Bone metastases are associated with considerable morbidity and can result in skeletal-related events (SREs), including pathologic fractures, the need for palliative radiotherapy, spinal cord compression, the need for surgery to bone to prevent or treat a pathologic fracture or spinal cord compression, and hypercalcemia of malignancy. Such SREs have been associated with decreases in survival and increases in healthcare costs. Skeletal morbidity and bone pain from metastases can also reduce patients’ functional capacity and undermine their quality of life. Patients who develop bone metastases from advanced cancers commonly receive bisphosphonates to not only delay the onset of SREs and reduce their frequency but also provide clinically meaningful palliative effects for bone pain. Ongoing research may lead to improvements in skeletal health monitoring and management for patients with malignant bone disease.

The skeleton is the most common site for distant metastasis in patients with cancer. For example, bone metastases form in more than 70% of patients with breast or prostate cancer, in 60% of patients with thyroid cancer, and in about 35% of patients with lung cancer or renal cell carcinoma (Coleman, 2004). Patients with multiple myeloma also develop bone lesions from myeloma colonization in the bone marrow that can affect bone metabolism. Bone metabolism involves resorption of old or damaged bone (osteolysis) by osteoclasts and the generation of new bone matrix by osteoblasts, the actions of which are stimulated by growth factors that are released during osteolysis. The bone microenvironment can provide fertile “soil” in which some metastasizing tumors may grow (Mundy, 1997). Many tumor cells that reach the bone can locally stimulate the body’s osteoclast cells to increase their rates of osteolysis, resulting in increased release of growth factors from the bone matrix in the areas near the metastatic tumor cells. Those growth factors, in addition to their effects on osteoblasts, can stimulate tumor growth (Mundy).

This “vicious cycle” of tumor growth and bone destruction can result in considerable morbidity for patients. Indeed, bone metastases are associated with skeletal-related events (SREs), which include pathologic fractures, bone pain requiring palliative radiotherapy, spinal cord compression, the need for surgical interventions, and hypercalcemia of malignancy (Coleman, 2004). Patients with bone metastases typically experience bone pain as their first symptom, and acute pain episodes may occur despite analgesia (“breakthrough pain”) (Simmonds, 1999). Moreover, because pain can be a symptom of the underlying bone pathophysiology (increased osteolysis resulting from malignant bone disease), the cause of bone pain is important to consider when selecting treatment for pain management.
multiple myeloma, 2.7 for lung cancer and other solid tumors, and 3.7 for breast cancer (Berenson et al., 1998; Lipton, 2003; Lipton et al., 2000; Rosen et al., 2004; Saad et al., 2004). Each type of SRE has been associated with decreases in patients' quality of life (QOL), and fractures have been associated with decreased survival (O'Connel, Ricchiuti, Conrad, & Resnick, 2002; Saad et al., 2007). SREs decrease patients' functional independence and thus limit their autonomy (Weinfurt, Anstrom, Castel, Schulman, & Saad, 2006; Weinfurt et al., 2004). In addition, SREs are associated with increases in healthcare costs (Botteman et al., 2006; Groot, Boeken Kruger, Pelger, & Uyl-de Groot, 2003). For example, in the United States, the average cost increase was $44,442 (2006 dollars) in patients with SREs versus no SREs for all tumor types with metastatic bone disease (Schulman & Kohles, 2007).

The introduction of bisphosphonates has provided an important tool to prevent or delay skeletal morbidity from bone metastases. Bisphosphonates, which inhibit osteoclast-mediated osteolysis, are the current standard of care for patients with bone metastasis from breast, prostate, or lung cancer or other solid tumors, or bone lesions from multiple myeloma (Heidenreich et al., 2009; Hillner et al., 2000; National Comprehensive Cancer Network, 2008). In clinical trials, bisphosphonates have been shown to not only delay the onset of SREs and reduce their frequency but also reduce bone pain and improve QOL in patients with advanced cancer (Pavlakis, Schmidt, & Stockler, 2005). This article presents the clinical implications of bone metastases in patients with advanced cancer, reviews pharmacologic treatment options, and provides practical guidance for the optimal management of patients with bone metastases.

