Letter to the Editor

Clinical Cancer Research

To B(MP-2) or Not To B(MP-2): Cytokines and Tumor Surgery—Letter

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In his editorial (1), Dr. Weiss divides his comments along two controversial themes within musculoskeletal oncology, the effects of surgical margins and of BMP-2 in the context of osteosarcoma. His comments regarding BMP-2 distill down to a belief that patient survival should never be compromised in exchange for improved orthopedic outcomes. Although we agree with this point in principle, additional discussion is warranted.

Many who care for osteosarcoma patients hold common the belief that until a new therapeutic approach becomes available survival is unlikely to improve. This belief is rooted in numerous phase III trials, all of which have failed to demonstrate improved outcomes with the addition of cytotoxic chemotherapy and immunotherapy agents. This notion is further underscored by a paucity of current phase III clinical trials. Although improving survival remains paramount, at this juncture, it may be a reasonable and timely to consider the improvement of orthopedic outcomes.

While we agree that survival remains more important than orthopedic outcomes, current standard of care appears discrepant in at least one manner. Given that the most recent international phase III clinical trial has definitively demonstrated the inability to salvage poor responders, tailoring chemotherapy with existing agents can no longer be considered advantageous. Furthermore, one could easily hypothesize that chemotherapy, in the context of a genetically unstable tumor, may lead to impaired survival through drug resistance. In addition, the impact of immediate versus delayed surgery has been previously explored (2). This markedly underpowered study has served as the basis for deeming delayed surgery as being safe, with immediate surgery having a survival advantage, but the result was not statistically significantly different. At a minimum, these results remind us that delayed surgery does not clearly improve overall survival. Beyond the smoothed logistical issues of delayed surgery, the only true benefit it provides is improving orthopedic outcomes.

Local BMP-2 administration may theoretically increase the risk of osteosarcoma metastases, but the data remain controversial (3–5). The warnings in the BMP-2 prescribing information are for all cancer risk, not specifically osteosarcoma. Conversely, BMP-2 is known to stimulate bone production and fracture healing, and it is plausible that it may decrease non-union. Indeed, well-conducted clinical trials will be the only manner with which to answer these questions. We would argue that it is hypocritical to dismiss a carefully monitored clinical trial investigating the use of BMP-2 to improve orthopedic outcomes, while administering neoadjuvant chemotherapy for the very same purpose.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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