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FAQ

GCT Frequently Asked Questions

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Here are the top questions related to giant cell tumors of the bone (GCTB) from general GCTB knowledge to treatment and what to expect. Every patient is different, and considerations may be unique to you. Consult and discuss with your healthcare team what is right for you.

ABOUT GCTB

1. What is GCTB?

GCT of the bone is a type of rare, locally aggressive, intermediate bone tumor that generally impacts the rounded ends of long bones (also called the epiphyseal location). It is non-cancerous but causes damage to bone and neighboring structures (e.g., ligaments).

2. Why is it called GCTB?

GCTB is named for its distinctive appearance under the microscope. It contains cells with very large centers, referred to as “giant cells.” The name reflects what pathologists saw long before the biology of the disease was understood. In the early 1900’s, “giant cell tumor of the bone” became the full name to include the description of the location of the tumor.

Early names also included “osteoclastoma,” reflecting the belief that the giant cells were cells responsible for bone resorption, known as “osteoclasts”. However, we now know that the giant cells have the ability to dissolve bone and are called “osteoclast-like” giant cells. While GCTB is named for the giant cells, those are not the mutated abnormal cells and instead they are recruited to become part of the tumor by the abnormal cells.

3. What causes GCTB?

Each cell in our body contains thousands of genes, which are made up of DNA. These genes act like instructions that tell our cells which proteins to make. Proteins carry out most of the important jobs that keep our bodies healthy and working the way they should.

In GCTB, a gene change (mutation) happens only in the tumor cells, nowhere else in the body. This means the mutation does not affect the rest of your cells.

The most common change happens in a gene called H3F3A, which helps make a protein called histone H3.3. This mutation occurs in 95% of GCTBs. Histones are special proteins that act like spools, helping to tightly wrap and organize DNA. By winding the DNA, they help control which genes are turned “on” or “off.”

In GCTB, the mutation in H3F3A changes how tightly the DNA is wound. The tumor cells gain easier access to certain genes that encourage them to grow. This also amplifies the signals they send out, which recruits other cells that break down bone, leading to the bone destruction seen in GCTB.

It is not known what causes the mutation in H3F3A.

4. What is the difference between GCTB and TGCT?

GCTB is a bone tumor typically found at the end of long bones and has a mutation to H3F3A which impacts growth. GCTB is treated by surgically scraping out the tumor (curettage) or removing the affected segment of bone (en bloc or wide resection). Denosumab is used when patients have untreatable disease or pre-operatively in some countries. Recurrence rate is between 10-40% depending on the research study, location, and severity of disease. GCTB can spread to the lungs in occasional cases and may be seen on x-ray. In general, GCTB is immediately more aggressive than TGCT because of its destruction of bone. GCTB almost always requires urgent treatment.

TGCT is a joint tumor caused by a mutation in CSF1, which drives the growth. It has two subtypes which drastically change prognosis. TGCT, depending on the subtype, has recurrence rate as high as 75-90%, but does not often damage bone. One in five patients have associated bone damage due to TGCT. TGCT can also be monitored and left untreated. When treated, TGCT is treated with surgery or oral targeted agents. Complete removal is not always possible, contributing to high recurrence. These tumors have no chance of spreading and are not seen on x-ray, making MRI the only way to detect or monitor.

These diseases are treated differently and don't share much in common besides their name, nonspecific symptoms (e.g., swelling and pain) and having cells that are "giant" (e.g., denosumab only works for GCTB).

5. How is GCTB diagnosed?

Often, a patient will go to a doctor due to a palpable lump, pain, swelling, or a fracture. The first test that is run is an X-ray. GCTB has a typical appearance on X-ray, often a "bubble-like" area at the end of a long bone. Due to the location of the "bubble", it may be confidently suspected to be GCTB from x-ray alone.

X-ray or CT scans use radiation which goes through skin and soft tissue and is absorbed by bone, therefore, the imaging captures bone well. Magnetic resonance imaging (MRI) is required to detect soft tissue masses directly. Following a bone mass identified on an X-ray, MRIs are used to determine how aggressive a tumor is, whether it extends into soft tissue, and helps plan surgery.

Biopsies are done to confirm diagnosis.

6. What drives the growth of GCTB?

GCTB grows because of a specific mutation in the tumor's own cells that changes how they behave. This mutation is called H3F3A mutation which only can be seen in the tumor cells. This sets off a chain reaction that leads to other cells being recruited, including the bone-dissolving cells. Bone destruction and tumor expansion are orchestrated by the tumor cells.

7. Who does GCTB affect?

GCTB can occur in any person or any bone. GCTB typically occurs at the end of long bones, commonly around the knee (such as the proximal tibia and distal femur).

GCTB commonly impacts skeletally mature adults between 20 and 40 years of age, and GCTB is rare in children and the elderly. We believe the reason it is more common in young adults is because the growth plates don't entirely develop until young adulthood and bone remodeling is still occurring. Bone cells turnover at high rates within this age range.

It is also slightly more common in women. It is unknown the reason currently, however, it has been speculated that this could be due to referral patterns or small biological differences such as inflammation and bone regulation. Overall, this difference in sex is not consistent across populations.

8. What does it mean that GCTB has a genetic abnormality?

Tumor growth is generally driven by a genetic abnormality in the tumor cells. These mutations are not present in genes throughout the body but acquired by a group of cells to enable them to grow uncontrollably. It is well documented that GCTB contains a genetic mutation called the H3F3A mutation which causes GCTB's growth by changing the microenvironment of tumor cells.

