Health-resource utilization attributable to skeletal-related events in patients with advanced cancers associated with bone metastases: results of the US cohort from a multicenter observational study

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Background: Patients with advanced cancer and bone metastases frequently experience skeletal-related events (SREs) including pathologic fracture, spinal cord compression, and radiation or surgery to bone. This prospective, observational study characterized health-resource utilization (HRU) associated with each SRE type across tumor types.

Methods: Patients with bone metastases secondary to breast, prostate, or lung cancer as well as patients with multiple myeloma were enrolled within 97 days of experiencing an SRE and were followed prospectively for up to 18 months. Data on hospitalization, length of hospital stay, outpatient visits, emergency department visits, nursing home or long-term care facility stays, home health visits, procedures, and medication usage were collected and attributed to SREs by investigators.

Results: In all, 238 patients were prospectively followed for a median of 9.5 months after enrollment. Bisphosphonates were prescribed in 77% of patients. Of 510 SREs recorded, 442 were included in the HRU analyses. Spinal cord compression and surgery to bone were associated with the highest rates of inpatient stays (mean, 0.6 hospitalizations per SRE), and length of stay was longest for pathologic fracture (mean, 16 days per SRE). Radiation to bone had the most outpatient visits (mean, 10 visits per SRE) and procedures (mean, 12 per SRE).

Limitations: HRU was likely underestimated because patient charts may not have been comprehensive, and the study design did not capture all potential HRU sources. Sample sizes were small for some SRE types.

Conclusions: Each SRE type was associated with substantial HRU, and patterns of HRU were unique across SRE type. The HRU burden of SREs in patients with bone metastases is considerable, even with bisphosphonate treatment.

Bone metastases are common in patients with advanced cancer and lead to serious sequelae that include local bone destruction, skeletal complications, pain, and hypercalcemia. About 70% of patients with advanced breast cancer, 90% of those with advanced prostate cancer, and 30%-40% of those with advanced lung cancer or other advanced solid tumors develop bone metastases.[1-4] The 5-year relative survival rates in patients with advanced cancer (defined as distant metastases to any site) at the time of diagnosis are 23.3% for breast cancer, 28.7% for prostate cancer, and 3.6% for lung cancer.[5] In advanced cancer patients with bone metastases and skeletal-related events (SREs), the survival rates are even lower and the mortality risk is

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high.[6-9] In these patients, survival time with bone metastases is measured in months to years.[2,6]

Patients with bone metastases frequently experience skeletal complications, including spinal cord compression, pathologic fracture, surgery to bone, and radiation to bone, which are collectively known as SREs. National Comprehensive Cancer Network (NCCN) guidelines recommend the use of denosumab for the prevention of SREs in patients with bone metastases secondary to advanced breast[10] or prostate[11] cancer. (Denosumab was not available during the conduct of the present study.) Intravenous (IV) bisphosphonates such as zoledronic acid and pamidronate are recommended by the NCCN for patients with bone metastases from breast cancer;[10] in prostate cancer, zoledronic acid is the only bisphosphonate recommended.[11] In lung cancer and other solid tumors, denosumab or bisphosphonate therapy can be considered.[12]

Despite treatment with bisphosphonates, about half of patients may experience SREs.[13-15] SREs may be associated with severe pain that could be incapacitating and difficult to treat, as well as other morbidities such as difficulty in walking or moving, instability, numbness, weakness, urinary or fecal incontinence, and paralysis.[2,16-20] Patients with SREs experience a compromised quality of life compared with those who have not had an SRE,[18,19,21,22] and their care may result in the use of considerable health-care resources.[23-30]

With the increase in cost constraints related to health care in the United States, it will become even more important to demonstrate both the burden of disease and the economic value of innovative medicines to inform health-care policy in the public and private payer segments. Numerous studies have evaluated various aspects of the burden of SREs; however, most report cost data alone, rather than health-resource utilization (HRU), and most are retrospective database analyses.[23-30] Many of these studies focus on a specific tumor type in a specific country; hence, the results cannot be generalized across other tumor types or regions. This prospective, observational, multinational study was designed to estimate HRU associated with each SRE type across the most common tumor types that metastasize to bone and predispose patients to skeletal complications such as SREs. In this report, we present data for the US cohort of this study.

Materials and methods

The primary objective of this study was to estimate HRU associated with SREs by tumor type, type of SRE, and country. Secondary objectives addressed here include the description of the usage patterns of systemic therapies for bone metastases.

