

## Safety and Efficacy of Repeat Administration of Samarium Sm-153 Lexidronam to Patients With Metastatic Bone Pain

*Sartor O, Reid RH, Bushnell DL, et al. Cancer. 2007;109:637-643.*

### Study Highlights

- The decrease in pain intensity scores and the percentage of patients responding was similar after multiple administrations of Samarium Sm-153 Lexidronam (Sm-153) to that after initial administration
- Treatment of bone pain with Sm-153 was repeated without significantly increasing toxicity

### Purpose

- To evaluate the use of 1.0 mCi/kg of Sm-153 for palliation of bone pain in patients who initially respond and are subsequently candidates for additional treatments upon recurrence of painful symptoms

### Study Design

- Multicenter, open-label study of 202 patients
  - Patients were included if they had painful bone metastases, recurrence after response to antineoplastic therapy, and a performance status  $\geq 50$
  - Patients were excluded if they had life expectancy  $< 2$  months, palliative radiation therapy within 6 weeks of dosing, chemotherapy within 4 weeks of dosing, white blood cell (WBC)  $< 4000/\text{mm}^3$ , platelets  $< 100,000/\text{mm}^3$ , serum creatinine  $> 2.0$  mg/dL; serum bilirubin  $> 2.0$  mg/dL
- Patients were eligible for Sm-153 retreatment if pain was improved by week 4 with initial treatment, but subsequently recurred after 8 weeks
- The most common primary tumors were prostate (77%) and breast (15%) cancer

## Study Design (cont'd)

### Percentages of patients receiving prior treatments

Prior treatment	All patients (n=202)	Patients receiving multiple administrations (n=55)
Surgery	97%	98%
Chemotherapy	26%	25%
Radiation	76%	71%
Chemotherapy plus radiotherapy	23%	24%

- Pain was reported using the Brief Pain Inventory (BPI) at baseline and weeks 4 and 8
  - Analyses were conducted in two patient groups—those who received  $\geq 2$  doses of Sm-153 (n=55), and those who received  $\geq 3$  doses of Sm-153 (n=11)
- Demographics and baseline hematologic parameters were similar among patients who received single doses and those who eventually received multiple doses
- The median interval between the first two infusions was 140 days, and the median interval between infusions after the second was 78 days
- For patients receiving multiple doses a mean of 2.4 doses were administered (range: 2 to 11 infusions)

## Results

### TOLERABILITY

- The only clinically significant toxicity noted was transient myelosuppression
  - WBC and platelet counts reached a nadir of approximately 50% of baseline at 4 weeks, and then recovered by week 8 in approximately 90% of patients after single or multiple administrations
  - There were no effects on hemoglobin levels

### WBC and platelet nadirs

	All patients dose 1 Nadir, (% of baseline)		Patients receiving multiple doses* Nadir, (% of baseline)	
	Dose 1 (n=188)	Dose 1 (n=54)	Dose 2 (n=51)	Dose $\geq 3$ (n=24)
Platelets	116 $\pm$ 66 (44%)	127 $\pm$ 36 (48%)	107 $\pm$ 50 (47%)	93 $\pm$ 38 (50%)
WBCs	3.6 $\pm$ 1.2 (50%)	3.7 $\pm$ 1.1 (49%)	3.6 $\pm$ 1.1 (54%)	3.5 $\pm$ 0.9 (61%)

\*Patients with  $\geq 21$  days postinfusion hematology data.

## WBC and platelet toxicity by grade

	Toxicity Grade	All patients dose 1 no. (%)		Patients receiving multiple doses* no. (%)	
		Dose 1 (n=188)	Dose 1 (n=54)	Dose 2 (n=51)	Dose ≥3 (n=24)
Platelets	0-2	167 (89%)	54 (100%)	45 (88%)	20 (83%)
	3	20 (11%)	0 (0%)	6 (12%)	4 (17%)
	4	1 (0.5%)	0 (0%)	0 (0%)	0 (0%)
WBCs	0-2	175 (93%)	52 (96%)	50 (98%)	23 (96%)
	3	13 (7%)	2 (4%)	1 (2%)	1 (4%)
	4	0 (0%)	0 (0%)	0 (0%)	0 (0%)

\*Patients with ≥21 days postinfusion hematology data.

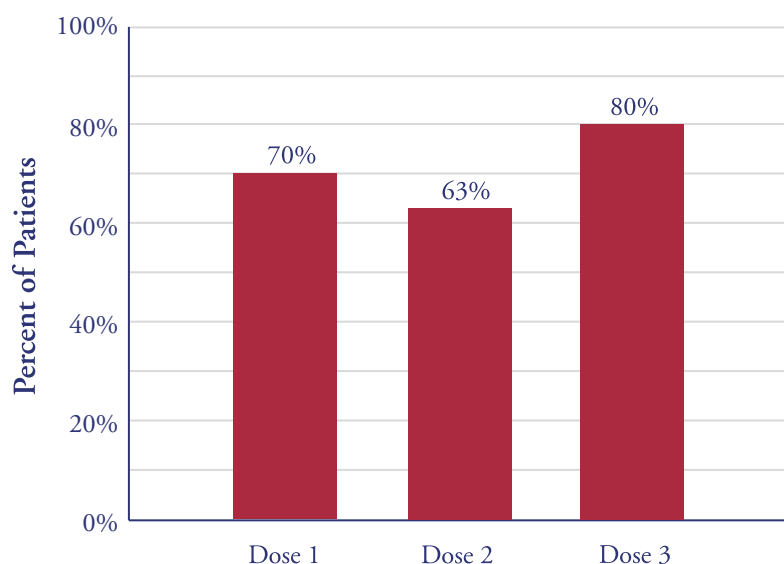
- The incidence of grade 3 WBC toxicity was similar after repeat administrations to that after initial administration
- There were no incidences of grade 4 WBC toxicity after any administration
- There were no incidences of grade 4 platelet toxicity among patients receiving multiple doses
- Nonhematologic adverse events were usually attributed to the patient's underlying disease or other medications
- Bone pain flares occurred in 2.5% of patients, all after initial administration

*“Recovery to  $PLT >75,000/mm^3$  and  $WBC >3,000/mm^3$  (toxicity grade 1 or less) by Week 8 occurred in 89.9% (160/178) of patients after an initial administration and 90.4% (66/73) after a second or greater administration.”*

## EFFICACY

- Patients receiving 2 doses reported significant alleviation of their bone pain at weeks 4 ( $P<.0001$ ) and 8 ( $P<.003$ )  
— After a third dose, decreases in pain were significant at week 4, but not at week 8

## Percent of patients with decrease in Week 4 pain scores by dose



## Conclusions

- Repeated administration of Sm-153 is both efficacious and well tolerated in the treatment of bone pain
- Sm-153 may be considered a reasonable treatment option for bone pain that recurs after an initial dose, provided that baseline hematologic criteria are adequate
- Adverse events did not increase with repeat dosing of Sm-153

## Indication

Quadramet® (Samarium Sm-153 lexidronam 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.

