Methods: C595 was reduced with 2-mercaptoethanol and labelling was performed by adding 200 MBq of 99mTc and 0.1 mL of methylene diphosphonate from a bone scanning kit. In vitro studies revealed the size, stability and immunoreactivity of the conjugate. The ability of the conjugate to bind to bladder tumours was initially tested in an ex-vivo model in which five fresh cystectomy specimens containing tumour were filled with 99mTc-C595 for 1 h. Bladders were imaged and biopsies of tumour and normal urothelium taken. The conjugate was then administered intravesically to five patients who had been diagnosed radiologically or endoscopically with bladder cancer. Patients underwent gamma camera imaging post-washout followed by Transurothelial Resection of Tumour (TURT) and biopsy 2 h later.

Results: The direct reduction mediated method produced a stable conjugate of 99mTc-C595 which had an immunoreactivity exceeding 85%. Gel filtration chromatography revealed a single peak of labelled material at the expected 150 kD region. Binding to bladder tumours was confirmed in the ex-vivo model; four out of the five tumours were successfully imaged with a mean tumour:normal ratio of 5.7:1. In the patient studies, four out of the five tumours were imaged with a mean tumour:normal ratio of 22:1.

Discussion: We have successfully labelled the monoclonal antibody C595 with 99mTc. The conjugate is stable in vitro and retains its high immunoreactivity. It has demonstrated its ability to localise to bladder tumours in an ex-vivo model and in patients when given intravesically. On the basis of these results we have embarked upon a study of intravenous 99mTc-C595 immunoscintigraphy in patients with invasive bladder cancer. This reagent may also have an application in diagnostic imaging of other intra-cavity tumours such as ovarian carcinoma.

1402 POSTER

Testicular self-examination (TSE) and testicular ultrasound (TUS) assisted follow-up for the early detection of secondary testicular tumors (STT)

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Purpose: To improve, by an analysis of the results of 3 years' experience, the early detection of STT assisted by monthly TSE and annual TUS.

Methods: Between April 1 1995 and April 1 1998 annually 702, 782, and 761 patients (pts) participated in our new follow-up program. We provided informative materials to our previously treated and controlled testicular cancer patients about the early signs of testicular cancer, the correct method of self-investigation and the importance of the early detection of STT. If any signs of tumor were palpable TUS was applied within a few days. During this period 14 STT cases were detected; 8 other STT pts were managed in our Department in the usual way. The clinical details of the two groups were compared.

Results: In the first group 4 stage I/A and 10 stage I/B tumors were detected; in 10 pts adjuvant chemotherapy was used and in 4 pts a wait and see approach was adopted. In group 2 the stage distribution was 2 I/A, 2 I/B, 1 II/A and 3 III/B. Three pts received adjuvant and 3 curative chemotherapy, 2 were managed by wait and see policies, and 1 received mediastinal irradiation with chemotherapy. Early detection helped to reduce the duration of symptoms, the number of chemotherapy cycles, the side effects and treatment costs.

Conclusion: With regular follow-up the prognosis of STT is good (CR: 100%), and a biopsy to detect CIS is unnecessary. The pts must be followed regularely for up to 5 years, must be prepared to use TSE-techniques and must recognize the impose of the early detection of STT. TUS, in combination with TSE, enhances the chance of early diagnosis; subsequently these tests can provide the basis for a cost-effective treatment with reduced side effects.

1403 POSTER

Radiotherapy (XRT) for testicular intraepithelial neoplasia (TIN)

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Introduction: TIN, also known as carcinoma in situ of the testis, has been recognized as the common precursor lesion of testicular cancer except for spermatocytic seminoma. In case of TIN in a solitary testis or double sided TIN local XRT with 20 Gy is the treatment of first choice yielding 100% cure rates. However, subsequent to XRT patients are at risk for delayed Leydig-cell insufficiency eventually necessitating testosterone substitution. Therefore new treatment strategies aim at the reduction of the total dose of XRT without compromising local control of TIN.