Patients

Eligible participants were aged 18 years or older with a diagnosis of bone metastases secondary to breast, prostate, or lung cancer, or were patients with multiple myeloma. They had an Eastern Cooperative Oncology Group (ECOG) performance status of grade 0, 1, or 2, and had experienced at least one SRE in the 97 days before enrollment. Informed consent was required from each patient before the collection of data. Patients with a life expectancy of less than 6 months or those who were currently enrolled in an investigational drug trial for the treatment of bone metastases or SREs were excluded.

Study design

This was a multicenter, prospective, observational study that was conducted in the United States, Canada, Germany, Italy, Spain, and the United Kingdom (planned sample size, 250 patients per country for a total of 1,500). Analysis of study results by country was specified in the protocol; the current report includes data from US sites only. The protocol and informed consent were approved by the Institutional Review Board at each site. The first US patient was enrolled in June 2008, and the planned study duration was 30 months after enrollment of the first patient. Patients were enrolled within 97 days of experiencing an SRE and were to be followed for about 18 months.

Patients' demographics and medical history were collected at enrollment. HRU data, including inpatient stays, outpatient visits, emergency department visits, nursing home or long-term care facility stays, home health visits, procedures (eg, imaging or surgery), and certain types of medication use were collected prospectively for the duration of the patient's participation in the study, and retrospectively through chart review for all SREs occurring in the 97-day period before enrollment. Investigators were responsible for attributing the HRU to SREs. Multiple related radiation sessions were counted as a single SRE of radiation to bone to which multiple procedures of radiation were attributed. The investigators were asked to collect data from the patient's chart at least every 90 days during the follow-up period to ensure collection of prospectively occurring SREs and HRU.

Outcomes

The primary outcome measures as specified in the protocol were:

- Inpatient stays—number of stays, duration of stays, reason for hospitalization, type of hospital unit, time spent on each type of hospital unit

- Outpatient visits—number of visits, reason for visits, provider type (eg, medical oncologist, physiotherapist, etc)
- Emergency department visits—number of visits, reason for visits, disposition (eg, admitted to hospital, discharged)
- Nursing home or long-term care facility stays—type of facility, reason for admission, length of stay
- Home health visits—number of visits, provider type, reason for visits
- Procedures—type (eg, imaging), reason, facility type
- Medications, including systemic therapies (eg, chemotherapy)

The secondary outcomes reported here include:

- Systemic bone targeted therapies (eg, bisphosphonates) for bone metastases—types of treatments prescribed, date of treatment initiation and discontinuation, dosing frequency.

Statistical methods

A target enrollment for the US cohort of 250 patients was based on the study objective of estimating the number of days of hospitalization per SRE type. This sample size included the assumption of the annual attrition rates of 20% for breast cancer and multiple myeloma, 38% for prostate cancer, and 55% for lung cancer.

The SRE that triggered enrollment (index SRE) and all subsequent SREs were classified as spinal cord compression, surgery to bone, radiation to bone, or pathologic fracture. SREs represent a composite of events and procedures. For patients with more than one retrospective SRE at the time of enrollment, the index SRE was selected in the following order: spinal cord compression; surgery to bone; pathologic fracture; or radiation to bone. For example, if a patient had both surgery to bone and pathologic fracture during the retrospective data collection period, then surgery to bone was identified as the index SRE.

Targets for the index SRE types were established for each country based on anticipated enrollment and the goal of ensuring adequate numbers of each SRE type per tumor type for the analysis. During the course of enrollment, when the target numbers had been reached for a particular tumor and SRE type, that index SRE enrollment group may have been closed.

Participants who met the eligibility requirements were included in the full analysis set. Some SREs were excluded from the HRU analyses because they were determined to be secondary to a primary SRE. For example, if a patient received surgery to bone after having had pathologic fracture, then the investigator may have attributed all HRU to the pathologic fracture SRE and no HRU to the surgery to bone SRE. In such cases, the secondary SRE with no HRU was excluded from the HRU analyses because inclusion would have led to an underestimation of HRU for that SRE type. Descriptive analyses of HRU were produced for each SRE type by tumor type.

The average duration of inpatient stay was computed as the total number of inpatient stay days attributed to SREs divided by the total number of SREs associated with an inpatient stay.

SREs were summarized by patient. SREs were summarized both retrospectively (up to 97 days before enrollment) and prospectively (after enrollment).

