

|                                     | BONE MARROW       | PBSC              | PBSC                 |
|-------------------------------------|-------------------|-------------------|----------------------|
|                                     | G-CSF<br>(n = 37) | G-CSF<br>(n = 11) | No G-CSF<br>(n = 14) |
| Neutrophils<br>>500/mm <sup>3</sup> | 12 (10-33)        | 11 (9-14)         | 12 (7-16)            |
| Platelets<br>>20000/mm <sup>3</sup> | 21 (18-36)        | 17 (10-25)        | 18 (9-33)            |
| Days Antibiotics                    | 12.5 (6-29)       | 11 (5-19)         | 10.5 (5-26)          |
| Days Hospitalization                | 25 (20-43)        | 22 (19-30)        | 25 (20-49)           |
| Packed red blood cells              | 5 (0-32)          | 3 (2-4)           | 4 (2-9)              |
| Random Platelets units              | 38 (7-247)        | 32 (8-98)         | 30 (5-200)           |

Although this is not a randomized survey, no difference with statistical significance could be proven for any of the other variables analyzed.

1136

PUBLICATION

# **LIMITED MOBILIZATION EFFECT OF G-CSF (LENOGRASTIM) FOR BLOOD STEM CELLS IN CHILDREN WITH SOLID TUMORS**

*Y. Kawano, Y. Takaue, Y. Kuroda, M. Ohira*

*Department of Pediatrics, University of Tokushima and National Cancer Center Hospital, Japan*

Autografts with G-CSF mobilized blood stem cell (PBSC) has been widely applied for cancer therapy. However, its dose response effect

has not been fully tested. To address this, we gave various doses of G-CSF to 31 children with solid tumors (age, 1 to 15 y) including 17 neuroblastoma, with concomitant measurement of circulating CD34+ cells. Eleven of 31 patients has >6 mo history of chemotherapy. They received a regimen incorporating CDDP and G-CSF was started from the nadir of WBC. Blood was drawn 3 times a week for CD34+ cell assay and CBC. There was no dose response effect for shortening the duration of neutropenia with 2 to 12.5 µg/kg of G-CSF. Increase of circulating CD34+ cells (>100/µl) was observed in patients whose platelet recovery was fast, reaching to a level of  $10 \times 10^9/l$  within 2 weeks (n = 14), but no apparent dose response effect was observed. While in the rest of slowly recovering patients, its effect was marginal. Comparing our historical data for children with ALL/NHL, these may suggest that G-CSF has only a limited effect for mobilizing PBSC in children with a solid tumor and/or those who were treated with a regimen specific for solid tumors.

## **Bladder cancer**

1137

ORAL

# **A PROSPECTIVE, RANDOMIZED, MULTICENTER, PHASE III CLINICAL TRIAL OF THE EFFECT OF DIFFERENT INITIAL THERAPY REGIMES AND MAINTENANCE PROPHYLAXIS IN SUPERFICIAL BLADDER CANCER USING MITOMYCIN C**

*D.W.W. Newling, D. Mulder*

*The Flemish Mitomycin C Study Group, Amsterdam, The Netherlands*

Doubts still exist over the appropriate initial regime and the length of maintenance necessary with intravesical chemotherapy for the best prophylaxis against recurrence in superficial bladder tumor. All patients with superficial bladder cancer were eligible apart from those with a solitary Ta lesion, in whom the protocol regimes would be generally unacceptable. After resection of tumors in the bladder, 1287 patients were randomized into 4 different groups. Group A received 8 weekly instillations with 40 mgs Mitomycin C in 50 cc's 0.9% saline, followed by 4 months, monthly prophylaxis with the same dose. Group B received 4 weeks initial therapy, followed by 5 months, monthly prophylaxis. Group C received the same therapy as group A but the prophylaxis was continued to 12 months and group D the same initial regime as group B but again with maintenance continued to 12 months. Groups were evenly matched with regard to stage and grade of their tumors and there was no significant sex difference between the 4 groups. The side-effects were similar in groups A and B, and groups C and D, but almost twice as many patients in groups C and D missed one or more instillations due to side-effects, compared with the two groups with the shorter maintenance regime. All patients have been treated for a minimum of 12 months and there are no significant differences in the recurrence rate of rate of progression between patients in group A and B compared with those in C and D.

