months; % S = 44). Total: 2 CR, 8 PR, 11 SD, 21 PD, 6 NE (MOS = 17 months; % S = 38). 21 patients died; 21 are still alive.

Conclusions: (1) we observed 43% of responses (CR + PR + SD) in all patients; (2) a higher (but not significant) rate of CR + PR was observed in the groups treated with IL-2 including regimens (27 and 26% vs 11%) (3) survival was in accordance with these observations.

469 POSTER

SERUM PSA 1-10 YEARS BEFORE THE DIAGNOSIS OF PROSTATE CANCER—COMPARISON WITH BPH AND HEALTHY CONTROLS

H. Mäenpää, U.-H. Stenman, O.P. Heinonen
Departments of Oncology, Clinical Chemistry and Public Health University of Helsinki, Finland

Background: Serum prostate specific antigen (PSA) is widely used for screening of prostate cancer, but little is known about its kinetics during development of the disease.

Patients: Twenty-five prostate cancers were detected among 5908 middle aged men participating in a primary prevention trial for coronary heart disease. Two age matched control groups were chosen: 50 subjects each with BPH and without urologic symptoms, resp. During 1980–1986 blood samples were drawn at 3 mo intervals and 1986–1990 at 6–12 mo intervals.

Results: Serum PSA was $\geqslant 4$ μg/l in 54% of samples drawn $\geqslant$ 4–<5 years before prostate cancer diagnosis. In samples from the same period the proportion was 28% among BPH patients and 3% among healthy controls. The respective proportions were 60%, 22% and 5% $\geqslant$2–<3 years before the diagnosis. In cancer patients the pattern of PSA kinetics was highly variable.

Conclusions: PSA is a valuable tool for prostate cancer screening, but overlapping with other clinical conditions is considerable. Prostate cancer is a heterogenous malignancy, and this is reflected on variable PSA kinetics.

470 POSTER

ORIGINAL REGIMEN OF SUBCUTANEOUS INTERLEUKIN 2 (IL2) AND INTERFERON ALPHA (IFN) IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA (MRCC) INELIGIBLE TO RECEIVE INTRAVENOUS (I.V.) IL2

B. Escudier, J.F. Rossi, A. Ravaud, J. Savary, K. Pignard, S. Négrier, The immunotherapy group of the French Cancer Center Federation, Coordinating Center: Centre L. Bérard, Lyon Cedex 69373, France

We are conducting a multicentric randomized study (IFN vs IL2 vs IL2 + IFN) called Crecy requiring an important selection of the patients. Indeed, only 40% referred patients (pts) are found eligible. For this reason, we set up a study using a more adopted regimen of immunotherapy: subcutaneous IL2 at 9×10^6 UI/day for 6 days associated with IFN 6×10^6 U/day 3 days a week; this cycle is repeated for 5 weeks with one week rest between each treatment cycle. All patients with measurable disease but ineligible for the Crecy study could be proposed to join this trial. 50 patients were treated on an out-patient basis in 18 centers in a period of 7 months. Toxicity was of concern with 2 grade IV (OMS) toxic events including massive pulmonary embolism and sudden death. Most toxic signs were fever, fatigue, anorexia, cutaneous rash, nausea and vomiting. All patients developed various degrees of inflammatory reaction at IL2 injection sites. In terms of tumor response, 2 partial and 1 complete tumor regression were observed among the initial 20 patients. This regimen appeared feasible in most patients ineligible for i.v. IL2 but toxicity is not negligeable and requires careful management. This study confirms that subcutaneous IL2 + IFN regimen can induce tumor responses despite a defavorable selection of the patients.

471 POSTER

THE MANAGEMENT OF PAIN IN ADVANCED PROSTATIC CANCER

D.W.W. Newling, J.A. van der Zee

Pain in advanced prostate cancer is mainly caused by boney metastases. Other causes, such as lower or upper urinary tract obstruction, infection and local spread of the tumor must always be considered. The most satisfactory treatment of pain is to stop the growth of the tumor by hormonal radiotherapeutic or chemotherapeutic measures. When these fail, there is a need for a structured program of analgetic therapy, to maximize its effect. In the early stages, the mainstay of therapy, is the prostaglandin synthetase inhibitors (P.S.I.). Possible side effects of this therapy must be considered in this elderly population. Later combination therapy with opiates with P.S.I. for breakthrough pain will be necessary. The treating physician must familiarize himself with the pain pathways involved, the various receptor proclivities of different opiate preparations and the possible side effects of combination therapy. A structured program for the management of these different patients used in the Free University in Amsterdam, will be presented.

