Conclusions: In this prospective study, low expression of BRCA1 and probably high expression of ERCC1 appeared to predict better prognosis in advanced relapsed OC. Unlike prior retrospective findings in T treated sarcoma, low BRCA1 and high ERCC1 levels did not predict longer PFS and OS in this trial. These results warrant further study to identify molecular biomarkers of outcomes with T therapy.

8006 ORAL

Improved outcome after first line chemotherapy in BRCA1- and BRCA2-associated ovarian cancer compared with sporadic ovarian cancer patients

C. Seynaeve[1], D. Hoogwerf[1], M. Kriege[1], S. Beugelink[1], A. Jager[1], J. Collee[2], E.M. Berns[1], M.E.L. Burg van der[1], C.W. Burger[3], P. Vencken[3]. *[1]Erasmus MC Daniel den Hoed Cancer Center, Medical Oncology, Rotterdam, The Netherlands; [2]Erasmus MC Daniel den Hoed Cancer Center, Clinical Genetics, Rotterdam, The Netherlands; [3]Erasmus MC Daniel den Hoed Cancer Center, Gynaecological Oncology, Rotterdam, The Netherlands*

Background: Data of *in vitro* and small retrospective studies suggest that ovarian cancer (cells) without functional BRCA1 of BRCA2 proteins are more sensitive to DNA-damaging chemotherapy, such as platinum-containing regimens. In some clinical studies a better survival has been observed for BRCA1/2-associated versus sporadic ovarian cancer patients. Data, however, are not consistent; moreover, separate data for BRCA1- and BRCA2-associated ovarian cancer are lacking. Therefore, we compared response to, progression free (PFS) and overall survival (OS) after first line chemotherapy between BRCA1-associated, BRCA2-associated, and sporadic ovarian cancer patients, respectively.
Patients and Methods: From the database of the family cancer clinic, we selected 86 BRCA1 and 12 BRCA2 mutation carriers diagnosed with ovarian cancer between 1980 and 2008, and having been treated with chemotherapy. Patients were matched in a 1:2 ratio for year of birth and diagnosis (within 5-years periods) with 194 sporadic ovarian cancer patients. A Chi-square test was used to test for differences in type of responses, and Kaplan-Meier survival analysis to calculate PFS and OS.
Results: Mean age at diagnosis was 52 years. Stage III/IV was observed in 73%, and was not significantly different between the groups. First line chemotherapy mainly consisted of platinum-based regimens (96%). A complete (CR) or partial response (PR) was significantly more often observed in both BRCA1- and BRCA2-associated than in sporadic ovarian cancer patients (88% vs 100% vs 65%, respectively). The median PFS was significantly longer in BRCA1- (2.3 years, $p = 0.008$) and BRCA2-associated patients (2.9 years, $p = 0.03$) than in the sporadic group (1.4 years). Also, the 2- and 5-years PFS rates were significantly higher in the BRCA1- and BRCA2-associated groups than in the sporadic group, being 55% vs 58% vs 34%, and 33% vs 50% and 18%, respectively. The median OS was 6.2 yrs vs >10 yrs vs 3 yrs in the BRCA1, BRCA2 and sporadic groups, respectively ($p = 0.004$; and 0.009). In multivariate analysis, corrected for FIGO-stage and differentiation grade, the longer PFS and OS in the mutation carrier cohorts remained significant.
Conclusion: The response to, as well as the outcome after chemotherapy is significantly better in BRCA-associated than in sporadic ovarian cancer. Further, BRCA1- as well as BRCA2-associated ovarian cancer are different entities, with a trend for BRCA2 being most sensitive to chemotherapy.

8007 ORAL

Enhanced expression of Annexin A4 in clear cell carcinoma of the ovary and its association with chemoresistance to carboplatin

A. Kim[1], S. Serada[1], T. Takahashi[1], B. Ripley[1], Y. Souma[1], M. Fujimoto[1], T. Naka[1]. *[1]National Institute of Biomedical Innovation, Laboratory for Immune Signal, Ibaraki, Japan*

