Conventional treatment of hypercalcemia of malignancy

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Hypercalcemia of malignancy (HCM) is the most common life-threatening paraneoplastic syndrome associated with cancer. Its prevalence rate is 10–20%, and it occurs primarily in patients with end-stage disease. It is more common in patients with tumors associated with bone metastasis, such as breast and lung cancer, multiple myeloma, and the hematologic malignancies (non-Hodgkin’s lymphoma and leukemia), than in patients with other tumor types.

HCM is associated with a variety of symptoms, such as anorexia, polydipsia, polyuria, nausea, vomiting, drowsiness, confusion, and, in severe cases, coma. Many patients have only nonspecific complaints like mild lethargy, whereas others have no symptoms at all. Clinicians, therefore, should closely monitor patients in whom HCM is most likely to develop.

A better understanding of the pathophysiology of HCM, including the identification of parathyroid hormone-related protein (PTHrP), which is the humoral factor primarily responsible for stimulating bone resorption, led to the development and marketing of several new agents for treating this condition. This article briefly reviews the treatment of HCM, compares available treatments, and suggests treatment guidelines. The recent FDA approval in August 2001 of a new bisphosphonate, zoledronic acid, may alter these suggested guidelines.
Options for managing HCM

HCM is caused by three mechanisms: increased osteoclastic bone resorption, increased renal calcium reabsorption, and increased gastrointestinal (GI) absorption of dietary calcium. The two principal contributors are increased bone resorption and increased renal tubular reabsorption. Most treatment strategies aim to decrease bone resorption, increase renal calcium excretion, or both, although simply restricting dietary calcium intake is appropriate in a few patients.

The most effective approach to HCM is treatment of the underlying malignancy with surgical resection or administration of chemotherapy or radiation therapy, because the tumor is the source of humoral and nonhumoral factors that stimulate bone resorption and decrease renal calcium excretion. This approach, however, is not always possible, and in some cases hypercalcemia persists despite attempts to eradicate the tumor.

Certain diseases, such as breast cancer and multiple myeloma, are often highly treatable, and data suggest that durable responses to second- and third-line therapies can be achieved. HCM in these patients is best treated with surgery, chemotherapy, or radiation therapy. In patients receiving chemotherapy or radiation therapy, the onset of antitumor action may not occur for a week or more. Therefore, treatment of HCM that has a more rapid onset of action may be required to decrease or stabilize the serum calcium concentration until the effects of antitumor regimens occur.

Other tumors, such as non–small cell lung cancer and renal cell cancer, do not respond well to chemotherapy or radiation therapy. Patients with these types of tumors require treatment directed at decreasing bone resorption and renal tubular calcium reabsorption to prevent progressive symptoms and death.

In patients in whom no effective cancer treatment is available and the prognosis is bleak, the most appropriate and humane approach to HCM may be no treatment at all. Left untreated, these patients generally have a rapid rise in serum calcium level and succumb to worsening encephalopathy, unaware of the severity of their illness.

The pathogenetic mechanism and the severity of hypercalcemia are the most important factors to consider in treating HCM (Table 1). Other factors, such as the rate at which the serum calcium concentration rises, renal failure and other contraindications to therapy, and the ultimate objective of therapy, are also important.

In the GI tract, dietary calcium is absorbed under the primary influence of 1,25-dihydroxycholecalciferol and the secondary influence of parathyroid hormone. In HCM, 1,25-dihydroxycholecalciferol and GI absorption of calcium are decreased because of a negative feedback mechanism; this supports the theory that increased absorption of calcium in the GI tract does not contribute or contributes minimally to HCM. Dietary calcium intake or administration of calcium supplements, therefore, does not need to be restricted except in patients whose tumors produce 1,25-dihydroxycholecalciferol, such as lymphomas. High levels of 1,25-dihydroxycholecalciferol released from a tumor increase GI absorption of calcium by overriding the negative feedback mechanism.

A patient with mild HCM may not require therapeutic intervention. For these patients, ambulation, which encourages the normal bone–remodeling process, may be enough to stimulate normal calcium homeostasis. Salt restriction should be avoided because it may promote volume contraction and renal calcium retention, leading to worsening dehydration and rising serum calcium concentrations. Patients with moderate or severe HCM should also be encouraged to ambulate and avoid salt restriction; because of the life-threatening nature of hypercalcemia, however, more aggressive treatments are needed to reverse the rise in calcium concentration.