Pathophysiology and Disease Burden From Bone Metastases

The human skeletal system provides structural support for movement and is necessary for hematopoiesis (Reich, 2003). All bone surfaces must undergo periodic bone remodeling to maintain skeletal integrity through the processes of osteoclast-mediated osteolysis and new bone formation by osteoblasts (as described in the introduction), which are tightly regulated (Berenson, Rajdev, & Broder, 2006). The intricate bone remodeling cycle is maintained by growth factors and cytokines embedded in the local bone matrix. The bone's abundant supply of growth factors, easily accessible supply of blood, and porous nature create an ideal microenvironment for tumor cells to metastasize. Figure 2 illustrates bone resorption.

If patients are left untreated, the vicious cycle of tumor growth and bone destruction can undermine skeletal integrity, and about half of all patients with bone metastases will develop an SRE. In addition to their effects on overall QOL, these events can result in substantial costs and increased risks for further complications. Bone metastases can result in severe pain, which may become refractory to standard pain medications. One of the most common SREs, and typically the first one experienced, is bone pain requiring palliative radiotherapy (Lipton, 2007). Palliative radiotherapy is costly and inconvenient to patients and can lead to usually temporary pain flares in some patients, in which bone pain intensifies rather than abates. Spinal cord compression, often presenting initially as back pain, may cause irreversible paraparesis or paraplegia if not detected and treated at an early stage. Patients with bone metastases also may experience pathologic fractures, which are associated with shorter survival compared with patients without a fracture (Lipton, 2007). A retrospective study of 123 patients with a solid tumor or multiple myeloma who experienced a long bone fracture revealed extended healing time, with fracture healing occurring in only 26% of patients who survived for more than six months after the event (Gainor & Buchert, 1983). Patients with a pathologic fracture may have to undergo surgery to stabilize the bone, which can lead to prolonged hospital stays and increased mortality from surgery-associated complications such as emboli (Choong, 2003). Additionally, in a study of older adult patients with hip fractures, patients with lower postfracture physical function are at increased risk for being institutionalized compared with patients who have higher physical function after a fracture (Cree et al., 2000). Hypercalcemia of malignancy, another serious SRE, can lead to heart failure or coma if not diagnosed and treated.

The negative impact of SREs on patients with bone metastases underscores the importance of bone-targeted therapies, such as bisphosphonates. Indeed, by breaking the cycle of tumor

**Figure 1. Skeletal-Related Events Among Patients With Bone Lesions (Trials of Approximately Two Years’ Duration)**

*Note.* Based on information from Berenson et al., 1998; Lipton et al., 2000; Rosen et al., 2004; Saad et al., 2004.

growth and bone destruction, normalizing the bone remodeling process, and preventing or delaying SREs, bisphosphonates provide a means to preserve functional independence and maintain QOL for patients with bone metastases.

**Prevention of Skeletal Complications**

Bisphosphonates significantly reduce the rate or risk of SREs in patients with malignant bone disease from advanced cancer (Coleman, 2004). Nitrogen-containing bisphosphonates, including zoledronic acid, pamidronate, and ibandronate, have demonstrated the most consistent efficacy compared with non-nitrogen-containing bisphosphonates, such as clodronate. The approved dosing schedules for the IV agents are summarized in Table 1 (Hoffmann-La Roche, 2004; Novartis Pharmaceuticals Corporation, 2008a, 2008b; Roche Products Ltd., 2007). Ibandronate has been approved for treatment of bone metastases from breast cancer only in Europe; clodronate has been approved only in Europe for treatment of bone metastases from breast cancer and bone lesions from multiple myeloma. Only pamidronate and zoledronic acid have received worldwide regulatory approval for treatment of bone metastases from breast cancer and bone lesions from multiple myeloma. In addition, zoledronic acid has received widespread regulatory approval for treatment of bone metastases from prostate cancer, lung cancer, and other solid tumors. Because of the approval of IV pamidronate and zoledronic acid in the United States, the American Society of Clinical Oncology consensus treatment guidelines specifically recommend IV bisphosphonates for patients with breast cancer and plain radiographic evidence of bone destruction (Hillner et al., 2003).

