8066 POSTER

Multi-institutional retrospective study of 64 patients with primary fallopian tube carcinoma treated with carboplatin and paclitaxel

G. Papaxoinis[1], C. Andreadis[2], G. Fountzilas[3], G. Aravantinos[4], C. Sykiotis[5], T. Akrivos[6], D. Pectasides[1]. *[1]"Attikon" University Hospital, 2nd Department of Internal Medicine Propaedeutic, Athens, Greece; [2]"Theagenion" Cancer Hospital, 3rd Department of Medical Oncology, Thessaloniki, Greece; [3]"Papageorgiou" Hospital Aristotle University of Thessaloniki School of Medicine, Department of Medical Oncology, Thessaloniki, Greece; [4]"Agii Anargiri" Cancer Hospital, 3rd Department of Medical Oncology, Athens, Greece; [5]"Attikon" University Hospital, Department of Gynecological Oncology, Athens, Greece; [6]Metaxa Memorial Cancer Hospital, Gynecology Department, Piraeus, Greece*

Background: The aim was to present the clinical outcomes of patients (pts) with primary fallopian tube carcinoma (PFTC) treated with carboplatin and paclitaxel.
Pts and Methods: The tumor registries of 3 Medical Oncology Departments from 1995 to 2007 yielded a total of 64 eligible pts with histologically documended PFTC and no prior chemotherapy.

Table 1

Number of pts	64
Age, Median, Range	61 (42−84)
ECOG performance status	
0	42 (66%)
1	13 (20%)
2	7 (11%)
3	2 (3%)
Histology	
Serous	33 (52%)
Poorly differentiated carcinoma	12 (19%)
Endometrioid	2 (3%)
Papillary	1 (1%)
Unspecified adenocarcinoma	16 (25%)
Histological grade	
1	3 (5%)
2	18 (28%)
3	40 (62%)
Unknown	3 (5%)
FIGO stage	
I	13 (20%)
II	16 (25%)
III	32 (50%)
IV	3 (5%)
Debulking surgery	
Optimal	40 (62.5%)
Suboptimal	24 (37.5%)
Measurable disease	
Yes	28 (44%)
No	36 (56%)
Type of surgery	
TAH+BSO+omentectomy	40 (63%)
TAH+BSO	13 (20%)
TAH+BSO+omentectomy+LNS	6 (9%)
TAH+USO+omentectomy	2 (3%)
Biopsies only	3 (5%)
Chemotherapy	
	11 (17%)
Cyclophosphamide+doxorubicin+cisplatin	
Cyclophosphamide+carboplatin	4 (6%)
Paclitaxel+carboplatin	48 (75%)
Carboplatin	1 (2%)

TAH: total abdominal hysterectomy, BSO: bilateral oophorectomy, USO: unilateral oophorectomy

Results: Pts and treatment characteristics are shown in table 1. There were 19 (68%) complete clinical and 7 (25%) partial responses (overall response rate = 93%). At the time of analysis 21 (33%) pts had relapsed and 16 (25%) had died. After a median follow-up of 40 months (m) (3±134+), the median overall survival (mOS) was not reached (5-years survival was 70%) and the median time to tumor progression (mTTP) was 81 m. The mTTP was not reached for pts with ST I/II and was 38 m for pts with ST III/IV ($p = 0.004$). The mOS for pts with ST I/II was not reached and was 62 m for pts with ST III/IV ($p = 0.057$). The mTTP was 86m vs 23m for pts with RD <2 cm and >2 cm respectively ($p < 0.001$). The mOS was not reached for pts with RD <2 cm and was 36m for pts withn RD >2 cm ($p < 0.001$).
Conclusion: Carboplatin/paclitaxel therapy is highly active in chemonaive pts with PFTC. These encouraging results lead us to suggest it as the standard chemotherapy.

