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.

Introduction/Background* As stated by ESGO-ESMO, there is a need for indicators of chemotherapy efficacy in ovarian carcinoma patients treated in first-line setting (Colombo et al, IGCS, 2020). The pathological chemotherapy response score (CRS) and the modeled CA-125 KELIM during neo-adjuvant chemotherapy were reported as potential markers. Moreover, changes in tumor infiltrating lymphocytes (TILs) after neo-adjuvant chemotherapy were reported as a prognostic factor (Leary et al, Cancer Immunol Immunother, 2021). We studied the relationships between changes in TILs, the pathological response (pR) and KELIM in patients treated with neo-adjuvant chemotherapy +/- interval debulking surgery (IDS) from CHIVA phase II trial.

Methodology The patients were enrolled in the randomized phase II trial CHIVA (NCT01583322, neo-adjuvant carboplatin-paclitaxel +/- nintedanib, +/- IDS, n=188 patients). KELIM were previously calculated (You et al CCR 2020). 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 >10% at least 2 mm epithelial surface with at least 1 lymphocytes/mm², poor response if no lymphocytes/mm²). Descriptive statistics assessed the relationships between KELIM, TIL changes, and pR.

Results* No relationship between KELIM and TILs infiltrates on baseline tumor samples were found. However, strong associations were found between KELIM and TIL 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).
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 TOB biobank (www.toc-network.de) and assessed for the immunohistochemical expression of MSLN on Tissue Microarray. For 51 paired primary and recurrent samples were included HGSOC patients, also paired recurrent samples were included. 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.

1075 CONTRIBUTION OF NETOSIS IN ADVANCED STAGES OF HIGH-GRADE SEROUS OVARIAN CANCER: DIAGNOSTIC IMPLICATIONS


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; 990.8-1233.5), 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 [(77.3 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,