9. Is GCTB hereditary? Can it be passed down?

No, GCTB is not passed down nor inherited. The H3F3A abnormality drives growth and this abnormality affects a minority of cells in the tumor and not the rest of the body.

10. Are there any risk factors for GCTB (dietary, occupational, genetic, lifestyle)?

No, GCTB occurs sporadically. There is no occupational, dietary, genetic, or lifestyle risk that has been identified to predispose anyone to getting this disease. GCTB cannot be passed down. GCTB is likely spontaneous and multifaceted, particularly since it affects young adults.

11. Are sex-based hormones (e.g., estrogen) affect growth or development?

GCTB growth is driven primarily by a mutation in the tumor cells (H3F3A). There is no evidence that links estrogen or other sex hormones directly cause GCTB or control its growth. Generally, estrogen influences bone remodeling and activity of bone resorption (contributing to women being affected by osteoporosis in older age). However, most researchers consider GCTB growth mutation-driven, with any hormonal influence being minor or theoretical.

12. How many people are diagnosed due to bone fractures?

20% of patients present with a pathological fracture, while other common symptoms include bone pain, swelling, tenderness, limited range of motion, and inability to weight-bear (1). Pathological fractures, or fractures due to GCTB, are a hallmark of GCTB that is considered aggressive.

13. What separates GCTB from sarcoma?

GCTB is considered an intermediate tumor. This means that GCTB sits between benign and malignant (cancerous). GCTB is locally aggressive, and damages bone. GCTB also has the potential to spread to the lungs. For these two reasons, it was classified by the World Health Organization as intermediate (2).

Sarcoma is a family of cancerous tumors that have a high risk of spreading and are life-threatening. Sarcomas are aggressive and are prone to spreading, way more often than GCTB. Sarcomas are always life-threatening and often must be treated with a combination of surgery, radiation, and chemotherapy.

GCTB is typically not life-threatening, with a few exceptions based on location. GCTB and sarcoma share some characteristics, such as, both can lead to damage and severe functional impairment when left untreated. Surgeries for sarcoma and GCTB can both be large and impact a patients' life and function.

14. Is there a correlation between symptoms and the size of GCTB?

There is no known relationship between size and GCTB symptoms. However, size and location of GCTB may impact whether the tumor breaks through the bone lining and a patient has a pathological fracture. The size of GCTB may impact how surgery can be performed and what technique is used.

15. Does GCTB spread?

In ~5% of patients, tumors can spread (metastasize) to the lungs (3, 4, 5). This is thought to be because the lungs are nutrient and oxygen rich, and blood flows directly from bone to the lungs. GCTB is not likely to spread elsewhere.

16. What is lung metastasis?

Lung metastasis refers to the spread of GCTB to the lungs. GCTB is not likely to spread to other locations.

17. Are there risk factors for lung metastasis?

There are a handful of evidenced risk factors (6). A commonly reported risk factor is prior recurrence of the primary GCTB location following surgery. Aggressive tumors in areas that are anatomically difficult-to-remove (e.g. spine) may lead to higher risk of metastasis. Younger patients may also have higher risk. Research is continuing to uncover additional risk factors and the strength of these relationships.

18. Are these tumors fast growing?

GCTB is generally considered locally-aggressive tumors that are somewhere between malignant and benign. Speed of growth is often viewed on a spectrum. GCTB are biologically closer to benign and may take several months to grow. However, GCTB growth is destructive to the bone and can extend in the most aggressive cases to the surrounding soft tissues. This means that it is important to seek urgent treatment to prevent further bone damage.

19. What is a H3F3A mutation and should I be tested?

The H3F3A mutation is present in up to 95% of GCTBs. It is believed to be the cause of the aggressive growth and bone destruction.

H3 is a histone, a type of protein around which our DNA wraps to regulate (turn on and off) its ability to produce proteins in our body's cells. H3 is present throughout a cell's life cycle, and the H3F3A mutation alters the gene controlling H3 in GCTB cells (7, 8). Research suggests that the changes this mutation makes to the tumor's environment drive growth (8).

The H3F3A mutation is considered a reliable diagnostic tool for GCTB and may be considered as a part of your diagnosis to rule out other giant-cell rich tumors, including chondroblastoma and aneurysmal bone cysts (ABC). The H3F3A mutation does not exclude or diagnose malignancy or change the course of your treatment (9, 10).

20. Does it manifest differently in adults and kids?

Yes, it can. GCTB is significantly more common in adults with fewer than 10% of cases occurring in children (11). GCTB shares common characteristics in the cells and growth patterns between children and adults.

However, in adults, GCTB is most common at the ends of long bones (epiphysis), near the growth plate. In children, GCTBs mimic other types of bone tumors more closely and grow away from the ends of bones (towards metaphysis) due to the immature growth plates (12, 13). Children have open growth plates, allowing continued growth spurts. Such differences can make it more challenging to diagnose a pediatric tumor as a GCTB on imaging and osteosarcoma is often considered.

21. Are there other abnormalities in my body because I have GCTB?

GCTB is typically a local disease with few known risk factors, so it is unlikely there are other abnormalities in your body because of your GCTB.