Results

Study population

In all, 238 patients were enrolled at US sites and met the eligibility criteria (full analysis set). By tumor type, 78 patients (33%) had breast cancer, 41 (17%) had prostate cancer, 71 (30%) had lung cancer, and 48 (20%) had multiple myeloma. Baseline demographics and disease characteristics are shown in Table 1.

The median length of prospective follow-up time was 9.5 months for all patients, 13.0 months for breast cancer patients, 9.4 months for prostate cancer, 6.6 months for lung cancer, and 10.7 months for multiple myeloma.

Skeletal-related events

Patients experienced a total of 510 SREs, of which 373 (73%) were experienced in the retrospective data collection period, and 137 (27%) were experienced during the prospective follow-up period. During the study, 43% of patients experienced one SRE, 25% had two SREs, 18% had three SREs, 6% had four SREs, 5% had five SREs, and 3% had six or more SREs.

HRU analyses

Of the 510 SREs reported in this study, 442 were included in the HRU analysis set. In all, 68 SREs (26 of surgery to bone and 42 of radiation to bone) were excluded from the HRU analysis because they were determined to be secondary to another (primary) SRE.

Overall, surgery to bone and spinal cord compression were more often associated with hospitalization than were other SRE types (mean, 0.6 hospitalizations per SRE for each; Table 2). Pathologic fracture was associated with longer hospital stays (mean, 16 days per SRE) and more home health visits (mean, 0.7 per SRE) relative to other SRE types. Radiation to bone was associated with the greatest number of outpatient visits (mean, 10 per SRE) and procedures (mean, 12 per SRE), but few other HRU types. Spinal cord compression was associated with mod-

TABLE 1 Baseline demographics and disease characteristics of the study population

Demographics/Disease characteristics	Cancer type: All Tumors (n = 238)	Breast (n = 78)	Prostate (n = 41)	Lung (n = 71)	Multiple Myeloma (n = 48)
Age, y					
Mean (SD)	65 (12)	61 (12)	73 (11)	66 (10)	64 (11)
Sex, n (%)					
Female	130 (55)	78 (100)	–	32 (45)	20 (42)
Male	108 (45)	–	41 (100)	39 (55)	28 (58)
Race/Ethnicity, n (%)					
White	208 (87)	66 (85)	36 (88)	64 (90)	42 (88)
Black	17 (7)	5 (6)	2 (5)	5 (7)	5 (10)
Hispanic/Latino	13 (6)	7 (9)	3 (7)	2 (3)	1 (2)
ECOG Performance, n (%)					
Grade 0	48 (20)	23 (30)	9 (22)	10 (14)	6 (13)
Grade 1	122 (51)	40 (51)	23 (56)	35 (49)	24 (50)
Grade 2	68 (29)	15 (19)	9 (22)	26 (37)	18 (38)
Time from cancer diagnosis to enrollment, mo					
No. of patients	237	78	40	71	48
Median	18	47	59	5	3
Mean (SD)	43 (61)	73 (76)	72 (65)	12 (24)	15 (24)
Time from diagnosis of bone metastases to enrollment, mo					
Median	3	3	7	2	2
Mean (SD)	12 (25)	16 (28)	20 (39)	4 (5)	11 (21)
History of SREs,[a] n (%)	101 (42%)	26 (33%)	23 (56%)	34 (48%)	18 (38%)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; mo, month; n, number of patients; SD, standard deviation; SRE, skeletal-related event; y, year.
Note: Some percentages do not add up to 100 because of rounding.
[a] Before the 90 days before enrollment (ie, before the retrospective data collection period).

erate to high HRU consumption in most categories, and had the highest frequency of emergency department visits (mean, 0.3 visits per SRE). Few nursing home or long-term care facility stays were recorded. The higher number of procedures associated with radiation to bone was influenced by the counting of each radiation session as an individual procedure in cases where a radiation procedure comprised multiple sessions.

