concentration ratio was 959. Cytotoxic concentrations of >0.1 μmol/L were detected in peritoneal fluid for a median period of 4 days (1−4) after HIPEC.
Conclusions: Cytoreductive surgery followed by HIPEC with paclitaxel seems feasible in stage III ovarian cancer patients. HIPEC with paclitaxel is associated with a highly advantageous pharmacokinetic profile. Locoregional drug concentrations are in the micromolar range rather than in the nanomolar range as for plasma levels after intravenous administration, while cytotoxic drug levels are maintained in the peritoneal cavity for several days after HIPEC.

5034 POSTER

Pharmacokinetics of trabectedin in women with recurrent ovarian cancer

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Background: Trabectedin (Yondelis®, ET-743) is an anticancer compound that has shown clinical activity in soft tissue sarcoma (STS), ovarian, prostate and breast cancer. Pharmacokinetics (PK) of trabectedin has been well defined in patients with STS and in other solid tumours during the Phase I and II program. This report describes the PK behaviour of trabectedin in women with platinum-sensitive, recurrent ovarian cancer (ROC) included in a Phase II study.
Methods: Adult women with ROC were randomised to receive trabectedin as 1.5 mg/m^2 over 24 hr infusion (schedule A) or 1.3 mg/m^2 over 3 hr infusion (schedule B) both every 3 weeks. All patients received dexamethasone premedication. Fourteen plasma samples were obtained within 168 hr after starting the first infusion. An LC/MS/MS assay was used to measure trabectedin in plasma. PK parameters were estimated by standard noncompartmental methods.
Results: The PK of trabectedin was characterised in 18 patients (11 schedule A, 7 schedule B) with adequate renal and hepatic function, and a median age of 58 y (range 41−72 y). Mean (SD) C_{max} and AUC_{inf} were 1.4 (0.7) ng/ml and 59.7 (27.2) ng*hr/ml for schedule A and 12.1 (6.4) and 73.6 (41.7) for schedule B. Mean (SD) Cl and V_{ss} were 47.4 (12.2) l/hr and 3848 (2319) l for schedule A and 38.2 (16.2) and 2698 (1423) for schedule B. Half-life was 95.8 (46.3) hr for schedule A and 96.1 (45.4) for schedule B. Interpatient variability was moderate/high, with variation coefficients ranging from 26% to 60%. Patients with grade 3−4 neutropenia during cycle 1 had longer half-lives than patients with grade 0−2. Patients with grade 3−4 ALT increases had higher C_{max} than patients with grade 0−2. Response rates (RR) were 44% and 36% in patients with (n = 18) and without PK (n = 89) respectively. Half-lives in responding patients showed a trend to be longer than those in nonresponders. Results about PK/PD relationships should be interpreted considering the low sample size. PK results with schedule A matched closely those from a prior study in STS patients [C_{max} = 1.22 (0.48), AUC_{inf} = 65.0 (37.8), half-life = 138.3 (109.2)]. Mean C_{max} in schedule B appeared higher than that in a prior Phase I trial [C_{max} = 6.41 (SD = 1.49; n = 6)].
Conclusions: PK characteristics of trabectedin in patients with ROC are in line with those observed in patients with other malignancies, showing a long terminal half-life, wide distribution, moderate total body clearance and moderate/high interpatient variability.

5035 POSTER

A protective role of magnesium salt supplementation against anaemia induced by paclitaxel and cisplatin in ovarian cancer (OC) patients