**Table 1. Hypercalcemia of Malignancy Severity Scale**

<table>
<thead>
<tr>
<th>Severity</th>
<th>Corrected Serum Calcium Concentration (mg/dL)</th>
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<tbody>
<tr>
<td>Mild</td>
<td>&lt;12.0</td>
</tr>
<tr>
<td>Moderate</td>
<td>12.0–13.5</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;13.5</td>
</tr>
</tbody>
</table>

Calciuric therapy

Most patients with HCM are dehydrated, presumably as a result of symptoms such as polyuria, anorexia, nausea, and vomiting. Patients may have fluid depletion of 5–10 L. Therefore, the initial treatment, calciuric therapy, aims to expand fluid volume, correct dehydration, increase the glomerular filtration rate, and promote renal calcium excretion. Hydration and saline diuresis restore fluids and enhance calcium excretion because sodium and calcium are excreted in parallel by the renal tubules. For patients with mild HCM, oral hydration with 3–4 quarts of fluid per day may be sufficient to correct fluid deficits. In patients with moderate to severe hypercalcemia, however, vigorous intravenous rehydration with 0.9% sodium chloride injection administered at a rate of 250–300 mL/hr is warranted until normocalcemia is achieved. The rate of infusion depends on the severity of hypercalcemia, the degree of dehydration, and the patient’s cardiovascular status.
Patients receiving vigorous hydration must be monitored carefully for signs of fluid overload. If fluid overload occurs, the rate of 0.9% sodium chloride infusion should be reduced, and administration of a loop diuretic, such as furosemide, should be considered. Administration of furosemide as standard therapy for HCM is not routinely recommended, however. Although loop diuretics control volume overload and promote sodium and calcium diuresis, they may have a more profound effect on sodium excretion than on calcium excretion. If sodium excretion exceeds intravenous sodium replacement, normal physiological renal sodium-conserving mechanisms are activated, decreasing both sodium and calcium excretion; this may aggravate HCM. Nonetheless, furosemide administration may be indicated for patients with congestive heart failure (CHF) or patients at risk for CHF resulting from aggressive fluid replacement.

Sodium diuresis also increases the excretion of potassium and magnesium. Low potassium and magnesium levels can result in cardiac arrhythmias. Serum concentrations of these elements should be routinely monitored, and supplements should be administered as needed to maintain normal serum concentrations. Unlike loop diuretics, thiazide diuretics cause dissociation between renal tubular absorption of sodium and calcium, thus decreasing calcium excretion. Thiazide diuretics may cause or aggravate HCM.

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Table 2 summarizes the effects of treatments for hypercalcemia of malignancy.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Regimen</th>
<th>Onset</th>
<th>Duration</th>
<th>Reduction in Serum Calcium Concentration*</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9% sodium chloride injection</td>
<td>2–4 L/day i.v.</td>
<td>24–48 hr</td>
<td>2–3 days</td>
<td>0.5–2.0 mg/dL</td>
<td>Fluid overload, hypokalemia, hypomagnesemia, hypotension</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>4–8 IU/kg s.c. or i.v. q 6–12 hr for 24–48 hr</td>
<td>4–6 hr</td>
<td>1–4 days</td>
<td>2–3 mg/dL</td>
<td>Nausea, inflammatory reactions at infusion site, flushing of face and hands, malaise, possibly vomiting</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Hydrocortisone 200–400 mg/day i.v. for 3–5 days</td>
<td>7 days</td>
<td>3–4 days</td>
<td>0.5–3 mg/dL</td>
<td>Hyperglycemia and hypokalemia, as well as immunosuppressant, catabolic, cushingoid, and osteolytic effects</td>
</tr>
<tr>
<td>Plicamycin</td>
<td>25 µg/kg i.v. over 4–6 hr; may repeat dose every 24–48 hr</td>
<td>12–72 hr</td>
<td>2–14 days</td>
<td>1–2 mg/dL</td>
<td>Hepatotoxicity, nephrotoxicity, thrombocytopenia, myelosuppression, nausea and vomiting, decreased concentrations of clotting factors</td>
</tr>
<tr>
<td>Etidronate disodium</td>
<td>7.5 mg/kg/day i.v. over 2–4 hr for 3–7 days</td>
<td>2–6 days</td>
<td>1–3 wk</td>
<td>&gt;1 mg/dL</td>
<td>Mild increases in blood urea nitrogen and serum creatinine concentrations, metalic or altered taste, transient hyperphosphatemia, transient fever, rash, nausea</td>
</tr>
<tr>
<td>Pamidronate disodium</td>
<td>60–90 mg i.v. over 2–24 hr</td>
<td>24–72 hr</td>
<td>3–4 wk</td>
<td>&gt;1 mg/dL</td>
<td>Fever, skin reaction at infusion site, mild gastrointestinal symptoms, mild hypophosphatemia, mild hypokalemia, mild hypomagnesemia</td>
</tr>
<tr>
<td>Zolendronic acid</td>
<td>4 mg i.v. over 15 min</td>
<td>24–48 hr</td>
<td>4 + wk</td>
<td>&gt;1 mg/dL</td>
<td>Fever, flulike syndrome, nausea and vomiting, skin reaction at infusion site, mild hypomagnesemia, mild hypokalemia, mild hypophosphatemia</td>
</tr>
</tbody>
</table>

