463 POSTER

CAN RT-PCR ANALYSIS OF RADICAL PROSTATECTOMY FLUIDS CONTRIBUTE TO CLINICAL DECISION-MAKING ABOUT THE ROLE OF POST-OPERATIVE IRRADIATION FOR PROSTATE CANCER?

B. Corn, J. Moreno, L. Gomella, D. Shupp-Byrne
Jefferson Medical College, U.S.A.

Objective: The decision to add post-op irradiation (RT) following prostatectomy (RP) is controversial. It was hypothesized that use of the Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) technique could lead to early detection of residual local cells to identify patients requiring adjuvant irradiation to prevent wound failure. A study was designed to determine if prostatic cells could be found in the operative site through RT-PCR targeted at PSA and to correlate this with margin status. *Methods:* 14 patients undergoing RP had 10 cc (blood, urine, irrigant) aspirated from the operative field after transection of the dorsal vein, urethra, and bladder. Ficoll gradient fractionation was performed on the specimens and RNA was extracted from the cell pellet. The quality of the RNA and the presence of the PSA RNA message was determined by RT-PCR targeted at actin and PSA. *Results:* 5 of 14 (36%) tested positive for prostate cells in the operative field. 9 were found to have positive surgical margins. All 5 men with positive RT-PCR PSA assays had positive margins. No patients have manifested wound failure at a median followup of 12 months. *Conclusion:* These data suggest that positive surgical margins may be associated with PSA-expressing cells during RP. Although no patients have yet manifested wound failure, it is impossible to detect an advantage for this new technology over conventional microscopical assessment of the margins because no patients with negative margins had positive RT-PCR PSA assays. Unlike frozen sectioning of lymph nodes, results from the assay *cannot* be acquired intraoperatively and therefore cannot be part of any clinical decision-making algorithm to abort the RP. Although this new technology is feasible, it appears to add no value in predicting which patients benefit from postoperative RT.

464 POSTER

INCIDENCE AND NATURAL HISTORY OF METASTATIC ADENOCARCINOMA OF THE PROSTATE AT DIAGNOSIS

S. Dal Fior, T. Iannone, G. D'Incà[1], G. Guatelli[1], G. De Marchi[1], A. Bordin, S. Guazzieri[1]
[1]Divisione di Radioterapia e di Urologia, ULSS n.1, Ospedale di Belluno

From January 1989 to June 1994, prostatic adenocarcinoma was diagnosed in 139 patients (pts) at the Department of Urology of Belluno Hospital. Thirty-two/139 (23%) pts had distant metastases at diagnosis (stage D2). Median age was 70 yrs (range 45–86). Seventeen/32 (53%) pts had only urinary symptoms, 8/32 (25%) both urinary and systemic symptoms, 6/32 (19%) just systemic symptoms, and in 1/32 (3%) asymptomatic patient the diagnosis was casual. The site of metastases was bone in 30/32 (94%) pts, 3 of which had also liver and 1 also brain metastases; 1/32 (3%) pt had only brain and 1/32 only peritoneal metastases. The grading was G1 in 2/32 (6%) pts, G2 in 12/32 (38%), G3 in 14/32 (44%) and unknown in 4/32 (12%). PSA was lower than 4 ng/ml in 2/32 (6%) pts, higher than 100 ng/ml in 23/32 (74%), in 6/32 (19%) was between 5 and 99 ng/ml and in 1/32 pt it was unknown. Thirty/32 (94%) pts were treated with hormonotherapy, the remaining two, one with brain metastases and the other with peritoneal metastases, died after a month from diagnosis before beginning the therapy, 21/32 (66%) had TURP and 8/32 (25%) chemotherapy with or without palliative radiotherapy. Twentysix/32 (81%) pts had a minimum follow-up of 20 months. Median survival was 15 months (range 1–48+).

In conclusion, prostate adenocarcinoma is often diagnosed in stage D2 (in 23% of cases in Belluno); 7/32 (22%) pts had only systemic symptoms or were asymptomatic at diagnosis; bone is the most frequent metastatic site (94%); systemic therapy is mostly ineffective and survival rate is low (median survival 15 months).

