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Use of Strontium⁸⁹ in Patients with Endocrine-Refractory Carcinoma of the Prostate Metastatic to Bone Practice Guideline Report # 3-6

Brundage MD, Crook JM, Lukka H and the Genitourinary Cancer Disease Site Group

ORIGINAL GUIDELINE: November 23, 1997

UPDATE: October 2001

This summary integrates the original practice guideline with the most current information (labeled NEW).

Part 1: Strontium⁸⁹ treatment for hormone refractory prostate cancer skeletal metastases: multiple painful sites of disease

Guideline Question

What is the role of Strontium⁸⁹ in effective palliation of patients with stage D endocrine-refractory prostate cancer and multiple sites of painful bony metastases?

Target Population

These recommendations apply to adult patients with stage D endocrine-refractory prostate cancer and multiple sites of painful bony metastases.

Recommendations

- Strontium⁸⁹ is recommended for use in patients with endocrine-refractory carcinoma of the prostate who have multiple uncontrolled painful sites of metastases on both sides of the diaphragm, not adequately controlled with conventional analgesic therapy and in whom the use of multiple single fields of external beam radiation is not possible.
- Strontium⁸⁹ has proven efficacy in the palliation of hormone-refractory painful bony metastases from prostate cancer.
- Strontium⁸⁹ has not been shown to lengthen the average duration of patient survival. There is limited evidence to determine its relative efficacy compared to wide-field irradiation. Specific indications, recommendations for administration, and the need for further data about the treatment are summarized in the report.

Indications for strontium⁸⁹ therapy in this clinical setting

All of the following are required:

1. Established diagnosis of prostate cancer metastatic to bone
2. Metastatic disease refractory to hormone therapy
3. Progressive sites of pain poorly controlled with conventional narcotics
4. Painful sites of disease on both sides of the diaphragm (otherwise, hemibody radiation is equally efficacious)

5. Patient or tumour factors (number of involved sites, location of involved sites, or level of pain control) are relative contraindications to the use of multiple single fields of radiation as an alternative
6. No evidence of impending spinal cord compression
7. Adequate bone marrow reserve
8. Painful bony lesions concentrate radionuclide on diagnostic scan

Methods

Entries to MEDLINE (1985 through September 2001), CANCERLIT (1985 through August 2001) and Cochrane Library (1985 through 2001, Issue 3) databases have been searched for evidence relevant to this practice guideline. The most recent literature search was performed in October 2001. No new evidence has emerged from review and updating activities.

Evidence was selected and reviewed by three members of the Practice Guidelines Initiative's (PGI) Genitourinary Cancer Disease Site Group (GU DSG) and methodologists. This practice guideline has been reviewed and approved by the GU DSG, which comprises medical oncologists, radiation oncologists, urologists, a pathologist, and a community representative.

External Review by Ontario practitioners was obtained through a mailed survey. Final approval of the original guideline report was obtained from the Practice Guidelines Coordinating Committee (PGCC). The Practice Guideline Initiative has a formal standardized process to ensure the currency of each guideline report. This consists of periodic review and evaluation of the scientific literature, and where appropriate, integration of this literature with the original guideline information.

Key Evidence

Three randomized controlled trials were available for evaluation. One randomized study compared the use of strontium⁸⁹ to conventional radiation (either hemibody or local field irradiation as determined prior to randomization), and the other two compared strontium⁸⁹ to placebo.

One of two studies comparing strontium⁸⁹ to placebo demonstrated the palliative efficacy of the intervention ($p < 0.01$), while the other showed no benefit. A third study comparing the efficacy of strontium⁸⁹ with conventional radiation concluded that all treatments provided equally effective pain relief, and that improvement was sustained for at least three months in similar proportions of patients. The median duration of patient survival was neither clinically nor statistically different between groups in this study.

The use of strontium⁸⁹ may cause bone marrow suppression, but clinically significant sequelae are uncommon. The use of strontium⁸⁹ may preclude further systemic chemotherapy and/or eligibility for clinical trials of systemic therapy. Symptoms other than those due to bone marrow suppression are rare.