22. What cells make up GCTB?

GCTB is named for its characteristic giant-center cells. These giant cells assume the function of osteoclasts, which are normal bone-absorbing cells. They are told to dissolve the bone by the abnormal tumor cells. The giant cells exist amongst other cell types in GCTB: macrophages, extracellular matrix cells, and tumor cells (14, 15). The tumor cells are known as stromal cells, a cell responsible for providing structural framework to tissues. These cells are oval (or spindle) shaped and express a protein called RANKL known to recruit and stimulate bone-dissolving osteoclasts (14, 15).

23. Are there any dietary or lifestyle changes that help with GCTB?

Many with GCTB change components of their diet and/or take supplements to improve overall health, well-being, and systemic inflammation. While anti-inflammatory diets and supplements can be used to aid in overall health, no specific diet or lifestyle modifications have been identified as helpful for GCTB or GCTB prevention.

Lifestyle changes to activities are often made based on GCTB symptoms (e.g., resting when there's pain). Modifying movements with the help of a physical or occupational therapist and regular maintenance of strength with targeted exercises can help many with GCTB return to very high levels of activity.

24. Is having GCTB considered a disability?

Having GCTB alone is not considered a disability. However, GCTB or its treatment may be considered a disability if it significantly limits your ability to perform daily activities or work.

GCTB and its treatment can cause chronic pain, reduced joint mobility, stiffness, and functional limitations. The qualification of GCTB as a disability depends on the severity of these symptoms and their impact on your daily life. If you are struggling, speak with your doctor about documentation that may be recognized under disability programs or for workplace accommodations.

DIAGNOSING GCTB

25. What is the gold standard scan for diagnosing and monitoring GCTB?

While an X-ray demonstrates that there is a bone tumor, defines the tumor boundary, and shows the extent of bone destruction, an MRI is considered the gold standard for local diagnosis and monitoring of GCTB. MRI enables visualization of soft tissue extension, the integrity of the bone, fluid filled levels such as neighboring cysts, and how involved the tumor is.

Following surgery, X-rays are commonly done to confirm no additional damage or change in the integrity of the bone, providing a quick snapshot of the status of the disease.

For monitoring or diagnosing lung metastasis, X-ray or CT are standard.

26. Do I need an expert or can I receive care locally?

Many specialty centers offer telemedicine visits and will work with you for local care (e.g., labs and scans may be done at local centers). It is encouraged that your local provider consults with a specialty center to ensure you are getting expert guidance for your GCTB.

27. What is a multidisciplinary review?

A multidisciplinary team (MDT) review includes a panel of experts of multiple specialties that reviews patient cases. Each specialty provides their opinion, and a collaborative treatment plan is created.

28. What is a core-needle biopsy? Are there other types of biopsies?

Core-needle biopsies refer to a procedure when a needle (typically 14-16 gauge) is used to remove tissue and confirm diagnosis. Typically, three samples are taken and the needle is guided by ultrasound or computed tomography (CT) scan.

There are other types of biopsies, such as surgical biopsies where tissue is removed during surgery. Surgical biopsies can be more definitive because they involve a larger sample of tissue but must be performed during an operation. In the case of GCTB, ruling out different tumor types is important and may dictate the type of surgery your doctor chooses.

29. Are core-needle biopsies required before surgery?

A core-needle biopsy is generally appropriate and the preferred biopsy approach. Core-needle biopsy is a standard first-step for diagnosing GCTB. These image guided core-needle biopsies have lower risks compared to surgical biopsies.

However, in some cases, such as if results are inconclusive from a core-needle biopsy or the location of the GCTB is difficult to biopsy by needle, a surgical biopsy may be performed to confirm the diagnosis.

30. When should the biopsy be done?

In most cases, a core-needle biopsy is performed before surgery to assist with the planning and confirm diagnosis/rule out cancer. In some cases, such as when the surgeon is fairly confident in the diagnosis, the biopsy may be performed at the beginning of surgery as confirmation.

31. What would I expect from the pathology report?

The pathology report will likely include a few sections: the type of biopsy and location, the “gross” or naked eye description of the sample, the cellular description of the sample under microscope, and the final diagnosis of tumor type. The report may also include any confirmatory genetic testing done if used to confirm or assess your diagnosis.

TREATING GCTB

32. What is the difference between a medical oncologist and an orthopedic oncologist?

Medical oncologists specialize in diagnosing and treating tumors with medications, including other bone and soft tissue tumors like GCTB. An orthopedic oncologist is a medical doctor specializing in surgery to treat tumors. Orthopedic oncologists consult medical oncologists for medications. These doctors should be part of the multidisciplinary team approach.

33. What is the difference between an orthopedic surgeon and an orthopedic oncologist?

An orthopedic oncologist is a medical doctor specializing in the surgical removal of tumors. They have specialized education for removing all types of tumors, benign and cancerous.

Generally, orthopedic surgeons fall into sports medicine, generalists, upper extremity, or lower extremity specializations. These surgeons are used to treating anatomical and mechanical injuries such as injuries related to sports and birth defects. These surgeons do not typically remove tumors.

It is important to have a multi-disciplinary team that includes an orthopedic oncologist and medical oncologist that specializes in bone tumors and sarcomas instead of a provider that specializes in the anatomical area of interest.

34. What type of provider should I see?

GCTB can require a multi-disciplinary treatment strategy that includes a team of healthcare providers familiar with musculoskeletal tumors, such as, an orthopedic oncologist, plastic surgeon, a medical oncologist, musculoskeletal radiologist, and physical therapist.

