

# A Dose-Controlled Study of $^{153}\text{Sm}$ -Ethylenediaminetetramethylenephosphonate (EDTMP) in the Treatment of Patients With Painful Bone Metastases

*Resche I, Chatal J-F, Pecking A, et al. Eur J Cancer. 1997;33:1583-1591.*

## Study Highlights

- Single doses of Samarium Sm-153 Lexidronam ( $^{153}\text{Sm}$ -EDTMP) alleviated the pain of bone metastases in the majority of patients
- $^{153}\text{Sm}$ -EDTMP provided rapid onset of pain relief with transient hematological toxicity

## Purpose

- To assess the comparative efficacy and safety of 0.5- and 1.0-mCi/kg doses of  $^{153}\text{Sm}$ -EDTMP in patients with bone metastases from a variety of primary tumors

## Study Design

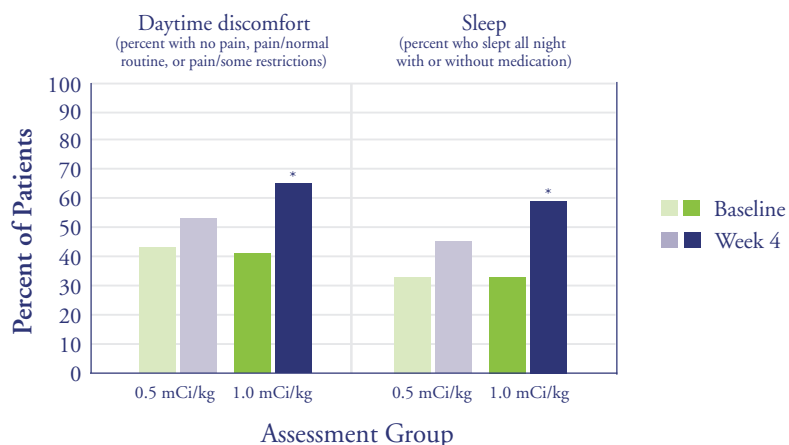
- Randomized, dose-controlled study of 114 patients
  - Patients had pain at one or more sites overlying abnormal uptake on the bone scan, a performance status  $\geq 40$ , and expected survival  $\geq 4$  months
  - Patients were excluded if they had granulocytes  $< 2000/\mu\text{L}$ , platelets  $< 150,000/\mu\text{L}$ , or serum creatinine  $> 2.0$  mg/dL
- Patients were randomized to receive either 0.5 (n=55) or 1.0 (n=59) mCi/kg  $^{153}\text{Sm}$ -EDTMP administered intravenously
  - Patients did not know which dose they were receiving
- All patients completed diaries to record pain intensity, sleep characteristics, and analgesic use
- Physician assessments were also completed
- The most common primary tumors were prostate (59%) and breast (32%) cancer
  - Approximately 1/3 of patients had received prior chemotherapy

## Results

### EFFICACY

- Patients reported alleviation of their bone pain at both doses, with a greater improvement in patients receiving the 1.0-mCi/kg dose
  - Onset of pain relief occurred during the first week for the majority of patients who responded in the 1.0 mCi/kg group
  - The difference in pain relief at week 4 between the two groups was statistically significant ( $P < .05$ )

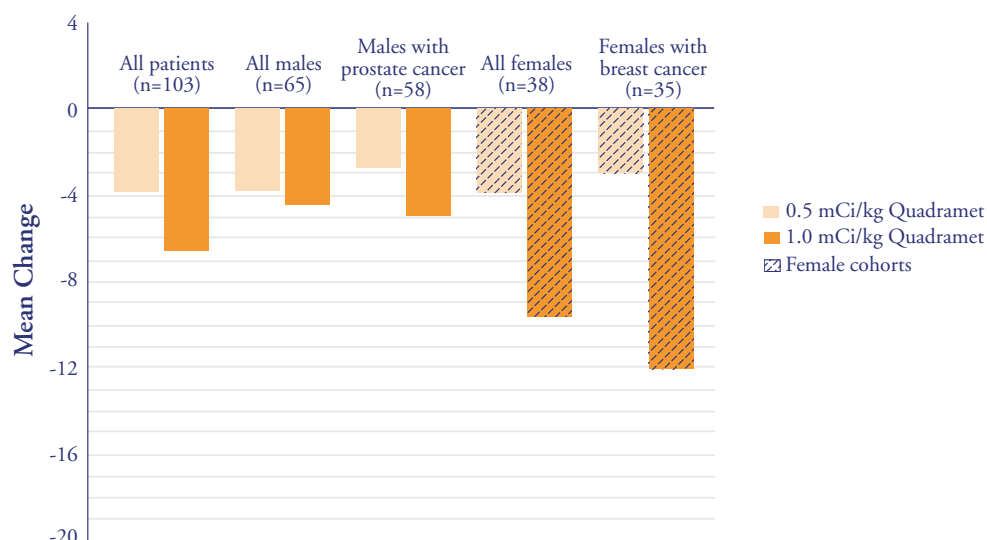
### Significant improvement in sleep and daytime discomfort



\* Statistically significant difference from baseline ( $P < .05$ ).

