marrow status (P= 0.054). The median distant disease free survival was 78 months (73 82, 95% CI) in patients with negative, and 72 months (61 82) in patients with positive bone marrow status (P= 0.051). Multivariate analysis revealed the presence of ITC as significant, independent risk factor for the subsequent development of distant metastases (relative risk 3.6, P= 0.046).

Despite the locoregional predominance of cervical cancer at the time of primary diagnosis, the presence of ITC in the bone marrow is frequent and indicates an increased risk for the development of distant metastases. This information may prove useful to stratify patients for systemic treatment.

161 POSTER

Radical pelvic radiation for uterine cervix cancer in the elderly

P. Vitek[1], P. Holeckova[1], M. Pala[1], J. Zamecnik[2], V. Stahalova[1]. [1] *Institute of Radiation Oncology, Dept. of Radiation Oncology, Praha 8, Czech Republic;* [2] *Insitute of Postgraduate Education in Medicine, Praha, Czech Republic*

Radical radiation treatment in the elderly remains a controversial issue. A sufficient number of recent references confirms comorbidity but not age itself as a limiting factor of both radio and chemotherapy. Upon the analysis of our historical group of patients with uterine cervix cancer we have tried to examine whether radical pelvic radiation in elderly patients could be advocated, whether it had the same effect and whether it did not compromise the patient status. 2 272 patients with uterine cervix cancer have been treated at the Institute of Radiation Oncology, Prague, Czech republic in the period 1972-1990. Median age was 56 years (18-89) (s=13,6). 1033 of them were eligible for a retrospective analysis i.e. there was a continuous evidence of their status within 5 years after their treatment. This group consisted of 111 pts. more (elderly) and 922 less (younger) than 70 years old at the time of treatment onset. There was a good correlation of disease stage between these subgroups (χ^2 = 5,47) (In the elderly: stage IA 1 pt., IB 18 pts., IIA 9 pts., IIB 38 pts., IIIA 5 pts., IIIB 30 pts., IV 11 pts.). All patients have been radically treated by a combined radiation therapy (40-48 Gy, Linac, Co and 30-35 Gy brachytherapy), predominantly by less sophisticated techniques than current patients (including 2 opposed fields technique). The retrospective data were not sufficient to provide reproducible information on late effects of therapy. However there are reliable data on mortality related to cancer.

The cause of mortality within 5 years after treatment - related vers. not related to cancer - was not significantly influenced by the age (p=0,141). Moreover the probability of death within 5 years related to cancer was very similar in both subgroups (0,32 younger vers. 0,39 elderly, p=0,58). There were no severe or lethal complications of radiotherapy. There was no significant difference between younger and elderly in survival time of those, who died for either reason within 5 years (20 vers. 18 months, p=0,805). The 5 year survival rate was 62% and 48% for younger and elderly patients respectively. These results confirm the age itself does not influence the natural history of the disease and the effects of pelvic radiation. Therefore radical radiation therapy should be administered in elderly patients except cases with a substantial comorbidity.

162 POSTER

Significant impact of integrin beta-3 expression in cervical cancer treated with radiotherapy +/- chemotherapy

G. Gruber[1], R.H. Greiner[1], J. Hess[1], P.W. Stiefel[1], H.J. Altermatt[2], V. Djonov[3]. [1] *University of Bern, Department of Radiation Oncology, Bern, Switzerland;* [2] *Pathology Laenggasse, Bern, Switzerland;* [3] *University of Bern, Institute of Anatomy, Bern, Switzerland*

Objective: To investigate the prognostic role of integrin beta-3 (b3) expression in patients with cervical cancer (cCa) treated with radiotherapy ± chemotherapy.

Patients and Methods: Eighty-two biopsy specimen from locally advanced cCa patients (median age: 63yrs) could be evaluated in regard to integrin beta-3 expression by immunohistochemistry (- / + / ++). All patients were treated with radiotherapy (median total dose: 69Gy), in 27 patients combined with cisplatin ± 5-FU. Mean follow-up was 41 months.

Results: Thirty-two out of 82 (39%) primary tumors were 'negative', 50 (61%) were 'positive' ('+': n=31; '++': n=19) for beta-3-expression. The actuarial 5-yrs-local-progression-free-survival difference was statistically significant (p=0.002) with 85% for 'negative' patients and 51% for 'positive' patients ('+': 46%; '++': 56%). The corresponding values are 85% vs 57% ('+': 67%; '++': 50%) for distant-metastasis-free-survival (p=0.037) and 78% vs 41% ('+': 44%; '++': 39%) for cause-specific-survival (p=0.013).

Conclusion: For the first time we could demonstrate that integrin-beta-3-expression offers the possibility to stratify between different risk profiles in patients with cervical cancer.