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Background: Paclitaxel and cisplatin are both well accepted drugs used in the treatment of ovarian cancer (OC) and anemia appears to be one of side effects. Cisplatin is a culprit of anemia by erythropoietin deficiency. We assessed the endogenous erythropoietin concentrations and other red blood cells parameters in OC patients given chemotherapy with magnesium salt supplementation vs. placebo.
Patients and Methods: A double-blind, placebo-controlled, randomised study conducted where magnesium sulphate was administered at a dose of 5 g as an iv infusion before each course of chemotherapy with PP (paclitaxel 135 mg/m^2 over 24 h infusion plus cisplatin 75 mg/m^2) every 3 weeks. Magnesium subcarbonate continuation at a dose of 500 mg given three times daily p.o. among courses. We performed analysis of serum concentrations of erythropoietin, haemoglobin and magnesium before treatment and before sixth course of chemotherapy.
Results: Between February 2003 and January 2006, 40 OC patients were enrolled. None of the patients received recombinant human erythropoietin or red blood cell transfusion. Haemoglobin levels decreased from 12.07±1.03 g/dl (mean±SE) (control 11.75±1.03 g/dl; p = 0.344) before treatment to 11.10±1.17 g/dl (control 10.04±1.17; p = 0.009) before sixth cycles in study group. Erythropoietin serum concentrations weren't changed significantly in both groups. Mg serum concentrations decreased significantly from 2.12±0.10 mg/dl to 1.63±0.19 mg/dl before sixth cycles (p < 0.0001) in placebo group.
Conclusions: Our results indicate that magnesium salt supplementation during chemotherapy may decrease anemia independently of erythropoietin serum changes.

5036 POSTER

Tumor advancement in uterine endometrial cancers patients

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Objective: The aim of this study was to investigate the expression of ephrinB2 and EphB4 in uterine endometrial cancers to analyze the ephrinB2/EphB4 functions against clinical backgrounds.
Methods: In 53 uterine endometrial cancers and 18 normal endometrium tissue samples immunohistochemistry and real-time RT-PCR to determine the histoscores and messenger RNA (mRNA) levels of ephrinB2 and EphB4, respectively, were carried out. Patient prognoses were analyzed with a 5-years survival rate.
Results: The localization of ephrinB2 and EphB4 was dominantly in the cancer cells of uterine endometrial cancer of all investigated cases. EphrinB2 and EphB4 histoscores were highly correlated with ephrinB2 and EphB4 mRNA levels, respectively (P < 0.01). Both the histoscores and mRNA levels of ephrinB2 and EphB4 significantly increased with clinical stages (I < II < III, P < 0.05), dedifferentiation (G1 < G2 < G3, P < .01) and myometrial invasion (A < B < C, P < .01 for ephrinB2 and P < 0.05 for EphB4) in uterine endometrial cancers. The 5-years survival rates of the 24 patients with high ephrinB2 and EphB4 expression were poor (57% and 63% respectively), for the 29 patients with low ephrinB2 and EphB4 expression, they were significantly higher (83% and 84%, respectively).
Conclusions: EphrinB2 and EphB4 were overexpressed during the tumor advancement as dedifferentiation and myometrial invasion. EphrinB2/EphB4 might work on tumor advancement and could be recognized as a novel prognostic indicator for uterine endometrial cancers.

5037 POSTER

Pelvic node control in locally advanced uterine cervical cancer treated with concurrent chemoradiotherapy

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Background: Several investigators recommend surgical debulking of enlarged lymph nodes prior to definitive radiotherapy for patients with locoregionally advanced uterine cervical cancer. The purpose of this study was to evaluate pelvic node control in patients with cervical cancer treated with concurrent chemoradiotherapy (CCRT) without surgical resection.
Material and Methods: Ninety-nine patients with uterine cervical squamous cell carcinoma treated with CCRT were analyzed. The stage distributions were: IB2 3; IIA 2; IIB 50; IIIA 1; IIIB 42; and IVA 1. Cervical tumor diameter and pelvic node status were assessed by MRI. The median maximum tumor diameter was 58 mm (range, 36−86 mm). Thirty-five patients had positive pelvic nodes (⩾10 mm, in the shortest diameter). The largest positive node diameter ranged from 10−50 mm (median, 18 mm). All patients received CDDP (20 mg/m^2 for 5 days every 21 days), pelvic external beam RT (PERT), and high-dose-rate intracavitary brachytherapy (HDR-ICBT). The planned RT schedule consisted of PERT with 40 Gy/20 fractions followed by HDR-ICBT with 18−24 Gy/3−4 fractions and PERT with 10 Gy/5 fractions using a midline block. Thirty-one of the thirty-five node positive patients received boost irradiation (6−10 Gy/3−5 fractions) to the involved nodes. The irradiation dose from HDR-ICBT to the pelvic nodes was estimated at a point 6 cm lateral to the midline at the level of the vaginal fornix. Doses of ERT and HDR-ICBT were simply summed and used for the pelvic node dose-response analysis. The median total dose was 60 Gy (range, 52−64 Gy) for positive nodes and 54 Gy (range, 51−55 Gy) for negative nodes. The median follow-up of the 81 surviving patients was 50 months (range, 8–102 months).
Results: Four-year overall survival (OAS), pelvic control (PC), and distant metastasis-free (DMF) rates for all 99 patients were 81%, 91%, and 80%, respectively. Four-year OAS, PC, and DMF rates for node-positive/node-negative patients were 62%/91% (P = 0.002), 82%/95% (P = 0.08), and