*Per course of therapy.
calcium therapy. Hydration with 0.9% sodium chloride injection expands intracellular volume, improves glomerular filtration, and enhances renal excretion of calcium. The onset of action is usually 24–48 hours, and calcium concentrations are generally reduced by 0.5–2.0 mg/dL. Calcitriol therapy alone rarely restores normocalcemia, but it can effectively ameliorate symptoms.7

**Antiresorptive therapy**

After volume-expansion measures are initiated, antiresorptive therapy should be administered to patients with moderate to severe HCM. Antiresorptive therapies aim to decrease the rate of bone resorption, which is stimulated by humoral factors produced by tumors. Antiresorptive therapies have a slower onset of action than calcitriol therapy, but the duration of effect is longer. Therefore, a combination of antiresorptive therapy and calcitriol therapy is optimal; antiresorptive therapy should be initiated with or immediately after initiation of calcitriol therapy.

Calcitonin, glucocorticoids, plicamycin, etidronate disodium, pamidronate disodium, and zolendronic acid are antiresorptive agents that have been used successfully to treat HCM. Table 2 summarizes the effects of these agents.

**Calcitonin.** Calcitonin is a naturally occurring peptide produced by the C cells of thyroid tissue, and it is one of the oldest drugs used to treat HCM.3,7 Calcitonin inhibits osteoclastic bone resorption and has a moderate calcific effect. Additionally, study results show that it produces a small analgesic effect, which may be an added benefit for patients who experience bone pain.7

The major assets of calcitonin are its rapid onset of action and safety in dehydrated patients and patients with preexisting renal failure.6 Serum calcium concentrations may decline by 2–3 mg/dL within a few hours, and the nadir may be reached within 24 hours after therapy is initiated.1 The usefulness of calcitonin may be limited beyond the first few days of therapy, however, because tachyphylaxis develops rapidly after administration. This reduced effectiveness results from loss of the calcic effects of calcium, possibly mediated by corticosteroid-sensitive receptor downregulation.5 Nevertheless, calcitonin plays a key role in treating patients with life-threatening increases in serum calcium concentrations because it has the most rapid onset of action and can be administered regardless of fluid or renal-function status.

The usual starting dosage of calcitonin is 1–4 IU/kg administered every six hours by subcutaneous (s.c.) or intramuscular injection for a maximum of eight days. Dosages as high as 8 IU/kg every six hours have been used. Common adverse effects associated with calcitonin include nausea, rash, flushing, and malaise.1

**Corticosteroids.** Corticosteroids, such as prednisone and hydrocortisone, are the therapy of choice for patients with HCM caused by vitamin D toxicity, steroid-sensitive malignancies like multiple myeloma and lymphoma, sarcoidosis, and other granulomatous diseases that produce 1,25-dihydroxycholecalciferol.7,8 Corticosteroids inhibit inflammatory cell proliferation within granulomatous tissue and hematologic malignancies, thereby decreasing 1,25-dihydroxycholecalciferol levels.7 Corticosteroid-induced decreases in 1,25-dihydroxycholecalciferol levels cause an increase in urinary calcium excretion and a decrease in intestinal calcium absorption by counteracting the effects of vitamin D. The maximum calcium-lowering effect does not occur for days to weeks after therapy begins, however.

