

group A were treated from October 1, 1992 to October 1, 1994 (51/T3, 4/T4, 4/N+, all Mo). Group B included 38 patients (28/T3, 2/T4, 8/N+, all Mo). In both groups radiotherapy was applied on LINAC (10 MV) with locoregional technique to a dose 65 Gy by conventional fractionation. Patients in group A received carboplatin weekly at daily dose of 150 mg, every fifth day, one hour prior to irradiation, up to total dose of 900 mg. Achieved response rates were in group A: CR = 89%, PR = 4%, PD = 7% and in group B: CR = 63%, PR = 11%, SD = 21%, PD = 5%. Hematological toxicity grade I and II (by WHO criteria), predominant leucopenia and thrombocytopenia, was registered in majority of patients in group A. Mean follow-up time was 20 months (range 3–26). Two-year overall survival as 86% and 70%, disease free survival as 69% and 50% in group A and in group B; respectively. Invasive local relaps occurred in 5/59 patients in group A and 6/38 patients in group B. Metastatic disease with local control confirmed in 7/59 patients in group A. Local relaps with disseminated disease had 5/38 patients in group B. Results showed that addition of carboplatin to radiotherapy increased complete response rate, local control and early survival in patients with locally advanced bladder cancer, but short follow-up, not permit definitive conclusion concerning long-term survival and bladder preservation.

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POSTER

NEOADJUVANT MVAC CHEMOTHERAPY IN BLADDER CANCER: THE CENTRE FRANCOIS BACLESSE (CFB) EXPERIENCE

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The efficiency of MVAC (Methotrexate 30 mg/m² J₁–J₁₅–J₂₂, Vinblastine 3 mg/m² J₁, Doxorubicine 40 mg/m² J₁, Cisplatin 70 mg/m² J₁) given as neoadjuvant chemotherapy (CT), was evaluated in a series of newly diagnosed patients treated at a single institution. From April 1988 to March 1993, 71 patients were referred to CFB of whom 40 were given MVAC as neoadjuvant CT. Initial patients' characteristics were: male/female ratio 4.7; mean age 57 years (range 31 to 75); there were 9 T₀T₁ with grade III, 16 T₂T₃, 7 T₄ and 8 T_x; 19 patients were N₀, 4 N₊, and 17 N_x. CT consisted of 3 to 4 courses of MVAC (35 patients); 5 patients were only administered 2 courses because of toxicity. Surgery was performed after CT in 30 patients (21 radical cystectomy); in 10 patients, secondary treatment consisted of irradiation.

After surgery, residual disease was present at histological examination in 20 patients; in the other 10 patients no tumour was microscopically found (objective and complete responses respectively 55% and 33%). Globally, at the end of therapy, 15 patients were in complete remission, 15 in partial remission, 7 had progressive disease, and 3 were not evaluable.

Toxicity (grade 2 to 4): CT induced haematological toxicity in 24 patients, renal toxicity in 5, cardiac toxicity in 3, and 3 patients died during CT.

With a median follow-up of 56 months, the 4 year overall survival rate from first CT course was 67%; the 4-year freedom from progression rate was 63%.

1152

POSTER

GEMCITABINE IN THE TREATMENT OF PATIENTS WITH ADVANCED TRANSITIONAL CELL CARCINOMA: A PHASE II STUDY

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Gemcitabine is a nucleoside analogue with broad-spectrum activity in several solid tumours. In a Phase I trial, responses were seen in patients with MVAC-refractory bladder cancer. Currently 21 patients with no prior chemotherapy for metastatic transitional cell cancer have been entered on a Phase II trial of gemcitabine at 1200 mg/m² weekly × 3 every 4 weeks. Patient characteristics include: 14 males, 7 females; median age 71 (range 42–88), median Karnofsky performance status 80 (range 60–100); 20 metastatic, 1 locally advanced disease; 2 prior adjuvant or neoadjuvant chemotherapy and 2 with prior radiation therapy. Currently 18 patients are evaluable for response with 3 too early. There have been 11 partial responses among the 18 evaluable patients. Sites of response

