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ORIGINAL ARTICLE

# Samarium-153Sm-EDTMP as an equivalent variant to pharmaceutical analgesic treatment

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## Summary

***Purpose:*** *Cancer pain is the most serious symptom for patients, especially during their terminal phase, when palliative medicine is needed. Our study tried to verify the usefulness of single-shot intravenous administration of Samarium (Sm)-153EDTMP in patients with bone metastases (group-A, N=53, males=25, females=28, age range: 30-69 years), as well as to compare a series of variables, using as a control group (group-B, N=37, males=17, females=20, age range: 30-69 years) with patients who were under drug treatment given from a physician specialized in palliative medicine.*

***Methods:*** *Both groups answered the following questionnaires: Greek Brief Pain Inventory (GBPI), Brief Multidimensional Life Satisfaction Scale (BMLSS), Hospital Anxiety Depression Scale (HADS) and ECOG performance status.*

***Results:*** *Pain severity and pain interference improvement p=0.0005 for both groups. HADS-anxiety: Samarium group, p= 0.397, drugs group p= 0.031. HADS-depression improvement for both groups p=0.031 and p=0.003, respectively. BMLSS improvement p=0.029 and p=0.265, while EGOG PS improvement was p=0.005 and p=0.014, respectively (numeric values).*

***Conclusion:*** *Intravenous administration of Sm-153EDTMP was equivalent to drug treatment against cancer pain for patients with multiple bone metastasis, an option for those patients who are intolerant or resistant to drug treatment. Samarium-treated patients needed less or not at all pain killers, having a better cost-effective result.*

***Key words:*** *anxiety, cancer pain, depression, quality of life, samarium (Sm-153EDTMP)*

## Introduction

Bone metastases often precede other metastases presenting usually a sign of advanced-stage disease. Survival of these patients can range from months to many years. The severe symptomatology of bony metastases, as well as their morbidity, require drastic and sometimes prolonged treatment and palliative care. The problem of pain management in cancer patients often eludes the interest of the treating physician, as his primary concerns are the communication of the diagnosis, or the way of treatment, or the preparation for the acceptance of the upcoming inevitable with all that it entails, such as anxiety, depression and grief. Given the fact that therapeutic progress requires the ethical and cognitive compliance, physicians nowadays have in their quiver a number of effective treatment methods. Medication with specialized formulations, suitable pharmaceutical combinations, the deep understanding of painkillers and radiotherapy, therapeutic administration

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of radioactive isotopes and analgesic operations are involved in the detailed planning of the therapeutic decision towards a holistic approach [1]. The fruitless efforts by untrained and inexperienced doctors often increasing the suffering, reduce the faith and trust towards them, and furthermore they alter personalities and heighten insecurity, causing stronger anxiety and deeper depression [1,2].

Various symptoms of cancer patients, primary pain, degrade the quality of their life. Two-thirds of cancer patients aged over 40 years suffer from pain caused by bone metastases [3]. The pain can be fast or slow in appearance, acute or chronic, benign or malignant with paroxysms (breakthrough pain). Pain can be categorized into body (nociceptive), visceral, neuropathic and pain caused by the continuous irritation of the sympathetic system. Furthermore, the emotional and psychic world of a cancer patient is extremely disturbed and chaotic. The stress because of his condition, his complicated treatment, his upcoming end, as well as the deconstruction of the relations with the surroundings, give off a different type of pain, which often the clinician ignores, the psychic pain [4,5]. The size of the stimulus, the awareness of pain and the response caused, are parts of an equation in which the essential and unique personality of the person is combined with the philosophical position towards the phenomenon of life. There are various theories about the interpretation of selective proliferation of bone metastases, including cancer embolic theory, the theory of slow blood flow in the red bone marrow that has a complex sinusoidal system and the theory of vertebral-vein grids without vein valves. The mechanisms of causing bone pain are mechanical, from the deformation of a bone, the precipitation of a vertebra or the compression of some nerve roots or they may be chemical, such as substances from alogones and cytokines that activate pain receptors. Bone metastases are primarily osteolytic, but they can also be osteoblastic or mixed [6].