In the past, corticosteroids were much more effective when administered in combination with calcitonin to increase the latter’s duration of effect. The combination quickly decreased serum calcium concentration, and the corticosteroid extended calcitonin’s duration of action. Because neither corticosteroids nor calcitonin is nephrotoxic, the combination can be administered to patients with renal impairment. Since the bisphosphonates became available, however, this combination has been used only occasionally.4

Corticosteroids are administered in hydrocortisone dose-equivalents of 200–400 mg/day i.v. for three to five days.1 The onset of action of corticosteroids is not well established, but most clinicians believe that it takes at least a week for corticosteroids to decrease the serum calcium concentration effectively. Corticosteroids’ duration of action is fairly short, and the reduction in calcium concentration is at the lower end of the range shown in Table 2. Adverse effects associated with corticosteroid administration include hyperglycemia and hypokalemia, as well as immunosuppressor, catastrophic, cushingoid, and osteolytic effects.1,6

**Plicamycin.** Before the bisphosphonates were available, plicamycin was the i.v. drug most commonly used to treat HCM. Produced by Streptomyces plicatus, plicamycin was initially used as an antineoplastic agent for the treatment of refractory testicular cancer. Although it was ineffective, it was shown to be a potent inhibitor of RNA synthesis in osteoclasts; presumably, this mechanism of action is responsible for plicamycin’s antihypercalcemic effect.1

Plicamycin is more potent than calcitonin, and its rapid onset of action is second only to that of calcitonin. However, it has a variable and unpredictable duration of response and causes numerous adverse effects. Hepatotoxicity, nephrotoxicity, thrombocytopenia, myelosuppression, nausea, vomiting, hypocalce-
mia, and decreased concentrations of clotting factors limit plicamycin’s short- and long-term use in certain patient populations. Many of these adverse effects can be decreased by administering plicamycin at the recommended dosage for less than four total doses. Plicamycin should not, however, be administered to patients with severe hepatic or renal dysfunction, thrombocytopenia, or coagulopathies or to patients who receive myelosuppressive chemotherapy or are dehydrated. Since plicamycin is a vesicant, it should be used cautiously if administered through peripheral veins. Because of these limitations, plicamycin is usually reserved for patients who are unresponsive to all other treatments for HCM.

The usual dosage of plicamycin is 25 µg/kg administered into a central i.v. line over four to six hours. The dosage may be repeated every 24–48 hours; most clinicians prefer waiting at least 48 hours or until a rise in serum calcium concentration is evident. Serum calcium concentrations begin to decrease as early as 12 hours after plicamycin administration and reach a nadir within 96 hours. The reduction in serum calcium concentration is 1–2 mg/dL per dose.

Gallium nitrate. Although no longer marketed in the United States, gallium nitrate was used to treat HCM in the early to mid 1990s. It exerted an antihypercalcemic effect by inhibiting bone resorption, probably by inhibiting PTHrP. Results of clinical trials showed gallium nitrate to be more effective than calcitonin, plicamycin, and etidronate disodium, normalizing serum calcium concentrations in 75–100% of patients with HCM.

Some of the bisphosphonates and other drugs used to treat HCM cause a slight increase in blood urea nitrogen (BUN) and serum creatinine (SCr) concentrations, but gallium nitrate caused overt nephrotoxicity characterized by renal tubular necrosis and obstruction of the tubular lumen. Other adverse effects included transient hypophosphatemia, mild respiratory alkalosis, anemia, nausea, vomiting, visual and hearing impairments, hypotension, and tachycardia.

Because of gallium nitrate’s adverse-effect profile, the need for five consecutive days of i.v. administration, and the availability of pamidronate disodium, gallium nitrate was withdrawn from the market in 1995.

Bisphosphonates. The bisphosphonates are a class of drugs that directly inhibit osteoclast resorption by inhibiting osteoclast precursors and exhibiting osteoclast cytotoxicity. The bisphosphonates also inhibit hydroxyapatite crystal dissolution and may prevent osteoblasts from recognizing bone. Three bisphosphonates are available in the United States for the treatment of HCM: etidronate disodium, pamidronate disodium, and zolendronic acid.