163 POSTER

Capecitabine chemoradiation for stage II B- III B cervical cancer: preliminary phase I results, Mexican Oncology Study Group.

L. Torrecillas, D. Ballesteros, G. Cervantes, P. Cortes, F. Aldaco, R. Martell, A. Fernandez, B. Ortega, L. Rosas, A. Erazo. *Medical Center 20 Noviembre ISSSTE, Medical Oncology, Mexico DF, Mexico*

Background: cisplatin (DDP) and radiotherapy for advanced locoregional cervical cancer has been adopted in many centers as standard first line treatment. However, toxicity and the need for weekly inpatient iv infusion makes DDP an inconvenient and intermittent radiosensitiser. Capecitabine (X) is an oral fluoropyrimidine which mimics continuous 5-FU infusion through twice-daily administration. Final conversion of X depends on thymidine phosphorylase (TP). Levels of TP are 5 times higher in cervical tumor cells compared with normal tissue and radiotherapy upregulates TP activity in tumor but not in healthy tissue. X dose with pelvic radiotherapy has been defined in phase I trials for rectal cancer, but fields, dose and local tissue toxicity differ in cervical cancer thus we performed a phase I trial.

Materials and methods: we escalated X to determine the maximum tolerated dose with simultaneous standard pelvic radiotherapy (1.8 Gy/day x 5/week total 4-field external dose 45 Gy followed by brachytherapy). X was administered twice daily, 5 days a week.

Results: to date, 21 patients with squamous cell cervical cancer, stage IIB 15, IIIB 6, median age 51 years (range 39-66) have been treated at: 2x250 mg/m^2 (n=4), 2x375 mg/m^2 (n=4), 2x500 mg/m^2 (n=4), 2x650 mg/m^2 (n=3), 2x825 mg/m^2 (n=6). Mild toxicity was: diarrhea 15 pts, stomatitis 2 pts, hand-foot syndrome 1 pt, vomiting 2 pts, external skin and vulvar dermatitis 3 pts, cystitis 3 pts, neutropenia 1 pt, thrombocytopenia 1 pt, liver ALT/AST rise 3 pts. The only dose-limiting toxicities (one patient with grade 3 ALT rise and one patient with bilirubin grade 2 rise for more than 1 week) were reached at a dose level of 2x825 mg/m^2. Three more patients are still under treatment for this dose level 2x825 mg/m^2. Twelve pts are currently evaluable for response: 10 CR with a median DFS of 5.5 months; one PR and one progression.

Conclusions: X can be safely administered concurrently with radiotherapy in cervical cancer with encouraging early efficacy results. X is a particularly convenient option for chemoradiaition and the final safe dose will be tested in a phase II study by MOSG.

164 POSTER

Primary therapy of ovarian cancer with Paclitaxel/Carboplatin/Gemcitabine (TCG): a Phase II Study (Ovar-8 protocol)

A.K. Belau[1], U. Wagner[2], J. Pfisterer[3], B. Richter[4], A. Stähle[5], C. Jackisch[6], H.J. Lück[7], W. Schröder[8], S. Olbricht[9], A. du Bois[10]. [1] *University of Greifswald, Gynecology;* [2] *University of Marburg;* [3] *University of Kiel;* [4] *Medizinische Klinik I, Dresden;* [5] *Vincentius Krankenhaus, Karlsruhe;* [6] *University of Marburg;* [7] *Medizinische Hochschule Hannover;* [8] *ZKH Bremen;* [9] *University of Magdeburg;* [10] *HSK Wiesbaden*

Introduction: The addition of a third, non-cross-resistant substance to Paclitaxel (T) and Carboplatin (C) might be considered as a method to improve the primary therapy of ovarian cancer. In preparation of a phase III study (*Ovar-9*), the addition of Gemcitabine (G) was tested under a multicenter, non-randomized 2-cohort study.

Methods: In the period from October 2000 until July 2002, the study included 55 female patients with a median age of 54 years (range 25-73). After the first operation of a primary ovarian cancer (FIGO Ic- IVa), they were treated with a combination of T (175 mg/m^2 3 h IV on day 1), C (AUC 5 IV on day 1) and G (800 mg/m^2 IV on days 1+8), q 3 weeks. G wasn't applied in the first cohort with ANC <1000/µl and in the second cohort with WBC <1500/µl on day 8 (dosage level -1). A prophylactic dose of G-CSF wasn't required in the protocol. The toxicity was recorded according to NCI-CTC and response was assessed per the RECIST (response evaluation criteria in solid tumors) criteria.