1138

ORAL

# **CLINICAL SIGNIFICANCE OF PROLIFERATING CELL NUCLEAR ANTIGEN EXPRESSION IN TRANSITIONAL CELL CARCINOMA OF THE BLADDER**

*H. Shiina, S. Urakami, H. Shirakawa, M. Igawa, T. Ishibe*

*Department of Urology, Shimane Medical University, 89-1 Enya-cho, Izumo 693, Japan*

To elucidate the clinical significance of cellular proliferation in transitional cell carcinoma (TCC) of the bladder, the proliferating cell nuclear antigen (PCNA) expression, p53 and nm23 immunoreactivities, 2c deviation index (2cDI) and 5c exceeding rate (5cER) were evaluated using an image analyzer. The paraffin embedded materials obtained from 77 patients with non-metastatic untreated TCC of the bladder who received

total cystectomy were used in this study. The PCNA expression significantly correlated with the p53 and nm23 immunoreactivities, 2cDI value and 5cER, respectively. The grade significantly correlated with all of the 5 parameters. Similarly, the stage as well as disease progression significantly correlated with all of the parameters except for the nm23 immunoreactivity. In univariate analysis, the prognostic relevance was noted in grade, stage, PCNA expression, p53 immunoreactivity, 2cDI value and 5cER, whereas not in nm23 immunoreactivity. In multivariate analysis, the PCNA expression, followed by 2cDI value, was the most important variable, however, the p53 immunoreactivity and 5cER were not of independent significance. The results suggest that the tumor growth fraction as assessed by the PCNA expression is an important and independent predictor for survival in patients with TCC of the bladder.

1139

ORAL

# **EFFECT OF PREOPERATIVE RADIOTHERAPY ON CLINICAL-TO-PATHOLOGIC DOWNSTAGING IN MUSCLE-INVASIVE BLADDER CANCER**

*A. Pollack, G.K. Zagars, C.J. Cole, C.P. Dinney, D.A. Swanson, H.B. Grossman*

*Departments of Radiotherapy and Urology, The University of Texas, M.D. Anderson Cancer Center, Houston, Texas 77030, U.S.A.*

Downstaging (DS) after preoperative radiotherapy is well-established; however, the prognosis of such patients relative to those who exhibit DS in the absence of any radiotherapy has not been described. The relationship between DS and local control for 301 patients treated with preoperative radiotherapy and cystectomy (PREOP) from 1960-1983, was compared to that for 225 patients treated with radical cystectomy alone (CYST) from 1984-1990. PREOP patients received 50 Gy in 25 fractions 4-6 weeks prior to cystectomy. DS was found in 73% treated with PREOP and 29% treated with CYST ( $p < 0.0001$ , chi-square). The only potential prognostic factors that correlated with DS were clinical stage and creatinine level ( $p < 0.05$ , chi-square). Multivariate analysis revealed that treatment (PREOP vs CYST) correlated with DS independently of these covariates. In terms of 5 yr actuarial local control, those who were downstaged fared better than those who were not; 93% vs 85% for PREOP ( $p = 0.01$ ) and 91% vs 83% for CYST ( $p = 0.13$ ). Local control for clinical Stage T2 and T3a patients was not related to the treatment, regardless of whether DS was documented. In contrast, downstaged T3b patients treated with PREOP had significantly greater local control rates than those receiving CYST. These data indicate that preoperative radiotherapy for clinical Stage T3b patients had a significant impact on local control beyond selection based on downstaging.