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

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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 (ieTILs, 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 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 ieTILs (median KELIM for ieTILs 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).

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 validation cohort (median follow-up 55 months IQR [41-69]), 61 (30%), 10 (5%), 52 (25%), and 82 (40%), had mismatch repair-deficient, POLE-mutated, TP53-mutated tumors, and tumors with no specific molecular profile, respectively. The 38-genes signature accurately predicted DSS (AUC=80%). Using a composite classifier accounting for the RNAseq signature and the TP53-mutated group, three groups were identified: good prognosis tumors based on RNAseq signature and without TP53 mutation, characterized by excellent outcome (N=103 patients, 5-years DSS rates of 99%) (reference), poor prognosis tumors based on RNAseq signature and without TP53 mutation (N=49 patients, 5-years DSS rates of 81%; HR: 5.86 [1.16; 29.7]), and TP53-mutated tumors whatever the RNAseq signature (N=52 patients, 5-years DSS rates of 52%; HR: 11.14 [2.40; 51.7]) (HR adjusted on FIGO stage). In 81 (38%) patients with adverse features (2020 ESGO/ESTRO/ESP