Radium-223 vs EBRT for Multiple Painful Bone Metastases: Is Less More?

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There is no question that radiopharmaceuticals have a role in the management of patients with metastatic bone disease. There is also no question that fractionated external beam radiotherapy (EBRT) is highly effective and generally well tolerated when delivered with large open or focal fields.[3] The answer to the question of which form of treatment is preferred should be based on: relative effectiveness, availability, and cost.[4]

It appears that the use of EBRT is largely driven by how far one lives from a radiation center.[4] Thus, it is also likely that whether one lives close to a place where radiopharmaceuticals can be easily obtained would impact patient and physician decisions about the use of such agents. Given the short half-life of radiopharmaceuticals, it is likely that more planning might be required to make use of these agents possible on short notice. In contrast, EBRT can be given the same day the patient arrives and within minutes. In addition, there appears to be a consensus among experts that a single treatment with simple techniques may be preferred in most patients, thus minimizing the need for return visits.[5-7] EBRT is evidence-based and extremely cost-effective when given in short courses.[8,9] For example, in Radiation Therapy Oncology Group (RTOG) 9714, we showed that a single treatment of 800 cGy × 1 was as good as 300 cGy × 10 and more cost-effective in the management of patients with prostate or breast cancer.[10,11] However, despite multiple trials favoring short courses of EBRT, to date expert panels have generally been hesitant to come out strongly for short courses of EBRT, even for prostate cancer.[12,13]

Although several areas can be treated effectively with EBRT, at some point in the spread of a cancer, management would certainly favor the use of radiopharmaceuticals. Another argument for radiopharmaceuticals hinges on whether their use can impact overall survival, as was suggested by one early study and also, more recently, by a study of radium-223.[14,15] Of note, however, in the only head-to-head trial completed to date that I am aware of, the authors concluded that “... pain treatment with local field radiotherapy is associated with a better overall survival compared to Strontium (89). The lower costs of local field radiotherapy also favour the use of this treatment in patients with HRPC [hormone-resistant prostate cancer].”[16] However, the study authors noted that the reason for an observed overall survival benefit with local field radiotherapy was not clear. Given that there is no level I evidence to disprove the observed association of an overall survival benefit with EBRT, can we safely ignore these findings? Clearly, clinical judgment will be key to selecting the appropriate modality for a given patient.

Looking forward, a key question will be whether the use of EBRT and radiopharmaceuticals in combination will yield additional benefits over the use of either alone.[17,18] With the promising results noted for radium-223, along with its relatively low toxicity profile, there are reasons to think that there could be a role for its use as an adjunctive therapy in patients with prostate cancer. Such patients might ideally have diffuse bone disease and an excellent performance status but one or two symptomatic lesions involving weight bearing bone(s). It is doubtful, however, that such treatment could displace EBRT, 800 cGy × 1, for a single symptomatic lesion as the standard of care without proof from a large phase III trial.

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