8067 POSTER

Platinum sensitivity in patients with brain metastases from ovarian cancer: results of a German multicenter study

K. Pietzner[1], K. El Khalfaoui[1], G. Oskay-Özcelik[1], R. Richter[1], P. Harter[2], K. Münstedt[3], S. Mahner[4], A. Hasenburg[5], P. Wimberger[6], J. Sehouli[1]. *[1]Charite-Universitätsmedizin Berlin, Department of Gynecology and Obstetrics, Berlin, Germany; [2]Frauenklinik Wiesbaden, Department of Gynecologic Oncology, Wiesbaden, Germany; [3]Universitätsklinik Giessen, Department of Gynecologic Oncology, Giessen, Germany; [4]Universitätsklinik Hamburg-Eppendorf, Department of Gynecologic Oncology, Hamburg, Germany; [5]Universitätsklinik Freiburg, Department of Gynecologic Oncology, Freiburg, Germany; [6]Universitätsklinik Essen, Department of Gynecologic Oncology, Essen, Germany*

Background: Ovarian cancer is one of the leading causes of mortality in women with gynaecological malignancies, but brain metastases are considered an uncommon metastatic site. Only few data exist on prognostic factors for this patient collective. Platinum sensitivity is a key factor in the management of ovarian cancer. But it is considered a secondary factor in the treatment of patients with brain metastases from ovarian cancer, due to the poor prognosis of this condition. The objective of this study is to evaluate the impact of different clinical variables on survival, focusing on platinum sensitivity.
Material and Methods: A multicenter, retrospective chart review was performed including patients with histologically confirmed ovarian cancer from six different German hospitals within the period between 1981 and 2008. Overall, 4277 cases of patients with ovarian cancer were analyzed. Cox regression analysis, Kaplan–Meier test, and log rank test were used to calculate survival and compare the impacts of clinical variables and treatment modalities.
Results: A total of 74 women with brain metastases were identified, resulting in an incidence of 1.73%. The median age at the diagnosis of central nervous system (CNS) metastases was 56.8 years (range, 33−83). The median interval between the time of the primary diagnosis and the occurrence of brain lesions was 28.8 months (range, 3.6−133.1). The median overall survival time from diagnosis of brain metastases was 6.2 months (range, 0.2−41.5). Multiple lesions were observed in 58 women (78.4%). Headache (36.5%), vomiting and nausea (17.1%) were the most frequent clinical symptoms. According to multivariate analysis following clinical parameters had a significant impact on overall survival: multiple lesions (hazard ratio [HR]: 4.1, 95% confidence interval [CI]: 1.9 to 8.9) and Grading I und II (HR: 2.8, 95% CI: 1.6 to 5.0) were associated with a negative impact. Platinum sensitivity (HR: 0.28, 95% CI: 0.15 to 0.52) was significantly associated with a positive impact on survival. A multimodal therapeutic management (surgery, radiotherapy and chemotherapy) (HR: 0.51, 95% CI: 0.28 to 0.92) and a good performance (HR: 0.52; 95% CI: 0.25 to 1.08) also showed a positive impact on overall survival. Tumor histology, ascites and age at the CNS diagnosis were not significant for the survival.
Conclusions: The most important finding of this study is the fact, that the sensitivity to platinum based chemotherapy was associated with a significant positive impact on overall survival. This novel finding should be considered in the conduction of multimodal therapy strategies for brain metastases from ovarian cancer.

8068 POSTER

High risk for ovarian carcinoma associated with polymorphisms of glutathione s-transferase GSTM1, GSTT1 and GSTP1 genes

R.A.M. Sagarra[1], G.J. Lourenço[1], S.F.M. Derchain[2], J.G. Segalla[3], C.S.P. Lima[1]. *[1]State University of Campinas, Clinical Oncology Service Department of Internal Medicine, Campinas SP, Brazil; [2]State University of Campinas, Gynaecology Oncology Service Department of Internal Medicine, Campinas SP, Brazil; [3]Amaral Carvalho Hospital, Clinical Oncology, Jaú SP, Brazil*

Background: Steroid hormones, such as estrogens, appear to be associated with ovarian carcinogenesis, although the exactly mechanism remains unclear. The 2- and 4-OH estrogens can be further oxidized to quinones that may cause DNA damage. The quinones can be deactivated by conjugation with glutathione by gluthathione S-transferases (GSTs), but it's not clear which of the GSTs are involved. Apart from that, *GSTP1* gene