After imaging suggests GCTB, you will likely be referred to an orthopedic oncologist. If you are seeking a second opinion on your surgical options at a specialized facility, look for orthopedic oncologists. If your tumor may not be able to be fully removed and you are considering medication (i.e., denosumab), you should see a medical oncologist as well.

35. Who is the right doctor to treat GCTB?

A multi-disciplinary treatment strategy may be necessary to treat GCTB. This could include a team of healthcare providers familiar with musculoskeletal tumors: an orthopedic oncologist, a medical oncologist, musculoskeletal radiologist, and physical therapist. A medical oncologist may not be necessary if a patient is likely to benefit from surgery alone, and the orthopedic oncologist is the primary provider for many with GCTB. In complex anatomical locations (e.g., sacrum, spine) or large GCTBs, a medical oncologist should be brought in to provide denosumab as an alternative option to surgery.

36. When should GCTB be treated? Is it urgent?

Yes, GCTB is considered an urgent diagnosis due to its local bone destruction. GCTB should be treated quickly to prevent further bone loss and preserve maximum mobility. GCTB growth causes the destruction of bone, and without treatment, this can lead to significant physical impairment, fractures, and long term joint damage.

37. What are my treatment options?

The primary treatment for GCTB is surgical removal. This means an orthopedic oncologist operates to remove the tumor by either scrapping it or removing a segment of bone. Surgery may include additional procedures such as ablation. The goal of ablation is to destroy microscopic remaining tumor cells and reduce recurrence risk and might include physical or chemical treatments. There are two types of ablation, either using argon beam or liquid nitrogen. Argon beam ablation uses heat to destroy remaining cells. However, argon beam ablation can also affect healthy nearby tissues. Liquid nitrogen is used to freeze the cells and kill any remaining, this is considered more conservative than argon beam ablation. At this time, researchers do not know whether ablation truly reduces recurrence rates or which type of ablation has better outcomes.

For tumors that cannot be removed via surgery due to their location or other healthcare system factors (e.g., long wait times for surgery), treatments will likely include denosumab. Denosumab is a medication (an engineered protein called a monoclonal antibody) that is used to harden the GCTB and prevent growth. Denosumab does this by blocking the tumor signals to the bone-dissolving cells.

Other treatment options could include in some cases: embolization (16). Embolization is a minimally invasive procedure where a catheter is used to block blood growth to inoperable tumors. This may be done with GCTBs in the spine, where symptoms are not improving following denosumab treatment.

38. What type of surgeries are performed for GCTB?

There are a few surgical options. The surgeon can remove the tumor from the bone by scrapping with a curette or remove the tumor alongside with a segment of healthy bone. The first procedure is called curettage referring to the sharp instrument called the curette which is used to scrape out the tumor from bone. The second is called en bloc or segment resection and is generally performed for more aggressive tumors.

After the tumor is removed via curettage, the cavity left after curettage is filled with either bone cement or bone graft, if it is small enough. Bone cement provides immediate structural support and may be stabilized with surgical screws or plates. Bone cement hardens with heat, quickly filling the hole from the scrapped out tumor. Bone cement has the added benefit of acting as an additional therapy because heat is released as it hardens. Bone cement and bone graft may be combined in cases where the tumor is very close to a joint. If too close to a joint, bone cement can cause damage to adjacent structures like cartilage.

After en bloc resection, the surgeon constructs a new joint or bone segment with prosthesis. A prosthetic bone, typically made of metal, is placed where the missing bone was (e.g., knee replacement).

39. Which surgery technique is the best?

The best surgical treatment for your tumor depends on the location and size of your tumor along with your health history. Curettage of the tumor is the ideal surgery, as it is the least destructive, but may not be an option in all cases. The nature of curettage surgery may also differ.

Small tumors may be best treated with curettage and bone grafting. Bone grafting requires the body to build new bone to stabilize the hole left by the tumor, which can take months to years. This may not be the best option in many cases, for example, when a GCTB is too large. As bone graft fills in, it can also be challenging to differentiate on x-ray from tumor recurrence.

Tumors removed by curettage and reconstructed with bone cement provide immediate long-term bone stability (17). Bone cement is commonly the preferred filler. It has been speculated that bone cement is associated with lower recurrence rate due to the heat reaction that occurs when the cement sets, potentially killing residual tumor cells.

En bloc resection, removing the segment of bone, are considered when the less invasive curettage procedures are not possible, due to tumor size, location, or multiple recurrences.

40. What type of bone cement is used for curettage?

Polymethylmethacrylate (PMMA) is the most common bone cement used after curettage to fill the remaining bone cavity. PMMA has been used in orthopedic surgery for decades (18). As the cement sets, it releases heat which may kill any remaining tumor cells in the surrounding millimeters of bone.

41. For segment resections of bone, what material is used in its place?

Segment or en bloc resections require the reconstruction of the removed bone and potentially a joint. This may be accomplished by a hardware implant (prosthesis) or through transplanted bone from another area (allograft). The materials used may include titanium or cobalt-chrome alloy for prosthesis and bone from either a donor or your own bone.

Carbon fiber may be used for plates, rods, and screws during reconstruction as it is a transparent material on X-ray, but it is not yet standard for large segment resection replacements.

42. Which is better, using cadaver or my own bone?

There are benefits to both allograft (cadaver) bone and autograft (your own) bone. Autograft can be more successful since it comes from your own body, meaning the immune system recognizes it. However, it requires a second incision and removal of an additional bone (typically from the hip/pelvis). Allograft may be preferred when the area is small. However, due to its potentially lower recurrence rate, bone cement is becoming the preferred treatment method (19).

