Results: Sensitivity and specificity of A. O. fluorescent staining in phase I study, were 80% and 100%, respectively, and all the cells from 10 healthy volunteers stained negative. Those in phase II study were both 100% in 16 patients with TCC, and all the cells from 13 healthy volunteers stained negative. p53 IMC and IMH were identical in 95% of the patients with TCC, and all the cells from 9 healthy volunteers did not expressed p53. mdm2 IMC and IMH were identical in 70% of the patients, and all the cells from 20 healthy volunteers did not expressed mdm2.

Conclusions: Our results confirm the usefulness of IMC as a non invasive method for diagnosis and intensive follow-up of TCC. A.O. fluorescent analysis of primary urine derived cell cultures is a promising non-invasive diagnostic technique.

128 POSTER

Ifosfamide (IFO) in the treatment of metastatic hormone refractory prostate cancer

P. Kellokumpu-Lehtinen, T. Lehtinen, T. Tammela. *Departments of Oncology and Urology, Tampere University Hospital, Finland*

Purpose: There is no good chemotherapy available for hormone refractory prostate cancer. To evaluate efficacy, schedule and toxicity of IFO fifteen patients (pts) with metastatic hormone refractory prostate cancer were treated.

Methods: IFO was given every third week at a dose of 5 gr/m^2 per 24-hour infusion on day one or at a dose of 1.5 gr/m^2 on days 1–4 as a short infusion with concomitant mesna uroprotection. Treatment was continued until disease progression (PD), untoward side effects or maximum 6 cycles.

Results: The mean age of the pts was 63 years (range 49 to 74 years). The mean time from diagnosis to the beginning of IFO was 21 months (range 5 to 46). All pts had bone metastasis and PSA from 16 to 1270. Nine (60%) pts received all six cycles with a cumulative IFO dose from 8 to 96 gr. Five pts responded with an over 50% decrease in PSA, and one with an over 45% PSA response and PR in his bone metastasis yielding a response rate of 40%. In three pts PSA remained stable and in six pts PSA increased (PD). The median survival has not yet been reached; the shortest was two months and the longest is 42+. Responses were equal in both treatment schedules, but there were more PD:s in 4-day arm. No serious adverse reactions occurred. Leukopenia grade 1–2 in 6 pts, anaemia grade 1–2 in 5 pts and no thrompocytopenia was reported. Dizziness, fatigue, nausea, vomiting, alopecia and bladder irritation were other adverse events.

Conclusion: IFO seems to be effective in the treatment of prostate cancer (RR 40%) and more pts should be treated to compare the two treatment schedules.

129 POSTER

Enhancement of radiation response of Dunning R3327 prostatic adenocarcinoma by IL-2 and histamine

S. Johansson[1], M. Landström[2], R. Henriksson[1]. [1]*Department of Oncology, Umeå University Sweden;* [2]*Department of Pathology, Umeå University Sweden, Sweden*

Purpose: The purpose of the present study was to investigate whether treatment with histamine alone, Interleukin-2 (IL-2) alone or IL-2 in a combination with histamine affects the result of irradiation (RT) of Dunning R3327 prostatic adenocarcinoma in rats. The growth pattern during treatment, and the effects of the various treatments on the tumours both macroscopically and microscopically at sacrifice were studied.

Method: Rats transplanted bilaterally in the flanks with the syngenic androgen-sensitive Dunning R3327 prostatic adenocarcinoma, were treated with histamine, IL-2 alone or with a combination of both histamine and IL-2. RT was delivered unilaterally to each of the animals, once daily, for 3 consecutive days, to a total dose of 18 Gy. The contra-lateral tumour served as intra-animal control. Treatment with IL-2, histamine and the combination treatment were started one week before RT and continued until the animals were sacrificed, 5 weeks after the RT was finished.

Results: All the tested agents alone but especially the combination treatment with histamine and IL-2 caused considerable reduction of the tumour growth. The effects of RT was potentiated and the most prominent decrease in tumour volume was seen in combination treatment. The microscopical analysis revealed pronounced alterations with e.g. decline in tumour cells and multiple appearance of cysts in the tumour tissue following IL-2/Histamine and RT.

Conclusion: Histamine and IL-2 in clinically tolerable concentrations seems to be a potent combination in enhancing the effects of RT. Further investigation on the underlying mechanisms of action are currently undertaken.