472 POSTER

ADJUVANT AND NEOADJUVANT CHEMOTHERAPY FOR NODAL METASTASES FROM SQUAMOUS CELL CARCINOMA (SCC) OF THE PENIS

G. Pizzocaro, L. Piva, N. Nicolai
Istituto Nazionale Tumori, Milano, Italy

The 5-year survival of patients with radically resected nodal metastases from SCC of the penis is approximately 40%, and the outcome of patients with fixed inguinal nodes is usually poor. Between 1979 and 1990, we submitted to 12 weekly courses of home administered adjuvant VBM (vincristine 1 mg. i.v. day 1, bleomycin 15 mg. i.m. 6 and 24 h. after vincristine, and methotrexate 30 mg. p.os day 3) 25 consecutive patients with radically resected nodal metastases from SCC of the penis. Other 13 patients received the same chemotherapy as primary treatment for fixed inguinal nodes, and 3 patients poorly responsive to neoadjuvant VBM plus other 3 fresh cases with fixed inguinal nodes were treated with 4 courses of PF combination chemotherapy (cisplatin 100 mg/m^2 day 1 followed by fluorouracil 1 g/m^2/day for a 96 h. i.v. infusion).

After a minimum follow-up of 4 years, only 4 patients (16%) relapsed in the adjuvant group, and the only poor prognostic indicator was bilateral nodal metastases (4 of 8 relapsed). As far as fixed nodes are concerned, 5 of the 7 partial responders (54%) to VBM primary chemotherapy could undergo radical surgery: 3 relapsed 15, 27 and 32 months after surgery, and 2 (15%) are alive disease free since 5 and 13 years, respectively, while 5 of the 6 treated with PF achieved a partial remission and 4 could undergo radical surgery with 3 patients (50%) being alive disease free from 3 to 10 years. Toxicity of both regimens was tolerable.

473 POSTER

INTERLEUKIN 2 (RIL2) IN THE TREATMENT OF METASTATIC RENAL CELL CARCINOMA-DURABLE COMPLETE RESPONSE WITH LONG TERM FOLLOW-UP

K.H.M. Rowley[1], D. Mort[1], C.W. Keen[2], M.D. Mason[1]
[1] Velindre Hospital, Whitchurch, Cardiff, U.K.
[2] Mid-Kent Oncology Centre, Maidstone, Kent, U.K.

Metastatic renal cell carcinoma has a poor prognosis with a 5 y survival < 10%. Results of treatment with conventional chemotherapy have been disappointing warranting the use of novel treatment regimens including rIL2 either alone or in combination with conventional chemotherapy. We report the Cardiff experience. 25 patients with metastatic renal cell carcinoma at various sites received rIL2 in the period 1989–1994. 18 patients received rIL2 by continuous intravenous infusion (3 MU/m^2/day for 5 days repeated after a 2-day break); 2 patients received subcutaneous rIL2 (9–18 MU daily, 5 days/week for up to 6 weeks initially) and 5 patients received rIL2 in combination with recombinant human interferon-alpha and 5-fluorouracil as described by Atzpodien (*Eur J Cancer* **29A Suppl.**5:56–58; 1993). Three patients (12%) achieved a complete response—2 after iv rIL2 and 1 after sc, 4 patients (16%) achieved a partial response and 5 patients (20%) had stable disease. The duration of response ranged from 3–64 months (median 8.5 months). The 3 patients achieving a complete response are alive and disease-free at 27, 59 and 64 months respectively. Overall 24% (95% CI 7.3%–40.7%) of patients in this series achieved an objective response which is consistent with results from other centres. Complete responses may be durable in some patients after rIL2 therapy.

474 POSTER

THE ROLE OF TRANSRECTAL ULTRASOUND (TRUS) AND SERUM PSA FOR CLINICAL EVALUATION OF RADICAL RADIOTHERAPY (RT) IN LOCALIZED PROSTATIC CANCER

S. Villa, M. Palazzi, F. Zanoni[1], V. Fossati, M.C. Leonardi, F. Milani
Radiotherapy Department and [1] Urological Department., National Cancer Institute Milan, Italy

Between 1/'93 and 12/'94, 50 patients with clinically localized (11-3,Nx,M0) prostatic adenocarcinoma histologically confirmed, were submitted to RT at our Department. Gleason Pattern Score averaged 5