Among bisphosphonates evaluated in a review of randomized, placebo-controlled trials investigating skeletal events in women with bone metastases from breast cancer, zoledronic acid yielded the largest reduction in skeletal morbidity (Body et al., 2003, 2004; Hortobagyi et al., 1996, 1998; Kohno et al., 2005; Kristensen et al., 1999; Paterson et al., 1993; Pavlakis et al., 2005; Tubiana-Hulin et al., 2001) (see Figure 3). Zoledronic acid is the only bisphosphonate that has been compared head-to-head with pamidronate in a double-blind, randomized, controlled, phase III trial; zoledronic acid produced benefits beyond those of pamidronate in patients with bone lesions from breast cancer or multiple myeloma (Rosen et al., 2003). After 25 months of follow-up, multiple-event analysis showed that the risk of SREs was reduced by a relative 20% (p = 0.03) with zoledronic acid compared with pamidronate (Rosen et al., 2003). The safety profiles of zoledronic acid and pamidronate were similar, with the most commonly reported adverse events for each treatment group being bone pain (58% and 57%, respectively), nausea (48% for both), and fatigue (43% for both). Grade 3 or 4 increases in serum creatinine occurred in 0.4% of patients treated with zoledronic acid (4 mg via 15-minute infusion) and in 1.9% of patients treated with pamidronate (90 mg via two-hour infusion).

Osteonecrosis of the jaw (ONJ) is an uncommon adverse event that has been reported in patients with cancer receiving complex treatment regimens, including bisphosphonates. Patients with ONJ have exposed bone in the maxillofacial area that occurs in association with dental surgery or spontaneously, with no evidence of healing after six weeks of appropriate dental care in the absence of metastatic disease in the jaw or osteoradionecrosis. In the largest database study to date of ONJ in patients with solid tumors or multiple myeloma treated with...
Zoledronic acid is the only bisphosphonate to significantly reduce the risk of SREs (p ≤ 0.05) versus placebo in patients with bone metastases from a broad range of solid tumors (Kohno et al., 2005; Lipton, Seaman, & Zheng, 2004; Major, 2007; Major, Cook, Chen, & Zheng, 2005; Rosen et al., 2004; Saad et al., 2004) (see Figure 4). Although several bisphosphonates have been studied in patients with bone metastases from hormone-refractory prostate cancer, only zoledronic acid has demonstrated significant, objective, long-term benefits at two years of treatment (Dearnaley et al., 2003; Elomaa et al., 1992; Ernst et al., 2003; Kylmala et al., 1997; Saad, 2002; Saad et al., 2004; Small, Smith, Seaman, Petrone, & Kowalski, 2003; Smith, 1989; Strang et al., 1997). Zoledronic acid not only reduced the proportion of patients who had an SRE (38% versus 49% with placebo; p = 0.03) (Saad et al., 2004) but also consistently reduced the proportion of patients who experienced each type of SRE (Saad et al., 2002). At 15 months, the safety profile of zoledronic acid 4 mg was comparable with that of placebo. The most commonly reported adverse events for each treatment group were bone pain (51% and 61%, respectively), nausea (36% and 37%, respectively), and constipation (34% and 35%, respectively). Grade 3 increases in serum creatinine occurred in 15.2% of patients treated with zoledronic acid (4 mg via 15-minute infusion) and in 11.5% of patients in the placebo group. Because earlier treatment may be more effective, studies in patients with hormone-sensitive disease are ongoing. Despite the differences in established efficacy among the bisphosphonates tested in the prostate cancer
setting, analyses have pooled all of the data, resulting in changes in healthcare policies. For example, zoledronic acid may be difficult to acquire in the United Kingdom because of National Health Service reimbursement issues in the urology setting, and many patients with prostate cancer may now go untreated or receive treatment with alternative bisphosphonates whose efficacy has not been established for tumors other than breast cancer.

