Radiopharmaceuticals: Present and Future

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Commentary on "Radiopharmaceuticals: When and How to Use Them to Treat Metastatic Bone Pain" by Paes et al. (page 197)

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In cancer patients, bone metastasis is a common complication, with the highest prevalence among breast and prostate cancer patients.[1] Pain is one of the most feared and debilitating cancer-related symptoms, with an incidence of 62%–86%.[2] Pain related to bone metastases constitutes the most frequent type of pain. The objectives of treating bone metastases are to palliate pain, improve quality of life, prolong pain-free survival, and eradicate tumor cells in the bone. Traditional treatment approaches include external beam radiation, orthopedic intervention, chemotherapy, hormone therapy, bisphosphonates, steroids, and radiopharmaceuticals.[3]

Radiopharmaceutical treatment of metastatic bone pain has been in practice for more than three decades. Currently, three radiopharmaceuticals are approved by the US Food and Drug Administration for the treatment of painful bone metastasis: samarium-153 lexidronam (Sm-153), strontium-89 chloride (Sr-89), and phosphorus-32 (P-32).[4] Rhenium-186 (Re-186) is widely used in Europe, and Re-188 is a promising investigational agent. P-32 has not been commonly used since the 1980s because of bone marrow toxicity. Radiopharmaceuticals have unique properties such as half-life, radiation energy, and tissue penetration that are associated with the onset of response, duration, and toxicity. Myelosuppression is the most common toxicity, which is often limited and reversible; this makes repetitive dosing practical, especially with short half-life radioisotopes. Several studies have demonstrated the palliative efficacy of radiopharmaceuticals, with similar overall reported pain response rates of 60%–90%.[5]

Radiopharmaceuticals have had relatively limited use in the oncology setting despite the overwhelming prevalence of metastatic bone pain, decades of clinical experience, and demonstrated efficacy with limited toxicity. Typically, physicians do not consider radiopharmaceuticals until several other treatment regimens have failed. Patients at this point may have developed low bone marrow reserve, consequently limiting the use of radiopharmaceuticals. In addition, physicians may be hesitant to give a marrow-toxic agent for pain relief because it might prohibit later cytotoxic therapies. The review "Radiopharmaceuticals: When and How to Use Them to Treat Metastatic Bone Pain" by Paes and colleagues addresses several of these misconceptions that hinder the use of radiopharmaceuticals. In addition, it addresses patient selection, monitoring, and areas of uncertainty including concomitant therapy with chemotherapy or bisphosphonates.

Accumulating evidence suggests that radiopharmaceuticals may not only provide palliative benefit but also improve clinical outcomes such as overall (OS) and progression-free survival (PFS), possibly by modulating the onco-niche.[6] Tu and colleagues[7] conducted the first study that demonstrated both improved clinical outcomes and palliative benefits in patients with metastatic castrate-resistant prostate cancer. The patients were treated with doxorubicin and Sr-89, and achieved a significant improvement in OS compared to doxorubicin alone. Recent studies by Amato et al[8] and Fizazi et al[9] with alternative chemotherapy regimens and radiopharmaceuticals have demonstrated similar improved PFS and OS. Randomized phase III trials to confirm these results are ongoing.

The foundation of radiopharmaceuticals in the treatment of metastatic bone pain for palliative benefits is well established. Physicians should not relegate radiopharmaceuticals to a

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treatment of last resort but should incorporate them into their multimodality treatment armamentarium. Further studies are needed to establish the palliative and potential clinical benefits of radiopharmaceuticals with concomitant chemotherapy and bisphosphonates, in addition to new therapies such as RANK ligand inhibitors and antiangiogenic agents.

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