0.015$). Transcriptome analyses suggested the underlying involvement of immune deprivation and wound healing processes in tumors with poor prognosis.

Conclusion* We demonstrate that RNAseq characterization can refine prognostication in EC beyond molecular subgroups and main prognostic features, and warrants validation for potential RNAseq-based adjuvant therapeutic strategies in EC.

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CLINICAL IMPACT OF MESOTHELIN EXPRESSION IN OVARIAN CANCER: A TISSUE MICROARRAY STUDY ON 113 PATIENTS

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10.1136/ijgc-2021-ESGO.603

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.

Result(s)* 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-GRADE SEROUS OVARIAN CANCER: DIAGNOSTIC IMPLICATIONS

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10.1136/ijgc-2021-ESGO.604

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).

Result(s)* Patients with HGSOc presented a higher concentration of cfDNA in plasma (median 1785,9 ng/mL; Q1-Q3, 1618,5-2181,6) compared to the controls (1526,7; 1452,0-1610,9) ($p<0,001$). 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,