43. Are there factors that impact the success of surgery?

Many factors can impact the success of surgery. These include the choice of surgery, i.e. curettage or segment resection and your tumor's characteristics, i.e. its size, growth rate, and location. It is also critical to be treated by a physician at a specialty center with experience in GCTB as the success of the surgery largely relies on the successful complete removal of your tumor.

44. What are the recurrence rates after surgery?

GCTB may recur after surgery. Recurrence rates with simple curettage surgery range from 27-65% but may differ based on tumor location, size, and whether a pathological fracture occurred (20). The use of bone cement is speculated to reduce recurrence rates to 12-27% (20). Recurrence rates after en bloc resection are even lower ranging from 0 to 12%, this is due to removing the entire segment of affected bone (20).

45. Does ablation reduce the risk of recurrence?

Yes, ablation may reduce recurrence risk (21, 22). There are multiple potential types of ablation, including argon beam and nitrogen-based ablation. Ablation causes cell death of any remaining tumor cells, which prevents these cells from growing into a recurrence.

46. How do I prevent future recurrence of GCTB?

There are no lifestyle choices that can prevent recurrence. Monitoring with x-rays, CTs, and MRI are the best way to identify a recurrence early.

47. Is there anything I can do, dietary or lifestyle, to reduce recurrence?

A generally active lifestyle and healthy diet are certainly recommended for overall health, however there is no specific set of recommendations for GCTB that can reduce recurrence. The most important thing you can do is attend regular screening to catch potential recurrence early.

48. If I have a recurrence, is surgery less likely to be successful?

Surgical options to treat recurrence are the same as for the primary original tumor, performed as either curettage or en bloc resection. Recurrence can cause further bone destruction and complicate surgery, but many patients have successful curettage to treat recurrence. The second recurrence rate after treatment is estimated around 20%, with en bloc resection having lower rates (23, 24, 25).

49. Are joint replacements curative?

Joint replacements accompany an en bloc resection, which have recurrence rates as low as 6% in some studies (26). Depending on the extent of the prosthesis and characteristics of the patient (e.g., overall health, weight, age), a revision surgery may be necessary later in life as a result of the wear or loosening of the interface between the prosthesis and your bone.

50. Can I have surgery again after a reconstruction/prosthesis?

Yes, you may have revision surgery as a result of complications or natural wear on the hardware over time.

51. What are the complications related to joint replacements/reconstructions/prosthesis?

Complications related to joint replacements following GCTB are similar to those of standard joint replacements. These can include infection, mechanical failure, dislocation, or loosening of the bond between the prosthesis and original bone (called aseptic loosening) (27). Risk of mechanical failure, dislocation, or aseptic loosening may increase over time, and revision surgery may be necessary in these cases.

Complications after curettage with hardware generally include the ongoing pain, pooling blood (hematoma), infection, or possible late development of osteoarthritis (28).

52. How are lung metastasis treated?

GCTB lung metastasis can be treated with surgery, denosumab, or monitoring (30). In most cases, lung metastasis are treated with denosumab. However, lung metastases are sometimes observed rather than immediately treated because their nature is often slow-growing and benign in nature (31).

53. How is recurrence or lung metastasis monitored?

Recurrence and lung metastasis are generally monitored by regular X-ray screenings or thoracic CT (chest CT). As GCTB are able to be diagnosed on X-ray and X-ray emit lower radiation than CT scans, X-ray is typically the first scan repeated regularly after GCTB treatment. If a recurrence is suspected from X-ray, your doctor will likely order an MRI or CT to confirm the recurrence and plan treatment.

54. How often should I get a scan for GCTB and my lungs?

The frequency of scans may depend on the patient, stage in their journey, symptoms, and stability of disease.

If a patient is newly out of surgery, scans are often performed every 3 to 6 months for the first 2 years. After the first 2 years, the frequency of scans may reduce to every 6 to 12 months for 3 additional years. The risk of recurrence is highest in the first 5 years. Of those that recur, most do so within the first 2-5 years post surgery.

The lungs are often scanned, using X-ray or CT, every 3 to 6 months for the first 2 years, and every 6 to 12 months thereafter. After 5 years, annual scans may be recommended. Monitoring for lung metastasis is considered preventative.

55. Are the scans for GCTB and my lungs different?

Often an X-ray will be performed to check both your lungs and the original tumor site. In bones, GCTB appears as a single well defined lesion with a “soap bubble” appearance typically at the ends of long bones. In the case of spread to the lungs, GCTB appear as calcified (white) spots or mass (nodule) possibly throughout the lungs.

56. Is radiation therapy a treatment for GCTB?

No, radiation therapy is generally avoided in GCTB due to the risk of cancerous transformation and other effective alternatives. Denosumab provides an alternative to surgery where GCTB is well-controlled in the majority of patients. For patients where their GCTB is unable to be removed by surgery and denosumab does not control the disease, radiation may be used after all other options have been depleted.

57. Is radiation from consistent scans a concern?

The risks associated with radiation exposure from consistent scans exists but does not typically outweigh the benefit and importance of continual monitoring for GCTB recurrence. X-rays emit lower doses of radiation than CT, and the frequency of scans is reduced over time.

