922 POSTER

NCIC CTG IND102: A phase II study of the oral platinum compound BMS-182751 in patients with advanced and or recurrent squamous cell carcinoma of the cervix

M. Trudeau[1], G. Stuart[1], H. Hirte[1], P. Drouin[1], M. Plante[1], P. Bessette[1], H. Dulude[2], D. Lebwohl[3]. *[1]NCIC CTG, IND Program, Kingston; [2]BMS, Canada; [3]BMS, Wallingford, United States*

Aim: BMS-182751 (JM-216) is an orally bioavailable platinum compound with activity in platinum and platinum resistant preclinical models.

Methods: We conducted a phase II study of BMS-182751 given at a dose of 30 mg/m^2 daily × 14 days every 5 weeks.

Results: 18 patients (pts) with advanced/recurrent squamous cancer of the cervix not amenable to curative therapy with measurable disease who had received no prior chemotherapy for systemic disease were entered, all of whom are evaluable for response and toxicity. Median age was 47 yrs (35–74 yrs); all pts had received prior pelvic irradiation (RT); 4 pts had received cisplatin as a radiosensitizer; PS was 0 (6 pts), 1 (7 pts) and 2 (5 pts); sites of disease included nodes (10 pts), pelvis (5 pts), lung (4 pts) and bone (3 pts). Median number of cycles was 2 (1–5) with 8 pts receiving 3 or more cycles. Toxicity was modest and usually grade 1 or 2 in severity with the most frequent drug related toxicity including nausea (56%), fatigue (50%), anorexia (39%), diarrhea (39%), vomiting (39%), constipation (28%) and altered taste (22%). 6 pts had grade 3 or 4 granulocytopenia and only 1 pt grade 3 or 4 thrombocytopenia. 2 pts had grade 2 or 3 creatinine increases. There were no treatment related deaths. 1 pt with a treatment free interval of 30 years achieved a partial response (PR), while 12 pts had a best response of stable disease (SD).

Conclusions: BMS-182751 is generally well tolerated, but has limited activity in pts with recurrent cervical cancer.

923 POSTER

Telomerase: The molecular marker for cervical cancer screening

V.G. Reddy[1], N. Singh[1], S.K. Jain[2]. *[1]All India Institute of Medical Sciences, Biochemistry, New Delhi; [2]All India Institute of Medical Sciences, Gynecology and Obstetrics, New Delhi, India*

Cervical cancer is one of the commonest cancers in women and is routinely screened by Pap smear. Screening for HPV 16 and 18 has augmented the sensitivity of this test. But still some cases escape. We focused on defining the utility of assaying telomerase activity as a possible screening marker for cervical cancer as telomerase activation is required for cellular immortality and oncogenesis.

With informed consent a total of 50 cases were studied, 20 confirmed carcinoma cervix cases, 20 control cervical samples from hysterectomy specimens and 10 cervical scraping from healthy young women.

We observed that all the cervical carcinoma cases (100%) were telomerase positive. Among the control cervical samples from hysterectomies the one's with any underlying risk factor like HPV-16/18 infection, abnormal cytology or histopathology were telomerase positive while the perfectly normal ones were telomerase negative. The cervical scraping samples, which did not have any underlying high risk factors, were also telomerase negative. The findings suggest that telomerase activity is a better screening marker for the early diagnosis of cervical cancer.

924 POSTER

Are vaginal bleedings in postmenopausal patients an early symptom of malignancies?

B. Gerber, A. Krause, H. Müller, T. Reimer, G. Kundt, J. Markowitzky, K. Friese. *Universität Rostock, Ob/Gyn, Doberaber strasse 142, Postfach 1008 88, D-18055 Rostock, Germany*

Purpose: Vaginal bleedings in postmenopausal patients (pts.) may be an indicator of malignancies, but will mostly disregard by the affected woman. Otherwise conservative management can delay the definitive, histological diagnosis of postmenopausal bleedings. The presented retrospective analysis was conducted to examine the relationship between delayed diagnosis and tumor stage as well as it's value as a prognostic factor.

Methods: Between January 1990 and June 1997 206 pts. with an endometrial cancer (EC) and 72 pts. with a cervical cancer (CC) were treated at our hospital. All together 248 of the 278 pts. stated abnormal vaginal bleedings. The time between the indicated first episode of vaginal bleeding and the definitive histological diagnosis (bleeding interval) was correlated retrospectively with the age, body mass index, hypertension, diabetes, endometrium thickness by transvaginal ultrasound, tumor stage, grading, and also analysed with regard to survival and recurrence. The median follow up time was 50 (min. 19–max. 84) months.

