Table 1

GI	stool-frequency	mucous/pain	bleeding
II°	3%	2%	21%
III°	1%	0%	1%

Table 2

URO	pollakisuria	nycturia	pain	hematuria	stenosis
II°	9%	23%	9%	5%	0.3%
III°	3%	3%	2%	1%	2%

vesicles, neoadjuvant HT, diabetes, cardiovascular disease, acute toxicity > I°. Univariate predictors for a higher incidence of late side-effects were: GI: prostate dose (p=0.035) and acute toxicity (p=0.005); URO: body mass index (p=0.059), cardiovascular disease (p=0.036) and acute toxicity (p=0.002). Multivariate predictors were: GI: acute toxicity (p=0.004) and prostate dose (p=0.032), URO: acute toxicity (p=0.002) and cardiovascular disease (p=0.023).

Conclusions: The incidence of moderate (III°) rectal or urologic late toxicity after CRT is low (<5%). The occurrence of acute symptoms > I° is a predictor for late II°/III° toxicity.

874 POSTER

Ir192 conformal brachytherapy and external beam radiation (EBR-CU.ir192) with or whithout hormonotherapy for locally advanced prostate adenocarcinoma: the Centre François Baclesse experience

D. Brune, F. Lesaunier, D. Benabid, M. M'vondo, M. Henry-Amar. *Centre François Baclesse, Radiotherapy Curietherapy, Caen, France*

Technique: We use temporary transperineal implantation with 2 to 6, 20 cm divergent needles. Implantation is made in 20 mn with general or rachianaesthesia. Needles are loaded with Ir^{192} (low dose rate, LDR) or linked to a projector (high dose rate, HDR).

Treatment protocol: The first protocol involved 15 Gy LDR Cu.Ir^{192} and 45 Gy pelvic EBR. The second protocol combined 2 x 4.7 Gy HDR Cu.Ir^{192} and 45 Gy pelvic EBR. The maximum dose delivered to urethra was 2 x 9 Gy. Within the prescribed radiation doses, the dose rate had no influence on clinical results as well as on toxicity. In locally advanced tumours (T2b-c,T3a-b), hormonotherapy (androcur, nonsteroid antiandrogens or LHRH agonists) was given to 83 patients because of dysuria, postponed therapy or based on recent published findings. Hormonotherapy duration was less than 6 months in 82% of patients.

Study population: From July 1989 to September 1999, 693 patients were treated of whom 291 presented with locally advanced N0, M0 tumours. 208 patients were given EBR-Cu.Ir^{192} only and 83 EBR-Cu.Ir^{192} and hormonotherapy. The two patient groups were similar for age (71 and 70 years in average) and WHO 2-3 performance status (36% and 37%); they differed for Gleason grade (grade ≥ 7: 35% versus 66%, p<0.001) and *ab initio* PSA level (> 20 ng/ml: 52% versus 81%, p=0.002).

Results: The 7-year cause specific survival rates were 85% and 75% in patients treated with and without hormonotherapy, respectively (p=0.59). The 7-year cumulative rates of local failure were 12% and 21% (p=0.10); that of distant metastases were 29% and 28% (p=0.79) and that of biological failure (PSA > 4 ng/ml) were 68% and 63% (p=0.58), respectively. Hormonotherapy duration (< 6 versus ≥ 6 months) had no statistical significant influence on local failure, distant metastases as well as biological failure rates although a trend was observed for less local failure with prolonged hormonotherapy (0% versus 15%). According to the Soma-Lent system, the 7-year cumulative rates of grade II-III urinary and digestive complications were 27% and 7%, respectively, similar in patients given or not hormonotherapy. Sexual complications could not be studied because of the deleterious impact of hormonotherapy on sexual performance.

Conclusion: The contribution of hormonotherapy to EBR-Cu.Ir^{192} is limited in patients with locally advanced prostate adenocarcinoma. Its impact might only concern the incidence of local failure. The administration of hormonotherapy immediately after radiation therapy only is questioned in the light of its efficacy when given at the time a local failure occurs.

875 POSTER

A prospectively randomized phase II trial of pegylated doxorubicin in hormone refractory prostate cancer

A. Heidenreich[1], P. Olbert[1], J. Goecke[1], F. Sommer[2], U.H. Engelmann[2]. [1] *Philipps - University Marburg, Department of Urology, Marburg, Germany;* [2] *University of Cologne, Department of Urology, Cologne, Germany*

Introduction & objectives: Liposomal encapsulation of doxorubicin (Caelyx™) has been shown to reduce non-specific drug delivery to normal tissues and improve the specific delivery to malignant cells. Caelyx™ may also reduce the peak plasma levels of doxorubicin that may be responsible for toxicity. Since doxorubicin shows response rates of 30% in HRPCA, we conducted a prospective randomized clinical phase II trial to evaluate the feasibility, toxicity and therapeutic efficacy of Caelyx™ in HRPCA.

