

¹⁷⁷Lu-EDTMP for Treatment of Bone Pain in Patients with Disseminated Skeletal Metastases

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¹⁷⁷Lu-labeled ethylenediaminetetramethylene phosphonic acid (¹⁷⁷Lu-EDTMP) is an agent that concentrates in areas of enhanced osteoblastic activity. The potential of ¹⁷⁷Lu-EDTMP for palliation of metastatic bone pain has been documented in the recent literature. The objective of the present work was to study the efficacy and safety of the agent after administration to a limited number of patients. **Methods:** Ten patients (median age, 68.5 y) with disseminated skeletal metastases received a single bolus infusion of ¹⁷⁷Lu-EDTMP (3.7 GBq). All patients had painful bone metastases in more than one anatomic region that were not relieved by narcotic analgesics. The efficacy of the agent was studied by following pain scores assessed at baseline and at 4, 8, and 12 wk after therapy, by using Karnofsky indices and mobility scores, and by determining the requirement for analgesics at baseline and 4 wk after therapy. The toxicity of the agent was assessed by analyzing complete blood counts. **Results:** A significant reduction in the mean pain score was noted in all patients. The initial mean pain score of 8.44 dropped to 5.73 within 1 mo of treatment. Six patients who required analgesics for pain management had either reduced or completely withdrawn from their use by 4 wk. Compared with initial scans, scans obtained 1 mo after therapy also showed a decreased uptake of the radiotracer. The mobility scores of all patients were higher at 4 wk. The mean Karnofsky performance score of all patients was initially 45 and increased markedly to 69 at 4 wk. None of the patients experienced blood-related toxicity. **Conclusion:** ¹⁷⁷Lu-EDTMP, with only low bone marrow toxicity, provided significant pain relief to patients and considerably increased their mobility, resulting in an overall improvement in the quality of life. The results of the preliminary clinical studies indicate that ¹⁷⁷Lu-EDTMP can be considered an effective and safe therapeutic radiopharmaceutical for pain palliation of patients with disseminated skeletal disease.

Key Words: ¹⁷⁷Lu-EDTMP; therapeutic radiopharmaceutical; bone pain palliation; osseous metastases

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Skeletal metastases are common in many malignancies. Patients with disseminated skeletal metastases often experience severe and refractory pain, and their condition is complicated by fractures, which may impair quality of life. Chemotherapy is ineffective in more than 50% of patients with multiple skeletal metastases. Although external-beam radiation therapy can provide significant palliation in up to three fourths of patients with osseous metastases, the amount of radiation the body can be subjected to in such therapy, even with regional fields, is limited. Furthermore, when one site is being treated for pain relief, other areas outside the radiation field may become symptomatic.

A second viable option for palliative therapy of bone pain is the use of radiopharmaceuticals. In patients with more than one metastatic bone site, the systemic administration of a radiotherapeutic substance has the potential to treat multiple metastases simultaneously. This approach has the advantage of presenting both an antitumoral effect and a secondary analgesic effect (1). The most commonly used radiopharmaceuticals in the treatment of bone are ⁸⁹SrCl₂, ³²P-orthophosphate, and ¹⁵³Sm-labeled ethylenediaminetetramethylene phosphonic acid (EDTMP). A characteristic of these radiopharmaceuticals is their affinity for skeletal tissue, especially in areas undergoing construction. Low radiation (β emissions) irradiates tumor cells while having only minimal effect on normal bone (1). The actual process by which pain palliation takes place is still unknown, but there are reports of patients experiencing a dramatic alleviation of their pain in a short period. The response is observed typically 1–3 wk after injection, and the response duration has a wide range from 2 to 12 mo, with a median response of 3–4 mo (2).

All 3 radiopharmaceuticals mentioned above are regularly used for the treatment of patients with metastatic bone pain and have already proven to be efficacious in alleviating the pain (3). Nonetheless, there is a need to develop radiopharmaceuticals with more favorable characteristics. The nuclear decay characteristics of ¹⁷⁷Lu are quite attractive for developing newer agents for bone pain palliation as it emits lower-energy β[−] radiation along with γ photons capable of being imaged and has an adequately long half-life, making it suitable for wider distribution (4). In the present

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TABLE 1
Demographic and Clinical Parameters in the 10 Patients of the Study Population

