Conclusions: Lymphopenia is an independent prognostic factor for survival in first-line treated OC and its physiopathology need to be investigated.

References

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8039 POSTER

New Dendritic Cell Vaccine Therapy Approach − Randomized Phase I/II Study in III-IV Stage Ovarian Cancer Patients

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Background: Currently, extensive studies to improve the immunotherapy approach based on DC-vaccine have been performed. Great emphasis is paid to finding new more efficient ways to load DC with tumour antigens. Our preclinical findings indicate that the lysate from tumour cells exposed to B.subtilis B-7025 cytotoxic lectins (LTCCL) used for DC loading is a very effective and promising approach. We report results of a phase I/II trial in advanced ovarian cancer (AOC) patients treated with DC pulsed with LTCCL.
Objective of the study: To examine clinical and immunological effects of specific immunotherapy with autologous DC loaded with LTCCL or conventional lysate of tumour cell (LTC) in advanced AOC treatment.
Patients and Methods: Eighty-one patient with III-IV stage AOC, ECOG 0−1, without autoimmune disorders were enrolled into randomized clinical trial. All patients received cytoreductive surgery and 6 courses of adjuvant polychemotherapy (PCT) on CP regimen (cisplatin 100 mg/m^2, cyclophosphan 800 mg/m^2). 41 patients after PCT had received DC-therapy (4−9x10^6 per injection). This group was divided into 2 subgroups: patient who received DC loaded with LTC (1 s/g) and patients who received DC loaded with LTCCL (2 s/g). Comparable groups and subgroups were similar by age of the patients, histology type of tumours, stages, volumes of surgical intervention and adjuvant chemotherapy. In the trial were used autologous DC of monocytic origin with expression of surface markers CD86 and HLA-DR at least 70%, CD83−50% obtained by flow cytometry. DCs were injected i.v. in 1−2 courses. One course consisted of 5 injections with one-month interval. Clinical and immunological monitoring of DC-vaccine therapy was performed. Special attention was focused on antigen specific cellular antitumour immune response.
Results: DC vaccine therapy was well tolerated without significant toxicity. DC vaccine therapy has improved of 1−3-year survival of patients. 1-year survival of 1 s/g patients was 88.8±3.7% and 2 s/g − 92.9±8.3 versus 80.1±3.4% in control group ($p < 0.05$). 2-year survival of patients in 1 and 2 s/gs was 47.8±4.5% and 53.1±8.5 respectively versus 20.5±4.7% in control group ($p < 0.01$). Overall survival of AOC patients with DC vaccine therapy for 3 year was: 1s/g − 26.7±5.6% and 2s/g − 39.8±8.7% versus 13.2±5.4% in control group. 95% of patients showed significant antigen specific immune response after 3−5 DC-vaccinations. In responding to DC-vaccination patients, immunotherapy significantly boosted the IFN-γ and IL-2 producting T-cell response to autologous tumour challenge. Moreover, the increased functionality of T-cells, indicated by increased expression of markers for CTL activation, differentiation and proliferation was revealed.
Conclusions: There was clear evidence of clinical benefit of vaccine therapy by DC pulsed with LTCCL for AOC patients. This approach warrants further study.

8040 POSTER

Diagnostic and Prognostic Significance of CA125 and HE4 in Ovarian Cancer Patients