Background: Clear cell carcinoma (CCC) of the ovary is known to be resistant to the platinum-based chemotherapy compared to serous or endometrioid adenocarcinoma of the ovary. Over 20% of all cases with ovarian cancer in Japan are classified as CCC and for unknown reasons this percentage is markedly higher (by approximately two-fold) than in Europe and the United States. The purpose of our study was to identify a candidate protein which is associated with chemoresistance of CCC, and to investigate the specific mechanism of chemoresistance conferred by the identified protein.
Materials and Methods: Two human ovarian cancer cell lines (OVISE-CCC/ OVSAHO-serous adenocarcinoma) were used for proteomic analysis. Enhanced expression of Annexin A4 was identified in ovarian CCC cells using 2-D differential gel electrophoresis (2D-DIGE) and mass spectrometry. Annexin A4 expression was further evaluated by real time RT-PCR and Western blot analysis using several ovarian cancer cell lines. Immunohistochemical analysis of Annexin A4 was performed in 126 epithelial ovarian cancer tissue samples. Chemoresistance (IC_{50} values) and intracellular platinum accumulation, following carboplatin treatment of Annexin A4-transfected non-CCC cells and empty vector control cells, were analysed by modified MTT assay and atomic absorption spectrophotometry.
Results: Annexin A4 levels were elevated in CCC cells compared with non-CCC cells as determined by real time RT-PCR and Western blot analysis. Immunohistochemical analysis demonstrated significantly high expression of Annexin A4 protein in ovarian CCC tumors compared with serous and endometrioid adenocarcinoma tumors ($p < 0.01$). Annexin A4-transfected cells were more resistant to carboplatin ($IC_{50} = 42$ mM) than control cells ($IC_{50} = 23$ mM). Intracellular platinum levels were significantly lower in Annexin A4-transfected cells compared with control cells following carboplatin treatment ($p = 0.0020$) and following an additional 360 min of carboplatin-free incubation ($p = 0.0004$).
Conclusion: Expression of Annexin A4 is elevated in ovarian CCC tumors and is associated with chemoresistance in cultured ovarian cancer cells. These results demonstrate that Annexin A4 confers chemoresistance in ovarian cancer cells in part by enhancing drug efflux. Annexin A4 may thus represent a novel therapeutic target of chemoresistance in patients with ovarian CCC.

Poster presentations (Tue, 22 Sep, 14:00−17:00)
Gynaecological cancer

8008 POSTER

Expression of inhibin/activin subunits (alpha, betaA and betaB) in normal and carcinomatous cervical tissue

J. Jückstock[1], T. Blankenstein[1], S. Kunze[1], U. Jeschke[1], K. Friese[1], I. Mylonas[1]. *[1]Klinikum der Universität München-Innenstadt, Gynaecological Oncology, München, Germany*

Background: Inhibins are dimeric glycoproteins composed of an alpha-subunit and one of two potential beta-subunits, (βA or βB), showing substantial functions in human reproduction and in endocrine-responsive tumours. In this study the expression of these different subunits was examined in normal and pathological cervical tissue.
Materials and Methods: Normal cervical tissue ($n = 10$) and cervical adenocarcinomas ($n = 6$) in archival specimens were examined by immunohistochemistry.
Results: Immunoreactivity of inhibin-α could be demonstrated in glandular cervical epithelium, while squamous epithelia cells did not express this subunit. Interestingly no analyzed cervical adenocarcinoma showed any staining reaction of this subunit. Both inhibin-βA and -βB subunits were seen in glandular epithelium of both normal and pathological cervical tissue. However, squamous epithelia cells also expressed these subunits, but with a lower intensity.
Conclusions: In this preliminary study we demonstrated an immunohistochemically detected expression of inhibin-α, -βA and -βB subunits in normal as well as in pathological cervical specimens. Possibly inhibin molecules are useful serological markers in cervical cancer. The subunits are expressed immunohistochemically to a certain amount, thus suggesting possible functions in normal and pathological cervical tissue. Moreover, inhibin-alpha is considered a tumour suppressor in several gynaecological malignancies, including endometrial and ovarian cancer. If this holds also true for cervical cancer will be evaluated in future studies.

8009 POSTER

Human papillomavirus type16 (HPV16) E6 gene variations in cervical intraepithelial lesion from Thai women

A. Chaiwongkot[1], I. Pientong[1], T. Ekalaksananan[1], B. Kongyingyoes[2], S. Siriaungkul[3], C. Suthippintawong[4], S. Vinyuvat[4], K. Tungsinmunkong[5], S. Triratanachat[6], T. Chuangsuwanich[7]. *[1]Faculty of Medicine, Khon Kaen University, Microbiology, Khon Kaen, Thailand; [2]Faculty of Medicine, Khon Kaen University, Pharmacology, Khon Kaen, Thailand; [3]Faculty of Medicine, Chiang Mai University, Pathology, Chiang Mai, Thailand; [4]Institute of Pathology, Ministry of Public Health, Medical Services, Bangkok, Thailand; [5]Faculty of Medicine, Prince of Songkla University, Pathology, Songkla, Thailand; [6]Faculty of Medicine, Chulalongkorn University, Obstetrics and Gynecology, Bangkok, Thailand; [7]Faculty of Medicine, Siriraj Hospital Mahidol University, Pathology, Bangkok, Thailand*

HPV16 infection is found as a major risk factor for cervical cancer in Thai women. Variations of HPV16 E6 gene that lead to amino acid changes may be associated with increased oncogenicity. This study aimed to investigate