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## FAST FACTS AND CONCEPTS #116

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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** The three isotopes available in this country –  $^{89}\text{Sr}$  (strontium-89),  $^{153}\text{Sm}$  (samarium-153), and  $^{32}\text{P}$  (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.

**Benefits** 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. Radiopharmaceuticals may delay onset of pain in pre-existing, clinically silent metastases.

**Procedure** The radiopharmaceutical is delivered in the outpatient setting by a single IV injection or orally ( $^{32}\text{P}$  only). 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. 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.

### Approximate retail costs (Note: dosing is calculated based on patient weight.)

- Strontium-89 chloride injection: \$3,097 / 5 mCi.

- Samarium-153 lexidronam injection \$2,770 / 150 mCi.
- Sodium phosphate P-32 solution: \$500 / 5 mCi.

**Comparative Data** There is little data comparing the three agents. However, the International Atomic Energy Agency sponsored a randomized, single-blind study comparing a single doses of oral  $^{32}\text{P}$  (12 mCi) and intravenous  $^{89}\text{Sr}$  (4 mCi). Patients were well-matched in terms of tumor type, degree of osseous involvement, and pretreatment pain scores. Partial (>50%) and complete (100%) analgesia responses were as follows:  $^{89}\text{Sr}$ : 7/15 and 8/15 patients, respectively;  $^{32}\text{P}$ : 7/16 and 7/16 patients, respectively. There were no significant differences in onset/duration/degree of analgesia or functional improvement. Hematologic toxicity was comparable save except that the  $^{32}\text{P}$  group had more thrombocytopenia.

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