HRU by SRE type in breast, prostate, and lung cancers is shown in Figures 1 and 2. Hospitalization was consistently high for surgery to bone, with 50% or more of surgery to bone events requiring a hospitalization across all solid tumor types (Figure 1a). Hospitalizations associated with spinal cord compression were also frequent. The length of hospital stay per SRE was longest for pathologic fracture across most solid tumor types (median, 11.5-25 days; Figure 1b). Median length of stay per SRE was 6.0-6.5 days for spinal cord compression for breast, prostate, and lung cancers; 6.0-8.5 days for radiation to bone across all solid tumors; and 4.0-4.5 days for surgery to bone across all solid tumors. Outpatient visits occurred with all SRE types across all solid tumor types, but were consistently high for radiation to bone (median, 9.0-12.0 per SRE) and consistently low for surgery to bone (median, 1.0-1.5 per SRE; Figure 2a). Emergency department visits occurred mostly with spinal cord compression and pathologic fracture, and were generally similar across solid tumor types (Figure 2b). Multiple myeloma data were generally similar to those for solid tumors. Home health visits were reported for pathologic fracture in breast cancer (mean [SD], 0.8 [4.8] per SRE) and for surgery to bone in lung cancer (mean [SD], 1.3 [3.5] per SRE), but the results were not consistent across tumor types and were zero or negligible for other SRE types.

TABLE 2 Health-resource utilization by type of skeletal-related event[a]

Health-resource utilization	Type of SRE			
	Spinal cord compression (35)[b]	Surgery to bone (37)[b]	Pathologic fracture (98)[b]	Radiation to bone (272)[b]
Inpatient hospitalizations				
Mean (SD)	0.6 (0.7)	0.6 (0.5)	0.4 (0.6)	0.0 (0.3)
Median	0.0	1.0	0.0	0.0
Length of stay, days[c]	(17)[b]	(22)[b]	(31)[b]	(9)[b]
Mean (SD)	11.8 (11.1)	6.4 (4.7)	15.8 (13.1)	8.0 (2.7)
Median	6.0	4.0	13.0	8.0
Outpatient visits				
Mean (SD)	8.1 (8.5)	3.3 (6.4)	6.0 (6.6)	10.1 (6.3)
Median	5.0	1.0	3.0	10.0
Emergency department visits				
Mean (SD)	0.3 (0.4)	0.0 (0.0)	0.1 (0.4)	0.0 (0.1)
Median	0.0	0.0	0.0	0.0
Nursing home/long-term care facility stays				
Mean (SD)	0.0 (0.0)	0.0 (0.0)	0.0 (0.1)	0.0 (0.0)
Median	0.0	0.0	0.0	0.0
Home health visits				
Mean (SD)	0.0 (0.2)	0.3 (1.7)	0.7 (3.4)	0.0 (0.0)
Median	0.0	0.0	0.0	0.0
Procedures (eg, imaging)				
Mean (SD)	11.5 (11.7)	5.4 (8.8)	8.6 (8.0)	12.1 (6.5)
Median	7.0	2.0	5.5	12.0

Abbreviations: SD, standard deviation; SRE, skeletal-related event.
[a] All tumors combined (breast, prostate, and lung cancer, and multiple myeloma); [b] Number of SREs; [c] Based on SREs associated with inpatient hospitalization.

Procedures were common with all SRE types, and were consistently high in number with radiation to bone (median, 12-14 per SRE). Results were also consistent across solid tumor types, with the exception of prostate cancer, which had a higher number of procedures for spinal cord compression (Figure 2c). For all tumor types combined (breast, prostate, and lung cancer, and multiple myeloma), the most common procedure type for each of the SRE types was external beam radiation, with an overall median of 10 procedures performed per SRE (Table 3). This is consistent with the common practice of conventional external beam radiation in the United States. The frequency of other procedure types varied with SRE type.

Bisphosphonate use

Most of the patients (71%) were being treated with bisphosphonates (both IV and oral) at or before enrollment (Table 4). The frequency of bisphosphonate use varied by tumor type, with the lowest use found in patients with lung cancer and the highest use in those with breast cancer. The length of time from first bisphosphonate dose administered to enrollment varied greatly among patients, with an overall median of 1.8 months across all tumor types (breast, prostate, and lung cancer, and multiple myeloma). Patients with breast cancer received the first dose of IV bisphosphonate sooner after the diagnosis of bone metastases than did those with prostate or lung cancer.