62%/87% (P = 0.008), respectively. Pelvic nodal recurrence was observed in 4 patients. One patient developed isolated pelvic node recurrence while the other 3 had concurrent recurrences at other sites, including 1 with a cervical tumor and 2 with cervical tumors and distant metastases. Nodal recurrence rates by the largest diameter were 1/64 for node-negative patients, 1/15 for nodes 10−14 mm, 0/13 for nodes 15−29 mm, and 2/7 for nodes ⩾30 mm.
Conclusion: Pelvic nodal metastases less than 30 mm were well controlled by CCRT without surgical resection using RT dose delivered. Thus, surgical debulking may be omitted for patients with enlarged pelvic nodes measuring less than 30 mm.

5038 POSTER

Prospective study on helical Tomotherapy as a new technique for whole abdominal irradiation in patients with advanced ovarian cancer

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Background: The prognosis for patients with advanced epithelial ovarian cancer remains poor despite aggressive surgical resection and platinum-based chemotherapy. Despite whole abdominal irradiation's (WAI) clinically proven efficacy, the use of radiotherapy in ovarian cancer has profoundly decreased mainly due to high toxicity. The purpose of this prospective study was to evaluate feasibility and toxicity of WAI applied by tomotherapy as a new method of image-guided IMRT.
Materials and Methods: Four patients who met our inclusion criteria (radically operated ovarian cancer FIGO stage III, R1 or R2 <1 cm and adjuvant platinum-based chemotherapy) were treated with WAI applied by tomotherapy to a total dose of 30 Gy in 1.5 Gy fractions as additional therapy. Organs at risk (OARs) were bone marrow, kidneys, liver, spinal cord, thoracic and lumbosacral vertebral bodies and pelvic bones. The planning target volume (PTV) included the entire peritoneal cavity. PTV was adapted according to breathing motion as detected in a 4D-respiratory-triggered computed tomography. Inverse treatment planning was done with the Hi-ART tomotherapy planning station. Daily control of positioning accuracy was performed with megavoltage computed tomography (MV-CT). Two patients are currently under therapy and more are about to be included in our study.
Results: Helical tomotherapy enabled a very homogeneous dose distribution with excellent sparing of OARs. A very satisfying target coverage was achieved, with a mean V90 of 94.0%, a mean V95 of 82.6%, a mean V105 of 6.5% and a mean V110 of 0.58%. Mean liver dose was 22.22 Gy and mean kidney doses were 8.62 Gy and 8.26 Gy respectively. Treatment could be performed in a mean time span of 21.3 minutes. No grade III/IV acute and late toxicity occurred. Until to date we did not encounter any relapse.
Conclusions: Helical tomotherapy is feasible and fast for WAI. It enabled excellent coverage of the PTV and effective sparing of liver, kidneys and bone marrow. No severe side effects occurred. Our technique provides a new promising alternative for intensity modulated WAI. Therefore we initiated a phase I/II study to evaluate the role of tomotherapy WAI in the treatment of advanced ovarian cancer.

5039 POSTER

Prognostic impact of pMI (mitotic index of proliferating cell population) in cervical cancer patients treated with carbon-ion beam