Parameter	Data
Median age (y)	68.5 (range, 52–78)
Mean duration of cancer (mo)	30 (range, 3–120)
Type of cancer (n)	
Lung	4
Prostate	3
Breast	2
Esophagus	1
Prior radiotherapy (n)	6 (60%)
Median time since last radiotherapy (mo)	8 (range, 4–10)
Prior chemotherapy (n)	4 (40%)
Median time since last chemotherapy (mo)	18 (range, 2–34)
Prior radionuclide therapy (n)	6 (60%)
Median time since last radionuclide therapy (mo)	8 (range, 5–27)
Median baseline scores	
Skeleton-based pain	8.44 (range, 7.2–9.8)
Mobility	2.99 (range, 2–4)
Karnofsky performance	45 (range, 40–50)
Median 4-wk scores	
Skeleton-based pain	5.73 (range, 4.8–6.9)
Mobility	1.3 (range, 1–2)
Karnofsky performance	69 (range, 60–80)
Median 8-wk skeleton-based pain score	3.82 (range, 3.3–4.8)
Median 12-wk skeleton-based pain score	1.71 (range, 1.2–2.2)

paper, we report our experience with and results from using ^{177}Lu -EDTMP in the treatment of bone pain in patients with disseminated skeletal metastases.

MATERIALS AND METHODS

Patients

The study group comprised 10 patients (7 men and 3 women) between 52 and 78 y old (mean age, 68.5 y). There were 4 patients with lung cancer, 3 with prostate cancer, 2 with breast cancer, and 1 with esophagus cancer. Among them, 6 patients had already undergone prior radionuclide therapy (4 with ^{153}Sm -EDTMP and 2 with ^{32}P -orthophosphate). The institutional review board approved this study, and all subjects signed a written informed consent form.

Eligibility Criteria

To be eligible for inclusion in the present study, patients had to have histologically proven carcinoma and be diagnosed with disseminated skeletal metastases through $^{99\text{m}}\text{Tc}$ -methylene diphosphonate whole-body scans. All patients also had to have consistent bone pain (baseline mean pain scores greater than 6 on the visual analog scale (5)) and insufficient response or intolerance to opioid analgesics. Adequate bone marrow function, including a hemoglobin level of less than 14 g/dL, total leukocyte counts greater than $3.5 \times 10^9/\text{L}$, and platelet counts greater than $100 \times 10^9/\text{L}$, was required. Performance status based on the Karnofsky score (6) needed to be 40 or above, and estimated life expectancy had to be at least 3 mo. Exclusion criteria included chemotherapy or radiotherapy within 4 wk before enrollment in this study; a super-scan finding on bone scintigraphy, pathologic bone fractures or spinal cord compression, age younger than 18 y, and pregnancy.

^{177}Lu -EDTMP Therapy

^{177}Lu -labeled EDTMP was prepared in the Radiopharmaceuticals Division (presently known as Isotope Applications and

Radiopharmaceuticals Division) of Bhabha Atomic Research Centre following the protocol approved by the Radiopharmaceutical Committee. ^{177}Lu was produced by irradiating an enriched Lu_2O_3 target (82% in ^{176}Lu) in the “Dhruva” reactor of the Bhabha Atomic Research Centre and was radiochemically processed using a reported procedure (4). EDTMP was also synthesized in-house following a procedure documented in the literature (7). A single patient dose of 3.7 GBq (100 mCi) of ^{177}Lu -EDTMP was prepared by incubating $^{177}\text{LuCl}_3$ with an aqueous solution containing 35 mg of EDTMP and 84 mg of sodium bicarbonate at room temperature for 15 min. The volume of the preparation was adjusted to 5 mL using normal saline, and the final preparation was subjected to Millipore filtration before its dispatch to Kovai Medical Center and Hospital for clinical applications. The agent was administered as a slow intravenous injection. Patients were examined and followed up at baseline and at 4, 8, and 12 wk after administration, usually as outpatients.

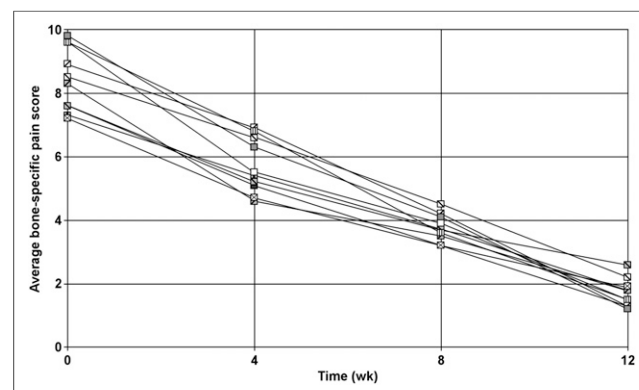


FIGURE 1. Individual bone-specific pain scores for 10 patients with skeletal metastases before and after treatment with ^{177}Lu -EDTMP.

