

# <sup>89</sup>Sr chloride (Metastron®)

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## 1. Introduction

The most common symptom of skeletal metastases is pain. This can be treated initially using simple analgesia but it is often necessary to switch to morphine-based preparations, which cause significant side effects. Local radiotherapy frequently gives good results, but metastases are often multifocal, as is the associated pain. In such cases, radionuclide treatment with <sup>89</sup>Sr-chloride provides a good alternative.

<sup>89</sup>Sr is a radionuclide that behaves as calcium *in vivo* and is therefore taken up by osteoblastic skeletal metastases. <sup>89</sup>Sr is a pure  $\beta$ -emitter. The  $\beta$ -radiation which is emitted during the radioactive decay process can produce a reduction in pain. Approximately 80% of patients with prostate carcinoma in whom hormone therapy is no longer effective report a reduction in pain following <sup>89</sup>Sr therapy. Ten to 40% of these patients are subsequently pain-free. The effects become evident 10-20 days following injection, reaching a maximum at 4-5 weeks post injection. The reduction in pain lasts 3-4 months on average. It is possible to repeat the therapy for recurrent symptoms although a minimum interval of 12 weeks is recommended. Osteoblastic skeletal metastases from breast carcinoma also respond well to treatment using <sup>89</sup>Sr-chloride.

## 2. Methodology

This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

## 3. Indications and contraindications

### *Indications*

Patients should meet the following conditions (at least a and b):

- Skeletal scintigraphy which shows uptake of bisphosphonate in multiple skeletal metastases from a prostate carcinoma
- Pain in several areas despite adequate pain management
- Recurring pain in an area previously treated with radiotherapy

### *Contraindications*

#### *Absolute contraindications:*

- Thrombocyte count  $<100 \times 10^9/l$
- Leucocyte count  $<3,0 \times 10^9/l$
- Pregnancy

#### *Relative contraindications:*

- Transient, treatable urinary incontinence. (Urinary catheters provided for this purpose should remain *in situ* for five days.)
- Serum creatinine value  $>130 \mu\text{mol/l}$  (creatinine clearance  $<50 \text{ ml/min}$ )

3. Preferably, patients should not have undergone chemotherapy or extensive radiotherapy in the previous six months (because of bone marrow reserve)
4. Pain in conjunction with a neurological deficit due to metastatic invasion (local treatment is then preferable)

#### 4. Relation to other therapies

The effectiveness of <sup>89</sup>Sr-chloride is, like <sup>188</sup>Re-HEDP and <sup>153</sup>Sm-EDTMP, comparable to that of external radiotherapy. External radiotherapy (or neurosurgery) is always preferable in patients with myelocompression or threatened/current neurological deficit. Extensive neurological examination should be a standard part of the analysis of patients with painful skeletal metastases. Previous external radiotherapy confined to a limited area is not a contraindication for treatment using <sup>89</sup>Sr-chloride.

Nowadays, patients with prostate cancer are often suitable for chemotherapy. Due to its long physical half-life, <sup>89</sup>Sr is not recommended in patients receiving (myelotoxic) chemotherapy. Therefore, the use of <sup>89</sup>Sr-chloride for bone metastasis of prostate cancer is nowadays limited. Short-lived radiopharmaceuticals such as <sup>188</sup>Re-HEDP and <sup>153</sup>Sm-EDTMP are to be preferred. In contrast to <sup>188</sup>Re-HEDP and <sup>153</sup>Sm-EDTMP, <sup>89</sup>Sr-chloride is not indicated for patient with bone metastases from primaries other than prostate cancer.

#### 5. Radiopharmaceutical

Strontium-89-chloride

##### a. Kinetics

<sup>89</sup>Sr is available as Strontium chloride (SrCl<sub>2</sub>) in a sterile water solution for intravenous administration. <sup>89</sup>Sr is a pure β particle-emitting nuclide with a physical half-life of 51 days and which decays into stable <sup>89</sup>Y. The maximum soft tissue range is approximately 8 mm (average 2,4 mm). Strontium behaves in a similar way to calcium in-vivo and is taken up in bone-forming cells (osteoblasts). Studies using intravenously administered <sup>89</sup>Sr-chloride show increased accumulation at the site of skeletal metastases compared to normal bone tissue. The biological half-life of <sup>89</sup>Sr-chloride in skeletal metastases is longer (approximately 50 days) than its half-life in normal bone tissue (14 days). This results in a higher radiation dose to the metastases compared to normal bone tissue (and bone marrow).

