

WHAT LUNG CANCER PATIENTS NEED TO KNOW ABOUT BONE HEALTH

**A PUBLICATION OF
THE BONE AND CANCER FOUNDATION**



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THIS PUBLICATION PROVIDES IMPORTANT INFORMATION ABOUT THE RELATIONSHIP BETWEEN LUNG CANCER AND BONE HEALTH.

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How Bone Works

To understand the impact lung cancer can have on bone, it is helpful for patients to understand what the skeleton does.

Bone is an active tissue with many functions. In addition to supporting the body, it serves as a storehouse for calcium and phosphorus, essential minerals needed throughout the body. Bone also contains marrow, the tissue that makes blood cells.

Normal bone constantly undergoes a process called remodeling. During the bone remodeling process:

- Bone cells called osteoclasts break down and remove (resorb) bone.
- Bone cells called osteoblasts make and deposit new bone at the site of bone removal.

Hormones and other substances produced by the body regulate the way these bone cells are formed and how they work.

What Lung Cancer Can Do to Bone

Radiation, chemotherapy, and steroids are treatments for lung cancer that can weaken bone. To determine whether the skeleton is being affected by lung cancer treatment, many doctors recommend that patients be given screening tests to measure their bone density before, during, and after cancer treatment.

Approximately 30 to 40 percent of people with lung cancer will have their cancer spread, or metastasize, to bone. When lung cancer metastasizes, tumor cells from the original cancer break off and travel through the blood stream to a new location, where they grow and multiply. Although lung cancer can spread to any part of the skeleton, tumor cells most often affect the bones that have the greatest blood supply. These include the ends of the arms and legs (nearest the torso), the pelvis, the ribs, and the spine.

When lung cancer spreads to bone, several factors can increase the process of bone destruction:

- Certain lung cancer cells produce a hormone, parathyroid hormone-related protein (PTHrP), that increases the number of osteoclasts and their level of activity.
- Bone destruction releases substances called growth factors that promote the growth of the cancer cells, creating a vicious cycle in which:
 - Growth factors are released as bone is destroyed.
 - The growth factors stimulate the growth of cancer cells.

— The increased number of cancer cells leads to the destruction of additional bone.

Lung cancer that has spread to bone can cause:

- **Bone pain.** Since pain is often the first sign that lung cancer has spread to bone, patients should tell their doctor right away if they detect pain that feels like it is coming from their bones. **Effective** treatments for bone pain are available and it is important to start them quickly.
- **Bone thinning and fractures.** Bone thinning and fracture can occur when a bone's hard surface is weakened by the growth of lung cancer cells. Weight-bearing bones such as those in the legs are at highest risk of fracture. Some people with lung cancer are prone to bone thinning in their vertebra because the radiation used to treat the lungs can affect the spine.
- **Pressure on the nerves of the spine** caused by compression fractures. This occurs when a tumor causes a vertebra to fracture and collapse on itself, pressing on the nerves of the spinal cord. Along with severe back pain, compression fractures can cause weakness or numbness in the arms or legs.
- **The formation of new blood vessels** that support the continued growth of the tumor.
- **Increased release of calcium from the bone** that can cause hypercalcemia—high levels of calcium in the blood. (See Hypercalcemia – What Patients Need to Know on page 5.)

Treating Bone Affected by Lung Cancer

The following therapies are used to treat bones affected by lung cancer:

- **Lung cancer treatment.** The prompt initiation of appropriate therapy for lung cancer is essential to minimize further bone loss and to improve symptoms related to bone disease.
- **Bisphosphonates.** Bisphosphonates are drugs that help stop abnormal bone loss by blocking the activity of the bone-resorbing cells (osteoclasts). (See Bisphosphonate Therapy on page 4.)
- **Denosumab (Xgeva™).** Denosumab is a drug that prevents bone breakdown or resorption by inhibiting RANKL, a protein that activates osteoclasts, the cells that are involved in bone breakdown or resorption. Denosumab is given by subcutaneous (under the skin) injection every 4 weeks and can be used with standard anti-cancer therapy.
- **Radiation.** If lung cancer spreads to bone in one location, radiation therapy may be used to relieve pain and prevent fractures at the site of the tumor.

- **Pain medication.** Patients experiencing bone pain should be given pain medication. This may include nonsteroidal anti-inflammatory drugs (NSAIDs) and/or drugs containing opiates (narcotic pain killers).

Bisphosphonate Therapy

Intravenous (given through a vein) bisphosphonates are the treatment of choice for lung cancer patients with:

- Cancer that has spread to bone.
- Increased levels of calcium in the blood (hypercalcemia).

