8049 POSTER

Epithelial Ovarian Carcinoma in Very Young Women: Age-specific Characteristics

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Background: Relative survival is classically more favourable in younger patients with epithelial ovarian carcinoma (EOC); however EOC is less common in younger women and our interest is to depict specific clinical features in these women and to determine whether patient age is an independent prognostic factor for survival.
Material and Methods: Using the tumour registry of the Institut Gustave-Roussy, we conducted a retrospective matched cohort study. The exposure definition is patient aged $\leqslant$30 years with a diagnosis of EOC between January 1990 and January 2009 (n = 75). Each of these exposed patients was matched to 2 randomly selected patients >40 years by date of diagnosis, stage (I/II or III/IV) and histology type (mucinous or non mucinous) (n = 150). The outcomes are the overall survival (OS) and relapse-free survival (RFS). A multivariable Cox proportional hazard model is used to compare these 2 outcomes between exposed and unexposed patients.
Results: The median age in exposed patients is 25 years (13 to 30). The 5-year-OS is 91% for early stages (FIGO I and II) and 46% for advanced disease (FIGO III and IV). Early stage and low grade are slightly more frequent (stage I, II, III and IV with 35, 4, 29 and 5 patients of 73 reported respectively, and grade 1, 2 and 3 with 36 patients, 20 and 4 patients out of 60 reported respectively). Serous and mucinous histology subtypes (35 serous, 25 mucinous, 1 with both) are the most represented ones. No BRCA mutation was found in 21 available samples. BRCA variants of yet unknown value are diagnosed in 5 patients. There is no statistically significant difference in OS and in RFS between exposed and unexposed patients. The 2-year-OS is 95% and 89% in exposed and unexposed group respectively, and the 2-year-RFS is 76% and 71% in exposed and unexposed group respectively.
Conclusions: The most relevant clinical features of EOC in younger women (<30 yrs) are early FIGO stage, serous and mucinous histology and low grade in an independent genetic context. No difference in OS and RFS is found between patients younger than 30 and older than 40 years of age.

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Cost-effectiveness of Trabectedin in Combination With Pegylated Liposomal Doxorubicin Hydrochloride for the Treatment of Women With Relapsed Platinum-sensitive Ovarian Cancer in the UK − Analysis Based on the Final Survival Data

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Background: Interim analysis demonstrated that trabectedin in combination with pegylated liposomal doxorubicin hydrochloride (PLDH) significantly improves progression-free survival (PFS) and shows longer overall survival (OS) in women with relapsed platinum-sensitive ovarian cancer (Monk et al, ASCO). The objective of this study was to estimate the cost-effectiveness of trabectedin plus PLDH compared to PLDH alone for patients with relapsed platinum-sensitive ovarian cancer in the UK, based on the final survival data published in June 2011.
Methods: A decision analytic model was developed to estimate the cost per quality-adjusted life year (QALY) gained for trabectedin plus PLDH compared to PLDH alone from the UK NHS and Personal Social Services perspective over a lifetime horizon. Effectiveness data for PFS and OS were based on the phase III randomised trial (OVA-301) in 672 patients with relapsed ovarian cancer. Parametric survival distributions were fit to the data from the platinum-sensitive subgroup to calculate mean PFS and OS for each treatment. Drug, administration, medical management and adverse event costs were based on British National Formulary prices and UK Healthcare Resource Group codes. Quality of life was measured by the EQ-5D data collected in the OVA-301 trial. Costs and outcomes were both discounted at 3.5%. Uncertainty was addressed by deterministic and probabilistic sensitivity analysis (PSA).
Results: The model estimated that trabectedin plus PLDH increased mean PFS by 3.0 months, and OS by 9.7 months compared to PLDH in the platinum-sensitive population. The total cost for trabectedin plus PLDH and PLDH alone were £41,657 and £23,579. The total QALYs gained for trabectedin plus PLDH and PLDH alone were 2.33 and 1.85. Therefore, the incremental cost per QALY gained was calculated as £37,206. PSA showed that the mean incremental cost per QALY based on 1000 stochastic simulations was £39,505.
Conclusions: Analysis based on the final survival data of the aforementioned trial showed a significant improvement in the mean OS and incremental cost per QALY originally calculated and submitted in the UK to the National Institute for Health and Clinical Excellence (NICE) based on interim analysis.