Zoledronic acid also is the only bisphosphonate that has demonstrated significant benefits and received widespread regulatory approval in patients with bone metastases from lung cancer and other solid tumors. In a randomized, placebo-controlled trial of zoledronic acid (4 mg) every three weeks for 21 months in patients with lung cancer and other solid tumors, zoledronic acid reduced the number of patients with any SRE (including hypercalcemia of malignancy) compared with placebo (39% versus 48%, respectively; p = 0.04) (Rosen et al., 2004) (see Figure 5). In addition, zoledronic acid significantly delayed the median time to first SRE (236 versus 155 days with placebo; p = 0.009) and significantly reduced the skeletal morbidity rate (1.74 versus 2.71 SREs per year with placebo; p = 0.01). The safety profile of zoledronic acid (4 mg via 15-minute infusion) was comparable with that of placebo. The most commonly reported adverse events for each treatment group were bone pain (51% and 61%, respectively), nausea (49% and 36%, respectively), and anemia (38% and 35%, respectively). Grade 3 or 4 increases in serum creatinine occurred in 1.8% of patients who received that zoledronic acid regimen or placebo.

Bone Pain and Quality of Life

Bone metastases are the most common source of chronic pain in the advanced cancer setting, yet they may remain underdetected and undertreated in many patients (Coleman, 1997; Peng, Wu, Sun, Chen, & Huang, 2006). Indeed, bone metastases have been identified as a source of pain that is typically not adequately treated, and the side effects associated with management of bone pain can impair patients’ QOL above and beyond the effects of the pain itself (Coleman, 1997).

Treatment of bone pain typically involves the concomitant use of focal radiotherapy and analgesic drugs, especially steroids and nonsteroidal anti-inflammatory drugs (often in combination with opioids) (Payne, 1989). Nonpharmacologic interventions can include heat and cold applications, therapeutic mattresses, massage, and relaxation exercises (Reich, 2003). Radiotherapy to bone is standard therapy for palliation of malignant bone pain that has become refractory to pharmaceutical interventions, and the need for palliative radiotherapy is one of the most prevalent SREs (Rosen et al., 2003, 2004; Saad et al., 2002, 2004). For example, in the placebo-control arms of long-term clinical trials of zoledronic acid and pamidronate in patients with malignant bone disease, 33%–37% of patients with bone metastases from solid tumors (breast, prostate, and non-small cell lung cancers) or bone lesions from multiple myeloma required palliative radiotherapy (Berenson et al., 1998; Lipton et al., 2000; Rosen et al., 2004; Saad et al., 2004). In a retrospective review of data from a clinical trial of zoledronic acid versus placebo in patients with prostate cancer (N = 248), radiation to bone reduced the extent to which bone pain interfered with patients’ daily activities (Weinfurt et al., 2005). However, having received radiotherapy also was associated with decreases in scores on the Functional Assessment of Cancer Therapy–General (FACT-G) for physical, functional, and emotional well-being at the patient’s subsequent FACT-G assessment, potentially because of adverse events from radiotherapy (Weinfurt et al., 2005). Therefore, palliative radiotherapy not only is a surrogate endpoint for bone pain but also is associated with decreases in health-related QOL (Weinfurt et al., 2005).

An additional class effect of bisphosphonates is clinically meaningful palliation for patients with refractory bone pain. In a randomized, placebo-controlled trial in patients with bone metastases from breast cancer (N = 144), the addition of the early-generation bisphosphonate clodronate (1,600 mg per day) to standard therapy for as long as 12 months was shown to significantly decrease pain according to visual analog scale pain scores (p = 0.01) and to reduce the need for analgesics (p = 0.02) (Tubiana-Hulin et al., 2001). Newer-generation nitrogen-containing bisphosphonates (e.g., pamidronate, ibandronate, risedronate, zoledronic acid) also decrease pain. Patients with bone metastases from breast cancer treated with pamidronate (90 mg; n = 185) had a smaller increase in bone pain compared with placebo (n = 195) after 12 months (p = 0.05) (Hortobagyi et al., 1996). In an open-label trial of zoledronic acid (4 mg) every three to four weeks for as many as six infusions in patients with breast cancer, prostate cancer, or multiple myeloma (N = 260), mean visual analog scale pain scores were significantly reduced after treatment compared to baseline in all patients overall and in each tumor type subset (p < 0.001) (Wiktor-Jedrzejczak, 2005). In the phase III trials, zoledronic acid significantly reduced the incidence of palliative radiotherapy to bone by 33% compared with placebo in men.
with prostate cancer (n = 422; p = 0.03), by 32% compared
with placebo in patients with lung cancer or other solid tu-
mors (n = 501; p = 0.01), and by 18% beyond the benefit of
pamidronate in patients with breast cancer (n = 766; p = 0.05)
(Major et al., 2005). The incidence of palliative radiotherapy
also was reduced in a randomized, placebo-controlled trial in
patients with advanced breast cancer (N = 227) treated with
zoledronic acid (8.8% versus 17.7% with placebo) (Kohno et
al., 2005).