The purpose of our study was a comparative analysis of pain palliative treatment evaluation of cancer patients with bone metastases, as well as their quality of life after therapy's administration. All patients who entered the study were distributed into two separate groups: group-A and group-B. Group-A received intravenous radioactive Samarium-153 [153Sm-EDTMP (ethylenediaminetetramethylenephosphonate)], and group-B the orthodox medication treatment suggested by the international guidelines. Our study took under consideration the psychological state of the patient, thus the manifestations of anxiety and depression. Finally, a comparative assessment between the medication taken during the allocation method of intravenous Samarium-153 and the pharmaceuticals taken during the method of the proper medication treatment, was attempted.

*Samarium-153 (153Sm-EDTMP) as a therapeutic pain killer*

Samarium-153 belongs to the group of Lanthanum (rare earths) and due to its size (large atomic radius) is characterized by creating complexes with substitution number 7 to 10. It is a relatively short-lived radioisotope ($T½$ = 28.8 hrs) and emits "β" and "γ" radiation. Connected with the EDTMP, it forms a highly bone-seeker radiopharmaceutical with the same fixation of the trend of bisphosphonates [7]. Fixation mechanisms of Samarium-153 are the following: (i) trivalent radionuclide (153Sm3 +) forms insoluble hydroxites and/or phosphate salts embodied in hydroxyapatite. These ions are transported in the form of soluble complexes and get bogged down initially by the formation of heteronucleus complexes with calcium on the surface of hydroxyapatite. Its final integration on the inorganic substance of the bone is kinetically stable with effective non-escaping of the radionuclide into the circulation; (ii) after the formation of heteronucleus complexes with calcium 153Sm-EDTMP the radiopharmaceutical with the aid of the available phosphate or carboxylic groups, which act as connection bridges, is being connected with the hydroxyapatite. Then befalls the incorporation of the radionuclides in the form of hydroxides and/or phosphate salts, as in mechanism (i) [8].

The recommended dose for the administration of the Samarium-153 is 1mCi/kg. A big part of the dose (40-90%) remains in bone metastases which absorb 99mTc-MDP, while the rest (98%) is excreted through the renal system within the first 6 hours. The analgesic effect of Samarium-153 varies in different studies from 61% up to 87%. Analgesia occurs within 1 to 2 weeks and lasts 1 to 8 months (2.6 months on average). Myelotoxicity appears between the 3rd and 6th week and is of moderate degree. Simultaneous use of bisphosphonates must be avoided, as they reduce the absorption of the radiopharmaceutical. Intravenous application of radio-spotted particles are being used for selective tumor irradiation, resulting a radiation dosage 20 to 30-fold higher than that which can be achieved by external radiother-

apy. Thus Samarium-153 delivers high radiation doses to bone metastases and micrometastases in the bone marrow, but only negligible doses to the hematopoietic marrow [3,8,9].

*Drugs' analgesic effect*

Opioids are among the oldest medications available for the management and control of pain in cancer patients. Opium contains high concentrations of both morphine and codeine, alongside with thebaine (paramorphine), which is used in the synthesis of various semi-synthetic opioid analgesics. Thus, it is not surprising that new agents were initially based on the morphine scaffold. First-line therapies for moderate to severe pain include prescriptions for common μ-opioid receptor agonists such as morphine and its various derivatives. Alternative approaches include novel opioids that target "δ" or κ-opioid receptors, or compounds that interact with two or more of the opioid receptors. Opioids play an essential role in the successful long-term care strategy for those patients in chronic cancer pain [10].

Nonsteroidal anti-inflammatory drugs (NSAIDs) represent a family of drugs that provide both analgesic and antipyretic effects, while in higher doses they provoke anti-inflammatory effects. NSAIDs could be given in patients receiving opioids, evaluating their benefit and weight on opioid therapy in individual patients who have a favorable response to justify a prolonged use. The role of NSAIDs that inhibit selectively the cyclooxygenase-2 (COX-2), leading to the anti-inflammatory, analgesic and antipyretic effects should be emphasized. Paracetamol, can also be used against cancer pain. In many occasions systemic analgesics could not provide a sustainable pain relief against cancer pain. Metastatic bone pain is characterized by the combination of nociceptive and neuropathic pain, that requires a low-dose of antiepileptic-antidepressant combination with opioids as a palliation method [11,12].

The management and palliative treatment for cancer patients usually requires a combination of paracetamol, NSAIDs and opioids [1,13] and multimodal therapy ensures adequate pain management [14].