Methods: A multicenter prospective trial was initiated for XRT of histologically proven TIN. Patients were treated with reduced total doses. A progressive dose reduction in 2 Gy steps was performed starting with 18 Gy. All patients had complete hormonal evaluation prior to XRT and again during follow-up. At least one control biopsy after XRT was required. Acute and possible late effects of treatment were prospectively documented using the EORTC-score.

Results: To date, 13 patients have been enrolled for the trial. 11 patients were treated with 18 Gy, 8 of which have so far undergone control biopsy showing complete eradication of TIN. 2 patients were treated with 16 Gy. Acute side effects of treatment are negligible. With a median time to follow-up of 6.8 months (range: 0–18.5 mo.) so far no significant decline in serum testosterone after XRT has been observed.

Conclusion: Preliminary data of the study indicate that XRT of TIN with 18 Gy may be sufficient for local control of this premalignant lesion. Further reduction of the XRT dose in the course of the study may provide a less toxic yet highly efficient therapy for TIN.

1404 POSTER

Inhibition of telomerase activity by antisense oligonucleotides in renal cell carcinoma

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With only a few exceptions, the ribonucleoprotein telomerase is found in malignant, but not in benign tissues. It has been previously shown by us and others that telomerase activity can be found in malignant tumors of bladder and kidney. Telomerase is obviously required for indefinite, malignant growth. Therefore, inhibition of telomerase activity would be a logical approach for therapy of malignant tumors such as renal cell carcinoma. Antisense RNA was chosen for telomerase inhibition in the present study. As tools for this type of therapy are not readily available, vectors were constructed allowing for expression of antisense telomerase RNA in murine RCC cells.

Murine renal cell carcinoma line RENCA, which is highly tumorigenic in mice, displays high telomerase activity, and a mean telomere length comparable to human cells (7–10 kb) was used as a model. After electroporation with eukaryotic expression vectors harboring the RNA template in antisense direction stable transfectants were isolated and tested for telomerase activty (TRAP assay), shortening of telomere length, and proliferative activity. After 35 population doublings 9 out of 13 antisense-transfected RENCA clones showed a reduced replicative potential compared to their non-treated counterparts. Fluorescence-based TRAP assay and measurement of the mean terminal restriction fragment length (TRF) gave evidence for reduced enzyme activity and resumption of telomere shortening in the transfectants. Growth inhibition was, however, of temporary nature only in some cell clones.

Antisense oligonucleotides may effectively inhibit telomerase activity, addition of telomeric DNA, and proliferation of murine renal cell carcinoma.

1405 POSTER

Gemcitabine/cisplatin in advanced transitional cell carcinoma of the urinary tract (TCC): A phase II multicenter trial

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Since January 1997, 54 patients (pts) affected by measurable advanced TCC were treated with gemcitabine 1000 mg/m^2 on days 1, 8, 15 and cisplatin 70 mg/m^2 on day 2 repeated every 4 weeks. Patients' median age was 67 (range 18 to 80), none had prior chemotherapy for metastatic disease, 7 had adjuvant cisplatin-chemotherapy concluded by >1 year, 52 were male and 2 female, 16 had prior cystectomy, 36 had ECOG 0–1 and 18 had ECOG 2 PS respectively. All patients entered on study have been evaluated for response and toxicity (*intent to treat*). Complete (CR) plus partial (PR) response were observed in 26/54 pts (48%) with 8 pts (15%) attaining CR. Twelve pts (22%) showed stable disease (SD) and 6 progressed (15.5%). G3–4 leukopenia was observed in 21 (39%) pts, and G4 neutropenia in 6 (11%). Grade 3–4 thrombocytopenia was recorded in 11 (20%) pts and g4 thrombocytopenia in 3 pts. The median number of cycles delivered was 4; 28 pts (52%) required dosage reduction of gemcitabine or omission to deliver it, on day 15 for neutropenia or thrombocytopenia. No other relevant side effects were recorded. Median time to progression and survival were 26 weeks and 36 weeks respectively. Out of 32 pts with disease related symptoms (haematuria, pain, weight loss), 16 (50%) improved.