465 POSTER

INFUSIONAL CHEMOTHERAPY BY IMPLANTABLE SUBCUTANEOUS PUMP: STUDY IN MULTIMETASTATIC KIDNEY CANCER

L.F. Frigerio, G. Giovannardi, R. Lanocita, A. Marchianò, G.L. Patelli, B. Damascelli
Special Radiological Procedure Department., Istituto Nazionale Tumori.-1, v. Venezian, 20133 Milano, Italy

65 patients with multimetastatic kidney cancer were treated by continuous infusional chemotherapy using a totally subcutaneous implantable pump. They were given from 8 to 78 fortnight cycles of fluorodeoxyuridine (FUDR) at doses ranging from 0.15 to 0.30 mg/kg/day. The sites of metastases were: lungs, liver, bone, lymph nodes, brain; moreover some patients had a contralateral kidney cancer or a recurrent disease at the site of the previous nephrectomy. The response rate was comparable to that of conventional iv chemotherapy, but to its comparison we obtained a dramatic decrease in side effects (6.1% anemia, 4.6% mucositis, 3% hepatitis-nausea-diarrhea). The infusional therapy is now being studied in a protocol including patients who were excluded from the IL-2/IFN protocol or showed a progressive disease during it.

466 POSTER

FREE AND α 1 ANTICHYMOTRYPSIN BOUND PSA IN PROSTATE DISEASES

J. Guillet, C. Role, D. Pons, V. Malard, N. Bedeau, L. Bellanger, P. Seguin
Hopital St Esprit, 47923 Agen Cédex, France
Cis Bio international BP 175-30203 Bagnols sur Cèze Cédex France

The discovery of prostate specific antigen (PSA) in the blood was a major step forward in the evaluation of prostate cancer. Nevertheless, at early stages, PSA assay has a low specificity: rather than a tumor marker, it has to be considered as a prostate (i.e. malignant and benign diseases) marker.

In order to evaluate the contribution of free PSA versus total PSA we tested 197 men (> 44 years) with RIACT CIS bio international techniques: 47 with prostate cancer, 128 BPH, 22 normal controls.

Results showed that Free/total PSA ratio is almost twice lower in patients with cancer than in patients with BPH or controls. Even if there is an overlap between cancer and BPH results, FPSA seems to provide a promising mean to differentiate benign and malignant prostate diseases at early stages.

467 POSTER

UPFRONT HORMONAL THERAPY, RADICAL PROSTATECTOMY AND RADIATION THERAPY FOR LOCALLY INVASIVE PROSTATE CANCER: A THREE YEAR FOLLOW-UP

G. Katz, Z. Wajsman
Gainesville, FL, U.S.A.

Combined treatment for clinical stage C carcinoma of prostate (CAP) in order to improve the disease free rate was done by upfront hormonal therapy (HT) followed by radical prostatectomy (RP) and radiation therapy (RT) or prolonged HT. Clinical staging was based on evaluation under anesthesia and metastatic work-up. Post RP pathological stage C patients in addition received adjuvant RT and D1 patients continued HT. Of 67 patients who entered the study, 54 were considered operable following HT therapy and underwent surgery, or whom 43 (80%) underwent PLND and RP (RP group). For the RP group the final pathological stage was B in 25/43 (58%), C in 13/43 (30%) and D1 in 5/43 (12%). For pathological stage C the mean follow-up period is 47 ± 19 months (range 12–87, median 47) with 1 patient dead of CAP, and 1 patient with detectable PSA. *Conclusions:* Upfront hormonal therapy, which successfully downstaged patients with clinical stage C prostate cancer followed by RP, can achieve a high disease free survival and compares favorably with other methods of treatments.

468 POSTER

METASTATIC RENAL CELL CARCINOMA (MRCC): RESPONSES TO DIFFERENT IMMUNOTHERAPIES

G. Landonio, C. Baiocchi, M. Ferrari, O. Gottardi, M. Majno, F. Scanzi
Department of Oncology. Niguarda Cà Granda Hospital, Milano, Italy

Aim: to compare clinical responses and survival (median overall survival -MOS- and 2 year survival -% S-) in 48 patients treated with different immunotherapies for MRCC (Interferon -IFN- and Interleukin-2-IL-2-).

Methods: the patients were treated in the following ways:
—18 with IFN—(9 MU s.c. 3 times/week × 6 months): group A;
—11 with IL-2 (18 MU/m2 i.v. × 4 days/months c.i.): group B;
—19 with IFN + IL-2 (at the same dosages): group C.

Responses were evaluated as complete response (CR), partial response (PR), stable disease (SD), progression (PD), not evaluable (NE).

Results: 1 CR, 1 PR and 5 SD were seen in the group A (MOS = 15 months; %S = 32); 0CR, 3 PR and 2SD in the group B (MOS = 16 months; % S = 36); 1 CR, 4 PR and 4 SD in the group C (MOS = 18

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