Palliation and Survival After Repeated $^{188}$Re-HEDP Therapy of Hormone-Refractory Bone Metastases of Prostate Cancer: A Retrospective Analysis

TO THE EDITOR: We read with great interest the article by Biersack et al. published in the November 2011 issue (1). Because our group shares with the authors a similar interest in the potentials of therapeutic bone-seeking radiopharmaceuticals not only for palliation of bone pain but also for some objective antitumor activity (especially when administered in combination with other therapies) (2,3), this article constitutes for us an additional source of inspiration and stimulates further impetus to our ongoing investigations in this field.

Considering this evolving scenario, we believe that clarifying somewhat further some of the issues addressed by Biersack et al. would contribute to enhancing the value of the overall information that the nuclear medicine community (as well as the medical oncology community at large) would derive from reading the article by Biersack et al. This need is felt by all specialists involved in the management of patients with bone metastases and is in fact spurring a growing number of systematic reviews and metaanalyses (3–10).

In the perspective of future reviews taking into account the works by Bonn’s group (1) along with other original contributions, it is essential (for the sake of clarity and for the purpose of statistical evaluation) to specify whether the patient population with long-term follow-up described in the latest publication (1) is totally independent from the population included in an earlier article by the same group describing the clinical benefit of repeated $^{186}$Re-hydroxyethylidenediphosphonate ($^{186}$Re-HEDP) administrations (11); this seems to be the case upon reading the last paragraph under “Discussion,” but perhaps a specific statement would help in this regard.

We certainly understand that there are some intrinsic limitations due to the retrospective nature of the study by Biersack et al. and to the fact that the patients’ response to $^{188}$Re-HEDP therapy in terms of bone pain palliation was reported with a crude, simplified scale by the referring physician (rather than recorded directly by patients according to, for example, the Visual Analog Scale). For instance, it would help the scientific community to know if the patient population described in this work represents a consecutive series or only those patients for whom the referring physician returned the questionnaire, and what percentage of questionnaires were correctly returned with respect to the total sent.

Still, for review and analysis purposes the results reported by Biersack et al. would be even better appreciated if they described in greater detail the duration of pain palliation and, above all, the reproducibility of the palliative effect after subsequent $^{188}$Re-HEDP administrations in the same patient, an issue that has already been addressed for other bone-seeking radionuclide agents, such as $^{153}$Sm-ethylidenediaminetetramethylene phosphonate (12). Furthermore, Biersack et al. do not specify the reason for repeated $^{188}$Re-HEDP therapies: was treatment repeated because of prior planning (perhaps as part of an ongoing protocol with the experimental drug $^{188}$Re-HEDP) or because of recurrent pain after palliation? In the latter instance, could retreatment of patients responding to the first treatment introduce a selection bias as to subsequent response to repeated therapy? Did the authors observe bone palliation after repeated treatment even if the first treatment was ineffective? Finally, for completeness of analysis the authors could provide the average number of administrations in the group receiving more than 3 $^{188}$Re-HEDP therapies (they only mention a maximum of 8, which is quite a bit greater than 3) and, above all, the overall duration of treatment from first to last administration. A further issue that is usually of great concern to medical oncologists is the possible hematologic toxicity of bone-seeking radiopharmaceuticals, especially after repeated administrations (and at relatively short intervals such as ~8 wk); a specific statement by the authors in this regard would be greatly welcome.

Concerning instead objective response to $^{188}$Re-HEDP therapy (as shown by declining levels of serum prostate-specific antigen [PSA] after radionuclide treatment), it would greatly help the reader to know on which occasion such a reduction was observed for patients treated more than once; in other words, do the data reported in Table 3 for groups B and C refer to the best response observed, and was such best response observed after treatment 1, 2, or 3? Conversely, it would help future analysis to know how the authors set thresholds defining serum PSA as “decreased,” “unchanged,” or “increased,” as well as to know how reproducible the serum PSA response was in each patient after repeated therapies.

Concerning survival analysis, the data provided by the authors would optimally be complemented by adequate information not only on the approximate burden of metastatic skeletal involvement (i.e., more precisely than simply “more than 5 lesions documented by a bone scan”) but also on the possible presence and extent of concomitant visceral metastatic disease. Still with reference to survival, as reviewed recently a crucial issue that is the object of increasing interest and attention in hormone-refractory prostate cancer patients with skeletal metastasis is possible combination therapy of bone-seeking agents with other proven or putative antitumor treatments, usually chemotherapy (3). In this regard, even if based on a retrospective study rather than on a prospective protocol, information on possible concomitant chemotherapy received by the patients described by Biersack et al. (or at least by a fraction of that population) would add to our understanding of the impact on survival of repeated $^{188}$Re-HEDP therapy per se compared with such a regimen in association with other antitumor agents.

REFERENCES


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