Results: The toxicity data of 52 female patients (261 cycles) were assessable. 40 women were assigned to the cohort 1 and 15 to cohort 2. As haematological toxicities of grade 3/4 in % of cycles occurred: anaemia 3.8/0, thrombocytopenia 11.8/1.5, leucopoenia 31.4/ 3.4 and febrile neutropenia 0.4/0. As non-haematological toxicities grade 3/4 were

observed: obstipation 6/0, diarrhoea 6/0, CNS/mood 2/2, pain/myalgia 8/2, dyspnoea 8/0, thrombosis 4/0 and infections 5/0. Due to toxicity, an alteration of the cycle became necessary for 4% of cycles. The intensity of dosage reached 90.5% for C and T, and 72.8% for G. The latter was due to the reduction of dosage on day 8 (level 1) in cycles 2-6.

Conclusions: Since the moderate haematological and mild non-haematological toxicity proved to be controllable the analysis were lead into an international, GCIG (Gynecologic Cancer Intergroup), randomized phase III intergroup study (*Ovar- 9*) that compares the standard therapy (T/C) with the triple combination. The study has been active since August 2002.

165 POSTER

Gemcitabine (G) plus carboplatin (C) in patients whose epithelial ovarian carcinomas (EOC) relapsed ≥6 months after platinum-containing first-line therapy: Preliminary results of a phase II study

F. Kose[1], J. Sufliarsky[2], S. Beslija[3], P. Saip[4], K. Krejcy[5], T. Minarik[2], E. Fitzthum[5], G. Tulunay[1], A. Melemed[5]. [1] *SSK Maternity and Women's Health Teaching Hospital;* [2] *Narodny Onkologicky Ustav Bratislava;* [3] *Klinicki Centar Univerziteta Sarajevo;* [4] *Istanbul University, Oncology Institute;* [5] *Eli Lilly and Company*

Background: Ovarian cancer, over 90% of which is epithelial in origin, remains the leading cause of gynecologic cancer deaths, accounting for 4% of all cancer diagnoses in women and 5% of all cancer-related deaths, collectively.

Objectives: The primary objective of this study was to determine the overall response rate (ORR) of G plus C in patients with EOC that relapsed e 6 months after discontinuation of first-line platinum therapy. Secondary objectives were to assess toxicity, duration of response, time to progressive disease, time to treatment failure, and survival time.

Methods: During each 21-day cycle, patients received G 1000 mg/m^2 on days 1 and 8 and C AUC 4.0 on day 1 (after G).

Results: From July 2001 to November 2002, 40 patients enrolled at 4 sites. The median age was 54.5 years (range, 38-79). Patients' World Health Organization (WHO) performance statuses were 0 (80%) or 1 (20%). Eighty percent of pts received prior paclitaxel in combination with a platinum. A total of 234 cycles were delivered (median 6; range, 2-8). Based on Southwest Oncology Group (SWOG) response criteria, 6 patients (15%) had complete responses, 18 patients (45%) had partial responses, and 1 patient (2.5%) had a partial response in nonmeasureable disease, for an ORR of 62.5% (95% CI, 45.8%-77.3%). CTC grade 3/4 toxicities were primarily hematologic, consisting of neutropenia (42.5%/35.0%), leukopenia (30.0%/0.0%), thrombocytopenia (15.0%/2.5%), and anemia (15.0%/0.0%). Two (5.0%) patients had grade 3 infection with grade 3/4 neutropenia. Other grade 3 toxicities were febrile neutropenia, anorexia, gastritis, epistaxis, abdominal pain, nausea, and vomiting (all in 1 patient each). No patients died on-study or within the 30-day post-study follow-up period.

Conclusion: These preliminary results show that G plus C has activity in EOC cancer, and a toxicity profile that is expected and manageable. Although analyses are ongoing, G plus C appears to be a promising treatment option for relapsed EOC in platinum-sensitive patients. Final data, including time-to-event results, will be available at the meeting.

166 POSTER

Ct scan-generated small bowel dvh's, and small bowel toxicity profiles, in post-operative gynaecological cancer patients. a prospective study assessing the impact of a bellyboard device

J. Martin, K. Fitzpatrick, R. McCloy, G. Horan, C. Faul. *St. Lukes Hospital, Radiation Oncology, Dublin 6, Ireland*

Aims: 1) To see if small bowel volumes in radiation portals were reduced by treating prone on a bellyboard versus supine without.This would be analysed using CT-planning 3D imaging and DVH's. 2) To establish relationships between small bowel DVH's and patients' RTOG/LENT-SOMA acute bowel toxicity scores, which were recorded prospectively.