58. What is denosumab?

Denosumab is a protein engineered to target the signal, called RANKL, that the GCTB uses to dissolve bone. These proteins are called monoclonal antibodies. Denosumab is used to prevent further bone loss and may shrink the existing tumor in some patients. While this drug is widely used in GCTB, it is also used in adult osteoporosis, cancer metastasis to the bones, and during hormone therapy for other cancers. Denosumab is administered as an injection in the fatty part of the arms or abdomen.

Denosumab is the active ingredient in two drugs marketed by a company as Prolia and Xgeva. Denosumab is the chemical name, also called the generic name, and Prolia or Xgeva are the branded names. Prolia is 60 mg of denosumab and administered every 6 months to prevent bone loss from osteoporosis. Xgevia is 120 mg of denosumab and administered every 4 weeks for bone tumors such as GCTB.

Denosumab was approved for the treatment of GCTB in 2013 ([34](#), [35](#)). In 2025, cheaper generic versions of denosumab were launched in the United States and others existed prior in other countries ([36](#)). It's important to note that generics have the same safety and efficacy as branded drugs due to the same active ingredient.

59. How does denosumab work?

Denosumab works by targeting the signal of GCTB to the bone dissolving cells. This signaling molecule is called RANKL. By blocking RANKL, denosumab prevents the activation of bone-dissolving giant cells. This prevents bone reabsorption.

60. Should I expect my GCTB to shrink on denosumab?

Yes, your GCTB may shrink on denosumab. However, if your GCTB does not shrink, that does not mean denosumab is not working.

You may also expect a decrease in pain, with or without tumor shrinkage. On imaging, you may see that the tumor has become mineralized and formed a calcified border. This means that the tumor is becoming inactive and unable to grow. In most cases, the tumor will not completely disappear on denosumab.

61. When is denosumab given?

Denosumab is generally given every week for the first 4 weeks at 120 mg and then once every four weeks thereafter. This first period of giving denosumab every week is called a “ramp up” period to make sure the tumor becomes inactive. The subsequent dosing, once every four weeks is called “maintenance dosing” to ensure the tumor remains inactive.

Denosumab may be administered prior to surgery in some cases or administered when tumors are recurrent or unresectable. Different health systems have different wait times. Denosumab is occasionally given in countries where surgery is unlikely to occur urgently.

62. What are the side effects of denosumab?

Side effects of denosumab are typically minimal and manageable. Side effects include nausea and muscle and bone pain. These can typically be well-managed with over the counter drugs (e.g., acetaminophen). More serious side effects, which are rare, include osteonecrosis of the jaw, unusual thigh bone fractures, hypophosphatemia, and hypocalcemia.

Denosumab should be avoided while undergoing dental work or during pregnancy. Reducing dental work while on denosumab also reduces the risk of osteonecrosis of the jaw.

63. Are side effects temporary or reversible?

Side effects of denosumab are generally temporary and reversible. Osteonecrosis of the jaw is a rare, severe possible side effect and can require minor surgical treatment in the worst cases but outcomes are good with fast treatment.

64. Does pausing and restarting denosumab reduce the side effects?

No, pausing denosumab may lead to the tumor becoming active again. Stopping denosumab must be carefully managed, and drug holidays are often not a strategy to manage side effects. However, patients and providers may decide to try an alternative dosing frequency (e.g., once every 6 weeks) to improve tolerability.

65. Is denosumab considered chemotherapy? Is it considered an immunotherapy?

Denosumab is not a chemotherapy or a traditional immunotherapy. It is a targeted therapy that acts on a signaling pathway within the tumor. It does not recruit your immune cells to attack the tumor or kill the tumor directly.

66. What is the risk of osteonecrosis of the jaw? Are there ways to prevent it?

It is estimated that the risk of osteonecrosis of the jaw is 1-6% ([37](#), [38](#)). The risk of osteonecrosis is higher in denosumab for tumor control than for managing osteoporosis due to the higher dose and frequent dosing (i.e., 60 mg vs 120 mg and 6 month dosing vs every 4 weeks dosing). A majority of individuals in clinical trials who developed osteonecrosis had existing dental risk factors ([37](#)). Prevention is usually carried out by good oral hygiene and clearance by dental care prior to administration.

67. What dental work should be avoided while on denosumab?

Tooth extractions and invasive dental work that include drilling should generally be avoided while on denosumab. Dental cleanings and fillings are generally safe.

68. What type of labs should I expect while on denosumab?

You should expect routine labs with your denosumab treatment. Calcium levels should be monitored for the prevention of hypocalcemia. Phosphate may be measured as well.

69. Are there any dietary lifestyle changes that improve the way denosumab works?

It is recommended that you take calcium and vitamin D supplements while on denosumab. This gives your body extra calcium while on treatment. Vitamin D is required for the calcium to be absorbed by the body, therefore they are often taken together. However, this does not improve the efficacy of denosumab and is specific to those receiving denosumab.

Calcium is typically given as 1000–1200 mg daily and vitamin D is usually recommended as 400–800 IU daily (sometimes higher if levels are low).

70. Should I still receive vaccines on denosumab?

Yes, you should generally still receive vaccines on denosumab, but there are considerations. Since denosumab is a protein-based drug, this can reduce the effectiveness of vaccines (39). You may consider spacing vaccinations from your denosumab doses (40). It is important to speak with your doctor about the risks for you individually.

71. Are there any medications or foods I should avoid on denosumab?

There are several drugs that can interact with denosumab, including corticosteroids, immunosuppressants, and some cancer immune therapies (41). It is important to talk to your doctor about medications you may be taking.