have included pelvic and periaortic lymph nodes, liver and lung metastases. Toxicity has been modest in this study with no Grade 4 drug-related side effects. Grade 3 nausea and vomiting have been encountered as have Grade 1 and 2 leukopenia, myalgias, skin rash and fever. One patient with a partial response developed pneumocystis pneumonia with lowered T-4 counts and was removed from study. When he subsequently progressed (approximately 5 months later) he was retreated with gemcitabine (and trim-sulfa prophylaxis) and again has had a partial response. These data suggest that gemcitabine has promising activity in patients with transitional cell cancer and merits combination studies with other active agents in this disease such as cisplatin (with which preclinical synergy has been demonstrated) and paclitaxel.

1153

POSTER

TRANSURETHRAL RESECTION (TUR) AND CHEMOTHERAPY FOR MUSCLE-INVASIVE BLADDER CANCER: LONG-TERM RESULTS

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116 patients with muscle-invasive bladder cancer (15 T₂, 94 T₃, 7 T₄; 23 G₂, 91 G₃, 2 G_X, 115 N_x, 1 N₁) were treated by "extensive" TUR and chemotherapy, either with high dose methotrexate (HDMTX) or cisplatin combinations. Follow-up is 3.9 to 15.2 years (median 11.6 years). The median age was 67 (range 37–88) and tumour size ranged from less than 2 to 7 cms. The median disease-specific survival is 7 years for the entire group, 4 years for HDMTX and has not been reached at 10+ years for the cisplatin combination group. T category and tumour size, but not histological grade, predict for outcome.

The results indicate that, for selected patients, this approach offers an excellent chance of bladder conservation without compromising cure rates. Results, in terms of local control and survival, are comparable with more conventional treatment approaches.

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POSTER

PRESERVATION OF THE ORGAN IN THE THERAPY OF INFILTRATING BLADDER TUMOURS

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From 1986 to 1994, in the II Clinic of Urology, 109 patients affected by invasive bladder carcinoma, without any random schedule, have been subjected to 3 different treatments: (1) Radical cystectomy; (2) Neoadjuvant chemotherapy (N.C.) + radical cystectomy; (3) N.C. + conservative surgical therapy. The difference of survival between group 1 and group 2 and 3 is important from the statistic point of view, and is respectively $P = 0.0209$ and $P = 0.0190$ after adjustment for age, stage, lymph node status (cox model). In the patients of group 3 (13 patients) we have considered it possible to carry out a conservative surgical treatment, in relation to the clinical-pathological response after N.C. In 9 cases, in which we have obtained 7 complete responses and 2 partial responses > than 90%, the conservative surgical therapy consisted of bladder TUR; in the remaining 4 patients for whom we have obtained a partial response > than 50% the therapy consisted of a bladder resection. These results seem to suggest that some patients affected by infiltrating bladder tumour, with a good response to N.C. and well selected, may be evaluated for a conservative treatment.

1155

POSTER

A PHASE III TRIAL OF NEOADJUVANT CHEMOTHERAPY (NCT) IN PATIENTS (PTS) WITH INVASIVE BLADDER CANCER (IBC). PRELIMINARY RESULTS: NCT IMPROVES PATHOLOGICAL COMPLETE RESPONSE RATE

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Introduction: As we reported previously (Eur J Cancer 1991;27(S12):107; Ann Oncol 1994;5(S8):66) treatment with CBDCA,

MTX and VBL is as effective as M-VAC in advanced bladder cancer with long-term survival and can be safely given in an outpatient basis and in pts with impaired renal function. We designed a multicentric study, randomizing pts to receive NCT followed by cystectomy (branch A) or cystectomy alone (branch B). We present the results of pts treated in one institution.

