Research Article

Health resource utilization associated with skeletal-related events in patients with bone metastases: Results from a multinational retrospective – prospective observational study – a cohort from 4 European countries

H. Hoefeler [a,*], I. Duran [b,c], G. Hechmati [d], C. Garzon Rodriguez [e], D. Lüftner [f], J. Ashcroft [g], A. Bahl [h], C. Atchison [i], R. Wei [j], E. Thomas [k], V. Lorusso [l,m]

[a] Forschungszentrum-ruhr, KliFoCenter GmbH, Pferdebachstr. 30, 58455 Witten, Germany
[b] Hospital Universitario Virgen del Rocio, Avda. Manuel Siurot s/n, 41013 Seville, Spain
[c] Centro Integral Oncologico Clara Campal (CIOCC), Calle Ona 10, 28050 Madrid, Spain
[d] Health Economics, Amgen (Europe) GmbH, Dammstrasse 23, 6301 Zug, Switzerland
[e] Institut Català d'Oncologia, Avinguda Gran Via de L'Hospitalet, 199-203, 08908 L'Hospitalet de Llobregat, Barcelona, Spain
[f] Universitätsmedizin Berlin, Charité Campus Benjamin Franklin, Charitéplatz 1, D-10117 Berlin, Germany
[g] Pinderfields Hospital, Mid Yorkshire Hospitals NHS Trust, Wakefield WF1 4DG, UK
[h] Bristol Haematology and Oncology Centre, University Hospitals Bristol, Bristol BS2 8ED, UK
[i] Health Economics, Amgen Inc., 1 Amgen Center Drive, Thousand Oaks, CA 91320, USA
[j] Biostatistics, Amgen Inc., 1 Amgen Center Drive, Thousand Oaks, CA 91320, USA
[k] Scientific Affairs, Amgen (Europe) GmbH, Dammstrasse 23, 6301 Zug, Switzerland
[l] Oncology Institute ASL, Via Antonio Miglietta, 5, 73100 Lecce, Province of Lecce, Italy
[m] National Cancer Institute, Istituto Oncologico Giovanni Paolo II, Viale Orazio Flacco 65, 70124 Bari, Italy

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ABSTRACT

Background: Skeletal-related events (SREs; pathologic fracture, radiation or surgery to bone, spinal cord compression) frequently occur in patients with advanced cancer with bone metastases/lesions. Limited data on the associated patient and economic burden are available to aid in resource planning and evaluating treatment options.
Methods: Patients with bone metastases/lesions secondary to breast, lung or prostate cancer or multiple myeloma; with at least one SRE within 97 days prior to enrollment; life expectancy of at least 6 months; and Eastern Cooperative Oncology Group performance status 0, 1 or 2 were recruited. Information on health resource utilization (HRU; including number/duration of hospitalizations, outpatient visits, procedures), attributed by investigators to be associated with a SRE, was collected retrospectively for up to 97 days prior to enrollment and prospectively for up to 18–21 months.
Results: A total of 631 patients contributing 1282 SREs, were enrolled across Germany, Italy, Spain and the United Kingdom. Approximately a third of all SREs required an inpatient stay. Mean duration of inpatient stay for patients with SREs requiring one ranged from 8.4 to 41.1 days across all countries and SRE types.
Conclusion: All types of SREs are associated with substantial HRU burden. Preventing SREs by using the best therapeutic options available may help to reduce the burden to patients and healthcare systems.

1. Introduction

Bone is a common site for metastasis in advanced cancer; reports suggest that approximately 65–75% of patients with advanced breast and prostate cancer, and 30–40% of patients with advanced lung, kidney or thyroid cancer, will develop bone metastasis. Almost all patients with multiple myeloma develop lytic bone disease [1,2]. Owing to the inherent nature of their manifestation, osteolytic lesions (commonly seen in patients who have lung or breast cancer or multiple myeloma) can be related to severe pain, pathologic fractures, life-threatening hypercalcemia, spinal cord compression and other nerve-compression syndromes [3]. In contrast, patients with prostate cancer have predominantly

osteoblastic lesions that can also be frequently associated with bone pain, as well as pathologic fractures and spinal cord compression owing to the poor quality of bone formed during the remodeling process [3] and the often osteoporotic state induced by prolonged castration. These skeletal complications are commonly categorized as skeletal-related events (SREs) and defined as pathologic fracture, radiation to bone, spinal cord compression and surgery to bone. History of previous SREs is associated with an increased risk for subsequent events and a poorer prognosis. Previous studies have demonstrated decreased survival rates in those patients who have bone metastases and prior SREs [4,5]. Although bone metastases/lesions and their associated SREs are predictors for increased mortality [4,6–8], patients with advanced cancer today are generally surviving longer as new and more effective treatment options are introduced into the therapeutic armamentarium. Thus, prevention of SREs becomes even more important as patient life-span is extended.