8051 POSTER

HER-2 Protein Overexpression in Ovarian Cancer − an Association With Other Prognostic Factors

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Introduction: The HER2 proto-oncogene encodes a protein with tyrosine kinase activity that functions as a growth factor receptor. Significance of HER2 expression/amplification in ovarian carcinomas is not clear enough. The pur-pose of this study was to determine the rate of HER2 protein overexpression in ovarian cancer, and to detect if any associations exist between HER2 protein overexpression and histological grade, histological type, tumour stage and patients age.
Material and Methods: A total of 34 cases of ovarian cancer were included in this study. The immunohistochemistry was used to determinate the HER2 protein overexpression in tumour tissue. Strong membrane reaction detected in more than 10% of tumour cells was considered a positive result.
Results: Positive expression of HER2 protein was found in 5 (14.7%) cases. All ovarian cancers with positive HER2 status were diagnosed in stage III ($p < 0.05$). Out of total 5 HER2 positive tumours, four (80%) were of serous type, and one (20%) of the mixed, serous-mucinous type. In the group of mucinous and endometrial tumours no positive HER2 expression was detected ($p = 0.05$). HER2 overexpression was seen in 7.7% of tumours grade III and in 33.3% of grade II. All well differentiated carcinomas were HER2 negative ($p > 0.05$). Patients with positive HER2 expression were 65 years old on average, whereas for those with HER2 negative status the average age was 56 ($p > 0.05$).
Conclusion: Positive expression of HER2 protein in ovarian cancer is significantly correlated with an advanced stage of tumour disease and could represent a factor of poor prognosis.

8052 POSTER

Evaluation of the Tumour Diameter Influence on the Treatment Results in Cervical Cancer Patients

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Background: The influence of the tumour diameter on the treatment results in cervical cancer patients, so far, has been the subject of not numerous studies.
Objectives: Evaluation of the tumour diameter influence on the overall (OS) and disease free survival (DFS) in cervical cancer patients.
Material: The clinical material constituted 242 cervical squamous cell and 142 cervical adenocarcinoma patients, treated between 1990 and 1999 year at Maria Sklodowska-Curie Memorial Cancer Centre and Institute in Warsaw. All patients were treated with surgery and complementary radiotherapy or with radiotherapy alone. During the analyzed period, radio-chemotherapy was not a standard treatment modality in cervical cancer patients. In all patients, during the diagnostic procedures, the tumour diameter was measured, using the transvaginal ultrasonography (USG TV). Method. The retrospective multivariate Cox's analysis of the most important clinic-pathological factors, in aspect of the OS and the DFS, was performed. As the cut point of the tumour diameter, 3 centimeters was accepted.

Results: Regardless of the other factors, the influence of the pretreatment tumour diameter on the OS, but not on the DFS in cervical squamous cell cancer patients, was demonstrated, HR = 1.7 [1.0, 2.8], p = 0.044, p = 0.08. We did not demonstrate the influence of the tumour diameter on the OS and the DFS in cervical adenocarcinoma patients.
Conclusion: The pretreatment assessment of the tumour diameter may be important in cervical squamous cell, but not in adenocarcinoma patients. Cervical adenocarcinoma is usually more aggressive and tends to disseminate earlier, than squamous cell cancer, regardless of the tumour size.

8053 POSTER

Knowledge and Applications of the Midwives and Nurses Working in the Woman Labor Clinics of an Educational Hospital on the Early Diagnosis of Cervix Cancer

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This study was made to determine the knowledge levels and application situations of the midwives and nurses working in the woman labor clinics of an educational hospital giving service in the European side of Istanbul. This descriptive study was made with the participation of 96 midwives and nurses. Data were collected with the survey form which was prepared by the researcher. Obtained data were evaluated in a computerized environment by using frequency distribution and chi-square significancy test. 62.5% of the midwives and nurses included in the research stated that they never go to a routine gynaecological control without any complaints, 54.1% of them stated that they did not see themselves as being under risk in the aspect of cervix cancer, 18.7% of them stated that they had no information about the risk factors related to the cervix cancer. 54.2% of the participants stated that they had at least one pap smear test, 20.8% of them stated that they did not see having a pap smear test as mandatory. 91.7% of the participants knew about the HPV vaccine, 54.2% of them learned about the HPV vaccine from visual and published media and 78.1% of them wanted to have HPV vaccination.
A statistically significant difference was found between the the knowledge levels and application situations of the midwives and nurses included in the research; and their age groups, educational status, and marital status ($p < 0.05$). It was also determined that the participants who were in the age group 32 and over, who had undergraduate or more education and who were married; had more desirable knowledge and applications.

Oral Presentations (Sat, 24 Sep, 11:15–13:20)
Head and Neck Cancer

8500 ORAL

Impact of Smoking Pack-years on Anatomic Disease Outcomes for HPV-related Oropharyngeal Cancer Treated With Radiotherapy With or Without Chemotherapy