Results: Pts. with EC and CC differed significantly with regard to the median age (67 vs. 62 years, p = 0.024). The median bleeding interval of pts. with EC was in tumor stage Ia/b: 12 weeks (25th–75th percentiles: 6–16); Ic: 16 (6–20); II: 16 (12–26) and III/IV: 28 (16–78) weeks. The bleeding intervals of prognostic favorable stages Ia/b were shorter than in stages Ic (p = 0.11), II (p = 0.0001), and III/IV (p = 0.0001). An increasing bleeding interval correlates with increased age (p = 0.032), endometrium thickness (p = 0.001) and tumor stage (p = 0.0001). Disease free survival and overall survival decreased significantly with longer bleeding intervals. By multivariate analysis with regard to disease free survival we confirmed age (p = 0.025) and tumor stage (p = 0.0001) as independent prognostic factors. Pts. with CC revealed median bleeding intervals of 16 weeks in stage Ib and 20 weeks in stages II–IV (p = 0.28).

Conclusion: In patients with endometrial cancer advanced tumor stages correlate with prolonged bleeding intervals. The presented data support the hypothesis that postmenopausal vaginal bleeding represents an early symptom for endometrial cancer. Bleedings due to postmenopausal cervical cancer represent a late symptom.

925 POSTER

Transvaginal color Doppler for predicting pathological response to preoperative chemoradiation in locally advanced cervical carcinoma: A preliminary study

J. Alcazar, M. Jurado, R. Cañón, I. Azinovic. *Clinica Universitaria, Pamplona 31008, Spain*

Purpose: In order to evaluate the role of transvaginal color Doppler ultrasonography (TCD) in predicting pathological response to preoperative chemoradiation in patients with locally advanced cervical cancer.

Methods: Ten patients with histologically proven locally advanced cervical cancer were evaluated by TCD prior to treatment. Tumour volumen, number of vessels within the tumour, lowest resistance index (RI), maximun peak systolic velocity (PSV), and the ratio between the number of vessels and tumour volume (Tumor vascular density, TVD) were calculated. All patients underwent preoperative chemoradiation and radical surgery. Complete pathological response (pathCR) was considered when no residual tumour was found on surgical specimen. Partial pathological response (pathPR) was considered when residual tumour was found.

Results: PathCR was achieved in three patients (30%), whereas 7 (70%) had pathPR. Mean tumoral volume was not statistically different between those with pathCR (33.2 cm^3) and those with pathPR (20.3 cm^3) (p = 0.305). Tumors with pathCR had lower mean number of vessels (3.3 vs 5.3, p = 0.01), lower TVD (0.1 vs 1.1, p = 0.05) and higher RI (0.41 vs 0.29, p = 0.03).

Conclusions: Although these data are preliminary, our results suggest that TCD may be useful for predicting pathological response to preoperative chemoradiation in patients whith locally advanced cervical cancer.

926 POSTER

Stepping source (Ir-192 HDR) versus linear distributed and fixed sources (Co-60 HDR) in brachytherapy of cervical cancer: Our clinical experience

S. Čikarić, S. Stupar-Petrović, I. Marjanov, Lj. Rudan, V. Plešinac, J. Stanković. *Institute for Oncology and Radiology of Serbia, Yugoslavia*

Purpose: A retrospective analysis is reported on the resuls of irradiated 216 patients with cervical cancer of all stages (FIGO) using stepping sorce (Ir-192 HDR: γ rays of 0.35 MeV – Microselectron) versus linear distributed and fixed sources (Co-60 HDR: γ rays of 1.25 MeV – Selectron) in brachytherapy and EBT (x-rays of 6–10 MeV).

Material: Distribution patients by stages was (Ir-192 group versus Co-60 group): St. I – 32 v. 17, St. II – 36 v. 49, St. III – 34 v. 37 St. IV – 6 v. 5 and all stages – 108 v. 108 pts. Squamous cell carcinoma was dominant hystopathological type (cca 95%). There were no patients younger than 20 years and peack incidence occurred in the 45–55 age group.

Methods: We combined transvaginal irradiation (Ir-192 HDR v. Co-60 HDR: 4–5 × 7–8 Gy/.A with uterine tube and 2 vaginal ovoids at radical irradiated group or 2 vaginal ovoids at post-operative irradiated group with doses 4 × 7–8 Gy/0.5 cm) with external beam therapy (36–46 Gy/18–22 fraction with or without central lead shield).

Results: ≥ 4-year survival (Ir-192 group v. Co-60 group) was (corrected

for cases lost to follow-up): St. I-24/27 (89%) v. 14/16 (88%), St. II-24/31 (77%) v. 28/36 (78%), St. III – 8/27 (30%) v. 10/22 (45%), St. IV – 0/3 (–) v. 0/4 (–) and all stages – 56/88 (64%) v. 52/78 (67%). Late post-irradiation sequelae were (French-Italian glossary): G1-20% v. 14%, G2 – 8% v. 10%, G3 – 10% v. 7%, G4 – 4% v. 1% and total – 42% v. 32%.