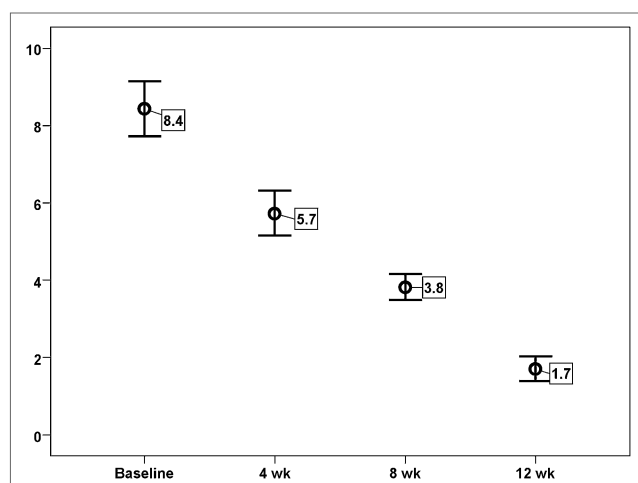


FIGURE 2. Comparison of mean pain score of study group.

Efficacy and Safety Assessments

Whole-body images of each patient were obtained on a dual-head γ camera (Symbia T-200; Siemens) at 1 d, 1 wk, and 1 mo after therapy. The 1-d image was used to determine the biologic distribution of the agent, whereas the 1-wk and 1-mo images were used to assess retention of the tracer in the body. Records of bone pain were evaluated at baseline and at 4, 8, and 12 wk after treatment. The pain score was calculated by taking the average score of all pain sites in each patient using a visual analog scale (5). A score of 0 indicated no bone pain, and a score of 10 indicated constant, severe bone pain. Use of analgesics was assessed by multiplying a score for the type of medication by the frequency of administration.

Data on analgesic use and quality of life were taken at baseline and at 4 wk. Regarding use of analgesics, a score of 0 indicated no analgesic use; a score of 1, use of nonsteroidal antiinflammatory drugs; a score of 2, mild narcotics; and a score of 3, strong narcotics. Regarding frequency of administration, a score of 0 indicated use of no analgesics; a score of 1, 1 tablet a day; a score of 2, 2 tablets a day; a score of 3, 3 or 4 tablets a day; and a score of 4, more than 4 tablets a day. Quality of life was assessed by mobility scores and Karnofsky (6) performance scores. A mobility score of 0 indicated pain-free mobility; a score of 1, mobility with some pain; a score of 2, mobility with moderate pain; a score of 3, mobility with severe pain; and a score of 4, complete immobility.

At baseline and at 2, 4, and 6 wk after therapy, vital parameters (e.g., blood pressure, pulse, and weight) were taken and a complete blood count (erythrocyte, leukocyte, and platelet counts) was performed. Toxicity was graded according to Common Terminology Criteria for Adverse Events, version 4.0.

Data Analysis

SPSS, version 20 (IBM) was used to calculate mean and SD. For each patient, the posttreatment data were compared with the pretreatment data (baseline) using a paired-sample *t* test. Assumption for using such statistics has been checked and found to be appropriate for this analysis. Values are presented with 95% confidence interval, and the *P* value for each comparison was measured, with a value of less than 0.05 being considered statistically significant. An error plot comparing the mean values of the 3 analyses was obtained.

RESULTS

^{177}Lu -EDTMP

The ^{177}Lu -labeled EDTMP was prepared with high radiochemical purity (mean, 99.41%; SD, 0.47%) as determined using paper chromatography with saline as the mobile phase (7).

Patient Characteristics

Patient characteristics are shown in Table 1. All patients had widespread skeletal involvement with painful metastases. In most patients, opioids were ineffective, and many patients had received prior palliative radiotherapy or systemic chemotherapy. Six patients had also undergone prior radionuclide therapy. The length of follow-up was 12 wk.

Pain and Performance Assessment

The individual pain scores showed a significant decrease in pain over the 12 wk of the study (Fig. 1). The mean pain score was 8.4 (SD, 1.0; range, 7.2–9.8) at baseline, 5.7 (SD, 0.81; range, 4.8–6.9) at 4 wk, 3.8 (SD, 0.46; range, 3.3–4.8) at 8 wk, and 1.7 (SD, 0.44; range, 1.2–2.2) at 12 wk. The score at 12 wk was 20.2% of the score at baseline (Fig. 2). The difference between the mean pain score at 4, 8, and 12 wk and the mean pain score at baseline was statistically significant ($P < 0.001$) (Table 2). All patients who were on analgesics before therapy had reduced or complete withdrawal from them by 4 wk.