Etidronate disodium. Etidronate disodium was the first bisphosphate to receive FDA approval for use in HCM. Etidronate disodium 7.5 mg/kg/day is administered intravenously over two to four hours to patients with moderate to severe hypercalcemia; the dose is repeated for a minimum of three days. Serum calcium concentrations begin to decline within two days and reach a nadir within seven days after administration of the first dose; the average onset of action is two to six days. This delay in onset of action is probably the biggest drawback to the use of etidronate disodium. Clinical studies indicate that etidronate disodium normalizes serum calcium concentrations in 40–92% of patients. Because the drug is excreted by the kidneys, it is important to adjust the dose in patients with renal failure.

Adverse effects associated with etidronate disodium include mild increases in BUN and SCr concentrations, transient increases in serum phosphorus concentrations, transient fever, rash, metallic or altered taste, and transient increases in serum phosphorus concentrations.

Etidronate disodium has limited appeal because of its demanding administration schedule. The drug is administered as a four-hour infusion every day for a minimum of three days, which requires patients to either return to the clinic daily or be hospitalized for the complete course of therapy. Additionally, the duration of action is extremely variable; some studies report the duration as three to four days, others as one to three weeks. Furthermore, despite etidronate disodium’s beneficial antiresorptive properties, it has the undesirable effect of inhibiting bone mineralization, a characteristic that is not observed with pamidronate disodium. Nonetheless, etidronate disodium is fairly effective in reducing calcium concentrations by more than 1 mg/dL per course of therapy.

Pamidronate disodium. Pamidronate disodium has become the bisphosphonate of choice for the treatment of HCM. Its mechanism of action is identical to that of etidronate disodium, except that it does not inhibit bone mineralization. Pamidronate disodium has been shown to be more potent and possibly less toxic than etidronate disodium. Studies comparing the two bisphosphonates show that pamidronate disodium decreases serum calcium concentrations faster and for longer. Other clinical studies show that pamidronate disodium results in normocalcemia in 60–100% of patients.

For patients with moderate HCM, pamidronate disodium 60 mg is administered intravenously over 2–24 hours; the dose for severe HCM is 90 mg. The dose can be repeated weekly, and the median duration of normocalcemia is three to four weeks. With an average duration of action of 28 days, a single dose of pamidronate disodium has the most sustained effect of all anti-
resorptive drug regimens discussed in this article.

Fever is a common adverse effect and can be treated with acetaminophen. Other adverse effects include nausea and induration or pain at the injection site, as well as decreased serum potassium, phosphorus, and magnesium concentrations. Nephrotoxicity does not appear to be associated with pamidronate disodium use, even in patients with concurrent renal dysfunction.4

Like etidronate disodium, pamidronate disodium decreases serum calcium concentrations by more than 1 mg/dL per dose. The greatest advantages of pamidronate disodium are its convenient single-dose administration schedule and long duration of action.

Zolendronic acid. In August 2001, the FDA approved a new bisphosphonate, zolendronic acid, for treatment of HCM. Results of a Phase III study comparing zolendronic acid with pamidronate disodium show that zolendronic acid has a higher response rate, faster onset, and longer duration of action. Furthermore, zolendronic acid is more convenient to administer (administered over 15 minutes) than pamidronate disodium. More information about zolendronic acid is provided in the Berensen article in this supplement.

**Overview of therapy options**

Figure 1 illustrates the mechanisms of action of the treatments discussed previously. The corticosteroids decrease intestinal calcium absorption, but these agents have a limited role since GI absorption of calcium is not altered in most patients with HCM. Hydration and furosemide increase calcium excretion, whereas calcitonin, plicamycin, gallium nitrate, etidronate disodium, pamidronate disodium, and zolendronic acid all inhibit osteoclastic bone resorption.

Figure 2 presents an overview of the onset and duration of action of the treatment regimens. Calcitonin has the fastest onset of action, but its short duration of action and tachyphylaxis limit its use. Calcitonin is most useful in the patient who has a very high serum calcium concentration that requires rapid reduction. Plicamycin has the second-fastest onset of action, but its duration of action is extremely variable and a variety of adverse effects limit its use.