In a Cochrane meta-analysis of bisphosphonates for relief of
bone pain secondary to bone metastases, their use was recom-
mended for patients with diffuse, painful metastases, especially
when analgesics (with or without radiotherapy) failed to provide
adequate pain relief or produced unacceptable adverse drug
reactions (Wong & Wiffen, 2002). Considering that pain is a
symptom of bone metastases, healthcare professionals should
consider therapies that are both palliative and able to treat the
underlying source of the pain. Therefore, bisphosphonates
should be considered for pain management in all patients with
bone metastases because they are the only class of supportive
therapy agents that has been demonstrated to not only relieve
pain but also affect the underlying pathophysiology of bone
metastases (malignant osteolysis).

Practical Implications

The role of nurses in the management of patients with meta-
static bone disease is multi-faceted, involving administering
anticancer therapy, conducting pain assessments, and counsel-
ing patients and caregivers about potential SREs and how
to prevent and manage them (Reich, 2003). Nurses provide
important ongoing support to patients by monitoring progress,
side effects, and therapeutic outcomes. In addition to ensuring
the safety of bisphosphonate administration (Berenson, 2005;
Maxwell, 2007; Maxwell, Swift, Goode, Doane, & Rogers,
2003), nurses also can educate patients with regard to moni-
toring pain status and reducing fracture risk by incorporating
changes in lifestyle and environment to prevent falls (Maxwell;
Maxwell et al.) (see Figure 6). Assessments at baseline and
throughout therapy are necessary to monitor how patients are
responding to therapy and whether changes in treatment regi-
mens are needed. Additionally, QOL assessments allow nurses
to monitor patients' well-being and ability to function in daily
activities. Any changes in QOL or decreases in performance
status during treatment may necessitate changes in disease
management.

Bone-Specific Quality-of-Life Assessment

A newly developed QOL assessment specific to symptoms
of bone metastases is being evaluated in phase III trials (Chow
et al., 2007). The tool was developed to capture morbidities
and effects not currently included in the European Organis-
a for Research and Treatment of Cancer Quality of Life
Questionnaire (also known as the EORTC QLQ-C30). The new
assessment tool consists of 22 questions rated on a scale from
1 (not at all) to 4 (very much) that are based on a patient’s
experiences during the previous week. Most questions concen-
trate on pain, such as where and when pain occurred and the
nature of the pain. The remaining questions address how the
symptoms may interfere with daily activities and any worries
that a patient may have about loss of mobility or decreased
health. When validated, the tool should enable the accurate
recording of QOL in patients with bone metastases and assist
with appropriate treatment decisions (Costa, Badia, Chow,
Lipton, & Wardley, 2008).

Patient Diary

Use of a patient diary for recording assessment results such as
pain scores, new bone events, or adverse events may facilitate
monthly interactions between nurses and patients (Schumacher
et al., 2002). A diary can be filled out at each visit and provides
an ongoing record of a patient's progress. The diary allows a
patient to record events and symptoms as they are experienced,
on an ongoing basis, and gives the patient a sense of control
over his or her symptoms (Reich, 2003). The diary also may as-
sist the patient in recognizing early and more subtle benefits
of therapy, which may improve adherence. Diaries promote discus-
sion between patients and healthcare professionals about what
has been recorded, help nurses motivate patients to continue
therapy, and establish connections with patients. Diaries also
may help nurses to identify when interventions are necessary
to enhance QOL.