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Background: Smoking pack-years (PY) has been reported to impact survival of HPV(+) oropharyngeal cancer (OPC) following radiotherapy (RT) +/- chemo (CX). However, the differential influence of PY on anatomic disease control (local, regional, and distant) vs. survival has not been emphasized in the recent literature. This study is designed to address this question.
Methods: All OPC patients treated with RT +/- CX from 2001–2009 on a prospectively assembled cohort with point of care outcome assessment were included. Actuarial 3-year overall survival (OS), cause-specific survival (CSS), local control (LC), regional control (RC), distant control (DC), and late toxicity (RTOG >= 3) were compared for HPV(+) vs. HPV negative [HPV(−)], and stratified by smoking PY (⩽10 vs. >10) for HPV(+) OPC. Univariate and multivariate analysis identified outcome predictors.
Results: HPV status (p16 staining) was assessed in 451/899 (50%) consecutive OPC revealing 346 HPV(+) and 105 HPV(−). Clinical characteristics including outcomes were identical for known vs. unknown HPV status. Median follow-up was 3.6 years. HPV(+) cases (n = 346) had higher OS (81 vs. 45%), CSS (87 vs. 59%), LC (93 vs. 77%), and RC (94 vs. 78%) with lower late toxicity (16 vs. 38%) vs. HPV(−) cases (n = 105) (all $p < 0.01$). The DC rate was similar (88 vs. 84%, p = 0.39). HPV(+) ⩽10 PY smokers (n = 173) had higher OS (88 vs. 74%, $p < 0.01$), marginally better CSS (92 vs. 83%, p = 0.04) vs. >10 PY smokers (n = 173), but identical LC (95 vs. 92%, p = 0.29), RC (96 vs. 92%, p = 0.12), DC (89 vs. 88%, p = 0.632), and late toxicity (12 vs. 19%, p = 0.11). Multivariate analysis revealed HPV status was the strongest predictor for OS, CSS, LC and RC (all $p < 0.01$), but not for DC (p = 0.21). N category was predictive for OS, CSS, RC and DC while T category was predictive for OS, CSS, LC and DC (all $p < 0.01$). Smoking PY was a strong predictor for OS, CSS, LC, RC (all $p < 0.01$) and DC (p = 0.02) in univariate but only for OS (Hazard Ratio 1.65, p = 0.03) in multivariate analysis (Table 1).
Conclusions: HPV(+) OPC has superior outcomes and lower toxicity compared to HPV(−) (except DC) when treated with RT +/- CX. HPV(+) minimal smokers fare especially well. Smoking PY affects overall survival but appears not to influence loco-regional control in HPV(+) OPC.

Table 1. Multivariate Analysis of Outcome Predictors

	Hazard Ratio (p)				
Variable	OS	CSS	LC	RC	DC
HPV(−)	2.64 (**<0.01**)	2.44 (**<0.01**)	3.28 (**<0.01**)	2.63 (**<0.01**)	1.51 (0.21)
>10 PY	1.65 (**0.03**)	1.62 (0.08)	1.32 (0.47)	2.05 (0.12)	1.21 (0.53)
Older age	1.03 (**<0.01**)	1.02 (0.11)	1.02 (0.27)	0.99 (0.43)	1.01 (0.47)
N2b–N3	2.15 (**<0.01**)	2.17 (**<0.01**)	1.30 (0.40)	2.63 (**<0.01**)	3.50 (**<0.01**)
T4	1.94 (**<0.01**)	1.91 (**<0.01**)	2.64 (**<0.01**)	1.47 (0.29)	2.68 (**<0.01**)

8501 ORAL

Phase II-trial of Concomitant Hyperfractionated-accelerated Radiotherapy (HART) With Cisplatin (Cis) Plus Cetuximab (Cet) for Locoregionally Advanced Inoperable Squamous Cell Head and Neck Cancer − Early Response and Acute Toxicities

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Background: Cet is a potent inhibitor of the epidermal growth factor receptor and has shown activity in squamous cell carcinoma of the head and neck (SCCHN) enhancing both radiotherapy and chemotherapy. We conducted a single arm phase II-trial to investigate the feasibility, efficacy and safety of combination therapy with Cis, Cet and HART.
Materials and Methods: Patients (pts) with stage III or IV, M0 SCCHN were enrolled and treated with an initial dosage of Cet (400 mg/m^2), followed by weekly dosage of 250 mg/m^2 during HART, which started with a prescribed dosage of 2.0 Gy per day for three weeks followed by 1.4 Gy twice daily to a total dosage of 70.6 Gy to the gross tumour volume. Cis 40 mg/m^2 was administered weekly (d1, 8, 15, 22, 29, 36).
Results: From February 2007 through November 2010, 74 pts were enrolled, 68 pts with a median age of 56 years (range 37 to 69 years) were evaluable. Of these 65 pts (96%) ⩾90% RT dosage, 50 pts (74%) ⩾90% Cet dosage and 56 pts (82%) ⩾4 cycles Cis 40 mg/m^2 were applied. Complete remission rate (CR) was observed in 23/68 (34%). Selective lymph node dissection was performed 6−8 weeks after end of radiation treatment for 16 pts (24%) with CR on primary tumour but residual neck disease. Furthermore partial remission (PR) was achieved in 29/68 (43%), so an overall response (OR) of 52/68 (77%) was reached. No change/stable disease occurred in 3/68 pts (4%) and progressive disease (PD) occurred 1 pt (1%). 3 pts have died due progression of disease. The most common grade ⩾3 toxicity were mucositis (59%) and dysphagia (52%), grade >2 Cet related toxicity included dermatitis acneiform (15%) within the radiotherapy portals.
Conclusions: Combination therapy of SCCHN consisting of HART-Cis-Cet is an highly active regimen. Further phase III-trials have to investigate the novel concurrent radiochemoimmunotherapeutic with the standard chemoradiation approach.