(range 2–9). Digital rectal examination, TRUS, TC or MR of the pelvis, radioisotope bone scan and measurement of serum PSA were performed for clinical staging, RT was delivered to the prostatic grand only, using 18 MV linear accelerator and a rotational technique. Total dose was 68–70 Gy (200 cGy/day 5 days/week) in continuous course. TRUS and PSA were repeated at 6 months after the end of the irradiation for clinical evaluation of RT effectiveness. At the present, 21 patients have a follow-up longer than six months. In 8/21 cases RT followed an hormonal therapy (OT) whereas 3/8 patients prolonged OT during RT. 11/21 patients had a lesion confirmed by TRUS before RT start and 10/11 showed no dimensional modification at the follow-up. 8/21 showed a reduction of the prostatic volume > 10%.

Pre-RT mean PSA was 6.4 ng/ml (range 0.1–19.4 ng/ml) versus 1.6 ng/ml (0.1–5.4 ng/ml) at the follow-up, six months after the end of RT.

The role of TRUS for the detection of local relapses is undisputed. On the other hand, PSA is a good index to evaluate clinical response to treatment.

475 POSTER

CONFORMAL RADIOTHERAPY OF LOCALIZED PROSTATIC CARCINOMA: ACUTE TOLERANCE AND EARLY EVALUATION OF EFFECTIVENESS

D. Zierhut, M. Flentje, R. Engenhart, V. Rudat, M. Wannenmacher
Department of Clinical Radiology, University of Heidelberg, Im Neuenheimer Feld 400, D-69120 Heidelberg, Germany

Acute tolerance and early effectiveness of conformal 3D-planned radiotherapy of prostate cancer was investigated in a prospective trial.

32 men (44–80 years old) with locally advanced carcinoma of the prostate (stage B2 or C) have been treated by 3D-planned conformal radiotherapy using high energy photons. Total doses from 50 to 70 Gy (mean: 63.9 ± 4.9 Gy) were applied with single doses of 2.0 Gy in 46 ± 4 days. 3D treatment volume was 274.1 ± 113.4 cm^3. Median follow-up is 1.5 years (11–30 months).

11 patients had none, 15 mild (WHO Grade 1) and 6 moderate symptoms (WHO Grade 2, mainly diarrhea, dysuria and polyuria). Acute complications leading to treatment interruption did not occur. In 19 patients symptoms disappeared within 6 weeks after radiotherapy. Only 2 men had symptoms which lasted longer than 3 months. Up to now no relapses and no late complications were detected. Incidence and severety of toxicity was significantly related to the size of treatment volume and to the irradiated volume of bladder and rectum quantified by dose-volume-histograms.

We conclude that 3D-planned conformal radiotherapy allows an effective and well tolerated therapy of localized prostatic carcinoma.

476 PUBLICATION

COMBINED MODALITY TREATMENT OF RENAL CANCER PATIENTS WITH TUMOR THROMBUS INVADING VENA CAVA INFERIOR

A. Mavrichev, S. Krasny, O. Sukonko, S. Polyakov
Research Institute of Oncology and Medical Radiology, Health Ministry of the Republic of Belarus, Minsk

To estimate the efficacy of various regimens of radiotherapy, the results of the treatment of 39 renal cancer patients with tumor thrombus in vena cava inferior, without distant and regional metastases and without tumor invasion of adjacent organs were studied. All the patients were administered radical surgery. The 5-year survival rate in 14 patients who received only surgical treatment (control arm) amounted to 26.92 ± 12.0%. In 14 patients administered preoperative large fraction radiotherapy (single dose 7 Gy to total target dose of 14 Gy), the five-year survival was 63.46 + 13.5% ($P < 0.05$). In 11 patients who received additional postoperative radiotherapy (single dose 2 Gy to total target dose of 40 Gy), the 5 year survival did not significantly differ from that in the 1st study arm and made up 52.94 + 15.37%. The data obtained indicate that combined modality treatment using preoperative large fraction radiotherapy of renal cancer patients with tumor thrombus in vena cava inferior significantly (more than two-fold) increases the 5-year survival rate compared with surgical treatment.