Adherence to Therapy

Adherence to an approved bisphosphonate dosing schedule
can have a direct effect on treatment efficacy. Given that bis-
phosphonates are administered as a preventive intervention,
patients might not appreciate the ongoing benefits of therapy
because no direct effects can be observed. Therefore, patients
may lose their motivation to take medication as prescribed
during long-term treatment, especially if they do not have
regularly scheduled follow-up visits. In an analysis of two U.S.
health-claims databases comparing fracture rates among post-
menopausal women with osteoporosis who were either persist-
ent or nonpersistent with their oral bisphosphonate therapy
(n = 6,391), only 20% of patients were persistent with their
therapy during 24 months, as indicated by no refill gaps of
more than 30 days for their prescriptions. Fracture rates were
significantly lower over 24 months among persistent versus
nonpersistent patients (p < 0.001) (Siris et al., 2006). Although
the analyses were in the benign setting, they illustrate that
nonpersistence with bisphosphonate therapy may reduce
treatment efficacy (Siris et al.). Moreover, in the overall patient
population (N = 35,537), better adherence correlated with
lower fracture risk. However, adherence with oral bisphos-
phonates may be poor because of administration requirements
such as fasting before a dose and remaining upright after a dose
to reduce gastrointestinal toxicity (Mangiapan, Hoer, Gothe,
Barghout, & Haeussler, 2006; Roche, 2006). For example,
a retrospective analysis of German health insurance claims
found that 50% of patients with cancer who initiated oral bis-
phosphonate therapy stopped treatment within three to four
months and that 65% of patients stopped treatment within six
months (Göl, Höer, Schiffhorst, Brandman, & Häussler, 2005).
By providing education on the benefits of bisphosphonate
therapy and enacting established supportive care protocols to
ensure patient safety and comfort during therapy, nurses may increase patients’ persistence and adherence to bisphosphonate therapy to avoid SREs.

In general, patients receiving IV bisphosphonates have high adherence to their treatment. A retrospective analysis of a German health-claims database found that only 8% of patients with cancer who initiated IV bisphosphonate therapy stopped treatment within six months compared with 64% of patients with cancer receiving oral bisphosphonate therapy (Mangiapane et al., 2006). Clinical outcomes could be maximized through patient adherence to and persistence with bisphosphonate regimens. For example, persistent treatment with zoledronic acid reduced the incidence of monthly SREs compared with untreated patients (Hatoum, Lin, Smith, Barghout, & Lipton, 2008). Additionally, zoledronic acid (4 mg every three to four weeks) correlated with a reduction of at least 48% in the first six weeks) correlated with a reduction of at least 48% in the first six months of treatment compared with less frequent administration or no administration.

### Supportive Care Measures

- **Acute-phase reaction:** Assess dehydration and electrolyte levels.
  - Nausea and vomiting: Administer antiemetics (e.g., thiethylperazine, prochlorperazine) and/or mild analgesics (e.g., acetaminophen) as necessary.
  - Fever: Monitor vital signs and nutritional status; administer antipyretics (e.g., acetaminophen) prophylactically for the first 24 hours after the first and second infusions and then as needed; admit patient for persistent fever.
  - Diarrhea: Monitor vital signs and nutritional status; administer anti-diarrheals (e.g., loperamide).
  - Acute-phase reaction tends to occur after the first bisphosphonate infusion and typically does not occur or is less severe with subsequent doses.

- **Anemia:** red blood cell transfusion and/or erythropoietin.

- **Myalgia or arthralgia:** Administer analgesics (e.g., acetaminophen) or nonsteroidal anti-inflammatory agents (e.g., ibuprofen), unless contraindicated.

- **Constipation:** Administer stool softeners; maintain adequate fluid intake; modify diet; increase fiber intake.

- **Headache:** Administer analgesics (e.g., acetaminophen).

- **Anorexia:** nutritional supplements, appetite stimulants.

