Methods This retrospective cohort study included patients treated for ovarian, tubal and primary peritoneal cancer in Wolfson Medical Center during the years 2000–2015. We classified three groups according to the site of recurrence: intraperitoneal only, retroperitoneal lymph nodes only, and both. Response to treatment was assessed by the RECIST criteria. Progression free survival (PFS), post-recurrence survival (PRS) and overall survival (OS) were estimated with the Kaplan-Meier method and compared with Log-rank test. The association between clinical variables and survival was established by Cox proportional hazards model.

Results Out of 135 patients in our cohort, 66 were diagnosed with intraperitoneal recurrence, 30 with retroperitoneal lymph node recurrence and 39 with combined recurrence. The clinical, pathological and surgical characteristics were similar among all groups, besides CA-125, which was significantly lower in the retroperitoneal recurrence group at diagnosis, end of treatment and recurrence. The median follow up period was 45.8 months. OS and PRS were significantly higher in the intraperitoneal and combined recurrence groups. (OS = 93.07 vs. 47.9 and 41.7 months, respectively, p=0.000, PRS = 68.57 vs. 29.67 and 19.7 months, respectively, p=0.000). In multivariate analysis, retroperitoneal recurrence was found to be an independent prognostic factor for survival.

Conclusions The site of recurrence has significant prognostic value regarding PRS and OS. Patients with retroperitoneal lymph node recurrence only, have a favorable prognosis with estimated survival longer than 5 years.

Abstracts

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Chemotherapy Reduces PAR Glycohydrolase (PARG) Expression in High-Grade Serous Ovarian Cancer Patients

Keywords: chemotherapy, PARG, ovarian cancer

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Objective: To evaluate the effect of chemotherapy treatment on PAR glycohydrolase (PARG), other member of poly (ADP-ribose) metabolism, in high-grade serous ovarian cancer patients (HGSOC).

Methods: Two HGSOC cohorts were evaluated by immunohistochemistry: 54 chemo-naïve HGSOC patients (45 HGSOC, 9 borderline, 4 normal tissue) and 53 HGSOC chemo-treated patients (44 HGSOC, 9 borderline, 7 normal tissue). In addition, we used in silico analysis to evaluate the effect of PARG mRNA expression in ovarian cancer and its relation with patient outcome.

Results: Our results showed that chemo-naïve patients have significant higher levels of PARG expression compared to borderline and normal (62.25%, 44.4% and 0% respectively). Interestingly, these levels were reduced in HGSOC patient samples that have received chemotherapy (45.44%, 44%, 0%, respectively, p<0.03). Indeed, this demonstrated that chemotherapy induces a reduction in PARG expression to levels equal to the borderline tumors. Furthermore, we found a dramatic re-localization of PARG protein to the cytoplasm in chemo-treated patients (100%) compared with chemo-naïve HGSOC samples that were localized in the nucleus (80%, P<0.05). In silico analysis of 1500 ovarian cancer patients revealed that PARG is up-regulated in ovarian cancer in comparison with normal tissue and highly expressed in advanced metastatic HGSOC. Moreover, its expression in advance disease was associated with shorter overall survival.

Conclusions: Our results showed that chemotherapy decreased PARG expression and re-localized it into the cytoplasm. Moreover, our findings highlights the possible use of PARG inhibitors as an adjuvant therapy to treat recurrent ovarian cancer together with chemotherapy and other new-targeted drugs such as PARP inhibitors.