Patients and methods: The inclusion criteria were transitional IBC T3b-4aN0M0, T2-3aN0M0 with obstructive uropathy or presence of diffuse Tis, and creatinine $<130 \times 1.25 \mu\text{mol/L}$. The schedule of NCT was: MTX 30 mg/m² and VBL 4 mg/m² (d +1, +8) and CBDCA 350 mg/m² (d +2); 3 cycles, every 4 weeks. All surgical specimens were reviewed by one pathologist*. The minimum follow-up was 2 years. Sixty-six pts were analyzed: 33 pts in branch A, 33 pts in branch B.

Results: Postoperative mortality was 3%. Response rates were: pCR and pPR 20% and 23% in branch A, and 3% and 12% in branch B. The pCR differences (17%, CI 2-32%) and the pCR + pPR differences (28%, CI 7-50%) were statistically significant with $p < 0.04$ and $p < 0.02$ respectively. There were no survival differences between the two branches. Five-year survival was 50%.

Conclusions: It's the first time that NCT in IBC has demonstrated more pathological responses than the transurethral resection alone. More pts and more trials are needed to confirm these results. The absence of survival differences could be due to chemotherapy selection of pts with a good prognosis in branch A.

1156 PUBLICATION TREATING UROTHELIAL TRANSITIONAL CELL CANCER (TCC) WITH METHOTREXATE (M), CARBOPLATIN (C), NOVANTRONE (N) AND VINCISTINE (O)

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Cisplatin combination chemotherapy (CT) is considered as standard therapy for TCC and MVAC as the mostly tested regime in this condition. The aim of this study was to test efficacy and toxicity of a combination by substituting the drugs of MVAC (except for M that was given in increased dose) by their analogues (MCNO) in pts with TCC. We administered M 300 mg/m² as a 4 h infusion (with fol. acid rescue), C 300 mg/m², N 12 mg/m² and O 1 mg/m², all given on d. 1, q 3w. 47 consecutive and CT-naïve pts aged 65 y. (43-74) received MCNO as follows: 16 pts as postsurgical adjuvant CT with 10 NED for 6+ (4-16+) mos, 5 relapsed/dead and 1 relapsed/alive on CT. 20 pts as neoadjuvant CT with 3 cCR (0 pCR), 7 cPR and 10 SD. 9 pts were operated (0 pCR/8 sCR), 5 of them are NED for 5+ (2-28+) mos, 6 survive on CT and 9 died. And 11 pts with metastatic disease and with 2 cCR/NED for 9+ and 23+ mos, 1 cPR, 4 SD and 4 PD. Alive off CT 2, alive on CT 3, dead 6. Toxicity gr. >2: Hb 21 (45%) pts, ANC 32 (68%), thrombocytopenia 20 (43%), G.I 14 (30%) with no toxic death. Our conclusion is that MCNO does not differ from other similar regimes in terms of efficacy/toxicity.

1157 PUBLICATION CMV AND CAMV IN THE TREATMENT OF ADVANCED BLADDER CANCER

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From June 1992 to March 1995, 28 patients (pts) with advanced bladder cancer were treated with CMV cytostatic regimen (14 pts; day 1: methotrexate 40 mg/m² e.v., vinblastine 4 mg/m² e.v.; day 2: cisplatin 90 mg/m² e.v.; day 8 = day 1; every 21 days) or with CaMV schedule, if serum creatinine was $> 1.5 \text{ mg/dl}$ (14 pts; cisplatin substituted by carboplatin, according to renal function, following Calvert formula; every 28 days).

Pts' characteristics were: 23 males, 5 females; median age: 62.5 (range 49-76) median performance status (ECOG): 1 (range 0-2). Sites of disease involvement: locoregional spreading in 13 pts; nodal metastases (mts) in 15 pts; pulmonary mts in 4 pts; hepatic mts in 3 pts; bone mts in 1 patient (pt).

Total number of administered cycles was 107 (median number of cycles per pt: 4; range 1-8). Grade 3 toxicity was: nausea and vomiting in 2 pts; anemia in 5 pts; leukopenia in 3 pts; thrombocytopenia in 2 pts; stomatitis in 3 pts. No grade 4 toxicity was reported.