Patients & methods: 48 patients with progressive HRPCA after hormonal therapy and antiandrogen withdrawal were randomized to receive Caelyx™ at 25mg/m^2 every 2 weeks for 12 cycles (group 1), 50mg/m^2 every 4 weeks for 6 cycles (group 2) and 50mg/m^2 every 4 weeks for 3 cycles followed by 40mg/m^2 every 4 weeks for 3 cycles (group 3). All patients received dexamethason 8mg bid on days 1 through 5 and vitamin B 300mg/day. 38/48 patients (79%) presented with severe pain due to osseous metastases equivalent to a pain score of 7.5 on a VAS ranging from 0 to 10. Therapeutic efficacy was recorded by serial PSA serum measurements, toxicity was recorded according to NCIC/CALBG and EORTC QLQ-C30.

Results: Median age was 68.9 (range 58-79) years; mean follow-up was 42 months. Mean pre-therapeutic PSA was 660.4 (8-6340) ng/ml. An objective response (>50% PSA↓) was observed in 17/25 (68%) patients in group 2 and the mean response duration was 6.5 months. None of the remaining patients developed a PSA response. Significantly more patients in group 2 had a pain response (52.6%) than patients in group 1 and 3 (28.6%, p=0.04). Mean 1-year survival was significantly higher in group 2 (42%) than in groups 1 and 3 (6% and 20%, respectively, p=0.02). Toxicity was severe with 24 pts (50%) demonstrating WHO stage III/IV toxicity. There was a significant difference in the type of toxicity between the different groups. Palmar-plantar erythema developed in 60% of group 1 patients (p<0.0005) whereas tachycardia developed predominantly in groups 2 and 3 (20% and 80%, p<0.0005). There was no dose-limiting cardio- or hematotoxicity.

Conclusions: Pegylated doxorubicin has a high palliative efficacy in HRPCA with painful osseous metastases; a short-term objective response was observed in the 40mg/m^2 group. Caelyx® might be a useful component of chemotherapeutic combination therapy in HRPCA.

876 POSTER

Protein microchips for the analysis of prostate specific antigen

E. Dementieva[1], E. Darii[2], A. Rubina[3], A. Zasedatelev[4], T. Osipova[5], T. Ryabykh[6], A. Baryshnikov[7], A. Mirzabekov[8]. [1] *Engelhardt Institute of Molecular Biology, RAS, Biochip-IMB center, Moscow, Russian Federation;* [2] *Engelhardt Institute of Molecular Biology, RAS, Biochip-IMB center, Moscow, Russian Federation;* [3] *Engelhardt Institute of Molecular Biology, RAS, Biochip-IMB center, Moscow, Russian Federation;* [4] *Engelhardt Institute of Molecular Biology, RAS, Biochip-IMB center, Moscow, Russian Federation;* [5] *N.N.Blokhin memorial Cancer Research Center, RF, RAMS, Institute of Experimental Diagnostics and Therapy of Tumors, Moscow, Russian Federation;* [6] *N.N.Blokhin memorial Cancer Research Center, RF, RAMS, Institute of Experimental Diagnostics and Therapy of Tumors, Moscow, Russian Federation;* [7] *N.N.Blokhin memorial Cancer Research Center, RF, RAMS, Institute of Experimental Diagnostics and Therapy of Tumors, Moscow, Russian Federation;* [8] *Engelhardt Institute of Molecular Biology, RAS, Biochip-IMB center, Moscow, Russian Federation*

Background. DNA and protein microchips found wide application in different fields of fundamental and applied science. Three-dimensional gel-based biochips with immobilized proteins developed by the Engelhardt Institute of Molecular Biology RAS can be used for different types of analysis including immunoassays. The goal of our studies was to create microchip-based technique for quantitative assay of prostate cancer marker, prostate-specific antigen (PSA, total and free) in sera of cancer patients.

Material and methods. Microchips with immobilized antibodies to total and free PSA were manufactured. The chip is an array of three dimensional semi-spherical gel elements separated from each other with hydrophobic surface. For the microchip fabrication, solutions of co-polymerization mixtures containing gel monomers and proteins were spotted on a glass slide by a robot. Diameter of gel drops was 50ñ300 μm depending on a robot pin. Polymerization of gel arrays was carried out under irradiation with UV