FOXL2 MUTATION DETECTION IN CIRCULATING TUMOR DNA OF ADULT GRANULOSA CELL TUMORS AS A POTENTIAL BIOMARKER FOR DISEASE MONITORING FROM THE RANDOMIZED ALIENOR TRIAL, A GINECO STUDY

Introduction/Background Adult granulosa cell tumors (aGCT) are rare ovarian malignant tumors harboring specific FOXL2 402C>G (C134W) mutation (96%) with multip le relapses. Serum markers are inaccurate in reflecting tumor burden, supporting the identification of new biomarkers.

Methodology Plasma samples were obtained at baseline and every 2–4 weeks for 6 months after C1D1 from patients enrolled in the ALIENOR trial (NCT01770301; 60 patients with relapsed sex cord-stromal tumors treated with chemotherapy +/- bevacizumab (Ray-Coquard, JAMA Oncol 2021)). Digital droplet PCR on circulating cell-free DNA was performed in 137 samples from 23 patients with FOXL2-mutated aGCT to investigate the clinical value of FOXL2 mutation on circulating tumor DNA (FOXL2mut ctDNA) for monitoring disease.

Results FOXL2mut ctDNA was detected in 10 of 23 aGCT patients’ plasma (43%). The sum of the largest diameter of target lesions was 52 mm for FOXL2mut ctDNA negative and 138 mm for positive samples. No clinical factors such as age, number of relapse, metastatic sites, chemotherapy lines or surgeries were correlated to FOXL2mut ctDNA levels. Looking at individual monitoring data, a trend between clinical progression and increased FOXL2mut ctDNA levels under therapy was noted. Among 19 patients with samples at baseline and for whom subsequent blood samples were also available at progression or end of study, sensibility, specificity, positive and negative predictive values of FOXL2mut ctDNA were 70%, 89%, 87% and 72% respectively. Only one of 4 patients without FOXL2mut ctDNA at baseline turned positive at progression. With a median follow-up of 42.6 months IC95%[36.8;48.8], 4 patients died (all in the FOXL2mut ctDNA group) (figure 1).

Conclusion In this small series of aGCT, monitoring FOXL2-mut ctDNA seems relevant to predict RECIST or clinical progression in relapse setting. All cancer deaths were in the FOXL2mut ctDNA group. Future studies are warranted to confirm if this biomarker can avoid repetitive CTscan for surveillance.

Abstract 2022-RA-830-ESGO Figure 1

2022-RA-830-ESGO EXPRESSION OF COL5A2 IN OVARIAN TUMOR MICROENVIRONMENT AND ITS MECHANISM OF PROMOTING OVARIAN CANCER

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Introduction/Background Recent studies have shown that the research of tumor cells alone cannot explain many phenomena in tumors, so the concept of tumor microenvironment has attracted more and more attention in tumor research. Studies have found that tumor cells need to interact with other cells, especially cancer associated fibroblasts (CAFs) to promote tumor progression. COL5A2 belongs to collagen family and is an important part of extracellular matrix in tumor microenvironment. Therefore, taking COL5A2 as the core to clarify the specific mechanism of the interaction between ovarian cancer cells and CAFs in the ovarian tumor microenvironment can provide a theoretical basis for the development of new treatment strategies for ovarian cancer.

Methodology We analyzed the expression of COL5A2 in 65 cases of ovarian cancer tissue specimens and explored the mechanism of altered COL5A2 expression in ovarian tumor microenvironment. Then we explored the underlying mechanisms of the effect of COL5A2 on cell proliferation, migration and invasion of ovarian cancer in vitro and in vivo.

Results (1) Compared with normal ovarian tissues, COL5A2 is highly expressed in ovarian cancer tissues, and when COL5A2 is highly expressed, the prognosis of ovarian cancer is worse.(2) COL5A2 mainly comes from CAFs.(3) The exosomes carrying ITGB1 secreted by ovarian cancer cells can activate the function of CAFs and promote the expression