The onset of action is similar for etidronate disodium and pamidronate disodium and coincides with the peak effect of calciuric therapy. Pamidronate disodium has the advantage of a longer duration of effect than any of the agents previously discussed. Zolendronic acid may supercede pamidronate disodium as the treatment of choice for HCM.

Table 3 shows a cost comparison of the treatment options. Calcitonin appears to be one of the less expensive regimens, but its cost is actually higher because repeated doses are necessary. Pamidronate disodium is less expensive than etidronate disodium and zolendronic acid costs slightly more. Although plicamycin is less ex-

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**Figure 1.** Mechanisms of action of treatments for hypercalcemia of malignancy.
Figure 2. Comparison of onset and duration of action of treatments for hypercalcemia of malignancy.

Table 3.
Cost Comparison of Treatments for Hypercalcemia of Malignancy

<table>
<thead>
<tr>
<th>Medication</th>
<th>Regimen</th>
<th>Cost ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcitonin&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4 IU/kg q 6 hr for 2 days</td>
<td>188.08</td>
</tr>
<tr>
<td>Calcitonin&lt;sup&gt;c&lt;/sup&gt;</td>
<td>4 IU/kg q 6 hr for 2 days</td>
<td>233.28</td>
</tr>
<tr>
<td>Etidronate disodium</td>
<td>7.5 mg/kg/day for 5 days</td>
<td>670.00</td>
</tr>
<tr>
<td>Pamidronate disodium</td>
<td>60 mg i.v. for 1 dose</td>
<td>533.07</td>
</tr>
<tr>
<td>Pamidronate disodium</td>
<td>90 mg i.v. for 1 dose</td>
<td>839.59</td>
</tr>
<tr>
<td>Plicamycin</td>
<td>25 μg/kg i.v. q 48–72 hr for 2 doses</td>
<td>197.48</td>
</tr>
<tr>
<td>Zolendronic acid</td>
<td>4 mg i.v. for 1 dose</td>
<td>856.38</td>
</tr>
</tbody>
</table>

<sup>a</sup>Cost based on recommended dose for a 70-kg patient with a body surface area of 1.73 m². Cost calculated using average wholesale price in 2001 Red Book<sup>13</sup> for full course of the regimen, excluding price of fluids, preparation, and administration.

<sup>b</sup>Generic calcitonin, Arcola.

<sup>c</sup>Miacalcin, Novartis.

Table 3. Cost Comparison of Treatments for Hypercalcemia of Malignancy

Discussion

The high prevalence of HCM and increased understanding of its pathophysiology led to the development of several new antiresorptive drugs during the past decade. The presence of symptoms, the rate of rise in serum calcium concentration, and the overall status of the patient are important considerations in selecting therapy. The selection should be based primarily on an agent’s effectiveness and adverse effects; secondary considerations include treatment cost, treatment duration, ease of administration, and duration of effect.

Future challenges in the treatment of HCM include the development of oral maintenance regimens and the prophylactic use of bisphosphonates in patients most likely to develop hypercalcemia.

Treatment strategy

Given the current options, a reasonable treatment strategy for moderate to severe HCM is as follows:

- Rule out other causes of hypercalcemia, such as primary hyperparathyroidism and vitamin D intoxication.
- Treat the underlying malignancy, if possible.
- Do not restrict dietary calcium intake.
- Mobilize the patient.
- Hydrate the patient with 0.9% sodium chloride injection at 250 mL/hr i.v.
- Use furosemide 20–380 mg i.v. only as indicated.
- Administer pamidronate disodium 60–90 mg in 250 mL of 0.9% sodium chloride injection i.v. over four hours beginning on day 1 or zolendronic acid 4 mg in 100 mL of 0.9% sodium chloride, USP, or 5% dextrose injection, USP, i.v. over 15 minutes beginning on day 1.
- In life-threatening cases only, use
calcitonin 4-8 IU/kg s.c. or i.v. every 6-12 hours for two to three days.

- In patients with tumors that are steroid sensitive or produce 1,25-dihydroxycholecalciferol, administer hydrocortisone 200-400 mg i.v. for three to five days.

Conclusion

The recent approval of a new bisphosphonate, zolendronic acid, was based on a favorable comparison with pamidronate disodium, suggesting that zolendronic acid is the drug of choice for HCM. The presence of symptoms, the rate of rise in serum calcium concentration, and the overall status of the patient are important considerations in selecting therapy.

References