## Methods

*Study material*

All patients included in the Control group-B started at point zero drug treatment according to the international palliative medicine protocols, a treatment which continued until the end of the study. All Samarium-153 group-A patients were administered an intravenous single shot of $Sm^{153}$EDTMP, while until the 10±3 day they continued their primary analgesic drug treatment. From this point on, when usually the effect of $Sm^{153}$EDTMP begins [3], their gradual release from the drug treatment started, so that the measurements during the 30±3 day should be independent from it.

A total of 53 patients suffering from diagnosed cancer with bone metastases that absorbed 99mTc-MDP, initially examined at the Anticancer Hospital "Agios Savvas", were included this study, forming the group-A of patients (25 males and 28 females, age range 30-69 years). Patients incorporated in the study had breast, prostate, lung, and colorectal cancers and sarcomas. Gathering data and monitoring patients lasted one year (June 2011 to June 2012). The diagnosis of malignancy was either histological or cytological and bone metastases were confirmed by nuclear medicine imaging and radiodiagnostic methods such as whole-body bone scintigraphy with γ-camera, PET-CT, computed tomography (CT), magnetic resonance imaging (MRI) and x-ray. For comparison a group-B was created, with 37 patients (17 males and 20 females) who were also diagnosed with cancer and bone metastases. Both groups, the intervention group-A to receive Samarium-153, and group-B to receive drug analgesia, were previously under pharmaceutical analgesic treatment proposed by their personal physician (internist, oncologist, general practitioner) for a median time period of 4 months (range -1.4 and +4.6). Their median number of bone metastases was 3.4 (range -1.4 and +4.6).

*Inclusion criteria*

Patients in both groups entered the study after a detailed study of their medical history. The admission criteria for the study were as follows: (i) Pain should have been at level 2 or 3 according to the Scale of Analgesia of the World Health Organization (WHO). In our study when we refer to pain, we mean "total pain" including the most important of all, the psychic pain; (ii) Multiple painful bone metastases (more than one), with pain localization that should coincide with them; (iii) Life expectancy of all patients >3 months; (iv) Platelet count $\geq 100\times10^3/mm^3$, hemoglobin at least 10g/dl, white blood cells >3.200, bilirubin not exceeding 2 mg/dl and creatinine levels <2 mg/dl; (v) Patients not having undergone chemotherapy, radiotherapy or hormone therapy for a period more than the last 4 weeks; (vi) All female patients should be necessarily tested with pregnancy test; (vii) Physician should take into account the patient's communication ability after his clinical examination.

*Exclusion criteria*

The exclusion criteria were as follows: (i) Patients allergic to EDTMP or in pain killers; (ii) All patients

with a high degree of intolerance towards medication [15].

All patients gave written informed consent. Both groups were randomly formed by the "total of patients", who were visiting the Anticancer Hospital "Agios Savvas", after consultation of both the nuclear medicine department and the hospital's pain clinic. Some patients dropped out for various reasons (intolerance, withdrawal from study, sudden death, etc) and both groups took their final composition.

After the administration of Samarium-153, group-A patients continued to receive the original medication. Group-B patients continued their medication administration until the end of the study, after a possible intervention by the medical staff for potentially improper or incomplete medication prescription from the treating physician (the primary therapist was not probably specialized in palliative care, and there was a strong possibility being ignorant of the basic principles of palliative care). On the other hand, in a short period of time (10±3 days), reduction of the dosage of the initial analgesic medication begun in group-A patients.

The recommended dose for the intravenous administration of Samarium-153 in group-A patients was 37 MBq/kg. All patients were monitored for myelotoxicity, via blood measurements at point zero, 10 ± 3 days after point zero, and 1 month after point zero [3]. All group-B patients were examined for potential side effects of the medications administered on the 1st, 3rd, 7th and 15th day after point zero. Patients of both groups had additionally the possibility of interactive discussion with the interviewing physician 24 hrs, 7 days a week, who also collected the survey data and maintained the anonymity of all patients.

*The questionnaires*

The questionnaires of this study were recorded twice, at point zero and 30 ± 3 days after the point zero, and included the following:

1. Greek brief pain inventory (GBPI), a short questionnaire with numbered scales from 0 to 10, in which pain is measured and recorded during the daily routine [16].
2. Brief Multidimensional Life Satisfaction Scale (BMLSS), a questionnaire which measures with the aid of numbered scales from 1 to 6 the satisfaction towards yourself, family, friends and life in general [17].
3. Hospital Anxiety and Depression Scale (HADS), a questionnaire with numbered scales from 0 to 3 which estimates stress and depression index [18].
4. ECOG/WHO/Zubrod score, a scale from 0 to 4 (4 represents worst condition), which ranks patients depending on the ability of their physical activity [19].