25 pts were evaluable for the response; we observed: 3 (12%) complete remissions (CR), 8 (32%) partial remissions (PR), 4 (16%) stable diseases and 10 (40%) progressive diseases.

Overall response rate was good (CR + PR = 44%) and toxicity was manageable and reversible.

1158 PUBLICATION ADJUVANT METHOTREXATE, VINBLASTINE, AND CISPLATIN CHEMOTHERAPY FOR INVASIVE TRANSITIONAL CELL CARCINOMA—TAIWAN EXPERIENCE

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We assigned 56 patients with high risk transitional cell carcinoma (vascular or lymphatic invasion in primary tumor, poorly differentiated P2, P3, P4 or N+ and Mo) to adjuvant chemotherapy after radical urological surgery. The chemotherapy was planned as 6 courses at 21-day intervals of methotrexate vinblastine and cisplatin. The median follow up time was 44 months. An average of 4.63 cycles of chemotherapy were administered with a range of 1 to 6 courses. The mean relative chemotherapy dose intensity was 62.1%. The median actual survival was 44 months; the 1 and 3 year survival probability were 92% and 50%, respectively. The median disease free survival was 15.5 months; the 1 and 3 year disease free survival probability were 66% and 28%, respectively. Disease relapse was noted in 33 cases which included 19 local regional relapses, 10 distant metastasis and 4 both local regional relapse and distant metastasis. With regard to treatment related toxicity, only 5 (9%) and 1 (2%) patient complicated with grade III and IV leukopenia, respectively and none died of sepsis. Further randomized study with appropriate patient stratification was needed to clarify the role of adjuvant chemotherapy for invasive transitional cell carcinoma.

1159 PUBLICATION THE CMV REGIMEN WITH CDDP OR CBDCA IN METASTATIC BLADDER CARCINOMA: REPORT OF A SERIES OF 29 PATIENTS

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From June 1986 to December 1994 29 patients (pts) with metastatic bladder carcinoma were treated with CMV regimen as originally reported by Harker *et al.*, *J Clin Oncol* 1985. Eight out of 29 pts were treated with CBDCA instead of CDDP with dose ranging from 200 to 300 mg/m² because of a pre-existing nephropathy, primary or due to the neoplasm (e.g. from pelvic masses).

We retrospectively evaluated responses rate, CR duration and survival from the beginning of treatment. Patient's characteristics in CDDP group were: median age 66 yr (48-79), PS ECOG 0-1, median follow-up 69 mos (6-107); in CBDCA group: median age 65 yr (60-71), PS ECOG 0-1, median follow-up 38 mos (26-51). In CDDP group 10 pts (48%) achieved an objective response, with 6 CR (29%) and 4 PR (19%), while in CBDCA group 3 pts (37%) showed an objective response with 2 CR and 1 PR. The median duration of CR was 30.5 mos in CDDP pts and 19 mos in CBDCA group, while the median survivals from the beginning of CT were 12 and 10.5 mos respectively. Two pts who received CDDP are still alive and free from relapse at 67 and 69 months.

Toxicities ≥ 3 WHO in CDDP group: neutropenia in 3, piastrinopenia in 2, anemia in 2 and gastroenteric toxicity in 4; in CBDCA group: neutropenia in 3, anemia in 1 and gastroenteric toxicity in 1; no piastrinopenia G3-G4 was observed.

Conclusions: Our results confirm the previous reports and the efficacy of CMV regimen in metastatic bladder cancer, the regimens containing CBDCA are slightly less effective.

1160 PUBLICATION RETROSPECTIVE ASSESSMENT OF PERFORMANCE STATUS (PS)—ACCURACY AND RELATION TO SURVIVAL IN PATIENTS (PTS) WITH URINARY TRANSITIONAL CELL CANCER (TCC)

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The aim of the study was to evaluate the reliability and validity of retrospective assessment of PS in pts with TCC. The clinical records of 149 pts with primary and 53 pts with recurrent TCC were scored twice by the two authors according to the WHO PS scale and related to survival. The results were analyzed in a Cox multivariate model together with other potential prognostic factors for survival. The median survival was