The observed relief in bone pain was accompanied by an improvement in the mobility score and the Karnofsky performance score. The mean mobility score was 2.9 (SD, 0.56; range, 2–4) at baseline and decreased markedly to 1.3 (SD, 0.48; range, 1–2) at 4 wk (Fig. 3), corresponding to 44.8% of the baseline score, primarily because of improved mobility. The mean Karnofsky performance score was 45 (SD, 5.27; range, 40–50) initially and increased signifi-

TABLE 2
Comparison of Mean Scores

Type of score	Paired differences			
	Mean	SD	95% confidence interval of difference	<i>P</i>
Mean pain (baseline) – mean pain (week 4)	2.7	1.2	1.8 to 3.6	<0.001
Mean pain (baseline) – mean pain (week 8)	4.6	1.1	3.8 to 5.4	<0.001
Mean pain (baseline) – mean pain (week 12)	6.7	1.3	5.8 to 7.7	<0.001
Karnofsky (baseline) – Karnofsky (week 4)	–24	6.9	–29 to –18.9	<0.001
Mobility (baseline) – mobility (week 4)	1.6	0.6	1.1 to 2.1	<0.001

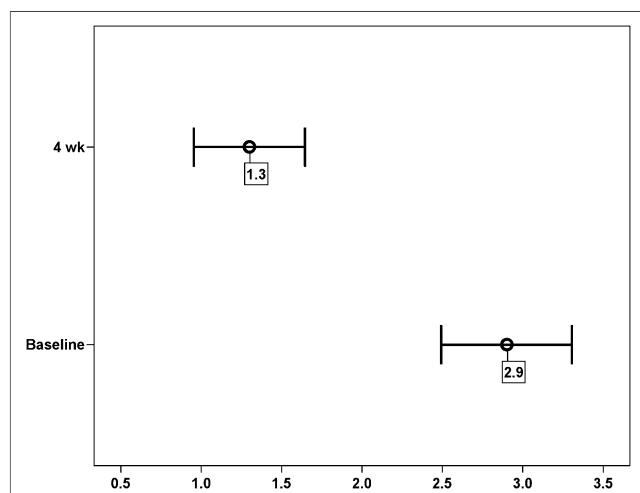


FIGURE 3. Comparison of mean mobility score of study group.

cantly to 69 (SD, 5.67; range, 60–80) at 4 wk, corresponding to 65.2% of the baseline score (Fig. 4). These differences between the mean scores at 4 wk and the mean scores at baseline were also statistically significant ($P < 0.001$) (Table 2).

Safety Assessment

The major limiting factor of ^{177}Lu -EDTMP was bone marrow suppression, which resulted in a reduction of peripheral blood counts. No significant change was seen in hemoglobin counts. The decrease in platelet and leukocyte counts began at 2 wk after radiopharmaceutical administration, reached a nadir at 4 wk, and quickly recovered by 6 wk. Two patients (20%) developed grade I platelet toxicity, and 1 patient developed grade II (10%) platelet toxicity. Four patients (40%) developed grade I leukocyte toxicity, and 2 patients (20%) developed grade II leukocyte toxicity. No clinically significant adverse reactions were noted. The changes in hemoglobin, platelets, and leukocytes during follow-up are illustrated in Table 3.

DISCUSSION

Bone pain is a major clinical challenge in most metastatic cancers, especially when the pain becomes resistant to opioid analgesics. The primary goal of palliative care is to provide these patients with a better quality of life while using minimum drugs, which otherwise might compromise their daily activity. Although local palliative radiotherapy is suitable for localized lesions, it is less applicable in patients with widespread skeletal metastases. Radiopharmaceutical therapy using bone-seeking therapeutic agents has been the prime choice of treatment for bone pain in such cancer patients. Although a few radiopharmaceuticals such as ^{32}P -orthophosphate, $^{89}\text{SrCl}_2$, and ^{153}Sm -EDTMP are regularly used for palliative care and have been proven efficacious, there is a need to develop radiopharmaceuticals with both better nuclear decay characteristics and better biologic behavior and make them available at a reasonable

cost to ensure greater accessibility to patients. Both ^{32}P and ^{89}Sr emit β^- radiation of comparatively high energy, thereby causing bone marrow toxicity; both are also pure β^- emitters, making it difficult to perform simultaneous scintigraphy and pharmacokinetic studies (8,9). Moreover, the high cost of ^{89}Sr , because of its limited production feasibility, is another drawback in its widespread use (10). ^{153}Sm -EDTMP is another effective bone pain palliative agent that is chemically and biologically stable and selectively accumulates in skeletal lesion sites (11–13). ^{153}Sm -EDTMP also results in lethal hemotoxicity at high doses (14) and may not be readily available, as ^{153}Sm has a short physical half-life of 1.9 d.