*Statistics*

Data was expressed as mean±standard deviation (SD) or median+range (in case of violation of normality) for continuous variables and as percentages for categorical variables. The Kolmogorov-Smirnov test was utilized for normality analysis of the parameters. The comparison of demographic or clinical variables between groups was performed using $x^2$ test and Fisher's exact test. The comparison of variables at each time point was performed using the Independent Samples t-test or the Mann-Whitney U test in case of violation of normality. Comparisons of variables during the observation period (baseline vs 1st month) for each group were performed using paired samples t-test. To indicate the trend from baseline to the 1st month of treatment the median percentage change from baseline to the 1st month was calculated. Comparison of percentage change from baseline to the 1st month of the parameters between the 2 groups was analyzed using the Mann-Whitney U test. Statistical analyses of qualitative variables were performed using $x^2$ test and Fisher's exact test. All tests were two-sided and statistical significance was set at $p<0.05$. All analyses were carried out using the SPSS version 16.00 (Statistical Package for Social Sciences, SPSS Inc, Chicago, Ill. , USA ).

## Results (Table 1)

Ten patients were excluded from study because they didn't meet the relevant criteria. Samarium group-A included 53 patients and the control group-B 37. No statistical difference for sex, age, pain localization and lodging was observed between groups (Table 2).

The results of our study showed that pain severity and pain interference changed over time in the same way and that in both groups a statistically significant improvement of both variables was observed (p=0.0005) for both groups. Using the Mann-Whitney and the t-test for independent samples, no statistically significant difference was noticed between groups. Response rates to pain, were as follows: 15% complete remission, 71% partial remission, and 7.5% pain progression. For HADS-anxiety, group-A showed no statistically significant improvement (p=0.397), something which was achieved for the control group-B which showed improvement (p=0.031). HADS-depression worsened significantly in both groups (group-A: p=0.003; group-B: p=0.031). HADS' variables changed over time in the same way in both groups. ECOG PS also changed over time in the same way in both groups, and a statistically significant difference for both group-A (p=0.005) and the control group-B (p=0.014) was noticed. The percent of patients who showed improvement in their qual-

**Table 1.** Summarized results of the study for both Samarium and Drugs groups

| *Questionnaire* | *Groups with p value* | *Baseline (mean±SD)* | *1st month (mean±SD)* | *Within group p-value* | *% change baseline-1st month (mean±SD)* |
|---|---|---|---|---|---|
| HAD anxiety | Samarium | 11.53±2.45 | 11.25±2.46 | 0.397 | -0.33%±20.97 |
| | Drugs | 12.19±2.62 | 11.30±2.21 | 0.031 | -4.92%±19.86 |
| | p-value | 0.225 | 0.918 | | 0.299 |
| HAD depression | Samarium | 7.34±2.19 | 819±2.16 | 0.003 | 15.36±32.08 |
| | Drugs | 7.84±2.43 | 8.70±2.22 | 0.031 | 17.41±36.68 |
| | p-value | 0.313 | 0.313 | | 0.779 |
| Pain severity | Samarium | 7.60±1.40 | 4.88±3.26 | 0.0005 | -35.47±41.38 |
| | Drugs | 7.96±1.47 | 5.34±3.11 | 0.0005 | -31.80±37.76 |
| | p-value | 0,248 | 0.497 | | 0.668 |
| Pain interference | Samarium | 8.06±1.48 | 6.17±2.39 | 0.0005 | -23.46±25.37 |
| | Drugs | 8.38±1.41 | 6.42±2.02 | 0.0005 | -23.57±19.26 |
| | p-value | 0,307 | 0.611 | | 0.982 |
| ECOG PS | Samarium | 2.15±0.89 | 1.85±1.05 | 0.005 | -12.58±37.11 |
| | Drugs | 2.35±1.06 | 2.00±1.13 | 0.014 | -11.97±39.50 |
| | p-value | 0.333 | 0.516 | | 0.876 |
| BMLSS | Samarium | 36.98±12.83 | 37.43±15.07 | 0.265 | 5.55±40.86 |
| | Drugs | 32.63±11.04 | 35.42±11.62 | 0.029 | 12.97±36.22 |
| | p-value | 0.186 | 0.498 | | 0.377 |