477 PUBLICATION

CHEMO-IMMUNOTHERAPY OF METASTATIC RENAL CELL CANCER (MRCC) WITH SUBCUTANEOUS LOW DOSES OF RE-COMBINANT INTERLEUKIN 2 (IL2) AND 4-EPIRUBICIN (EPI)

G. Colucci, E. Naglieri, V. Gebbia, E. Durini, S. Lucarelli, A. Pellegrino, N. Gebbia, F.P. Selvaggi
Department Medicine, Oncology Institute, Bari and GOIM (Gruppo Oncologico dell'Italia Meridionale), Italy

The clinical use of IL 2 and anthracycline in MRCC is based on preclinical studies that have shown a synergistic antitumor activity, due to an increased specific antitumor immunity (Gautam, Cancer Res. 1991; 51:6133–7). Seventeen pts (6 females and 11 males) with MRCC have been treated in a multicenter phase II study to test the safety and efficacy of low dose subcutaneous IL 2 in combination with EPI. The cycle consisted of IL 2 at 9 million I.U. for the first two days of the first week followed by 4.5 million I.U. for the remaining three days of the first week and for five days/week for five weeks, plus EPI at 25 mg/mq the first day of each week. Median age was 56 years (46–71); median Karnofsky index was 90. Thirteen pts had prior nephrectomy. Three of these had syncronous metastases and were subjected to debulking surgery. Only two pts received prior chemotherapy or immunotherapy. The disease sites were: lung in 9 pts, lymph nodes in 7, kidney in 2, adrenal glands in 2, bone in 3 and renal bed in 2 pts. Fourteen pts are evaluable for response and toxicity, 3 are early to evaluate. We observed one CR and one PR lasting 14+ and 6 months, respectively. In the 8 pts with SD (57%) the median time to progression was 9 months (range 4+ to 12+). CR was obtained after two cycles in superficial lymph nodes and bone lesions while PR was noted in the lung. The toxicity was mild: only one pt had grade 3 hypotension; the most frequent toxicities (grade 1–2) were fever (9 pts) and malaise (5 pts). No pts required a decrease in IL 2 or EPI dosage. This study is ongoing and a larger number of patients are necessary to draw definitive conclusions concerning the efficacy of this chemo-immunotherapy combination in MRCC.

478 PUBLICATION

BRAIN METASTASES FROM HYPERNEPHROMA

C. Nieder, M. Niewald, U. Nestle, K. Schnabel
Department of Radiotherapy, University Hospital, 66421 Homburg/Saar, Germany

A retrospective analysis of 22 cases treated between Oct 83 and Dec 94 was performed. 13 patients had solitary, 9 multiple brain metastases (b.m.). 19 suffered from extracranial metastases too. In 7 cases (6/7 with solitary b.m.) surgery plus whole-brain irradiation was performed (OP + RT). 15 patients received RT alone. The median total dose was 30 Gy. Median survival was 311 days (OP + RT), 116 days (RT, $P = 0.006$), and 132 days (all). After OP + RT improvement of performance status was more frequent. Only 4 patients achieved partial remission of their b.m. after RT alone. Extracerebral metastases and number of b.m. were prognostic factors. *Conclusion:* OP + RT was sign. better than RT alone. A standard palliative schedule of 30 Gy failed to achieve local remission of b.m. and clinical improvement in most of the cases. For hypernephroma metastases a higher total dose might be useful if RT alone is applied.

479 PUBLICATION

RADICAL IRRADIATION TREATMENT IN PATIENTS WITH PROSTATE CANCER: RESULTS AND PROGNOSTIC FACTORS

P. Peczkowski, M. Pilichowska
Urology-Oncology Dept, Cancer Center & Institute, Warsaw, Poland

From October 1984 to June 1991, 261 patients with prostate cancer registered in Cancer Center, Warsaw. A group of 133 pts were selected for radical irradiation. The material was divided into two groups: an "early"-stage T1 (9 pts) and T2 (36 pts) and an "advanced"-stage T3 (73 pts) and T4 (7 pts).

8 pts with Tx were eliminated from the analysis. Overall actuarial 5-years survival, 5-years local control and 5-years disease-free survival were analyzed. Actuarial 5-years survival rate was 98% in the "early" group and 44% in the advanced group ($P < 0.00001$). The actuarial 5-years local control was 93% and 60% respectively ($P = 0.004$). The actuarial 5-years disease-free survival was 85% in the "early" group and 20% in the "advanced" group ($P < 0.00001$). Multivariate analysis demonstrate that T stage, age, elongation time of treatment were independent covariates for overall survival. A log-rank test and Cox regression model were performed for statistic. The late radiation related morbidity was acceptable. The results of radiotherapy of intracapsular disease were very good, but they were not satisfactory in patients with direct extracapsular extension.