The proportion of patients receiving bisphosphonates increased during the course of the study, with a total of 184 patients (77%) across all tumor types (breast, prostate, and lung cancer, and multiple myeloma) receiving bisphosphonate during the retro- and/or prospective data collection periods. Among those who received bisphosphonates, the median duration of use was 11.0 months across all tumor types (breast, prostate, and lung cancer, and multiple myeloma; 184 patients), 15.6 months for breast cancer (66 patients), 8.8 months for prostate cancer (32 patients), and

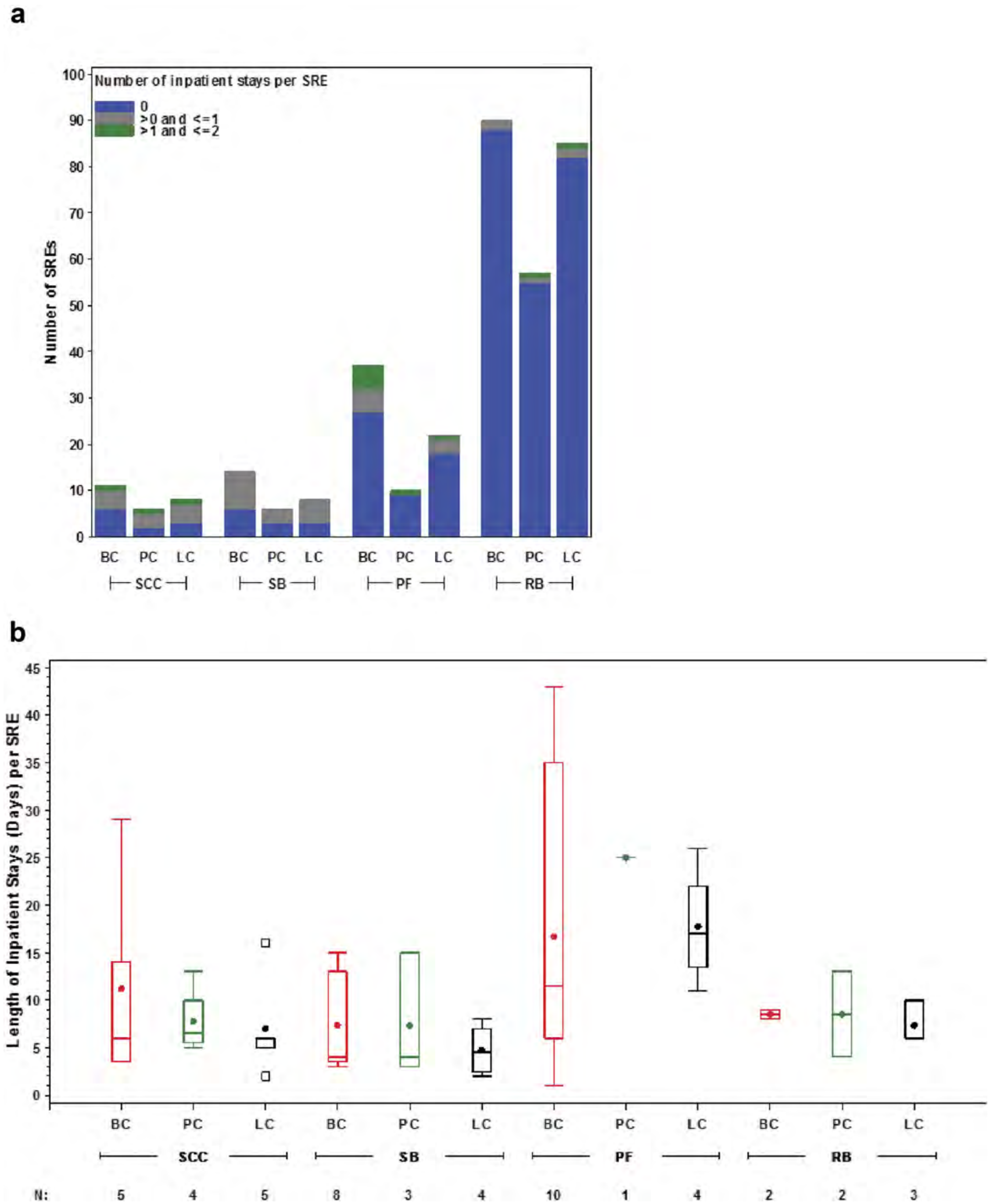

FIGURE 1 The frequency of skeletal-related events by number of inpatient stays per SRE, tumor type, and SRE type (1a). Duration of inpatient stay per SRE by tumor type and SRE type (1b). The horizontal line in each box indicates the median, the dots indicate the mean, and the top and bottom borders of the box mark the 75th and 25th percentiles, respectively. The upper edge of the whisker indicates the maximum observation below the upper fence (75th percentile +1.5 IQR); the lower edge of the whisker indicates the minimum observation above the lower fence (25th percentile −1.5 IQR), and the squares show observations outside the upper and lower fence. BC indicates breast cancer; PC, prostate cancer; LC, lung cancer; SCC, spinal cord compression; SB, surgery to bone; PF, pathologic fracture; RB, radiation to bone; IQR, interquartile range.

