8035 POSTER

The Combination of Weekly Carboplatin and Paclitaxel is Active and Tolerated for the Treatment of Advanced Ovarian Cancer in Elderly Patients

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Background: Platinum/taxane doublets have long been considered the standard treatment regimen for advanced-stage ovarian cancer. Common side effects seen with the use of these drugs include gastrointestinal symptoms, myelosuppression and neurological toxicity. The purpose of this study was to evaluate the feasibility, effectiveness, toxicity and quality of life of a weekly schedule, containing carboplatin and taxanes in elderly patients.
Methods: From January 2009 to December 2010 24 patients (pts) with advanced ovarian cancer were included in the study. Median age was 74 years, and PS was 1, 2 and 3 in 15, 6 and 3 patients respectively. The pts received carboplatin AUC 2 (days 1, 8, 15), and paclitaxel 80 mg/m^2 (days 1, 8, 15) of a 28-day cycle. Primary endpoints were response rate, progression-free survival and overall survival. The results were retrospectively analyzed according to feasibility, toxicity (National Cancer Institute Common Toxicity Criteria) and quality of life (QoL).
Results: All patients were evaluable for the primary endpoint. The overall response rate was 80% (14 complete responses, 5 partial responses); the median survival has not yet been reached after a median follow-up of 24 months. Toxicity was: neutropenia grade 2/3 (33.3%); nausea grade 2 (40%); grade 1 vomiting (5%). No patient reported a worsening of QoL to report the side effects of treatment.
Conclusions: A weekly carboplatin and paclitaxel regimen is highly active for women with advanced-stage ovarian cancer. The regimen is well tolerated in elderly patients.

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The Value of the Risk of Ovarian Malignancy Algorithm (ROMA) as a Predictor of Platinum Resistance and Survival for Ovarian Cancer Patients

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Background: A Risk of Ovarian Malignancy Algorithm (ROMA) based on Human Epididymis Protein 4 (HE4) and CA125 has been developed and reported to categorize women with a pelvis mass into high or low risk of ovarian malignancy. Originally, the ROMA score was developed for diagnostic purposes but the clinical application for HE4 for other purposes such as a predictor of platinum resistance has not been investigated. The objective of the present study was to change the diagnostic ROMA score and develop a new prechemotherapy "ROMA" score. This new Risk of Platinum resistance Algorithm (ROPA score) score was developed for prediction of platinum resistance and prognosis.
Material and Methods: Serum from 170 patients with newly diagnosed ovarian cancer was analyzed for CA125 and HE4 using ELISA assays. The new ROPA score at baseline (just before initiation of chemotherapy) was developed incorporating HE4 and CA125 into an algorithm resembling the algorithm used for the diagnostic ROMA score. Samples were collected just prior to first line chemotherapy and all patients were treated with carboplatin/paclitaxel combination chemotherapy. All patients signed informed consent and permission was obtained from the relevant regulatory authorities.
Results: The ROPA score before initiation of chemotherapy was to some extent able to predict platinum resistance depending on the cut off level for specificity and sensitivity. At specificity level of 75% the sensitivity for platinum resistance was 60% for the ROPA score at baseline before chemotherapy. Increasing ROPA score was in multivariate survival analysis (adjusted for age, FIGO stage, histology, histological grade and residual tumour) negatively associated with progression-free survival (HR = 4.7, 1.3–17.1, 95% CI, p = 0.020) and overall survival (HR = 6.3, 1.3–31.6, 95% CI, p = 0.025).
Conclusions: Increasing ROPA score calculated from a serum sample just before initiation of chemotherapy seems associated with platinum resistance and decreased progression-free and overall survival.

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Linking XRCC1 Arg399Gln and GGH −401C>T Polymorphisms to Cervical Cancer Risk

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Introduction: Cervical cancer is still a key health issue worldwide. *X-ray Repair Complementing Defective Repair in Chinese Hamster Cells 1* (*XRCC1)* codifies a scaffold protein in Base Excision Repair pathway, through which it regulates other DNA repair enzymes. *Gamma Glutamyl Hydrolase* (*GGH)* regulates folate intracellular reserves. It is an important regulatory enzyme since folate has been involved in epithelial carcinogenesis.
Objective: With this study, we intended to explore what is the influence of *XRCC1* Arg399Gln and *GGH* −401C>T genotypes in conditioning cervical cancer risk.
Methods: DNA samples were extracted from peripheral blood cells of 581 patients with cervical disease and 334 healthy controls. The XRCC1 and GGH polymorphisms were evaluated through Real-Time PCR. The odds ratio (OR) and its 95% confidence interval (CI) were calculated as a measure of the association between genotypes and cervical cancer risk.
Results: Concerning *GGH* −401C>T polymorphism, we found a protective role for advanced cervical cancer development. Our results demonstrated that patients carriers of the variant T allele present 30% lower risk of advanced disease according to grouped genotype analysis (CC/CT Vs TT, IIB+III+IV Stages: OR=0.696, 0.541–0.897 95% CI, p = 0.002). Regarding *XRCC1* Arg399Gln a statistically significant association with cervical cancer risk was not observed (p = 0.842). Additionally, no association was found neither for grouped genotypes analysis (GG Vs A carrier) (p = 0.797), nor for cervical cancer stages (p = 0.567).
Discussion/Conclusions: We postulated that *GGH* over-expression could disturb folate and cell metabolism for which folic acid is essential. Since tumour cells should not be able to survive with sub-optimal folate levels, they could putatively be eliminated by apoptosis before advanced stages start to develop.

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Lymphopenia is an Independent Prognostic Factor in Ovarian Cancer and Could Be Associated With Immune Activation

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Background: The interaction between the host immune system and tumoral cells plays a major role in tumour progression. We recently showed that lymphopenia is an independent prognostic factor associated with poor outcome in a large series associating metastatic breast cancer, sarcomas and lymphomas patients [1]. Here the impact of lymphopenia on ovarian cancer (OC) patients was investigated.
Materials and Methods: A retrospective study on 146 patients treated for epithelial OC was conducted in Centre Léon Bérard, Lyon, France, between 1992 and 2009 to investigate the impact of lymphopenia on outcome. In addition a prospective study was conducted on 50 newly diagnosed OC patients comparing the percentage of activated $CD4^+$Tcells ($CD3^+CD4^+CD25^{int}$) and memory $CD4^+$T cells ($CD3^+CD4^+CD45RO^+$) evaluated by flow cytometry in lymphopenic and non-lymphopenic and the plasmatic levels of pro-inflammatory cytokines measured by multiplex ELISA.
Results: Median levels of lymphocytes were correlated with advanced FIGO stages (III/IV) when compared to early stages (I/II, $p = 0.04$). By using a cut-off of 1000/mm3, 13.7% of patients presented lymphopenia. In multivariate analysis of overall survival, in addition to "well known" prognostic factors (such as stages and residual disease), lymphopenia was an independent prognostic factor associated with short survival (HR = 2.24, $p = 0.02$). We hypothesized that lymphopenia is due to chronic immune activation. Our preliminary datas showed that lymphopenic patients present increased levels of activated $CD4^+$Tcells and memory $CD4^+$T cells among total lymphocytes when compared to non-lymphopenic patients. Comparison of plasmatic levels of pro-inflammatory cytokines, in particular IL-6 and TNF-α measured by multiplex ELISA in lymphopenic and non-lymphopenic patients are on-going and will be presented in the ESMO annual meeting.