has also been involved in cell proliferation and apoptosis. We tested in this study whether the polymorphisms of the glutathione *GSTM1*, *GSTT1* and G*STP1* might alter the risk for ovarian carcinoma (OC).
Material and Methods: Genomic DNA from peripheral blood of 137 consecutive OC patients and 137 controls were analysed by the multiplex-PCR for identification of the *GSTM1* and *GSTT1* genotypes and PCR-RFLP for identification of genotypes of the *GSTP1*. The differences between groups were analysed by χ^2 or Fisher exact test. Multivariate analysis served to obtain age and ethnic origin adjusted crude odds ratios (ORs).
Results: Similar frequencies of the *GSTM1* (37.6% versus 31.4%, $P = 0.37$) and *GSTT1* (30.6% versus 24.8%, $P = 0.25$) null genotypes were seen in patients and controls. In contrast, the *GSTP1* Ile/Ile genotype was more frequent in patients than in controls (59.1% versus 44.5%, $P = 0.01$). Individuals with this genotype had a 1.84 (95% CI: 1.14−3.01) fold increased risk for the disease. The frequency of the combined *GSTM1* null and *GSTP1* Ile/Ile genotypes was higher in patients than in controls (43.5% versus 24.6%; $P = 0.02$). Carriers of the genotype were under a 2.59 (95% CI: 1.18−5.64) fold increased risk for OC than others. Moreover, an excess of the *GSTM1* null, *GSTT1* null and *GSTP1* Ile/Ile combined genotype was seen in patients compared to controls (30.3% versus 7.1%; $P = 0.01$). Individuals with the genotype had a 8.00 (95% CI: 1.77−35.87) fold increased risk for OC than carriers of the remaining genotypes.
Conclusions: The results suggest that the variant *GSTT1*/*GSTM1* null and *GSTP1* Ile/Ile genotypes combination are linked to a substantial increased risk of development of OC. We hypothesised that *GSTT1* and *GSTM1* null genotypes leads to a loss of enzymatic conjugation activity, favouring the exposure of ovarian to estrogens. Apart from that, the *GSTP1* Ile/Ile genotype may add OC risk through different effects on cell cycle by protecting cells against apoptosis promoting tumour cells survival.
Financial support: FAPESP and CNPq.

Head and neck cancer

Oral presentations (Tue, 22 Sep, 14:45−16:30)
Head and neck cancer

8500 ORAL

Expression of EGFR and HPV-associated p16 in head and neck cancer: correlation and influence on prognosis after radiotherapy in 1088 patients from the randomised DAHANCA 5, 6 & 7 trials

P. Lassen[1], J.G. Eriksen[1], T. Tramm[2], S. Hamilton-Dutoit[2], J. Alsner[1], J. Overgaard[1]. *[1]Aarhus University Hospital, Department of Experimental Clinical Oncology, Aarhus, Denmark; [2]Aarhus University Hospital, Department of Pathology, Aarhus, Denmark*

Background: Expression of p16 is highly correlated to infection with Human Papillomavirus in squamous cell carcinoma of the head and neck (HNSCC). Previous reports have demonstrated an inverse correlation between expression of epidermal growth factor receptor (EGFR) and p16 in HNSCC. The aim of this study was to examine the correlation between EGFR and p16 and to asses their influence on response to radiotherapy (RT) and survival in a large cohort of HNSCC patients treated with RT alone in the randomised DAHANCA 5, 6 & 7 trials.
Material and Methods: Between January 1986 and December 1999 The Danish Head and Neck Cancer group (DAHANCA) conducted the nationwide DAHANCA 5, 6 & 7 randomised trials, focusing on overcoming the disadvantages of tumour cell hypoxia and accelerated tumour cell proliferation in relation to RT. In the present study 1088 pre-treatment tumour tissues from patients in these trials were examined by immunohistochemistry for EGFR-expression (high/low) and p16 status (pos/neg).
Results: In total 258 of 1088 (24%) tumours were p16pos and 885 (81%) had high EGFR-expression. The correlation between EGFR and p16 was found to be inverse with p16pos tumours tending to have lower EGFR-expression (27%) compared to p16neg tumours (16%, $p < 0.0001$). In the oro-pharynx the frequency of p16 was highest (132/329, 40%) and the inverse correlation between EGFR and p16 most pronounced (63% of tumours with low EGFR were p16pos). Prognosis was significantly improved for p16pos tumours compared to p16neg: loco-regional tumour control (66% vs 51%, $p < 0.0001$), disease specific survival (75% vs 58%, $p < 0.0001$) and overall survival (59% vs 41%, $p < 0.0001$) at 5 years. In multivariate analysis p16 remained an independent prognostic factor for loco-regional tumour control [OR: 0.49 (95% CI 0.38−0.62)], cancer specific death [OR: 0.43 (0.33−0.56)] and overall death [OR: 0.52 (0.43−0.63)]. EGFR-expression did not influence on prognosis, neither in the total cohort nor in subgroup analysis stratified by p16 status.
Conclusions: In this large cohort of patients with HNSCC treated with RT alone HPV-associated p16pos tumours had lower expression of EGFR than p16neg tumours. p16 status was found to have major prognostic impact on outcome after RT whereas EGFR-expression had no prognostic implication on its own and did not contribute to a refinement of the prognostic value of p16 status.
Presented on behalf of the Danish Head and Neck Cancer group (DAHANCA)