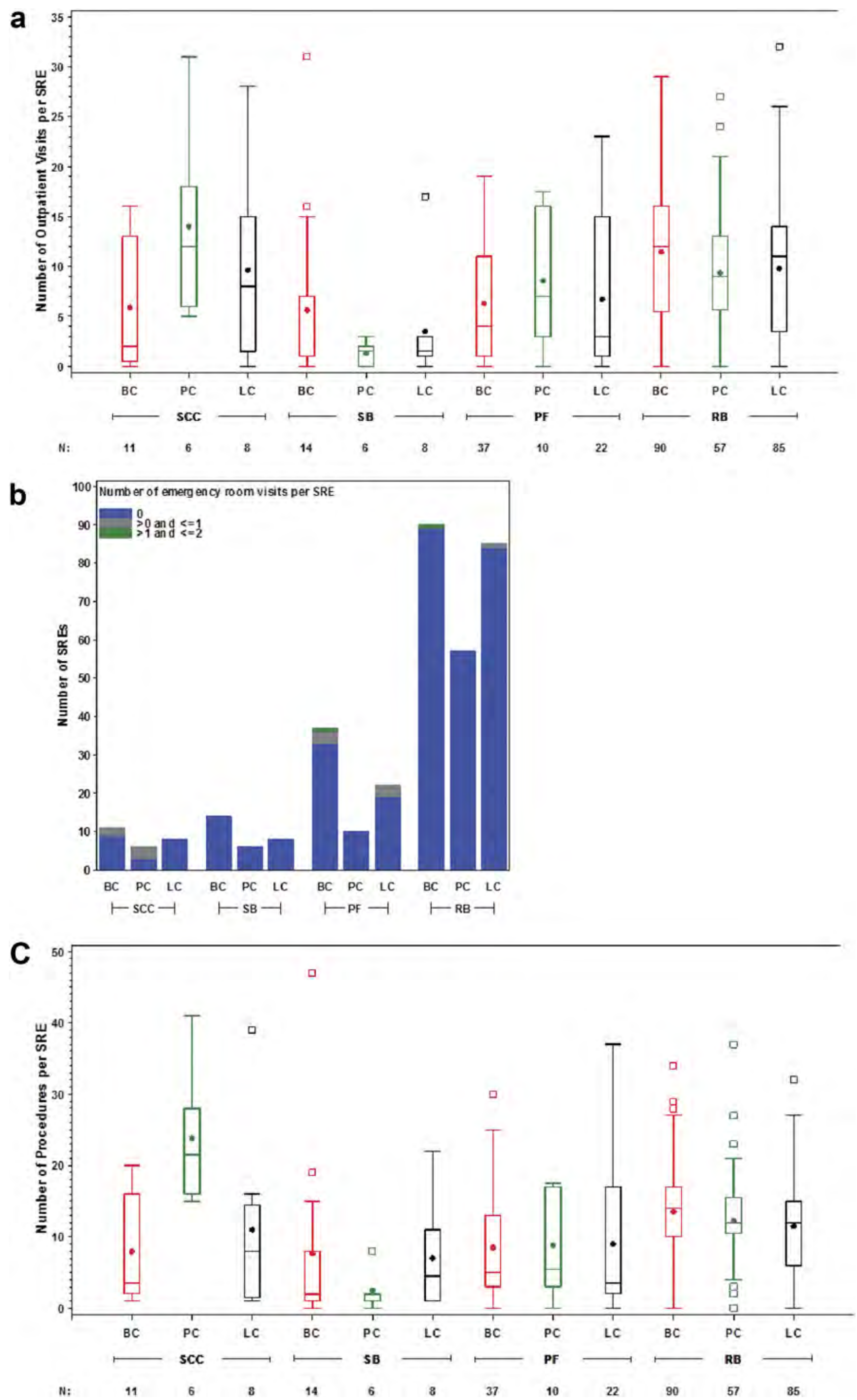

FIGURE 2 The number of outpatient visits per SRE by tumor type and SRE type (2a). The horizontal line in each box indicates the median, the dots indicate the mean, and the top and bottom borders of the box mark the 75th and 25th percentiles, respectively. The upper edge of the whisker indicates the maximum observation below the upper fence (75th percentile +1.5 IQR); the lower edge of the whisker indicates the minimum observation above the lower fence (25th percentile −1.5 IQR), and the squares show observations outside the upper and lower fence. Frequency of SREs by number of emergency department visits per SRE, tumor type, and SRE type (2b). Number of procedures per SRE by tumor type and SRE type (2c). The horizontal line in each box indicates the median, the dots indicate the mean, and the top and bottom borders of the box mark the 75th and 25th percentiles, respectively. The upper edge of the whisker indicates the maximum observation below the upper fence (75th percentile +1.5 IQR); the lower edge of the whisker indicates the minimum observation above the lower fence (25th percentile −1.5 IQR), and the squares show observations outside the upper and lower fence.