In recent years, ^{177}Lu -EDTMP has emerged as a potential candidate for palliation of metastatic bone pain. Major advantages of using ^{177}Lu as a radionuclide include a lower β energy (maximum, 497 keV), which results in little hemotoxicity, and the presence of γ energies (113 and 208 keV), which can be used for imaging and dosimetry studies. There is also a production advantage, as it can be produced in large scale with sufficiently high specific activity and an excellent radionuclidic purity using medium-flux research reactors. Moreover, ^{177}Lu has a half-life of 6.73 d, which provides logistic advantages (4). On the other hand, the use of EDTMP as the carrier moiety while formulating bone-specific radiotherapeutic agents using radiolanthanides is already well established. It has been reported that EDTMP forms stable complexes with various radiometals and that these localize in the skeleton in proportion to the osteoblastic activity and exhibit other favorable biologic characteristics (15). The biologic behavior of ^{177}Lu -EDTMP studied in animal models such as mice, rats, and dogs has shown encouraging results (7,16) and prompted us to study the clinical behavior of the agent initially in a limited number of cancer patients with disseminated skeletal metastases.

In the present study, a notable reduction in pain was observed within a week in all 10 patients, and complete

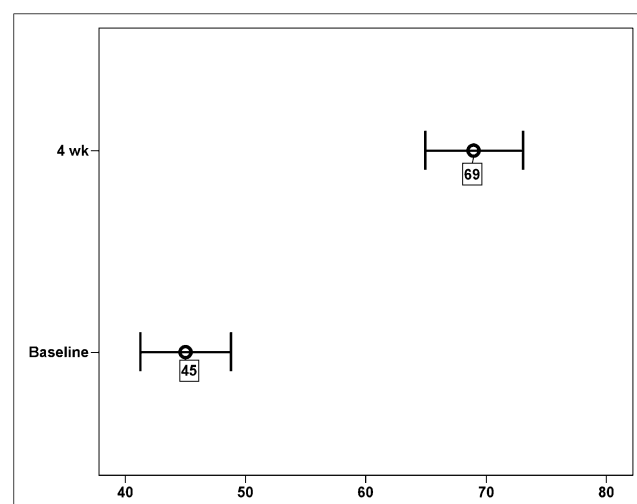


FIGURE 4. Comparison of mean Karnofsky performance score of study group.

TABLE 3
Toxicity of ^{177}Lu -EDTMP for Painful Bone Metastases

Grade	HGB	PLT	LEU
I	0	2 (20)	4 (40)
II	0	1 (10)	2 (20)
III	0	0	0
IV	0	0	0

HGB = hemoglobin ($\times \text{g/L}$); PLT = platelets ($\times 10^9/\text{L}$); LEU = leukocytes ($\times 10^9/\text{L}$).

Data are number followed by percentage.

pain relief was seen in all patients by 12 wk (Fig. 2). At 4 wk, all patients had reduced or completely withdrawn from analgesics. Whole-body images taken at 1 d after therapy showed excellent biologic distribution and minimal soft-tissue uptake, similar to that seen in a corresponding $^{99\text{m}}\text{Tc}$ -methylene diphosphonate scan (Fig. 5). This scan was also comparable to that obtained using ^{153}Sm -EDTMP (Fig. 6). The whole-body scans obtained at 1 mo showed significant tracer retention (Fig. 7). Our study also demonstrated that the benefits of our treatment using ^{177}Lu -EDTMP lasted for more than 4 mo. Pain relief along with a higher Karnofsky performance score and mobility score at 4 wk indicates a definite improvement in the patient's quality of life, which is the major goal of palliative care. All differences between scores were statistically significant.

A recent study by Yuan et al. indicated that ^{177}Lu -EDTMP was an effective and safe treatment for palliation of metastatic bone pain in patients with prostate or breast cancer and showed that a dose as low as 1,295 MBq (35 mCi) was sufficient for bone pain palliation; however, the percentage of patients showing early pain relief was comparatively less when a lower dose was administered than when the dose was higher (2,590 MBq [70 mCi]) (17). Sola

et al. also demonstrated the ease of preparation as well as the feasibility and efficacy of ^{177}Lu -EDTMP as a safe agent for pain palliation in metastatic bone involvement (18). The major dose-limiting factor with bone-seeking radiopharmaceuticals is bone marrow toxicity, which results in peripheral blood cell counts (19). In our study, grade I platelet toxicity was seen in 2 patients and grade II platelet toxicity was seen in 1 patient. In addition, grade I and II leukocyte toxicity was seen in 4 and 2 patients, respectively. The hemotoxicity caused was mild, acceptable, and fully reversible without the use of replacement therapies or stem cell growth factor support. Our study also found immediate and efficacious pain relief with ^{177}Lu EDTMP, similar to other studies, and our dosing of 3.7 GBq (100 mCi) proved to be well tolerated by all patients and had the added advantage of earlier and sustained pain relief even at 12 wk without significant hematologic toxicity (17,18).

