CAN CHEMOTHERAPY CHANGE TUMOR BRCA STATUS AND AFFECT SUSCEPTIBILITY TO TREATMENT?

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Introduction Ovarian cancer (OC) development in BRCA-heterozygotes is due to somatic inactivation of the remaining BRCA-allele. For patients with a long history of systemic treatment, secondary tumor mutations are described in the literature, leading to a possible change in the response to the therapy. The objective of our study was to assess whether short-time chemotherapy can cause BRCA-molecular changes in the tumor.

Material Retrospective single-institutional study on HGSOC patients who had at least double tumor BRCA assessment during chemotherapy.

Results A total of 19 paired-tumor-BRCA (p-BRCA) were identified between January-2017 and December-2018 among HGSOC patients treated at primary diagnosis or recurrence.

Primary tumor BRCA assessment showed somatic wild-type variant (s-WT) in 14/19 (73.7%), pathogenic-variant (PVs) in 4/19 (21.0%) and variant of uncertain-significance (s-VUS) in 1/19 (5.3%). Twelve patients (63.2%) received second tumor BRCA assessment at time of interval-debulking surgery (IDS) (Group A) and 7 patients (36.8%) at time of secondary cytoreductive surgery (Group B). Treatment consisted of standard carboplatin and taxol. Six (31.6%) cases received additional Bevacizumab or PARP-i. The median number of cycles was 3 (range: 3–4) for Group A and 6 (5–7) for Group B.

No reversal of tumor BRCA status was observed between two consecutive samplings.

Conclusion In a small cohort of HGSOC patients there is no plasticity of somatic BRCA-status after few cycles of standard chemotherapy. These results need to be confirmed in a larger sample-size and compared with those obtained after long biological treatments.