Approximately 85% of the Strontium chloride is ultimately excreted into the urine with a renal plasma clearance of approximately 1,5 to 11,5 l/day. Less than 10% is excreted on the first day. This rate of excretion is usually lower in patients with skeletal metastases. The total body retention after three months varies between 11 and 88% depending on the extent of metastasis.

##### b. Dosage

The effectiveness of treatment with <sup>89</sup>Sr-chloride has been shown to be optimal using a dose of 1,5 MBq/kg body weight per treatment. A standard total dose of 150 MBq is given (irrespective of body weight). The dose is administered intravenously. This must be done slowly (over at least four minutes) as too rapid an injection can cause a 'calcium flush'.

#### 6. Radiation safety

##### Dosimetry

The dose conversion coefficient (ingestion DCC) of <sup>89</sup>Sr is  $3,4 \times 10^{-9}$  Sv/Bq. The inhalation DCC is  $1,2 \times 10^{-8}$  Sv/Bq.

The radiation dose to individual bone metastases is between 9-92 Gy depending on the size of the lesion. The average bone marrow dose following administration of 150 MBq is approximately 3 Gy. The effective dose (H50,E) to the patient is 0,4 Sv per treatment. The effective dose to persons continually present in the direct environment as a result of external irradiation from a patient is approximately 10 µSv. This dose can increase to a maximum of 40 µSv in the event of internal contamination.

#### *Toxicity/side effects*

During the first 48 h following administration of the radionuclide, a small number of patients may experience an increase in pain (known as the 'flare phenomenon') which recedes spontaneously and is generally followed by a good response to the Strontium therapy.

The thrombocyte count is the most sensitive parameter with regard to bone marrow toxicity. Thrombocytopenia to the order of approximately 70% may occur reaching its lowest point after 4-6 weeks; recovery is seen within 3-6 months. Severe thrombocytopenia is rare and may occur in patients with known bone marrow deficiency, for example as a result of chemotherapy. Bone marrow toxicity also increases with repeated <sup>89</sup>Sr-chloride treatments.

### **7. Patient preparation/essentials for procedure**

- Laboratory facilities required
- Preparatory work must be carried out in a radiopharmacy department compliant with GMP-z.

#### *Data on request form*

- a. Type of carcinoma, location of primary tumour and locations of known metastases
- b. Medical history, including details of hormonal therapy, chemotherapy and radiotherapy
- c. Result of recent scintigraphy (2-8 weeks) and a copy of the scintigraphy if performed elsewhere
- d. Blood results, including a recent serum calcium level, thrombocyte and leukocyte count, serum creatinine level and, if relevant, creatinine clearance
- e. Co-medication

#### *Method*

Confirm that the patient has not been given biphosphonates (APD) in the previous 48 h. Calcium therapy should be discontinued for at least two weeks prior to treatment. The radiopharmaceutical should be slowly administered intravenously, through a drip or butterfly needle and three-way tap, over a period of four minutes and subsequently flushed with saline. The syringe containing <sup>89</sup>Sr-chloride should be protected with a Perspex syringe shield. The product can be administered on an out-patient basis, and there are no restrictions on normal interactions with friends or relations.

#### *After-care*

The radiopharmaceutical is excreted mainly into the urine and the toilet to be used should therefore be connected to sewage, and not a septic tank. Special sewage tanks are not required (see Aanbevelingen VROM (recommendations of the Dutch Ministry of Housing,

Spatial Planning and Environment)). Haematological values should be checked every two weeks following therapy to determine whether the thrombocyte levels have returned to normal (after approximately 8 weeks). The first outpatient follow-up appointment should be scheduled for three weeks after treatment. In the event of a significant reduction in thrombocytes, the patient should return for weekly follow-up appointments until the thrombocyte level has returned to normal. Follow-up nuclear medicine appointments should be scheduled in close collaboration with the patient's lead specialist. The patient should be instructed to use adequate contraception for the four months following treatment. Incontinent patients should be given sufficient incontinence materials to last five days. It is important to note that patients excrete significant amounts of <sup>89</sup>Sr in the urine for a significant period of time following the treatment. The ADL (activities of daily living) guidelines recommended by the VROM (Dutch Ministry Housing, Spatial Planning and the Environment), SZW (Dutch Ministry of Social Affairs and Employment) and the NVNG (Dutch Society of Nuclear Medicine) should be issued to and discussed with patients and their carer(s). Operating theatres and pathology laboratories are not required to take any additional radiation safety measures (other than normal radiation safety procedures) when working with patients who require surgery within two weeks of receiving <sup>89</sup>Sr therapy.

Death of the patient following administration of <sup>89</sup>Sr: Cremation of the patient is not prohibited although scattering of the ashes over land is not permitted.

## 8. Literature

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