Conclusion: ≥4-year survival of stage III was better in Co-60 group and late postirradiation complications were more frequent in Ir-192 group of patients.

927 POSTER

Phase II trial of paclitaxel and cisplatin in advanced or recurrent adenocarcinoma of the endometrium

M. Dimopoulos[1], C. Papadimitriou[1], G. Aravantinos[2], L. Moulopoulos[1], D. Gika[1], P. Athanassiades[1], V. Georgoulias[3]. [1]*Department of Clinical Therapeutics, University of Athens School of Medicine;* [2]*Department of Medical Oncology, Agii Anargiri Hospital;* [3]*Department of Medical Oncology University of Crete School of Medicine, Greece*

Purpose: To evaluate to activity and toxicity of the combination of paclitaxel with cisplatin in patients with primary stage IV or recurrent endometrial adenocarcinoma.

Methods: The treatment consisted of paclitaxel 175 mg/m^2 IV over 3 hours followed by cisplatin 75 mg/m^2 every 3 weeks for a total of 6 courses.

Results: Twenty-four patients were included. The median age was 62 years (range: 45 to 75 years). Histology consisted of endometrioid adenocarcinoma in 16 patients, the median PS was 1 and twelve patients had previously received radiotherapy. Objective response was documented in 16 patients (67%) including 7 complete and 9 partial responses. The median remission duration was 7 months, the median time to progression was 8 months and the median overall survival was 21 months. Grade 3 or 4 toxicities consisted of neutropenia in 22%, neurotoxicity in 13%, and nausea and vomiting in 9%. No patient died due to toxicity.

Conclusions: The combination of paclitaxel and cisplatin is a relatively well tolerated and active regimen for the treatment of patients with advanced or recurrent endometrial cancer.

928 POSTER

Combined radio-chemotherapy (CR) in advanced cervical cancer: A phase-II trial with cisplatin and bleomycin

N. Kantardzic[1], S. Beslija[2], M. Musanovic[1], A. Cardzic[1], N. Kazic[1], N. Mahic[1], N. Paraganlija[1], J. Lomigoric[1], M. Banjin[2]. [1]*Institute of oncology, Radiation therapy, Sarajevo, Yugoslavia, Bosnia-Herzegovina;* [2]*Institute of oncology, Medical oncology, Sarajevo, Yugoslavia, Bosnia-Herzegovina*

Cancer of the cervix is the first or second most common form of cancer in the female population in developing or poor countries. It is the one of the most frequent malignancies in Bosnia and Herzegovina since the war. The problem of large numbers of young women with late diagnosis, and advanced stage tumors is compounded by the poor results of conventional therapy.

In our efforts to prevent high frequency of pelvic recurrences and distant metastasis, we performed single Institution study, in which from January 1997 to June 1998, 25 previously untreated women with advanced cervical cancer were treated with a therapy consisting of fractionated external beam irradiation (45 Gy), administered using 1.8–2.0 Gy/day, 5 days a week, to the whole pelvis with local boost if indicated, followed by two intracavitary cesium (Cs) applications (2 × 15 Gy), combined with cisplatin (50 mg m−2) and bleomycin (20 mg m−2). Cytotoxic agents were given intravenously on every 3 weeks for a total of four courses during the irradiation. The patients ages ranged from 34 to 52 years, median 49 years. There were 11 FIGO stage IIB, 2 IIIA, 11 IIIB, and 1 IVA. Acute toxicities (g WHO grade 2) were leucopenia (14 of 25 patients), diarrhoea (10/25), cystitis (2/25), abdominal pain (19/25), nausea (13/25) and skin desquamation (10/25). Clinically diagnosed pelvic response was achieved in 84.0% (21/25) with a complete response of 32.0% (8/25). As yet, after a median follow-up of 11.2 months, 21 of 25 patients (84.0%) are alive and well (persistent complete/partial remission), two patients (8.0%) are alive with local progression, two (8.0%) have died from pelvic and/or distal recurrence.

Concomitant cisplatin and bleomycin and radiotherapy is a safe and tolerable mean of treatment for locally advanced cervical cancer. The true advantage for survival, however, can be demonstrated only after completion of randomised trials comparing CR with conventional radiation therapy which is in plan to be performed on our Institute.