BC indicates breast cancer; PC, prostate cancer; LC, lung cancer; SCC, spinal cord compression; SB, surgery to bone; PF, pathologic fracture; RB, radiation to bone; IQR, interquartile range.

TABLE 3 Number of procedures performed per SRE by SRE type[a]

Procedure type (n)	Mean (SD)	Procedure type (n)	Mean (SD)
All SRE types (442)		Cont./Surgery to bone (37)	
External beam radiation[b]	7.47 (6.55)	Chemotherapy	0.11 (0.52)
Physical exam	1.03 (1.68)	Computed tomography	0.11 (0.31)
X-ray	0.34 (0.81)	Other	0.46 (1.45)
Magnetic resonance imaging	0.27 (0.55)	Pathologic fracture (98)	
Intensity-modulated radiotherapy[b]	0.21 (1.87)	External beam radiation[b]	3.81 (6.09)
Laboratory assessment	0.20 (0.79)	X-ray	0.91 (1.26)
Computed tomography	0.18 (0.48)	Physical exam	0.69 (1.45)
Other	0.56 (1.58)	Magnetic resonance imaging	0.50 (0.65)
Spinal cord compression (35)		Computed tomography	0.36 (0.63)
External beam radiation[b]	5.71 (6.46)	Laboratory assessment	0.27 (0.96)
Physical exam	1.86 (2.92)	Radionucleotides	0.16 (1.52)
Magnetic resonance imaging	0.71 (0.70)	Radionuclide scan	0.12 (0.32)
X-ray	0.54 (1.09)	Chemotherapy	0.13 (0.87)
Laboratory assessment	0.40 (1.17)	Surgery to bone (spine)	0.13 (0.41)
Computed tomography	0.34 (0.76)	PET Scan	0.11 (0.32)
Surgery to bone (spine)	0.26 (0.44)	Surgery to bone–extremities	0.10 (0.34)
Ultrasound	0.14 (0.49)	Other	1.07 (2.52)
Chemotherapy	0.11 (0.53)	Radiation to bone (272)	
Other	1.14 (2.35)	External beam radiation[b]	9.83 (5.73)
Surgery to bone (37)		Physical exam	1.01 (1.36)
External beam radiation[b]	1.49 (4.54)	Intensity-modulated radiotherapy[b]	0.34 (2.38)
Physical exam	1.22 (2.38)	Magnetic resonance imaging	0.14 (0.43)
Laboratory assessment	0.41 (1.40)	Laboratory assessment	0.13 (0.50)
Surgery to bone (extremities)	0.41 (0.50)	X-ray	0.11 (0.30)
X-ray	0.35 (0.72)	Computed tomography	0.10 (0.35)
Surgery to bone (spine)	0.30 (0.52)	Other	0.32 (0.79)
Magnetic resonance imaging	0.27 (0.45)		
	Cont./		

Abbreviations: n, number of procedure types; SRE, skeletal-related events.
[a]For procedures with mean ≥ 0.10 per SRE, all tumor types combined (breast, prostate, and lung cancer, and multiple myeloma); [b]A radiation procedure with multiple sessions is captured as multiple procedures.

5.8 months for lung cancer (47 patients). The most commonly prescribed bisphosphonate was IV zoledronic acid, which was prescribed in 164 patients (69%).[31] Pamidronate was less frequently prescribed (22 patients; 9%).

Discussion

To our knowledge, this is the first large, prospective, observational study to report investigator-attributed HRU by SRE type in clinical practice across four common tumor types. Most previous studies on SRE burden have reported results from retrospective database analyses or bisphosphonate clinical trials, and many have been limited to a single tumor type. In the United States, a few publications have reported on the substantial cost associated with SREs, particularly for SREs requiring inpatient hospitalization.[21-23,27] Those studies have focused primarily on costs of hospitalization and length of stay, whereas the present study captured a more complete picture of the spectrum of oncology practices involved in caring for patients with SREs. Of note, this study collected SRE-specific HRU data, which have not been reported in most prior studies, including outpatient and emergency department visits, as well as detailed information on procedures performed. For this reason, comparisons of the present results with previously reported data are limited.

