PERGAMON

European Journal of Cancer 39 (2003) 2566

European Journal of Cancer

www.ejconline.com

Letter

A comment on "Scandinavian Sarcoma Group Osteosarcoma Study SSG VIII: prognostic factors for outcome and the role of replacement salvage chemotherapy for poor histological responders"☆

G. Bacci*, A. Longhi, C. Forni, E. Setola, E.S. Ferrari

Chemotherapy Unit at the Istituto Ortopedico Rizzoli, Bologna, Italy

Received 5 June 2003; accepted 13 June 2003

We read with interest the paper of Smeland and colleagues [1] about prognostic factors in 113 patients with osteosarcoma of the extremities treated in the last neoadjuvant study of the SSG. In their paper, the authors reported that only three factors appeared to influence the prognosis of these patients: gender, tumour volume at a cut-off of 190 ml, and the mean serum level of methotrexate (MTX) at the 24th hour.

We recently reviewed our data on prognostic factors for non-metastatic osteosarcoma of the extremity of approximately 620 patients treated with neoadjuvant chemotherapy at our institution between 1983 and 1999. Chemotherapy was performed according to six different protocols that were successively activated. In our series, in the univariate analysis, patients with tumour volumes less than 150 ml, with a normal serum value of Alkaline Phosphatase (AP), with normal serum values of lactic dehydrogenase (LDH), and with a good histological response to preoperative chemotherapy had a significantly better prognosis. However, in the multivariate analysis, only a high serum level of LDH (Relative Risk (RR) 1.8, 95% CI 1.2–2.8, $P<0.003$), high serum level of AP (RR 3.3, 95% CI 2.3–4.8, $P<0.0001$), and a poor histological response to chemotherapy (RR 2.3, 95% CI 1.6–3.4, $P<0.0001$) maintained their statistical significance.

As regards gender, we were not able to confirm any better prognosis for females. In fact, the 5-year event-free survival (EFS) was almost the same in males and females (55 versus 58%). Instead, we confirmed the very poor prognosis for patients who relapsed with local recurrence (5-year overall survival after relapse: 5% for patients who had local recurrence versus 24% for patients who relapsed with metastases only). We were not able to evaluate the prognostic value of the serum MTX level on the whole series because patients were given different protocols and the doses of this drug ranged between 750 and 12 000 mg/m^2. However, when evaluating only the patients who were treated according to the second protocol (IOR/OS-II), we found their prognosis to be significantly ($P=0.001$) related to the MTX mean serum concentrations at the end of the infusion.

Smeland and colleagues stated that the lack of prognostic value for histological response could be due to the relatively limited number of patients evaluated. According to our experience, we believe that the lack of prognostic value for serum LDH and AP levels might also be due to the small numbers of patients studied. In fact, in addition to our present series, another study on a large series of patients ($n=279$) by the Memorial Sloan Kettering Center [2] reported a prognostic significance for serum AP levels ($P=0.001$) and serum levels of LDH ($P=0.001$).

However, the better prognosis of females reported by the Scandinavian authors remains more difficult to explain.

References

1. Smeland S, Muller C, Alvegard TA, *et al*. Scandinavian Sarcoma Group Osteosarcoma Study SSG VIII: prognostic factors for outcome and the role of replacement salvage chemotherapy for poor histological responder. *Eur J Cancer* 2003, **39**, 488–494.
2. Meyers PA, Heller G, Healey J, *et al*. Chemotherapy for non-metastatic osteogenic sarcoma: the Memorial Sloan Kettering experience. *J Clin Oncol* 1992, **10**, 5–15.

☆ European Journal of Cancer 2003, **39**, 488–494. Doi of article referred to: 10.1016/S0959-8049(02)00747-5.

* Corresponding author. Tel.: +390 51 6366 829; fax: +390 51 6366 277.

E-mail address: gaetano.bacci@ior.it (G. Bacci).

doi:10.1016/S0959-8049(03)00546-X