Two intravenous bisphosphonates are approved by the United States Food and Drug Administration (FDA) for treating cancer that has spread to bone. Pamidronate (Aredia®) was approved in 1995. Zoledronic acid (Zometa®), a stronger bisphosphonate, was approved in 2002. Both drugs are given by intravenous infusion every three to four weeks and can be used with standard anti-cancer therapy.

Side Effects

Treatment with these two intravenous bisphosphonates and denosumab can cause both short- and long-term side effects. **Short-term side effects** that may occur immediately after receiving intravenous bisphosphonates drugs are flu-like symptoms such as fever, chills, and muscle aches. These side effects are often mild, do not last long, and tend not to recur following future bisphosphonate treatments. Intravenous bisphosphonates and denosumab can cause lowering of the serum calcium level that can cause side effects such as lethargy and cardiac complications. The following **long-term side effects** have been reported in some cancer patients treated with these intravenous bisphosphonates:

- **Osteonecrosis (dead bone) of the jaw (ONJ)** is a rare dental condition. It is an area of exposed jaw bone that shows no sign of healing after eight weeks. The condition can cause feelings of pain or numbness in the affected area.

As most cases of osteonecrosis of the jaw have occurred in patients treated with intravenous bisphosphonate drugs – mainly pamidronate and zoledronic acid – there is concern, but no proof, that ONJ is a side effect of these medications.

Denosumab use has also been associated with osteonecrosis of the jaw.

Osteonecrosis of the jaw is much more likely to occur after an invasive dental procedure (such as having a tooth removed). Therefore, lung cancer patients should have their dentist give them a careful examination before starting therapy with pamidronate or zoledronic acid. Patients should also be sure to follow good oral health procedures.

Additional information can be found in the Bone and Cancer Foundation publication “Osteonecrosis of the Jaw – Information for Cancer Patients” available online at www.boneandcancerfoundation.org or by calling 1-888-862-0999.

- **Kidney problems.** As intravenous bisphosphonate treatment can affect kidney function, zoledronic acid or pamidronate should not be given to patients with severe kidney problems. Lung cancer patients being treated with these drugs should have their kidneys checked before each infusion. This is done with a blood test that measures kidney function. Physicians can manage most problems with kidney function that are caused by bisphosphonate therapy.

Hypercalcemia – What Patients Need to Know

Even if their cancer has not spread to bone, lung cancer patients can develop a serious condition called hypercalcemia — a high level of calcium in the blood.

As previously noted, lung cancer cells produce and release a hormone (PTHrP) into the bloodstream that can increase the rate at which bones release calcium. Lung cancer that has spread to bone can also cause an increased release of calcium from the site of the tumor. Hypercalcemia occurs when the amount of calcium in the blood rises to a certain level.

It is important for lung cancer patients to be aware of the symptoms of hypercalcemia, which include:

- Being very thirsty and urinating a lot.
- Constipation (difficult bowel movements).
- Irregular heart beat.
- The development of kidney stones.
- Loss of appetite.
- Being very sleepy.
- Confusion.
- Coma (this is rare).

Patients experiencing any of these symptoms should seek medical attention at once because there are good treatments for hypercalcemia and it is important to start them quickly.

Glossary

Bisphosphonates: Drugs used to prevent the breakdown of bone.

Chemotherapy: Drugs used to kill cancer cells.

Growth Factor: A substance that promotes growth, especially cellular growth.

Nonsteroidal Anti-inflammatory Drugs: Drugs such as acetaminophen, aspirin, and ibuprofen used to treat pain and inflammation.

Metastasis (plural: metastases, verb: metastasize): The spread of cancer cells throughout the body. The cancer cells that have spread to other parts of the body are the same as those in the original tumor.

Radiation therapy: Treatment with radiation to kill cancer cells.

RANK Ligand: A protein that activates osteoclasts, the cells that are involved in bone breakdown or resorption. Denosumab (Xgeva™) is a RankL targeted therapy.

Steroids: A natural or synthetic compound that reduces inflammation and can decrease growth or survival of some types of cancer cells.

Tumor: An abnormal mass of tissue. Tumors are either benign (noncancerous) or malignant (cancerous).

Vertebra: The bony segments that make up the spinal column.

The mission of The Bone and Cancer Foundation is to:

- Provide information to cancer patients and family member on the causes and current treatment of cancer that involves the bone.
- Provide information and serve as a resource for physicians, nurses, and other health professionals regarding the management of cancer that spreads to the bone.



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