Randomized, controlled trials have shown that pain relief induced by radioisotopes is not significantly different from external palliative radiotherapy (20,21). However, the impact of radionuclides on survival of patients is controversial. A notably reduced survival was reported with ^{89}Sr versus local-field radiotherapy for bone pain in metastatic prostate cancer in a European randomized, multicenter trial (20). These data are in direct contrast to data reported from a similar trial from the United Kingdom, which noted no difference in survival rates in patients who received ^{89}Sr and palliative radiotherapy (21). On the other hand, improved survival has been reported with radioisotopes in randomized, placebo-controlled trials (22).

Recent or concurrent systemic chemotherapy has thus far been regarded as a contraindication to radionuclide therapy. However, the combined use of radionuclides and chemotherapy may act synergistically and improve pain palliation (23). Several reports have documented improvement in pain

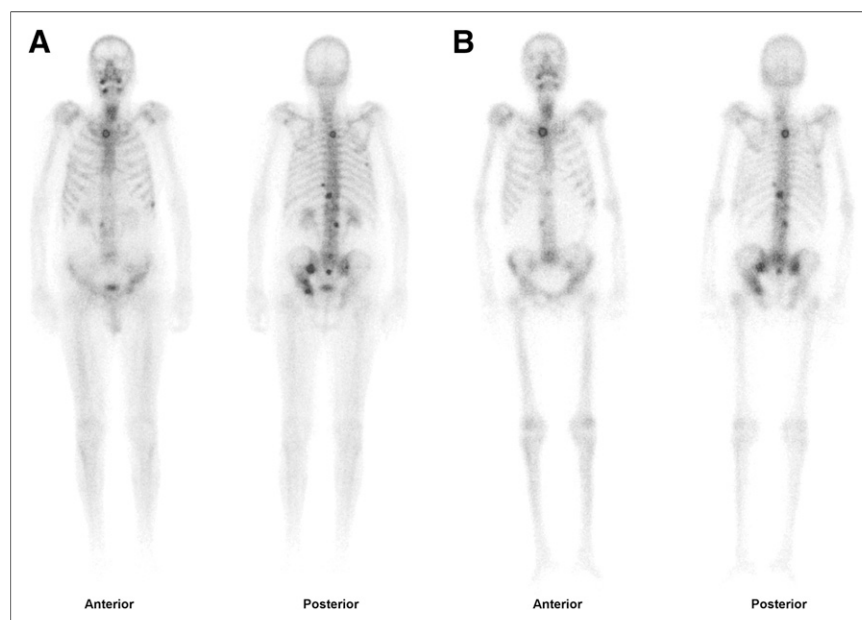


FIGURE 5. $^{99\text{m}}\text{Tc}$ -methylene diphosphonate bone scan (A) and corresponding ^{177}Lu -EDTMP scan (B) showing excellent tracer localization in osteoblastic areas. A color version of this figure is available as a supplemental file at <http://tech.snmjournals.org>.

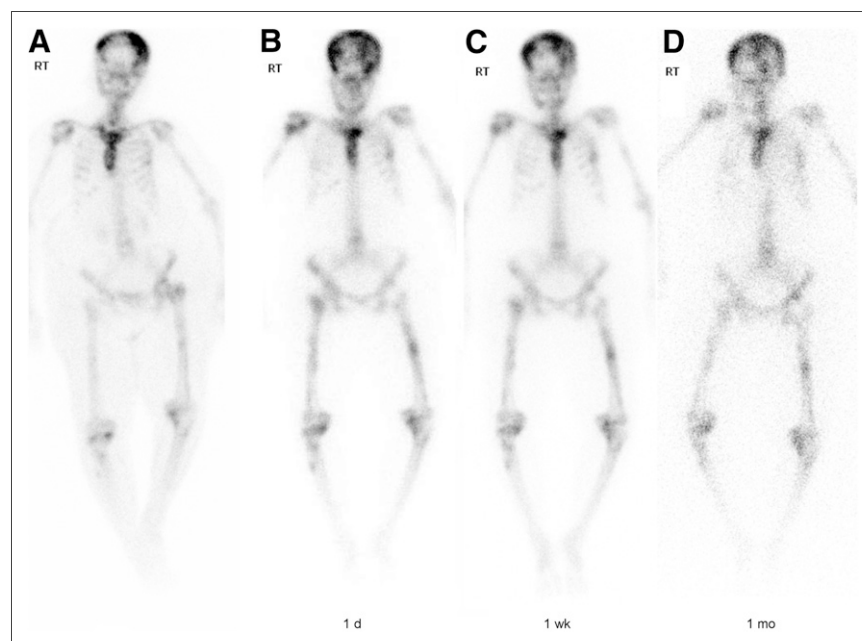


FIGURE 6. ^{99m}Tc -methylene diphosphonate scan (A) and corresponding ^{177}Lu -EDTMP images (B–D) of same patient.