Future Research

- At present, many factors related to cost (such as need for hospitalization, expensive analgesics, further radiotherapy, and so on) have not been evaluated in a prospective analysis. Further information is also required regarding validated palliative outcome measures in studies enrolling larger numbers of patients, before a full cost-effectiveness analysis can be considered.

Part 2: Strontium⁸⁹ treatment for hormone-refractory prostate cancer skeletal metastases: adjunctive strontium⁸⁹ for patients receiving local radiotherapy

Guideline Question

What is the role of strontium⁸⁹ in effectively palliating patients with stage D hormone-refractory prostate cancer receiving local radiotherapy for isolated painful bony metastases?

Target Population

These recommendations apply to adult patients with stage D hormone-refractory prostate cancer receiving local radiotherapy for isolated painful bony metastases.

Recommendations

- Strontium⁸⁹ is not recommended for routine use as an adjunct to local radiotherapy in this clinical setting.
- Strontium⁸⁹ is known to temporarily reduce analgesic intake and to modestly delay the need for treatment of sites of new pain, when used as an adjunct to local field radiotherapy and when compared to placebo adjunct therapy. The clinical significance of these benefits is not certain.
- Strontium⁸⁹ has not been shown to lengthen the average duration of patient survival in this setting and there is no evidence to determine its relative efficacy compared with wide-field irradiation. The need for further data about the treatment is summarized in the report.

Methods

Entries to MEDLINE (1985 through September 2001), CANCELIT (1985 through August 2001) and Cochrane Library (1985 through to Issue 3, 2001) databases have been searched for evidence relevant to this practice guideline. The most recent literature search was performed in October 2001. No new evidence has emerged from review and updating activities.

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Key Evidence

One randomized controlled trial was available for evaluation. This study compared the use of strontium⁸⁹ to placebo injection as adjunctive treatment of patients receiving local radiotherapy for painful bony metastases from prostate cancer.

The randomized trial demonstrated that patients receiving strontium⁸⁹ had fewer analgesic requirements, fewer sites of new pain, and less need for additional local-field radiotherapy than patients receiving placebo. All of these differences were statistically significant. Differences in relief of pain at the index site and the duration of survival were neither statistically nor clinically significant.

The use of strontium⁸⁹ may cause bone marrow suppression, but clinically significant sequelae are uncommon. The use of strontium⁸⁹ may preclude further systemic chemotherapy and/or eligibility for clinical trials of systemic therapy. Symptoms other than those due to bone marrow suppression are rare.

Future Research

- At present, many factors related to cost (such as need for hospitalization, expensive analgesics, further radiotherapy, and so on) have not been evaluated in a prospective analysis. Further information is also required regarding validated palliative outcome measures in studies enrolling larger numbers of patients, before a full cost-effectiveness analysis can be considered.

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*The Practice Guidelines Initiative is sponsored by:
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The Practice Guidelines Initiative (PGI) is a project supported by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care, as part of the Program in Evidence-based Care. The purpose of the Program is to improve outcomes for cancer patients, to assist practitioners to apply the best available research evidence to clinical decisions, and to promote responsible use of health care resources. The core activity of the Program is the development of practice guidelines by multidisciplinary Disease Site Groups of the PGI using the methodology of the Practice Guidelines Development Cycle.¹ The resulting practice guideline reports are convenient and up-to-date sources of the best available evidence on clinical topics, developed through systematic reviews, evidence synthesis, and input from a broad community of practitioners. They are intended to promote evidence-based practice.

This practice guideline report has been formally approved by the Practice Guidelines Coordinating Committee, whose membership includes oncologists, other health providers, patient representatives, and Cancer Care Ontario executives. Formal approval of a practice guideline by the Coordinating Committee does not necessarily mean that the practice guideline has been adopted as a practice policy of CCO. The decision to adopt a practice guideline as a practice policy rests with each regional cancer network that is expected to consult with relevant stakeholders, including CCO.

Reference:

- ¹ Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. *J Clin Oncol* 1995;13(2):502-12.

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