- **Edema lower limb:** Maintain elevation of extremities; use compression stockings, if needed.

- **Fever or malaise:** Monitor vital signs and nutritional status; administer antipyretics (e.g., acetaminophen) prophylactically for the first 24 hours after the first and second infusions and then as needed; admit patient for persistent fever.

- **Urinary frequency:** Monitor vital signs and nutritional status; administer antidiuretics (e.g., furosemide) as necessary.

- **Nausea and vomiting:** Administer antiemetics (e.g., thiethylperazine, prochlorperazine) and/or mild analgesics (e.g., acetaminophen) as necessary.

- **Flu-like symptoms:** Assess hydration and electrolyte levels.

- **Pain and analgesic assessment:**—Severity
  - Site
  - Type of pain

- **Concomitant medications:**—Dose and schedule
  - Calcium and vitamin D supplementation

- **Concomitant treatments (e.g., radiotherapy, chemotherapy):**—Mobility and activity

- **Hydration status:**—Discussion of any adverse events since last visit

- **Psychosocial distress:**—Determination of whether the patient has experienced any new skeletal-related events

- **Mobility and activity:**—Effectiveness of treatment from patient’s viewpoint

- **Observations for a Patient Diary:**—What to do when side effects occur
  - Ensure availability of therapy for common adverse events.
  - Advise patients of adverse events for which they should contact the healthcare team.
  - Ensure patient’s accessibility to the hospital.
  - Reassure patients who experience flu-like symptoms that the symptoms will be less severe after each subsequent infusion and will not likely occur after the second or third infusion.

**Assessment Information Checklist**
- Height and posture
- Weight
- Serum creatinine and corrected serum creatinine (corrected for age, weight, and gender) (0.6–1.3 mg/dl or 70–120 µmol/L)
- Hydration status
  - Signs and symptoms of dehydration
  - Adequate fluid intake (2–3 L per day) unless patient is on restricted fluid intake
  - Diarrhea or vomiting in previous 24 hours
- Pain and analgesic assessment
  - Severity
  - Site
  - Type of pain
- Concomitant medications
  - Dose and schedule
  - Calcium and vitamin D supplementation
- Concomitant treatments (e.g., radiotherapy, chemotherapy)
- Mobility and activity
- Oral condition
- Hydration status
- Serum creatinine and corrected serum creatinine (corrected for age, weight, and gender) (0.6–1.3 mg/dl or 70–120 µmol/L)
- Weight
- Height and posture
- Calcium and vitamin D supplementation

**Observations for a Patient Diary**
- During the first five days after each infusion
  - Urinary frequency
  - Fever or malaise
  - Other symptoms

- Ongoing symptoms
  - Pain level (visual analog scale or Brief Pain Inventory)
  - Locations of any bone pain
  - Analgesic use or other medications
  - Physical activity or ability to move

**Patient Education—Side Effects**
- Possible adverse events
  - Flu-like symptoms (after initial infusion) and skeletal pain (Acetaminophen [paracetamol] can be administered prophylactically.)
  - Renal function deterioration (serum creatinine and creatinine clearance)
  - Osteonecrosis of the jaw (spontaneously or after dental procedure)—uncommon

**Figure 6. Administration Guidelines for Patients Treated With Bisphosphonates**


Conclusions

Bone metastases are common in patients with advanced malignancies, especially those with breast or prostate cancer, and are associated with bone pain and SREs. Because SREs and bone pain are associated with decreases in QOL and functional independence, any therapy that can reduce the number or severity of SREs also should reduce the negative effects of skeletal complications on QOL. Nurses can enact management strategies to ensure patient safety and comfort and to maximize adherence with effective treatment regimens.

Bisphosphonates prevent or delay potentially debilitating SREs and reduce bone pain. Further research may allow improvements in skeletal health monitoring and management for patients with metastatic bone disease. Such improvements may enable patients to better maintain their QOL and functional independence throughout the course of their disease. Nurses play an important role in assessing, administering treatment, and monitoring responses to therapy for patients with metastatic bone disease to reduce SREs in this population.

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