PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #116
RADIOPHARMACEUTICALS FOR PAINFUL OSSEOUS METASTASES

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Introduction This *Fast* Fact reviews bone-seeking radiopharmaceuticals (radionuclides), which occupy a valuable niche in the palliation of painful bone metastases. See *Fast Facts* #66 and 67 for a general discussion of palliative radiation.

Isotopes and Physiology Many isotopes available in this country – ^{89}Sr (strontium-89), ^{153}Sm (samarium-153), and ^{32}P (phosphorus-32) – work by binding with high affinity to hydroxyapatite in regions of rapid bone turnover near osteoblastic metastases, delivering therapeutic doses of localized beta radiation, with a tissue penetration measured in millimeters. The precise mechanism of analgesia is unknown but is probably not dependent solely on cell kill. Rather, analgesia may also be a function of inhibition of lymphocyte-associated cytokines or alterations in osteoclast and/or osteoblast activity. Radium-223 is a newer isotope which is a targeted alpha emitter with more selective binding to areas of increased bone turnover in bone metastases. It thereby leads to highly localized cytotoxic effects.

Benefits The benefits of many of the radiopharmaceuticals have been limited to pain relief and delay of skeletal events. Analgesia may begin within 3-7 days, but more typically begins within one to two weeks after administration. Analgesia will last from two to six months; treatment may be repeated. Symptom improvement is noted in 60-80% of patients, with complete analgesia in 20-30% of responders. Only radium-223 has shown a survival benefit compared with placebo in select patients. Patients with castration-resistant metastatic prostate cancer lived 3 months longer. In addition, radium-223 appears to be associated with less myelosuppression and adverse events.

Procedure The radiopharmaceutical is delivered in the outpatient setting by a single IV injection or for radium-223, six injections given at 4 week intervals. Administration requires no special monitoring.

Patient selection Patients with multiple painful bone metastases, demonstrated by bone scan and/or plain X-ray, corresponding to site(s) of pain and an expected survival of >12 weeks are appropriate for radiopharmaceutical therapy. For patients with castration-resistant prostate cancer and bone-predominant disease, radium-223 should be strongly considered. Evidence supporting efficacy in prostate and breast cancer is substantial; data for other tumor types are limited.

Contraindications

- Preexisting myelosuppression (e.g. WBC <3.0K and Platelets <60-100K).
- Oncological urgencies/emergencies in which radiopharmaceuticals will be of no benefit (e.g. actual or impending spinal cord compression or pathologic fracture).
- Renal insufficiency (relative contraindication).
- Evidence of disseminated intravascular coagulation (relative contraindication).
- Pregnancy

Adverse effects

- Marrow suppression: Reversible, moderate neutropenia and thrombocytopenia – manifested by approximately 30-70% drop in leukocyte and platelet counts – is a predictable side effect. Depending on the specific agent this begins two to four weeks following administration, with a nadir between weeks four to six. Bone marrow recovery occurs by weeks eight to twelve.
- Pain flare: Increasing pain occurs in 10-20% of patients, usually within the first week of administration. It is transient and may be predictive of a good therapeutic response.

Comparative Data There is little data comparing agents. However, the International Atomic Energy Agency sponsored a randomized, single-blind study comparing a single doses of oral ^{32}P (12 mCi) and intravenous ^{89}Sr (4 mCi). There were no significant differences in onset/duration/degree of analgesia or functional improvement. Hematologic 32P was associated with significantly more thrombocytopenia. Because ^{32}P is also known to have a long half-life and be incorporated into marrow cells, it is rarely used in the US.

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