8501 ORAL

Larynx preservation using induction chemotherapy followed by radiation – five-year evaluation of swallowing and laryngeal functions for patients enrolled in the GORTEC 2000−01 randomized study

C. Debelleix[1], S. Chapet[1], C. Sire[2], C. Tuchais[3], S. Faivre[4], M. Alfonsi[5], J.L. Lefebvre[6], G. Calais[1]. *[1]CHU de Tours - Hopital Bretonneau, Radiotherapie, Tours, France; [2]Centre Hospitalier de Lorient, Radiotherapie, Lorient, France; [3]Centre Paul Papin, Radiotherapie, Angers, France; [4]Institut Gustave Roussy, Oncologie Médicale, Villejuif, France; [5]Institut Sainte Catherine, Radiothérapie, Avignon, France; [6]Centre Oscar Lambret, Chirurgie Cervico Faciale, Lille, France*

Background: Larynx preservation, using induction chemotherapy followed by radiation or concomitant chemoradiation, could be achieved for patients with locally advanced larynx and hypopharynx tumors. However this kind of approach should cure the patient but also keep the function. The objective of this prospective study was to evaluate the 5-year functional results, focused on voice and swallowing, for patients treated with induction chemotherapy followed by radiation.
Materials and Methods: 213 patients have been enrolled in the GORTEC 2000−01 randomized study which compared induction chemotherapy with Cisplatin (P) and 5 Fluorouracil (F) with or without Docetaxel (T) followed by radiation in case of good response. Radiation therapy was proposed for 142 patients. The others were treated with total laryngectomy and post operative radiotherapy. With 61 months median follow-up, 67/142 are alive with their larynx. Questionnaires have been sended to all of these patient. The quality of the voice was evaluated using the “Voice handicap index 30” (VHI30). The impact on quality of life and swallowing function were assessed through the EORTC Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) and the “Quality of Life Head and Neck module” (QLQ-H N 35).
Results: 61 patients (91%) answered to questionnaires. Voice disability is very low for 57% of patients (VHI score <30) moderate for 28% (VHI score 30 to 60) and severe for 15% (VHI score >60). 1 patient have permanent tracheostoma. Mulivariate analysis has been done to test potential factors that would affect the results of the VHI. Recovering larynx mobilty following induction chemotherapy was the only predictive factor for a good VHI score ($p = 0.035$). The VHI score was correlated with the global quality of life scale and functional scales of the QLQ C 30. 25 patients (40%) had no eating or swallowing problems (eating HN35 score = 0). 17 patients (27%) used daily nutritional supplements and 5 patients (8%) had an enteral feeding tube. Patients who received induction chemotherapy with PF are taking more opioid treatments and nutritional supplements compared to those who received th TPF regimen.
Conclusions: Using induction chemotherapy followed by radiation for larynx preservation the quality of the functional result regarding voice was poor for 15% of the patients and for 8% of the patients regarding the swallowing function. These data would be useful for designing the future larynx preservation trials.

8502 ORAL

Long term (Five-year) results of Tax324: A Phase III Trial of Sequential Therapy comparing TPF with PF in Patients with locally advanced squamous cell cancer of the head and neck

J. Lorch[1], R.I. Haddad[1], J. Fasciano[1], O. Goloubova[2], K. Cullen[2], M. Posner[1]. *[1]Dana Farber Cancer Insitute, Head and Neck Oncology Program, Boston Massachusetts, USA; [2]University of Maryland, Center of Biostatistics, Baltimore Maryland, USA*

Background: In the original TAX324 report, after a minimum follow up of two years and a median of 42 months, sequential chemotherapy with Taxotere, cisplatin and 5FU (TPF) significantly improved survival by 30% compared with cisplatin and 5FU (PF). TAX324 and TAX 323 established Induction and Sequential therapy with TPF as treatment standards for patients with Locally Advanced Head and Neck Cancer (LAHNC). We are now presenting the long term results of the TAX324 study.
Material and Methods: After IRB approval, the study group used the anonymous study codes of the patients who were alive or lost to follow