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Letter to the Editor

A comment and update on "Does the histological subtype of high-grade central osteosarcoma influence the response to treatment with chemotherapy and does it affect overall survival? A study on 570 patients of two consecutive trials of the European Osteosarcoma Intergroup"

We read with interest the article of Hauben and colleagues [1] that provides important information on the relationship between the osteosarcoma pathological subtype, histological response and survival, after an evaluation of 570 patients with primary high grade osteosarcoma of extremity that were included in two consecutive multicentric studies of the European Osteosarcoma Intergroup (EOI).

As mentioned by the authors, in a previous paper published 4 years ago, we reported very similar results [2]. The way we classify osteosarcoma subtypes is the same as that used by Hauben and colleagues. On the basis of predominant cell type and intercellular material (osteoid, cartilage, collagen and vascular spaces) osteosarcoma is classified as conventional (osteoblastic, fibroblastic, chondroblastic, anaplastic) telangiectatic, small cell osteosarcoma. This diagnosis is always made on surgical specimens, and the histological response is defined as: (a) total vs incomplete; (b) percentage of the necrotic tumour, (c) according to the Huvos' classification [3]. In our paper [2], the histological response was registered as total (100%) or incomplete.

We would like to update the experience of the Rizzoli Institute on this topic by reporting the results of a recent review on a larger number of cases and using the same cut-off level as Hauben and colleagues to classify good and poor responders. Thus, a good response to chemotherapy was defined as 90% tumour necrosis or more, and a poor response as less than 90% necrosis). This review includes 827 patients with non-metastatic high-grade osteosarcoma of the extremity treated at Rizzoli Institute between 1983 and 1999 with different protocols of chemotherapy and followed-up for 3–15 years. With this review, performed by two experienced pathologists in our institution, we can entirely confirm the results reported in the paper by the pathologists of the European Osteosarcoma Intergroup.

In fact:

(a) the rates of cases of conventional (or osteoblastic), chondroblastic and fibroblastic tumours in the Hauben series were 71, 10 and 9%, respectively. The corresponding rates in our series were: 66.5, 9.9 and 9.6%; and, as in the series reported by Hauben and colleagues:

(b) the rate of good responder-patients (tumour necrosis $\geqslant 90\%$) was significantly higher for fibroblastic tumours than for chondroblastic tumours (57/80, 71% vs 41/82, 50%; $P = 0.009$), while for conventional (osteoblastic) tumours, the rate of good histological response was 64% (352/551);

(c) in addition our patients had a significantly better prognosis in cases of good response: the rate of 5-year disease-free survival was 69% for good responders vs 52% for poor responders; $P < 0.0001$);

(d) in our series, in spite of the lower rate of good response in chondroblastic tumours, the patients with this osteosarcoma subtype had a prognosis that was not different from that of the other histotypes. In fact, the 5-year disease-free survival was 60% for chondroblastic, 58% for osteoblastic and 75% for fibroblastic tumours. These differences were not statistically significant.

The similarity of our results to those reported by Hauben and colleagues, seems to indicate that a subtype classification is highly reliable, even if performed by different pathologists, and that osteoblastic, chondroblastic and fibroblastic osteosarcomas respond differently to preoperative chemotherapy. However, a larger series of patients is needed to determine whether these three different subtypes, besides having a different histological response to preoperative treatment, also have a different prognosis that could justify a specific therapeutic approach.

References

1. Hauben EI, Weeden S, Pringle J, Van Marck EA, Hogendoorn PCW. Does the histological subtype of high grade-central osteosarcoma influence the response to treatment with chemotherapy

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and does it affect overall survival? A study on 570 patients of two consecutive trials of the European Osteosarcoma Intergroup. *Eur J Cancer* 2002, **38**, 1218–1225.
2. Bacci O, Delepine N, Bertoni F, *et al*. Predictive factors of histological response to primary chemotherapy in osteosarcoma of the extremity: a study of 272 patients preoperatively treated with high dose methotrexate, doxorubicin and cisplatin. *J Clin Oncol* 1998, **16**, 658–663.
3. Huvos AG, Rosen G, Marcove RC. Primary osteogenic sarcoma: pathologic aspects in 20 patients after treatment with chemotherapy en block resection, and prosthetic bone replacement. *Arch Pathol Lab Med* 1977, **101**, 14–18.

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