relief, prolonged duration of response, reduced development of new painful sites, and improved progression-free and overall survival in patients treated with radioisotopes along with chemotherapy versus chemotherapy alone in various cancers (24–26). The combination of radioisotopes and chemotherapy, including docetaxel, is currently being pursued in several clinical trials.

This study was limited by the small sample size, absence of a control group, and lack of long-term follow-up. Survival rates could not be assessed because of our short observation period. Further studies of longer duration and a larger population group are needed to assess survival rates, safety, and efficacy of ^{177}Lu -EDTMP.

CONCLUSION

This study indicated that systemic administration of ^{177}Lu -EDTMP was an effective, well-tolerated, feasible, and safe treatment option for palliation of metastatic bone pain in patients with disseminated skeletal metastases. All patients in the study benefited from this therapy. Best results were seen at 4 wk after treatment. The imaging possibilities, mild hemotoxicity, and economic factors make ^{177}Lu -EDTMP stand out among other radiopharmaceuticals used for palliative therapy of metastatic bone pain. ^{177}Lu -EDTMP shows promising results and should be considered the preferred option among other palliative modalities.

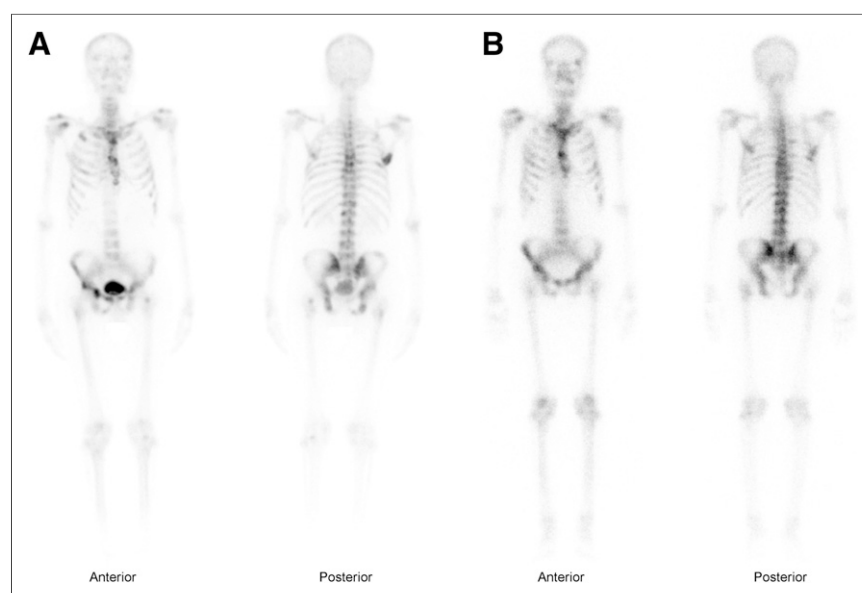


FIGURE 7. ^{177}Lu -EDTMP image (B) demonstrating biologic distribution similar to ^{153}Sm -EDTMP (A) in same patient.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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REFERENCES