Apart from their association with severe pain and reduced quality of life, SREs require substantial healthcare resource utilization (HRU) in their treatment and management. Previous retrospective studies have attempted to quantify various aspects of the burden of SREs across specific tumor types/countries, with studies in the United States of America (USA), France, Portugal and Spain all reporting high costs associated with SREs [9–14]. However, these studies did not address the overall HRU burden. With the current cost restraints across European healthcare systems influencing resource reimbursement, this information is important when planning future healthcare requirements and evaluating new treatment options to prevent skeletal complications. Thus, our observational, multinational study was designed to estimate HRU related to each of the defined SRE types in patients with breast, lung or prostate cancer, or multiple myeloma. Owing to the high incidence of these malignancies [15] and the frequency of associated bone metastases [1,2] these cancers can be considered to be responsible for the majority of the burden associated with bone metastases and their related complications in clinical practice. The study was carried out in Canada, Germany, Italy, Spain, the United Kingdom (UK) and the USA. Herein we report data for a cohort from 4 European countries.

2. Materials and methods

2.1. Patients

Patients were eligible if they were aged at least 18 years, had evidence of one or more bone metastasis secondary to breast, prostate or lung cancer or had multiple myeloma with focal lytic bone disease, and had experienced at least one SRE in the 97 days prior to enrollment. Other eligibility criteria included an Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2 and life expectancy of at least 6 months; these criteria were used because patients with shorter life expectancies or worse performance statuses are more likely to be treated in hospices or managed care facilities, where information is often not transferred to hospital patient charts and thus not accessible to the study investigators. Patients provided signed, informed consent prior to collection of their data. Exclusion criteria included participation in an investigational drug trial for the treatment of bone metastases or SREs.

2.2. Study design

A multicenter, observational study was conducted in centers across four major European countries (Germany, Italy, Spain and the UK) as well as Canada and the USA. Large countries were chosen to help meet our enrollment targets. Planned enrollment was 250 patients per country; annual attrition (dropout and death) was assumed to be 20% for breast cancer and myeloma, 38% for prostate cancer and 55% for lung cancer. Therefore, a country accruing 250 participants had an expected total follow-up of 281 patient-years. Analysis of study results per country was pre-specified in the protocol; these analyses review HRU by country and SRE type.

SREs were classified by the investigators as one of the following: pathologic fracture, radiation to bone, spinal cord compression or surgery to bone. In order to ensure that adequate numbers of each SRE type per tumor group were recorded for the analysis, enrollment targets for the index SRE types were established for each country. Patients were enrolled within 97 days of experiencing the index SRE and patients were planned to be followed for up to 18–21 months. In case of a patient experiencing more than one SRE in the 97 days prior to enrollment, the index SRE was selected using the following hierarchy: (1) spinal cord compression; (2) surgery to bone; (3) pathologic fracture; and (4) radiation to bone.

The study was planned to run for 30 months after enrollment of the first patient and thus not all patients received the full duration of follow-up. Baseline demographics and medical history were collected at enrollment. HRU data were collected retrospectively for up to 97 days before study enrollment and prospectively for up to 18–21 months or until the end of the study. Associated HRU data collected from patient charts included information relating to inpatient stays, outpatient visits, emergency room visits, nursing home/long-term care facility stays, home health visits, procedures and certain medications. HRU was independently attributed to each SRE by the investigators. Data were requested to be collected from the patient's chart at least every 90 days during the follow-up observation period to ensure the identification and collection of any prospectively occurring SREs and resource use.

Enrollment began in 2008 and the data cut-off for this primary analysis was 31 May 2010.

2.3. Objectives

The primary study objective was to estimate HRU associated with SREs by type of SRE, tumor type and country. Secondary objectives, not discussed in this paper, included measurement of utility-based health-related quality of life following incident SREs, description of patterns of bisphosphonate use in patients with bone metastases and description of the association between bisphosphonate use and changes in renal function.

2.4. Outcome measures

This paper reports the primary outcome measures for HRU, including inpatient stays, outpatient visits, procedures, emergency room visits, nursing home/long-term care facility stays and home health visits. Details of these outcome measures are listed in Table 1. Secondary outcome measures, not discussed here, included measures of patient-reported outcomes (the 5-domain EuroQol questionnaire), bisphosphonate use (type, date of initiation/discontinuation, dose and frequency) and renal data (serum creatinine level, creatinine clearance rate, glomerular filtration rate, date of renal impairment/failure, and end-stage renal disease and dialysis).

2.5. Statistical methods

All analyses in this observational study were descriptive. Participants who met the eligibility criteria and were enrolled