929 POSTER

Neoadjuvant chemotherapy in locally advanced cervical carcinoma (LACC): Mitomycin C (M), bleomycin (B) and cisplatin (C) combination (MBC)

R. Peredo, F. Delgado, S. Bonicatto. *Fundación Oncológica Argentina FUNDONAR, Hospital San Roque, La Plata, Argentina*

Objective: To evaluate the toxicity and efficacy of MBC in pts with squamous cell LACC.

Methods: Between January 1993 and June 1998, 43 pts with squamous cell LACC were treated with MBC: Mitomycin 10 mg/mq d1, Bleomycin 15 IU d1–3 and Cisplatin 40 mg/mq d1–3, repeated every 3 weeks for 3 cycles, prior to radical histerectomy plus pelvic lymphadenectomy. Eligible pts had histologically confirmed squamous cell carcinoma of the cervix, age =/< 70 years, ECOG PS =/< 2 and adequate pulmonary, hematopoietic, liver and renal function, FIGO Stage IIB, IIA and IIIB, no prior chemotherapy (CT) or radiotherapy (RT) and measurable or evaluable disease by CT scan. Pts received 3 cycles and were the assessed for feasibility of surgery.

Results: 43 pts were included, and 41 were evaluable for response and toxicity. Median age 51.3 years (range 24–70). After NCT, partial objective response was achieved in 28/41 (68.3%) pts and radical histerectomy was possible in 5/42 (11.9%) pts. 13/42 (30.9%) pts experienced no change. Mean of duration of response in not operable pts was 3.21 months (range 1–5). With a total of 122 cycles, toxicity resulted in ECOG G3-4 myelosupression 10 cycles (8.2%) and gastrointestinal 6 cycles (5.4%). There were no toxic death, and all toxicities were reversible.

Conclusion: MBC is a feasible and well tolerated regimen in LACC, with significant anti-tumor activity and reduced toxicity. Operability can be achieved in 11.9% of cases. Nevertheless, the duration of response in pts who remain not operable after NCT was short.

930 POSTER

Results of treatment in patients with cervical carcinoma Stage II distal B

C. Haie-Meder[1], W. Gargouri[1], C. Breton[1], P. Morice[2], C. Lhommé[3], A. Gerbaulet[1]. [1]*Institut Gustave-Roussy, Radiotherapy, Villejuif;* [2]*Institut Gustave-Roussy, Surgery, Villejuif;* [3]*Institut Gustave-Roussy, Gynecology, Villejuif, France*

From 1985 to 1995, 58 patients with cervical carcinoma with a distal involvement of the parametrium stade IIB were treated with a combination of external irradiation and brachytherapy. Pelvis irradiation (+/– para-aortic area) consisted of 45 Gy delivered in 5 fractions per week of 1.8 Gy. Endocavitary brachytherapy, using the mould technique, delivered 15 Gy within the refeence volume according to the ICRU recommendations. Brachytherapy characteristics: the mean 15 Gy reference volume was 340 cc (139 cc–689 cc). The mean bladder dose was 25 Gy (13 Gy–48 Gy) and the mean maximal rectal dose was 26 Gy (5 Gy–55 Gy). The total reference air kerma was 1.94 cGy/m^2 (0.9 cGy/m^2–3.2 cGy/m^2). The overall 3-year and 5-year survival was 75% and 65%. Four patients presented a non sterilization of the tumor. Nine patients presented a local recurrence: 6 central and 3 lateral pelvic recurrences. Three patients presented grade 3 or 4 complications: 2 urinary complications and 1 digestive complications. In this series of patients with advanded stage IIB disease, a combined therapeutic approach with external irradiation and endocavitary brachytherapy following ICRU recommendations gave good results with a satisfactory local control.

931 POSTER

I–II stage endometrial carcinoma: Is tumoral volume a prognostic factor?

A. Bonetta[1], N. D'Abbiero[2], C. Iotti[2], G. Zini[2], L. Armaroli[2]. [1]*Radioterapia, Istituti Ospitalieri, Cremona;* [2]*Radioterapia, ASMIN, Reggio Emilia, Italy*

Purpose: to evaluate retrospectively the impact of the tumoral volume on the outcome in the treatment of endometrial carcinoma in I–II stage.

Material and Methods: from 1/1/85 to 31/12/94 219 patients were admitted in this study; among these, 113 patients received postoperative radiotherapy (isocentric box technique, median dose of 46 Gy (min 40, max 55) with 1.8–2 Gy per fraction. Among the well known prognostic factors we have also analysed the tumoral volume, distinguishing two groups: endometrium infiltrated for more (>1/2) or less (>1/2) than half of its volume. This data is defined on anatomo-pathological macroscopic description of the tumor (extension on endometrial mucosa, diameter of the cancer mass compared to uterine cavity). The group is stratified as follow: for volume