HAD: Hospital Anxiety and Depression scale, BMLSS: Brief Multidimensional Life Satisfaction Scale, ECOG PS: Eastern Cooperative Oncology Group Performance status, SD: standard deviation

ity of life was 24.3% in the control group-B and 15.1% in the Samarium group-A. While ECOG PS changed similarly in both groups, as previously mentioned, in group-A 77.4% (60.4±17) of patients did not show any change in their general condition, while 22.6 % did ( improved 15.1%, worsened 7.5% ). In group-B 24.3% showed improvement, while 8.1% worsened. BMLSS changed over time in the same way in both groups. For this variable a statistically significant difference was observed for the control group-B (p=0.029), but not for the Samarium group-A (p=0.265). However, using the Mann-Whitney U test and t-test no statistically significant difference was noticed in parametric (p=0.377), and in non-parametric (p=0.192) values. Myelotoxicity for the Samarium group-A was in general moderate and reversible, as well as the side effects for the control group-B (Table 3). Finally, an equivalence test between the two approaches was made, showing that both treatment regimens were equivalent for all variables: pain severity, p=0.034, pain interference, p=0.009, HAD-anxiety, p=0048, HAD-depression, p=0.033, BMLSS, p=0.016, ECOG PS, p=0.0005.

**Table 2.** Control of demographic or clinical variables

| *Clinicodemographic variables* | | *Samarium N (%)* | *Drugs N (%)* | *p value* |
|---|---|---|---|---|
| Gender | Male | 25 (47.2) | 17 (45.9) | 1.000 |
| | Female | 28 (52.8) | 20 (54.1) | |
| Age, years | 30-49 | 31 (58.5) | 16 (43.2) | 0.219 |
| | 50-69 | 22 (41.5) | 21 (56.8) | |
| Cancer type | Breast | 26 (49.1) | 15 (40.5) | 0.494 |
| | Lung | 6 (11.3) | 6 (16.2) | |
| | Prostate | 17 (32.1) | 10 (27.0) | |
| | Other | 4 (7.5) | 6 (16.2) | |
| Residence | Athens | 36 (67.9) | 20 (54.1) | 0.363 |
| | Province | 14 (26.4) | 15 (40.5) | |
| | Resident abroad | 3 (5.7) | 2 (5.4) | |

Analyzing the drug dosages, we observed that group-B medication varied at much higher dosage levels than that of group-A. Morphine and fentanyl dosage were noticeably reduced among patients of group-A. It was also noticed that in group-A the strongest opioids dosage was lowered, while in group-B it was increased. For 5% of the group-A patients it was sufficient taking paracetamol alone for pain relief. What is worth noticing was that for group-B patients antidepressants were a key part in the therapeutic approach, while in group-A patients these drugs were given

**Table 3.** Side effects

| | *Myelotoxicity grade I (WBC 3.0-3.9 and PLT 75.0-normal) N (%)* | *Myelotoxicity grade II (WBC 2.0-2.9 and PLT 50.0-74.9) N (%)* | *Myelotoxicity grade III (WBC 1.0-1.9 and PLT 25.0-49.9) N (%)* |
|---|---|---|---|
| *Group-A "Samarium"* | | | |
| N= 53 | 23 (43.4) | 2 (3.8) | 1 (1.9) |
| M= 25 | 8 (32.0) | 1 (4.0) | 1 (4.0) |
| F= 28 | 15 (53.6) | 1 (3.6) | 0 |
| *Group-B "Drugs"* | *Nausea* | *Gastric pain* | *Vomiting* |
| N= 37 | 11 (29.8) | 4 (10.8) | 3 (8.1) |
| M= 17 | 7 (41.18) | 1 (5.9) | 1 (5.9) |
| F= 20 | 4 (20.0) | 3 (15.0) | 2 (10.0) |

N: number, M: males, F: females, WBC: white blood cells, PLT: platelets

only to a small percentage. In general drug dosage among group-A patients was stable or significantly reduced, while in group-B it was significantly increased.

It was observed that 3 cases of the Samarium group-A showed stabilization of bone lesions, and in one case complete remission of the bone metastases was achieved.