There is no known association between denosumab and any food or alcohol (41).

72. Can orthopedic oncologists prescribe denosumab?

GCTB management may require an interdisciplinary team that includes a medical oncologist who manages denosumab. However, orthopedic oncologists also can prescribe denosumab and often lead GCTB treatment due to its primary surgical component.

73. Is denosumab the only medication available?

Denosumab is the only FDA approved medication currently. Bisphosphonate drugs have also been used to prevent bone reabsorption in GCTB and have been shown used effectively (42, 43). However, bisphosphonates are less likely to stabilize or control the GCTB compared to denosumab. Thus, denosumab is the preferred medicine alternative to surgery.

74. When would bisphosphonates be useful in GCTB?

Bisphosphonates act to coat the bone, strengthening it and preventing bone reabsorption (44, 45). It is speculated that bisphosphonates may target neoplastic cells contributing to their cell death (44). They have become less common after the availability of denosumab and are used in countries that do not have access to denosumab or when denosumab is costly. Transition to bisphosphonate therapy after the cessation of denosumab may be a possibility for those that have complications from denosumab (46).

75. Will I remain on denosumab forever?

If surgery is not a viable option for your GCTB, then in most cases, it is possible you may need to remain on denosumab for an indefinite period. However, patients have successfully stopped treatment as well. This often depends how long a patient was on denosumab prior, the location of the tumor, and risks associated with stopping. Since denosumab does not destroy tumor cells, GCTB can recur after treatment cessation.

The long-term continuation of denosumab is an ongoing area of research (47, 48, 49). There are currently no protocols for how long patients should remain on denosumab or how to effectively go off. Stopping denosumab may also have rebound effects causing severe bone loss, thus there is careful planning for treatment cessation.

76. Does taking denosumab before surgery reduce recurrence risk?

There is some evidence that taking denosumab prior to surgery can increase recurrence risk, and it is therefore prescribed with caution (50, 51). However, in cases where the tumor is inoperable or operation would cause significant physical morbidity, denosumab prior to surgery may improve outcomes. Additionally, different healthcare systems may have different wait times which impact whether denosumab is given prior to stabilization while waiting for surgery.

77. Is anyone too young for denosumab? Too old?

Denosumab is approved for GCTB in all skeletally mature patients, but may be given to children. Older patients may receive denosumab due to osteoporosis.

Because denosumab suppresses bone resorption and breakdown, your body does not release calcium from the bone. Instead, denosumab causes the bone to strengthen and harden. Vitamin D and calcium are recommended while a patient is receiving denosumab to supplement the calcium that would typically be released from bone. Vitamin D is essential for your intestines to absorb the supplemented calcium.

78. Does denosumab make you immunocompromised?

Most patients do not experience significant immunosuppression and there is a slightly increased risk of skin infections. However, this risk has been disputed and the risks associated may decrease over the course of treatment (52).

79. If I try to go off denosumab, how long should I remain on before?

Denosumab may be taken for a short period of 3-6 months to notice a significant reduction in tumor activity, pain, or size. Typically, 6 injections are given before surgery in the pre-surgical space.

Denosumab used to manage unresectable GCTB is considered an indefinite treatment duration (53). Family planning is a consideration for going off GCTB, as it is advised against during pregnancy.

It is not known what the optimal duration of denosumab treatment is for unresectable GCTB or how to prevent recurrence once denosumab is stopped (54, 55). Considerations before stopping would include the duration of stability of your disease and your side effects. Treatment dose interval extension may be considered as an alternative by your oncology team prior to stopping. For instance, patients may increase their dosing interval from every 4 weeks to every 6 weeks, then every 8 weeks, then every 12 weeks.

It is also possible to go back on denosumab after having stopped treatment if GCTB recurs and see benefit (56).

80. Can I take denosumab while pregnant?

No, the use of denosumab is advised against while pregnant to prevent possible harm to an unborn baby. It is advised to use birth control for at least 5 months after stopping denosumab and prior to conception. Ask your doctor about how to manage pausing denosumab during pregnancy.

81. Does denosumab affect male or female fertility?

There is some evidence that denosumab may improve male fertility, but a recent clinical trial did not show significant effect (57, 58, 59). Denosumab is believed to have no effect on female fertility (60).

LIFESTYLE WITH GCTB

82. Can I have GCTB forever?

The majority of people with GCTB achieve complete remission with surgical removal of their tumor. In this case, you will no longer have GCTB. GCTB management includes long term screening for recurrence and to adapt to changing physical function after GCTB.

In the case that GCTB is managed with denosumab and not fully removed, GCTB may be present long-term, but the tumor is likely inactive. This means scans are given throughout the entire treatment duration to confirm the tumor remains inactive. You may still have GCTB, but symptoms and progression can be completely controlled.

83. What does followup with GCTB look like?

Follow up with GCTB is centered around monitoring for recurrence and managing long-term symptoms associated with reconstructive surgery. You will likely have regular screening to check for recurrence and visits with your orthopedic oncology team for 5 years after treatment. If you received treatment with denosumab, your medical oncology team will monitor the effects of denosumab on imaging and in labs and manage your side effects. Denosumab treated patients will continue to receive imaging for years after treatment cessation to monitor for recurrence as well.

Depending on the location of your tumor and severity of the functional changes caused by your treatment, it is important to seek a physical therapist to help manage and prevent pain from joint wear.