- There was a statistically significant improvement in patients daytime comfort and ability to sleep through the night from baseline to Week 4 in the 1.0 mCi/kg cohort ( $P < .05$ )
- At Week 4, 70% of patients in the 1.0 mCi/kg group and 67% of those in the 0.5 mCi/kg group thought that  $^{153}\text{Sm-EDTMP}$  treatment lessened their pain

### Change in AUPC at Week 4 in subgroups of patients



- Patient diaries also indicated a statistically significant mean decline in area under the pain curve (AUPC) scores from baseline to Week 4 in the 1.0 mCi/kg cohort ( $P < .05$ )
- At week 16, 39% of patients receiving the higher dose were classified as responders, compared with 31% of patients receiving the lower dose
- Response was highest in women, particularly in those with breast cancer, occurring in 40% of breast cancer patients in the 0.5-mCi/kg group, and 80% of breast cancer patients in the 1.0-mCi/kg group

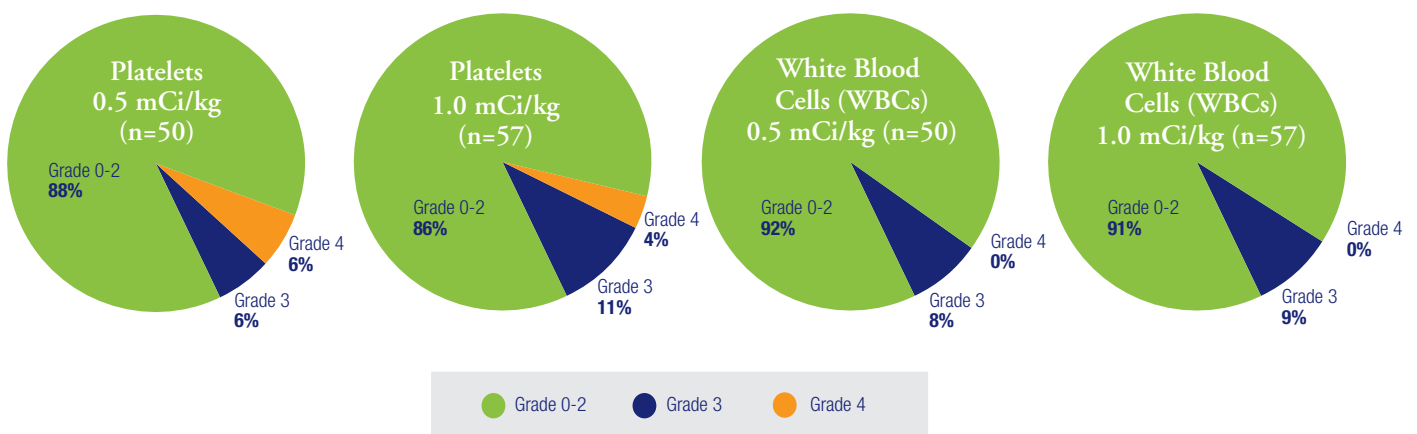
## TOLERABILITY

- Transient pain flares occurred in 11% of patients receiving 0.5 mCi/kg and in 8% of patients receiving 1.0 mCi/kg
- There was a predictable level of dose-related marrow suppression
  - Mean white blood cell (WBC) and platelet nadirs were lower, and the changes from baseline greater, for the 1.0 mCi/kg group than for the 0.5 mCi/kg group
  - In both groups, WBC and platelet counts reached a nadir at 3 to 4 weeks, and then generally recovered by week 8

## Platelet and WBC nadirs

	0.5 mCi/kg (n=50)	1.0 mCi/kg (n=57)
<b>Platelets</b>		
Mean nadir (/μL)	154,000 (±12,000)	119,000 (±9,000)
Mean % of Baseline	56%	43%
Time to nadir (weeks)	4	4
<b>WBCs</b>		
Mean nadir (/μL)	4400 (±212)	3600 (±172)
Mean % of Baseline	60%	49%
Time to nadir (weeks)	4	3

## Hematologic toxicity by grade



- Three patients (6%) in the 0.5 mCi/kg group and 2 patients (4%) in the higher dose group developed grade 4 platelet toxicity (<25,000/μL); one of these patients had a baseline count of 31,000/μL, and the other four received either external beam radiation (n=3) or chemotherapy (n=1) after receiving the study agent
- Grade 3 WBC toxicity occurred in 8% (n=4) of the lower dose cohort and 9% (n=5) of the higher dose; there were no incidents of grade 4 WBC toxicity

## Conclusions

- The 1.0 mCi/kg dose was found to be safe and effective for the treatment of painful bone metastases
- Pain relief results observed in the women with breast cancer suggest that the 1.0 mCi/kg dose would be expected to work well in this highly pretreated patient population
- Excellent efficacy and well-defined toxicity may make  $^{153}\text{Sm}$ -EDTMP appropriate for use in earlier stages of treatment of metastases

## Indication

Quadramet® (Samarium Sm-153 leixidronam injection) is indicated for relief of pain in patients with confirmed osteoblastic metastatic bone lesions that enhance on radionuclide bone scan.

## Important Safety Information

Because of the unknown potential for additive effects on bone marrow, Quadramet should not be given concurrently with chemotherapy or external beam radiation unless the clinical benefits outweigh the risks. Commonly observed adverse events for Quadramet: bone marrow toxicity occurred in 47% of patients in clinical trials. Myelosuppression may increase the risk of infectious and hemorrhagic adverse events. Non-hematologic adverse events that occurred in  $\geq 5\%$  of patients and greater than placebo were pain flare (7%), diarrhea (6%), infection (7%), spinal cord compression (6.5%), arrhythmias (5.0%) and hematuria (5.0%). Patients taking Quadramet should have blood counts monitored for at least 8 weeks, or until recovery of adequate bone marrow function. Quadramet should not be used in patients who have known hypersensitivity to EDTMP or similar phosphonate compounds; women of childbearing age should have a negative pregnancy test before administration of Quadramet. If Quadramet is administered to a nursing mother, formula feeding should be substituted for breast feeding. Patients who receive Quadramet should be advised that for several hours following administration, radioactivity will be present in excreted urine. To help protect themselves and others in the environment, precautions need to be taken for 12 hours following administration.

Please see accompanying full prescribing information.