Methods: 45 Post-op gynae. cancer patients to be prospectively assessed, first underwent conventional simulation supine and prone, as for standard 3 or 4 field pelvic radiotherapy. Planning CT scans were then done in the above two treatment positions. Small bowel was outlined on all slices, and DVH's acquired for both positions. The volume of small bowel in the radiation portals was analysed for supine and prone. Actual treatment was delivered prone, and acute bowel toxicity recorded prospectively. Observations:1.) Small bowel in the lateral radiation portals significantly reduced when prone on the bellyboard - 6-111cc reduction at 95% CI; p=0.04. 2.) Patients with no or negative reduction when prone had significantly smaller abodomino-pelvic volumes as calculated by CT planning; p, E. Wong, J. Chen, T. Coad, G. Rodrigues, M. Lock, G. Bauman (Canada)

Background: Whole pelvic IMRT is complex, requiring multiple fields, often with field splitting and junction problems. We developed an Intensity Modulated Arc Therapy (IMAT) radiation technique that simplifies treatment planning and delivery.

Materials and Methods: Five women with high-risk carcinoma of the endometrium received 4-6 cycles of paclitaxel and carboplatin sequentially with radiotherapy. Using axial CT slices, the tumor bed, iliac and pre-sacral vessels, ± lower para-aortic region were contoured as GTV. A CTV with 5-10 mm margin and PTV with 7 mm margin were generated. The small bowel, iliac crests, femoral heads, bladder and rectum were contoured as critical organs. Balancing the complexity of the arc technique with normal organ sparing, two anterior intensity modulated arcs, from 300° to 30° (IEC convention) and 330° to 60° were used. DVH, dose distribution, dynamic MLC patterns, and comparisons to conventional treatment and 5-field IMRT inverse plans were generated.

Results: Using the IMAT, 95% of the tumor volume received dose above 45 Gy, the nodes 40-45 Gy and bladder/ rectum ≤ 45Gy. This technique allowed sparing of the small bowel, iliac crests and femoral heads. The dose to the iliac crests was reduced compared to conventional radiation therapy and similar to IMRT. The volume of small bowel receiving dose above 45Gy was 80%, 10%, 15% for conventional, IMRT, and IMAT technique respectively. Treatment has been well tolerated with no significant acute toxicities.

Conclusions: IMAT provides an effective technique to treat the tumor bed and regional nodes while allowing a conformal avoidance of the bone marrow and small bowel compared with conventional radiation therapy. While critical structure sparing is similar to multi-field IMRT, our method is simpler to plan and deliver and was well tolerated. Ongoing work will assess both the clinical outcome and long term toxicity of this multi-modality treatment strategy.

167 POSTER

Is 5-year survival rate a real measure of outcome in cervix cancer patients treated by radiotherapy? Long-term results in patients treated with external beam radiation therapy and high dose rate brachytherapy

L. Souhami[1], R. Corns[1], M. Duclos[1], G. Stanimir[2]. [1] *Radiation Oncology,* [2] *Gynecology, McGill University, Montreal, Canada*

Background: To evaluate the long-term outcome of patients with carcinoma of the cervix treated with a combination of external beam radiation therapy (EBRT) and high dose rate brachytherapy (EBRT).

Material and Methods: From 1984 and 1977, a total of 283 previously untreated patients (pts) with cervix cancer were treated with a combination of EBRT and HDRB. The median age was 62 years and there were 23 pts with stage IB disease (9%), 50 with IIA (18%), 116 with IIB (43%), 7 with IIIA (3%) and 77 with IIIB (27%). EBRT consisted of irradiation to the whole pelvis to a median dose of 46 Gy (range: 40-54.6 Gy) and HDRB typically in 3 insertions given weekly, each insertion delivering a dose of 8 Gy to point A. Chemotherapy was not given to any of these pts. The primary endpoints assessed in this analysis were survival, pelvic control and toxicity. In an attempt to determine predictive variables for survival and pelvic control, multivariate analyses, using a Cox proportional hazardous model were performed. Variables investigated were stage, age (<47 vs >47 years), overall duration of treatment (<47 vs >47 days), HDRB scheduling (<25th vs >25th day) and total dose (<98 Gy vs >98 Gy).

Results: At a median follow-up time of 84 months for pts at risk, the 5-, 10- and 15-year overall survival rates are 60%, 55%, and 49%, respectively. There was a continuous decrease in survival from cervix cancer with longer follow-up. The long-term survival rates and pelvic control rates for the different stages are shown in the table below. A total of 78 pts (24%) failed in the pelvis. On multivariate analysis, stage ($p < 0.0001$), age ($p = 0.019$) and treatment duration ($p = 0.057$) had a significant impact in survival, while stage, age, treatment duration and brachytherapy scheduling

Stage	5-year Survival/ Pelvic Control	10-year Survival/ Pelvic Control	15-year Survival/ Pelvic Control
Overall	60%	55%	49%
IB	62%/78%	62%/78%	62%/78%
IIA	75%/90%	67%/86%	57%/86%
IIB	70%/80%	63%/74%	58%/74%
IIIB	48%/55%	40%/55%	40%/55%