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Introduction: Epithelial Ovarian cancer (EOC) is the most frequent cause of death from gynaecological cancer, being characterized by few early symptoms, presentation at an advanced stage and poor survival. At the moment, CA125 is the unique biomarker used for EOC diagnosis. Therefore, there is a pressing need to develop new methods for early detection and prognosis. The aims of this study were to investigate: a) the diagnostic performances of CA125 and HE4; b) the association of CA125 and HE4 with the established EOC clinicopathological prognostic characteristics; c) the value of CA125 and HE4 in predicting overall survival (OS), disease-free survival (DFS) and progression free survival (PFS) for EOC patients.
Material and Methods: The study included 114 EOC patients, 131 patients with ovarian benign cysts, 34 patients with endometriosis and 140 healthy controls. Pre-operative serum samples were analyzed for CA125 and HE4 by a chemiluminescent microparticle immunoassay on automated ARCHITECT instrument (Abbott Diagnostic Division, Chicago, IL). Cutoff value was 35 U/ml for CA125 and it was 70 pM (in pre-menopausa) and 140 pM (in post-menopausa) for HE4.
Results: Serum HE4 and CA125 levels in EOC patients were significantly higher compared with healthy controls, endometriosis and ovarian cysts (all $p < 0.001$). Comparison of CA125 and HE4 at set cutoff showed that CA125 levels were above the threshold values more frequently than HE4 in EOC and in endometriosis patients. CA125 and HE4 values were positively associated with FIGO stage, histological grade, lymph node involvement, residual tumour after cytoreductive surgery, ascites and positive peritoneal cytology (all $p < 0.05$). In univariate analysis, CA125 and HE4 levels were significant associated with OS, DFS and PFS (all $p < 0.02$). Multivariate analysis showed that HE4, but not CA125, was an independent prognostic factor for OS, DFS and PFS (all $p < 0.02$).
Discussion: Our data show that CA125 is more sensitive than HE4 for EOC diagnosis, whereas HE4 is more specific than CA125 for the discrimination of endometriosis from malignant diseases. The combination of CA125 and HE4 will improve the differential diagnosis between subjects with different ovarian pathologies. The positive correlation of CA125 and HE4 levels with other established prognostic factors suggests that CA125 and HE4 could be involved in tumour aggressiveness. Finally, for the first time, we find HE4 as an independent prognostic factor in EOC patients.

8041 POSTER

Relevance of Gamma-glutamyltransferase − a Marker for Apoptotic Balance − in Predicting Tumour Stage and Prognosis in Cervical Cancer

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Background: Recent large epidemiologic population-based studies identified gamma-glutamyltransferase (GGT) as a marker for increased cervical cancer incidence. Furthermore, high levels of GGT seem to increase the risk of progression of high-grade cervical dysplasia to invasive carcinoma. Therefore, we evaluated the association between pre-therapeutic serum GGT levels, tumour stage and prognosis in patients with cervical cancer.
Materials and Methods: In this multi-center trial, pre-therapeutic GGT levels were examined in 692 patients with cervical cancer. GGT levels were correlated with clinico-pathological parameters. Patients were assigned to previously described GGT risk groups and uni- and multivariate survival analyses were performed.

Table 1. Survival analyses of 692 patients with cervical cancer.

	Disease-free survival			Overall survival		
	Univariate[1,2]	Multivariate[3]		Univariate[1,2]	Multivariate[3]	
	P-Value	*P*-Value	HR (95% CI)	*P*-Value	*P*-Value	HR (95% CI)
Tumour stage (FIGO I vs. II vs. III vs. IV)	<0.0001	<0.0001	2.0 (1.6−2.5)	<0.0001	<0.0001	2.0 (1.5−2.5)
Lymph node involvement (negative *vs.* positive)	<0.0001	<0.0001	2.5 (1.7−3.9)	<0.0001	<0.0001	2.9 (1.8−4.7)
Histological grade (G1 *vs.* G2 *vs.* G3)	0.001	0.02	1.7 (1.2−2.3)	0.003	0.046	1.5 (1.1−2.2)
Patients' age	0.001	0.5	1.0 (0.9−1.0)	0.001	0.7	1.0 (1.0−1.1)
GGT groups (A and B *vs.* C and D)	0.01	0.7	1.1 (0.7−2.0)	<0.0001	0.3	1.4 (0.7−2.6)
Histopathological Type (Squamous cell carcinoma *vs.* Adenocarcinoma)	0.04	0.3	1.3 (0.8−2.1)	0.05	0.06	1.7 (1.0−2.9)

[1]Log rank test; [2]univariate Cox-regression analysis; [3]multivariate Cox-regression analysis, HR = Hazard Ratio, 95% CI = 95% Confidence Interval; GGT = g-glutamyltransferase.

Results: GGT serum levels were associated with FIGO stage ($p = 0.002$), but not with lymph node involvement ($p = 0.2$), histological grade ($p = 0.7$)