84. Should I avoid activities due to GCTB?

Activities to avoid depend on the size and location of your tumor. It is important to speak with your medical team about this for your particular case.

GCTB around the knee joint (proximal tibia or distal femur) may require avoiding high-impact activities including running and hiking to prevent joint wear and pain, particularly if osteoarthritis develops. High-impact activities may be avoided for GCTB of the hip or spine as well for similar reasons.

The need to avoid activities is, however, highly individual. Smaller tumors that can successfully be treated with curettage and bone graft may have very minimal impact on mobility, and it is possible that no activities will require avoidance.

85. Can I still exercise?

Yes, you can still exercise after treatment of GCTB. Mobility after GCTB and treatment are generally quite good, particularly following curettage. Wide resection may cause greater changes to function long-term. It is important to talk with your oncology team about considerations based on the location of your tumor and the type of treatment you received.

86. Do patients with lung metastasis have symptoms?

Lung metastasis is uncommon, affecting approximately 5% of patients with GCTB. However, for those that do develop lung metastasis, it typically occurs within the first 24 months of surgery.

Patients with lung metastasis are often entirely asymptomatic; therefore, scans are performed regularly to check for metastasis.

87. Do hormonal birth controls impact GCTB?

There is currently no evidence that hormonal birth control affects GCTB growth. GCTB is driven by mutations and the degradation of bone, which is unrelated to sex hormones. Patients taking hormonal contraceptives, such as birth control pills, patches, or implants, are not thought to have an increased risk of tumor growth or recurrence. Males and females are affected in similar proportions by GCTB, despite slight predilection in females.

88. Are there any supplements I can take to support my bone health?

Bone health is supported by calcium, vitamin D, and magnesium. Supplementation is particularly important while taking denosumab or after treatment with bone graft which requires growing new bone. Talk to your health team about doses in your case.

89. Are there any ways to treat pain with diet or physical therapy?

Yes, some patients report benefits in pain by managing diet and physical therapy. Anti-inflammatory foods support reducing chronic pain, and protein supports building muscle to reduce joint pain. Physical therapy can help increase joint mobility, build strength, and even desensitize to neuromuscular pain after surgery. It is best to find a physical therapist who is familiar with treating patients after surgery, especially with hardware.

90. Are there any modifications to my house that will help recovery?

During initial recovery, depending on the location of your GCTB, it may be helpful to reduce the need to go up stairs and install temporary accessibility tools, such as a shower handle and chair. An occupational therapist may be present after your surgery to help review managing household tasks in the initial recovery phase where mobility may be very limited.

91. Is there any way I can manage the symptoms from surgery or GCTB such as swelling and pain?

Rest, compression, ice, heat, and elevation may all be beneficial to managing surgical recovery. Ice is generally recommended in the initial recovery window. Elevate the affected area above your heart to reduce swelling if possible. You will likely receive information about these techniques from your surgical care team. You may also be prescribed pain medications (including ibuprofen, gabapentin, or opioids) to help manage the pain which are optional based on your needs and health history.

92. Will this affect my ability to have children?

GCTB itself does not affect fertility or prevent you from having children. For women with GCTB that require denosumab treatment, you may need to delay pregnancy until you can safely transition off before expanding your family.

Long term arthritis, joint, or bone pain caused by GCTB may be exacerbated by pregnancy as these conditions due to any cause can worsen due to body changes during pregnancy. These should not prevent pregnancy, but seeking aid from a medical or physical therapy team to prepare for pregnancy may be beneficial.

93. Should I have continuity of care after recovery from an operation? How often should I go back to my doctor?

Yes, you should have continuity of care after recovery from an operation. You will likely see your surgeon and their team within a month of the operation and then on regular intervals alongside screening. These screenings allow the surgical team to check on any hardware you may have and monitor for complications. These visits are also critical due to the high recurrence rate of GCTB.

94. Is physical therapy helpful before or after surgery?

Improving balance and strength prior to any surgery can aid in recovery, but physical therapy may not be tolerable prior to surgery due to the location and size of GCTB. Physical therapy is critically important shortly after surgery to restore range of motion and prevent scar tissue from building in joints (arthrofibrosis). Physical therapy longer term helps build strength that leads to long term recovery.

95. Is there anything I can do to improve bone and joint stability?

Improving bone and joint stability can depend on your treatment. If your GCTB was removed with curettage or wide resection, it is critical to have a nourishing diet post-operatively to rebuild tissue and assist bone modeling (e.g., high protein). If your GCTB is unresectable, denosumab and supplementation (with calcium, vitamin D) help to build bone stability as well.

In all cases, bone and joint stability can be improved by maintaining healthy and strong muscles. It is recommended to work with a physical therapist to find targeted exercises that build strength within any limitations caused by changes to your body during GCTB and its treatment.

96. How often should my provider request scans to monitor my GCTB? Does this differ if I'm symptomatic or asymptomatic? If I'm more than 5 years out?

Your provider should request frequent scans in the first 2-5 years after GCTB. Since the risk of recurrence after surgical removal is highest in the first two years, providers may request scans (typically X-rays) of your primary tumor site and lungs up to every 3-4 months. Scans may decrease to every 6 months or annually for the next 3-7 years. Many providers do not screen for recurrence after 5 years in asymptomatic individuals due to the very low risk of recurrence after this window. If you ever develop new pain at the location of your GCTB, even after 5 years, CT or MRI scans are suggested immediately to rule out recurrence.