- Mertens WC et al. Systemic bone-seeking radionuclides for palliation of painful osseous metastases: current concepts. *CA Cancer J Clin*. 1998;48:321, 361–374.
- McEwan AJ. Palliative therapy with bone seeking radiopharmaceuticals. *Cancer Biother Radiopharm*. 1998;13:413–426.
- Paes FM, Serafini AN. Systemic metabolic radiopharmaceutical therapy in the treatment of metastatic bone pain. *Semin Nucl Med*. 2010;40:89–104.
- Pillai MR, Chakraborty S, Das T, Venkatesh M, Ramamoorthy N. Production logistics of ^{177}Lu for radionuclide therapy. *Appl Radiat Isot*. 2003;59:109–118.
- Bijur PE, Silver W, Gallagher EJ. Reliability of the visual analog scale for measurement of acute pain. *Acad Emerg Med*. 2001;8:1153–1157.
- Buccheri G, Ferrigno D, Tamburini M. Karnofsky and ECOG performance status scoring in lung cancer: a prospective, longitudinal study of 536 patients from a single institution. *Eur J Cancer*. 1996;32A:1135–1141.
- Chakraborty S, Das T, Banerjee S, et al. ^{177}Lu -EDTMP: a viable bone pain palliative in skeletal metastasis. *Cancer Biother Radiopharm*. 2008;23:202–213.
- Pandit-Taskar N, Batraki M, Divgi CR. Radiopharmaceutical therapy for palliation of bone pain from osseous metastases. *J Nucl Med*. 2004;45:1358–1365.
- Nishio M, Sano M, Tamaki Y, et al. A multicenter study to determine the efficacy and safety of strontium (^{89}Sr) chloride for palliation of painful bony metastases in cancer patients [in Japanese]. *Nihon Igaku Hoshasen Gakkai Zasshi*. 2005;65:399–410.
- Das T, Pillai MR. Options to meet the future global demand of radionuclides for radionuclide therapy. *Nucl Med Biol*. 2013;40:23–32.
- Ratsimanohatra H, Barlesi F, Doddoli C, et al. Use of ^{153}Sm -EDTMP to relieve pain from bone metastasis in lung cancer. *Rev Mal Respir*. 2005;22:317–320.
- Tripathi M, Singhal T, Chandrasekhar N, et al. Samarium-153 ethylenediamine tetramethylene phosphonate therapy for bone pain palliation in skeletal metastases. *Indian J Cancer*. 2006;43:86–92.
- Maini CL, Bergomi S, Romano L, et al. ^{153}Sm -EDTMP for bone pain palliation in skeletal metastases. *Eur J Nucl Med Mol Imaging*. 2004;31(suppl 1):S171–S178.
- Sandeman TF, Budd RS, Martin JJ. Samarium-153-labelled EDTMP for bone metastases from cancer of the prostate. *Clin Oncol (R Coll Radiol)*. 1992;4:160–164.
- Ando A, Ando I, Tonami N, et al. ^{177}Lu -EDTMP: a potential therapeutic bone agent. *Nucl Med Commun*. 1998;19:587–591.
- Máthé D, Balogh L, Polyák A, et al. Multispecies animal investigation on bio-distribution, pharmacokinetics and toxicity of ^{177}Lu -EDTMP, a potential bone pain palliation agent. *Nucl Med Biol*. 2010;37:215–226.
- Yuan J, et al. Efficacy and safety of ^{177}Lu -EDTMP in bone metastatic pain palliation in breast cancer and hormone refractory prostate cancer: a phase II study. *Clin Nucl Med*. 2013;38:88–92.
- Solá GA, Argüelles MG, Bottazzini DL, et al. Lutetium-177-EDTMP for bone pain palliation: preparation, biodistribution and pre-clinical studies. *Radiochim Acta*. 2009;88:157–161.
- Liepe K, Kotzerke J. A comparative study of ^{188}Re -HEDP, ^{186}Re -HEDP, ^{153}Sm -EDTMP and ^{89}Sr in the treatment of painful skeletal metastases. *Nucl Med Commun*. 2007;28:623–630.
- Oosterhof GO, et al. Strontium(89) chloride versus palliative local field radiotherapy in patients with hormonal escaped prostate cancer: a phase III study of the European Organisation for Research and Treatment of Cancer, Genitourinary Group. *Eur Urol*. 2003;44:519–526.
- Quilty PM, Kirk D, Bolger JJ, et al. A comparison of the palliative effects of strontium-89 and external beam radiotherapy in metastatic prostate cancer. *Radiother Oncol*. 1994;31:33–40.
- Buchali K, et al. Results of a double blind study of ^{89}Sr -strontium therapy of skeletal metastases of prostatic carcinoma. *Eur J Nucl Med*. 1988;14:349–351.
- Tomblyn M, et al. The role of bone-seeking radionuclides in the palliative treatment of patients with painful osteoblastic skeletal metastases. *Cancer Control*. 2012;19:137–144.
- Sciuto R, Festa A, Rea S, et al. Effects of low-dose cisplatin on ^{89}Sr therapy for painful bone metastases from prostate cancer: a randomized clinical trial. *J Nucl Med*. 2002;43:79–86.
- Palmedo H, Grünwald F, Wagner U, et al. Remission of bone metastases after combined chemotherapy and radionuclide therapy with Re-186 HEDP. *Clin Nucl Med*. 1998;23:501–504.
- Sideras PA, Stavra A, Gouliamos A, Limouris GS. Radionuclide therapy of painful bone metastases: a comparative study between consecutive radionuclide infusions, combination with chemotherapy, and radionuclide infusions alone—an in vivo comparison of their effectiveness. *Am J Hosp Palliat Care*. 2013;30:745–751.



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