1301

CARBOPLATIN, MITOXANTRONE, VINBLASTINE, METHOTREXATE AND LEUCOVORIN COMBINATION CHEMOTHERAPY FOR URINARY BLADDER CARCINOMA

E Gez-1, B Nussbaum-1, C Servadio-2 and A Sulkes-1. Institute of Oncology-1 and Department of Urology-2, Beilinson Medical Center, Petah Tiqva, Israel

Nineteen patients (pts), median age 75 (range 67-82), with infiltrating bladder carcinoma were evaluated for the efficacy and side effects of combination chemotherapy: Carboplatin 200, Mitoxantrone 10, Vinblastine 3, and Methotrexate 50mg/m², given IV on day 1 and Leucovorin 15mg x 4, orally on day 2, every 4 weeks. Nine pts received chemotherapy for metastatic disease with a response rate of 22%. Ten pts received neoadjuvant chemotherapy and radical radiotherapy for $T_{2-3}N_{x}M_{0}$ disease. Irradiation dose was 45Gy to the pelvis and 65Gy to the urinary bladder, 1.8Gy x 5/week, over 7 weeks. Following this treatment, in 7 pts (70%) a complete response was achieved for median duration of 13 months. One patient died of leukopenia and sepsis.

1302

NEO-ADJUVANT CHEMOTHERAPY WITH CISPLATIN AND METHOTREXATE IN BLADDER CANCER. Leal Silva J, Cardoso A, Carvalho R, Pinho T, Escobar C, Vasconcelos A, Pinto S., Ferreira P. Instituto Portugnês de Oncologia, Porto, Portugal

Both cisplatin and methotrexate have activity in advanced bladder cancer. Between 1988 and 1992 we have treated 46 patients with invasive carcinoma of the bladder, grade II-III, stage III-IV, with a regimen of neo-adjuvant chemotherapy of methotrexate, 40 mg/m2, IV, day 1 and cisplatin, 70 mg/m2, IV, days 1 and 15, q 3 weeks.

The purpose of this study is to assess the response rate and toxicity in patients with a poor performance status and / or old age.

Clinical characteristics: 46 pts, 38 male, 8 female, age 43 - 80 (median 64), performance status WHO 1-2, with a pathologically confirmed diagnosis of bladder cancer.

Number of cycles: 147, median 3 / pt (range 2 - 5).

Toxicity: the main toxicity of the treatment was leucopenia, ocurring in 9 / 46 patients (nadir 2.400) and thrombocytopenia in 2 / 46 (nadir 74.000)

Results: O.R. 23 / 46 (50%), CR 8 / 46 (17.3%) - 3 of them without histologic confirmation, and PR 15 / 46 pts (32.7%).

Conclusion: CDDP + MTX in this schedule results in a elevated objective response with a very acceptable toxicity, beeing a good alternative regimen for patients with poor performance status.

1303

COMBINED TREATMENT FOR INVASIVE BLADDER CANCER

T Čufer, J Červek, B Zakotnik, B Kragelj, M Stanonik
Institute of Oncology, Ljubljana, Slovenia

Forty-five pts with invasive bladder cancer had (TUR), followed by 3-4 cycles of poly-ChT incl. cis-platin. Cytologic reevaluation was done after ChT. In pts with residual ca. cystectomy was performed whenever feasible. Pts with CR received additional RT (40-65 Gy). CR after TUR and ChT was achieved in 24/45 pts (53%). Of 19 pts with recurrence after TUR and ChT, 14 underwent cystectomy. After completed ChT and RT, CR was achieved in 28/45 pts (62%), of these Stage T2T3: 23/34 (67%), Stage T4: 5/11 (45%). After 20-61 mos follow up (median 39), 8/31 (26%) pts with preserved bladders have had local relapse and 3/31 (10%) distant metastases; 20/31 pts (64%) with completed ChT and RT, and 20/45 (44%) with completed protocol are living NED. Of pts with cystectomy, 8/14 (57%) had distant metastases. The estimated survival rate at 52 months has been 68% for pts with CR after ChT, and 53% for pts with residual disease after ChT. Complete tumor eradication was achieved in more than 50% of our pts, and after 3 yrs median follow up, bladder was free of disease in 64% of pts treated by full ChT and RT. This therapy was much more effective in T2T3 tumors, whereas a large tumor size (T4) rendered this treatment less effective.

1304

INTERLEUKIN-2 INTRAVESICAL CONTINUOUS PERFUSION IN THE PREVENTION OF POST TUR RELAPSE OF OPERATED SUPERFICIAL BLADDER CANCER

Ferlazzo,G., Magno,C., Lupo,G., Rizzo,M., Adamo,V., Cavaliere,R., Iemmo,R., Silipigni,A.M.
Istituto di Clinica Oncologica e di Ricerca sui Tumori - Università di Messina

A new immunotherapic approach in the prevention of post-TUR superficial bladder cancer (Ta,T1; G1,G2) relapse has been evaluated. We studied 7 patients who underwent 5 day intravesical continuous perfusion with ricombinant interleukin-2 (rIL-2) (EUROCETUS) after trans-urethral resection. rIL-2 was diluted in urological solution in amount of 3.000.000 UI/day (2 pts), 9.000.000 UI/day (3 pts) and 27.000.000 UI/day (2pts). To allow a 24h continuous bladder perfusion, catheterized patients received rIL-2 solution at 2 ml/min. (3 litres/day). Another 5 day cycle was repeated after 4 weeks.

Flow cytometric analysys and cytology of the cellular immunological reaction in the urine of patients was performed before and after the 5 day intravesical perfusion. The number of leucocytes in the urine was greatly increased after treatment: even if all leukocyte subtypes were increased, the relative increase of eosinophilis in the urine after treatment tended to be higher compared to the other subtypes (3+-2.4% vs 7.5+-9.1%). As lymphocytes may be considered the effector cells in IL-2 mediated anti-cancer activity, subsets of urine lymphocytes were further characterized by flow citometry. The lymphocyte population was mostly represented by T cells and Natural Killer cells percentage was significantly lower than in related peripheral blood lymphocytes (PBL) (p<0.02) both before and after therapy. Most of T cells were CD4+ and the expression of IL-2 receptor (7.9+-3.3% vs 13.9+- 3.3% p<0.03) and HLA-DR antigens (16.5+-4.5% vs 23+-2.8% p<0.03) on T cells was increased at the end of therapy. Related PBL did not present any percentage increase nor in IL-2 receptor neither in HLA-DR expression. Urine lymphocytes phenotype suggest they may represent the lymphocytes in the bladder wall and that they are different from PBL. Side effects were very limited and they did not appear to be dose related: only 2 pts presented enaturia after 1 week the end of therapy. None of the treated patients showed relapse at cystoscopic control 3 monthes after the end of therapy. We have demonstrated a great presence of leukocytes and T lymphocyte activation in the urine of pts treated with rIL-2 intravesical continuous perfusion. Furthermore increased number of eosinophills is known to be a specific marker of IL-2 activity. Our data indicate a local cellular immunological reaction induced by this rIL-2 intravesical administration method. The continuous perfusion allow a prolonged presence of rIL-2 in the bladder and next monthes follow up could explain the real usefulness of this immunotherapic strategie in the profilaxis of post TUR recidiva.