130 POSTER

p53 gene mutations in primary bladder carcinoma

X. Garcia del Muro[1], A. Torregrosa[2], M. Verdú[1], E. Condom[3], J. Muñoz[4], F. Vigués[4], A. Fabra[2], J.R. Germá[1]. [1]*Servei d'Oncología, Institut Català d'Oncología (ICO), Barcelona;* [2]*Institut de Recerca Oncològica (IRO), Barcelona;* [3]*Servei d'Anatomia Patològica, Hospital Princeps d'Espanya, Hospital Duran i Reynals, Ciutat Sanitaria Bellvitge, Barcelona;* [4]*Servei d'Urologia, Hospital Princeps d'Espanya, Hospital Duran i Reynals, Ciutat Sanitaria Bellvitge, Barcelona, Spain*

Transitional cell carcinoma of the urinary bladder is an heterogeneous disease with very different pathologies and clinical outcomes. Superficial lesions recur in 30–80% of patients and 20% of these recurrences become invasives and potentially metastatic. Besides, metastatic diseases appears in 50% of patients with invasive carcinomas after radical cystectomy. Thus, it is very important to identify patients who might benefit from more accurate therapy. To achieve this purpose we studied p53 protein over-expression and the presence of mutations. We evaluated histological sections from 46 patients with bladder cancer using immunoperoxidase technique. p53 was assessed with three different antibodies (PAb 1801, DO-1 and MU-195). TCC tumors were also analysed for p53 mutations using frozen samples by SSCP and direct sequencing analysis of exons 4 through 9. Overall, 20 of the 46 (43%) TCC tumors were positive for at least one antibody. Mutations were identified in 19 of the 41 samples showing a good concordance between positive immunohistochemical staining ($p < 0.05$). Interestingly, p53 mutations occurred more frequently in exons 4.5 and 6. The presence of mutated p53 was correlated with tumor grade ($p < 0.01$) (1 of 15 low-grade tumors vs 18 of 27 high-grade tumors) and stage ($p < 0.01$) (6 of 23 superficial vs 13 of 19 infiltrant tumors). These findings support that mutations in p53 gene appear later in progression and that its presence in superficial and/or low-grade tumors defines a subset of patients with more aggressive tumors which might warrant new strategies of treatment.

131 POSTER*

Correlation between PSA, post-treatment biopsy and clinical outcome in irradiated prostate cancer patients

C. Landmann. *Radiation-oncology, University Hospital Basel, Switzerland*

Purpose: The role of PSA in the detection of local recurrence after radiotherapy (RT) is unclear. The main objective of this study was to examine the correlation between post-treatment PSA values and histopathologic finding in the prostate after definitive external beam RT.

Methods: 61 transrectal ultrasound (TRUS) guided biopsies were performed on 57 asymptomatic patients during routine clinical follow-up after RT for prostate cancer. Median follow-up from conclusion of RT was 26 months.

Results: Out of 61 biopsies 33% showed normal prostatic tissue, 40% showed dysplasia and 26% were positive for cancer. The median PSA value for the negative biopsy group was 1.6 μg/ml. For the positive biopsy group it was 8.4 μg/ml. Only 25% of the patients with positive biopsies developed a clinical recurrence during a 5-year follow-up.

Conclusion: A low PSA value does not exclude a positive biopsy. There is no rationale for routine post-irradiation biopsies in prostate cancer as they rarely reflect therapy outcome.

132 POSTER

High-dose rate interstitial brachytherapy followed by percutaneous irradiation for prostate cancer – First results of a prospective trial

T. Wiegel[1], U. Höller[1], M. Nausner[1], U. Steiner[2], S. Dinges[3], S. Deger[4], W. Hinkelbein[1]. [1]*Dept. of Radiotherapy;* [2]*Dept. of Urology; University Hospital Benjamin Franklin;* [3]*Dept. of Radiotherapy;* [4]*Dept. of Urology, Charite, Berlin, Germany*

Aim: To test the effectiveness and side effects of a combined high dose rate brachytherapy and percutaneous irradiation (RT) for localized prostate cancer in a prospective phase II trial.

Material: Between 10/92 and 6/96 58 patients (pts.) were treated. All pts. were node negative. 4 pts. had T1 tumors, the others T2/T3 tumors. Two