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Background: We previously reported that the pMI (Mitotic Index [MI] of Proliferating Cell Population) was a strong prognostic factor in cervical cancer patients treated with photon beam (Nakano and Oka. Cancer 1993). In this study, we investigated whether pMI predicted prognosis in cervical cancer patinets treated with carbon ion beam, or not.
Materials and Methods: Tissue sections were obtained from all of 27 patients with stage IIIB bulky (19 patients) and IVA (8 patinets) squamous cell carcinomas of the cervix treated with carbon ion beam at National Institute of Radiological Sciences between 1995 and 1997 as a phase I&II study with dose escalation fashion (protocol: 9403). The treatment was started with an initial dose of 52.8 GyE/24 fraction, and was increased by 4.8 GyE per step to total 72.0 GyE/24 fraction. Their ages ranged from 36 to 72 years old (mean and median: 56 and 54 years old). All patients were followed for a minimum of 5 years or until death. The MI and Ki-67 labeling index (Ki-67-LI) were determined by H&E and immunohistochemical staining, respectively. More than 1000 tumor cells were evaluated in each specimen. The pMI was calucurated as following formula; (pMI)=(MI)/(Ki-67-LI). Cut-off value of the pMI was defined as 3.5, according to the result of our previous report. The Fisher's exact probability test were used for the statistical analysis of differences. The data of the multivariate analysis for local control and survival were assessed with the Cox proportional multivariate analysis.
Results: The pMI ranged from 0.6 to 8.9 (mean and median: 3.9 and 3.2). A total of 44% (12/27) of tissue specimens had greater than 3.5 of the pMI. Nine of 12 patients with greater than 3.5 of the pMI had local recurrence, while only 4 of 15 patients with less than 3.5 of the pMI had local recurrence (p = 0.02). Ten of 12 patients with greater than 3.5 of the pMI were died of the disease within five years, while 6 of 15 patients with less than 3.5 of the pMI were died within five years (p = 0.047). The multivariate analysis indicated that the pMI had the strongest impact on both local control (standard regression coefficient = 0.48 and p = 0.019) and survival (standard regression coefficient = 0.48 and p = 0.017) among the variables, including clinical stage and irradiated dose.
Conclusions: Theses results suggest that high pMI predict a poor prognosis in patients with squamous cell carcinomas of the cervix treated with carbon ion beam.

5040 POSTER

Recurrent or metastatic endometrial cancer: Prognostic factors after taxane-based systemic chemotherapy

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Background: Taxane-based chemotherapy has been recently introduced as an effective therapeutic option in recurrent or metastatic endometrial carcinoma (RMEC), exhibiting considerable efficacy even in the more aggressive types of uterine papillary-serous carcinoma (UPCC) and clear-cell carcinoma (UCCC). The aim of the current study was to determine the potential prognostic factors in RMEC after taxane-based chemotherapy.
Patients and Methods: 110 eligible patients who received pacitaxel-containing regimen for RMEC were retrospectively evaluated and follow-up data were recorded. Potential prognostic factors for overall survival (OS) were identified with the Kaplan-Meier method in univariate analysis and the Cox regression model in multivariate analysis.
Results: Although non-endometriod (UPSC and UCCC) histology is associated with a worse prognosis compared to endometriod adenocarcinoma (14.46 months, 95% CI: 8.66−20.26 months vs 17.57 months, 95% CI: 11.91−23.24, p = 0.093), histology does not constitute an independent prognostic factor for OS in multivariate analysis (HR = 1.43, 95% CI: 0.82−2.48, p = 0.21). Performance status (PS) at diagnosis and histological grade are independent prognostic factors for overall survival (p = 0.007 and 0.045 respectively). Patients who do not relapse within the field of previous external radiation have a 45% reduction in the risk of cancer-associated death compared to patients who do so (HR = 0.55, 95% CI 0.32−0.93, p = 0.026).
Conclusion: Despite the documented efficacy of paclitaxel-containing regimens against UPSC and UCCC, patients bearing such tumours continue to be associated with a worse prognosis compared to those with endometriod tumours, albeit not significantly. PS at diagnosis, histological grade of the tumour and relapse within the field of previous external radiotherapy constitute a valid prognostic model in the RMEC setting after taxane-based chemotherapy.

5041 POSTER

Non-dysgerminomas of the ovary: a retrospective analysis at N.N. Blokhin Russian Cancer Research Center

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Purpose: This is a retrospective review of treatment results of patients with malignant ovarian germ cell tumors (MOGCT) except dysgerminomas in Clinical Pharmacology and Gynecology Departments, N.N.Blokhin Russian Cancer Research Center (NNBRCRC) between 1990 and 2006.
Methods: A total of 56 patients with nondysgerminomas were retrospectively reviewed. The histologic subtypes included endodermal sinus tumors (n = 13), immature teratomas (n = 13), embryonal carcinoma (n = 1),