TABLE 4 Bisphosphonate use

	Cancer type			
	All Tumors[a] (n = 238)	**Breast (n = 78)**	**Prostate (n = 41)**	**Lung (n = 71)**
Received bisphosphonates[b] at or before enrollment, n (%)	168 (71)	63 (81)	30 (73)	40 (56)
Median time from diagnosis of bone metastases to first IV bisphosphonate dose, mo	1.8	1.4	5.1	2.6
Median time from first bisphosphonate dose to enrollment,[b,c] mo	1.8	2.7	1.4	1.0
Treated with bisphosphonates during study,[b,d] n (%)	184 (77)	66 (85)	32 (78)	47 (66)
Median duration of bisphosphonate use,[b,c,d,e] mo	11.0	15.6	8.8	5.8

Abbreviations: IV, intravenous; mo, months; n, number of patients.
Note: If bisphosphonate use was initiated before the retrospective data collection period, ie, > 90 days before enrollment, then the actual bisphosphonate start date was used; in patients who switched bisphosphonate medications or who used bisphosphonates noncontinuously, duration of use was the sum of all administration periods.
[a]Includes breast, prostate, and lung cancer, and multiple myeloma; [b]Includes oral and intravenous; [c]In patients treated with bisphosphonate; [d]During the retro- and/or prospective data collection periods; [e]Based on stop/start dates recorded in the case report form in subjects receiving bisphosphonates during the retro- and/or prospective data collection periods.

Among the US cohort of this multinational study in patients with bone metastases, all SRE types were associated with substantial HRU, and the pattern of HRU was consistent with that expected for each SRE type. All SRE types were associated with multiple outpatient visits and many procedures, whereas the SRE types most likely to result in hospitalization were surgery to bone and spinal cord compression. Lengths of hospital stay differed for the four SRE types, but were fairly consistent across the tumor types. A recent US payer database study of inpatient costs for SREs in patients with bone metastases reported mean lengths of stay ranging from 6 to 12 days, depending on SRE type and tumor type, a finding that is consistent with the estimations reported in our study.[29]

The bisphosphonate usage data collected in this study offer some interesting insights into prescribing patterns in the United States. Most of the patients were already receiving a bisphosphonate at or before study enrollment. Bisphosphonate use was less frequent and shorter in duration in lung cancer, compared with the other tumor types, possibly because of the shorter life expectancy and/or the lack of a strong recommendation by the NCCN guidelines.[12] Zoledronic acid was prescribed in the majority of patients in all tumor types, whereas pamidronate was used only occasionally.

This study has several limitations. First, the HRU reported in this study may underestimate actual HRU for a number of reasons. The HRU reported here reflects only information available from patient charts, which may not have been comprehensive. For example, few home health visits and nursing home or long-term care facility stays were captured in this study. This may be a result of underreporting because the information may not have been available in patient charts at the oncologists' offices. Emergency department visits were also less common, which may be explained by differences in regional oncology practice. For instance, in investigators' practices in Texas (AM) and Kentucky (HG), patients have 24-hour access to their oncologists and rarely receive care through the emergency department, whereas in a California practice (MF), patients are more often sent to the emergency department to receive rapid access to diagnostic testing. We also note that the number of procedures may have been underestimated, as physical examination was not captured in relation to inpatient stays. Furthermore, transportation for patients from hospital to radiation centers by ambulance was not included in this study and represents an additional source of resource burden.

Another limitation of the study is that the sample sizes for surgery to bone and spinal cord compression were limited and may not have been sufficient to provide a generalizable HRU estimation. Similarly, the length of stay estimations may have been limited by small sample sizes. Finally, we note that the distribution of SRE types was influenced by the index SRE targets and should not be considered to represent a normal population distribution.

The results of this study in other countries will be presented separately and will allow the opportunity to compare practice patterns and HRU between the United States and Europe in future publications.

Conclusion

Results of the US cohort of this observational study have shown that SREs of all types are associated with substantial HRU in patients with bone metastases and breast, prostate, or lung cancer, most of whom were receiving bisphosphonates. The considerable burden of SREs on both the patient and health-care system points to the strong need for more effective therapies or interventions to prevent these events.

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