

Samarium-153-lexidronam Complex for Treatment of Painful Bone Metastases in Hormone-Refractory Prostate Cancer

Sartor O, Reid RH, Hoskin PJ, et al. Urology. 2004;63:940-945.

Study Highlights

- The results of this study demonstrated that Samarium-153-lexidronam (¹⁵³Sm-lexidronam) is safe and effective for the relief of the pain of bone metastases in patients with hormone-refractory prostate cancer
- Myelosuppression was mild and transient

Purpose

- To evaluate the safety and efficacy of ¹⁵³Sm-lexidronam for the palliation of bone pain in patients with hormone-refractory prostate cancer

Study Design

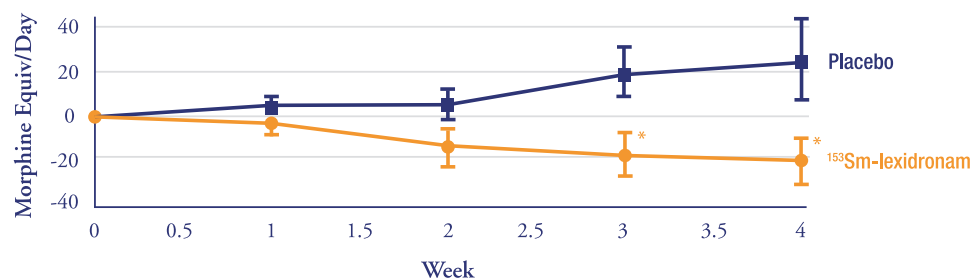
- Prospective, randomized, placebo-controlled study of 152 patients with painful bone disease secondary to prostate cancer disease progression
 - Among the inclusion criteria were: a positive bone scan, significant bone pain, and/or use of opioid analgesics in daily doses equivalent to 60 mg oral morphine
 - Patients were excluded if they had received hormonal therapy within 8 weeks of dosing or radiotherapy within 6 weeks of dosing
- Patients were randomized to receive either 1 mCi/kg ¹⁵³Sm-lexidronam (n=101) or placebo (n=51) administered intravenously over 1 minute
 - Patients also received 1000 mL oral or intravenous fluid 4 hours before and/or 6 hours after administration of study drug
- All patients completed daily diaries to record pain intensity and analgesic use
- 80% of patients were taking opioid analgesics at baseline, at a mean oral morphine dose equivalent of 78.6 mg in the placebo arm and 96.5 in the active treatment arm
- Nonresponders were unblinded at week 4 so that those randomized to placebo would have the opportunity to switch to potentially active treatment

Results

EFFICACY

- There was a significant improvement in analgesic consumption and rapid pain relief in patients treated with ^{153}Sm -lexidronam
 - Pain intensity was evaluated using a linear 100-mm visual analog scale (VAS) and a pain descriptor scale (PDS) as recorded in patient diaries

Change in opioid use

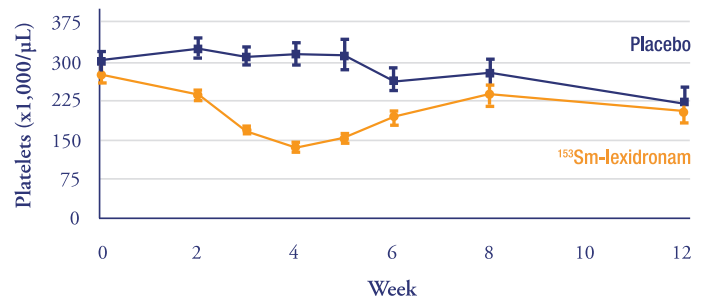
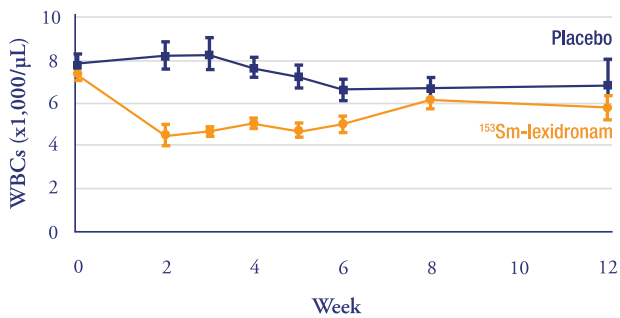


- The difference in opioid use indicated that the pain relief achieved among ^{153}Sm -lexidronam responders was not attributable to increased use of analgesics in that cohort
- Complete pain response occurred more frequently in patients receiving ^{153}Sm -lexidronam compared to those receiving placebo (38% vs 18%, respectively, $P=.008$)
- 35% of ^{153}Sm -lexidronam-treated vs 55% of placebo-treated patients were unblinded after 4 weeks due to lack of response
 - 43% chose to receive open-label treatment with ^{153}Sm -lexidronam
- PSA levels decreased by more than 50% in 9% of ^{153}Sm -lexidronam-treated patients and in 5% of placebo-treated patients

TOLERABILITY

- The only clinically significant toxicity associated with treatment was mild transient myelosuppression
 - In the active treatment group, white blood cell (WBC) and platelet counts decreased after drug administration, reached a nadir at 3 to 4 weeks, and then recovered to normal values by week 8
 - Nadir WBC and platelet counts averaged 3800/μL (\pm 1400/μL) and 127,000/μL (\pm 53,000/μL), respectively
 - None of the patients experienced a grade 4 WBC or platelet toxicity
- Pain flares occurred at the same frequency (6%) in both treatment groups

WBC and platelet counts



Hematologic toxicity by grade

	Toxicity Grade	Placebo (n=47)	¹⁵³ Sm-lexidronam (n=93)
Hemoglobin	0-2	41 (87%)	82 (88%)
	3	5 (11%)	10 (11%)
	4	1 (2)	1 (1)
Platelets	0-2	47 (100%)	90 (97%)
	3	0 (0%)	3 (3%)
	4	0 (0%)	0 (0%)
WBCs	0-2	47 (100%)	87 (95%)
	3	0 (0%)	5 (5%)
	4	0 (0%)	0 (0%)

Toxicity grades defined as hemoglobin: grade 0-2, \geq 8.0 g/dL, grade 3, 6.5-7.9 g/dL, grade 4 <6.5 g/dL; platelets: grade 0-2, \geq 50,000/μL, grade 3, 25,000-49,900/μL, grade 4, <25,000/μL; WBCs: grade 0-2, \geq 2,000/μL, grade 3, 1,000-1,900/μL, grade 4, <1,000/μL.

Conclusions

- This study demonstrated that ^{153}Sm -lexidronam effectively reduces the pain of bone metastasis in patients with hormone-refractory prostate cancer
- The safety profile of ^{153}Sm -lexidronam makes it a valuable treatment option for this patient population

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.