## Discussion

A variety of studies, and reviews such as Turner's and Claringbold's, Ilora's and Glenn's, have dealt with the analgesic action of Sm153EDTMP for pain caused by bone metastases of various cancers, recording analgesia rates from 60% up to 95% [20-26]. International literature includes also extensive reports for the analgesic pharmaceutical action, mainly of paracetamol, NSAIDs agents and opioids, with high rates of reduction of pain intensity, as the Manzini's and Radovanovic's studies presented, recording rates from 85% up to 90% [27-31]. Results in both cases are in complete agreement with the results of our study. As the newest data show improvement in quality of life and overall survival after controlling bone metastases with nuclear local radiotherapy and/or general radiotherapy, but also with proper use of drug choices [32], the research for the usefulness of intravenous application of Sm153EDTMP in comparison with drug administration or a combination of both options, will enable patients and medical staff to enjoy the best palliative result according to their needs.

HAD variable, demonstrated that HAD-anxiety varies over time with the same pattern in both groups, while there is a statistically significant difference between the baseline time and the 1st month of the indicator HAD-anxiety concerning only group-B (p=0.031). This could be explained with the limited personal contact between patients and Nuclear Medicine physician, as the implementation of treatment is only a single shot. On the other hand, repetition of the doctor-patient contact, when for example the physician controls the pharmaceutical analgesic action, greatly increases the likelihood of the diagnosis of stress, anxiety and depression, while it alleviates the fatigue associated with cancer. The variety of different treatment formulations and applications against pain produces itself a feeling of optimal palliative effect in total contrast to a single-injection therapy [33,34].

Depression among cancer patients appears at a rate that exceeds 50%, and is constantly increasing over time during the progression of disease [35,36]. Our study recorded an upward trend in the index of depression in both groups, whereas the behavior of the index over time was again similar. While depression is certain to affect the quality of life of cancer patients, recent studies demonstrated the aggravating role of cytokines in tumor inflammation and IL- 1b -511T/T genotype on the occurrence of depression, presenting pathophysiological genetic mechanisms, a fact that could explain the depression's progressiveness, irrespective of the treatment strategy [37].

Although statistics ignore the ECOG rates of improvement (concerning the rates of condition changed), is it the physician of a patient who suffers from cancer capable to ignore improvement rates of 15-24 %? Given that the data on long-term results on the quality of life in patients with cancer are scarce and usually the prognosis and long-term expectations are poor [38], physicians must have as their primary objective to improve patients' quality of life in every possible way [39].

The satisfaction index of life altered similarly in both groups, but again group-B was benefited by the extraction and exchange of information, which is directly linked to the satisfaction of life [40]. The international literature indicates that between two treatment strategies with similar efficacy, patients would choose oral and/or transdermal therapy compared to intravenous drug administration, believing in a greater personal gain, in a reduced feeling of being sick, and finally in a better deal against the disease [41]. On the other hand, patients who have undergone both oral and intravenous therapy, eventually tend towards

intravenous, thinking firstly the safety protocols when hospitalized (even for a few hours), and secondly the minimized family's intervention in their treatment [42]. It should be said that the decision has to be taken jointly between physician and each individual patient.

Analgesia levels achieved in both groups were similar. As cancer pain affects general activity, mood, walking ability, normal work, sleep and above all the enjoyment of life [43-47], it is strongly related with the quality of life, despite the clinical symptoms and socio-demographic factors, and usually requires a higher dose of analgesics than the physical pain [48-51]. The difficulty to distinguish the different types of pain and their intensity, as well as to correctly measure them, represents a timeless quest, while the establishment of appropriate diagnostic calculating tools is strongly necessary [52].

The reduction in medication, alongside with the local radiation effect that synergistically reduces pain [53] among the patients of group-A, and on the other hand the constantly elevation of the drug dosage, combined with the additional use of antidepressants to control neuropathic pain in later stages of cancer in group-B, give a potentially better cost-effectiveness result for the Samarium-153 variant [54,55].

## Conclusion

Our study compared two groups of patients suffering from solid tumors with multiple bone metastases, who received either the appropriate medication treatment or an intravenous dosage of Samarium-153. While usually medical studies are analyzing single-dimension treatments only, our study juxtaposed two completely different approaches, proposing Samarium as a fully equivalent method to the pharmaceutical approach, that can meet the needs for patient palliation. It can also be applied in patients with allergies or intolerance to pain killers, or with inability towards the application of the program administration. Furthermore Samarium-153 reduces the use of pain killers and the outpatient visits in hospitals, resulting in resource savings.

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