



Treatment with Denosumab for giant cell tumour of bone

Giant cell tumours (GCT) of bone are benign (non-cancerous) growths, which develop in bones, most often around the knee and forearm. These tumours can cause severe damage by causing the bone to dissolve. This can result in the bone breaking or the joint being damaged so badly that it has to be replaced. Treatment usually involves either scraping the tumour out of the bone and strengthening the bone with metal plates or a type of plastic cement or replacing the bone with an artificial metal and plastic joint.

Recently a new treatment has become available. This is a drug called Denosumab. It has been used for several years to treat patients with age related bone weakness (osteoporosis) and to treat patients with cancer where they are having problems with the cancer attacking their bones. Denosumab has been found to work well to control Giant Cell Tumour of bone by stopping it dissolving the surrounding bone.

How Does Denosumab Work?

Bone is constantly being replaced, being absorbed and re-made in a cycle throughout adult life. Bone is made by cells called osteoblasts and eroded by cells called osteoclasts. In Giant Cell tumour it is thought that some osteoclasts in a specific area of the skeleton become overactive and so breakdown bone too quickly weakening the bone.

Does Denosumab work?

Denosumab has been shown to be effective in treating GCTs of bone with the vast majority of patients demonstrating a response both in terms of the appearance of their x-rays and by a reduction in their symptoms, particularly pain. In the majority of patients, the Giant Cell Tumour is seen to become more ossified

(boney) showing that the osteoclasts have been stopped from being overactive and the osteoblasts are repairing the bone returning some of its strength.

Why Have Denosumab Rather Than Standard Treatment?

Standard surgical treatment for patients with a GCT has been an operation to scrape out the tumour from the bone and filling the cavity with bone graft or bone cement. Generally this was effective for small tumours completely within the bone. Normal treatment for larger tumours extending out of the bone, causing the bone to break, or extending into the nearby joint, was removal of the affected segment of bone, often including the affected joint, and replacement with a prosthesis. Whilst effective at removing the tumour, such procedures are often associated with a significant reduction in function.

Denosumab is being offered to patients who have one or more of the following problems:

- Patients with a GCT in an area of the body where removal of the tumour is not possible because it would cause a very high risk to life or a significant reduction in function (eg the pelvis, spine, skull base). Some of these patients may have Denosumab as a treatment for their GCT for many years or possibly for the rest of their lives.
- Patients with a large GCT which has grown out of the bone where normal treatment would need an operation to replace the bone or joint. In these patients it is hoped that the Denosumab would reduce the size of the tumour and allow an operation where the tumour is scraped out to be performed. This allows the patient to keep their own joint and not have a replacement. These patients are



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usually given Denosumab for a short period of time (between 3 and 6 months) and would then undergo a lesser operation than would have been expected if not treated with Denosumab.

- The last group of patients treated with Denosumab are patients where the GCT has returned after previous surgery. In these patients the Denosumab is used to either help further surgery to be successful or to control the tumour if no further surgery is possible.

Do I Have to be Treated With Denosumab?

No. It is your choice to start the treatment but you are being offered it because the multi-disciplinary team (surgery, pathologists, oncologists, radiologists and nurses) who have reviewed your case feel it is the best treatment for you.

What Will Happen To Me If I Agree to Denosumab Treatment?

In the first instance, you will be seen in clinic to explain your diagnosis and proposed treatment. It will be checked that it is safe for you to receive Denosumab. You will of course be given an opportunity to ask questions about the treatment. Your doctor will take a history from you, examine you and blood tests will be done. You will be encouraged to think about and discuss your options for treatment.

If I Wish To Have Denosumab, What Happens Next?

If you are happy to proceed with treatment the drug can be given at that clinical appointment. If you wish to think about things then an appointment will be made a week later to start treatment. The drug is given as an injection under the skin (usually the abdomen). A very small needle is used, similar to that used to give insulin to patients with diabetes. The treatment

follows this plan so that the drug level builds up in your body to block the GCT from dissolving your bone.

- Week 1 First Dose
- Week 2 Second Dose
- Week 3 Third Dose
- Week 4
- Week 5 Fourth Dose
- Week 6
- Week 7
- Week 8
- Week 9 Fifth Dose
- Every four weeks after fifth dose

At each visit, you will be asked a few questions about how you are responding, for example, if you have any symptoms from the injections (see below) and if the pain of your GCT has changed at all. You will have blood tests taken at each clinic visit.

What Do I Have To Do Between Injections?

Because Denosumab inhibits the cells that absorb bone some patients experience changes in the levels of calcium in their blood. Therefore it is essential that all patients on Denosumab take a daily calcium tablet to prevent levels of calcium falling.

Pregnancy and Denosumab

Denosumab must not be given to women who are pregnant as it may harm an unborn child. If you think you maybe pregnant before starting treatment please tell your clinical team. They will then review your treatment plan.

If you are a female of child bearing age you must avoid getting pregnant whilst being treated with Denosumab. You must use a reliable method of contraception if you are sexually



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active. Men being treated with Denosumab do not need to make any changes to their contraceptive use. There is no evidence that Denosumab has an effect of sperm production.

When Will The Denosumab Be Stopped?

This depends on why the denosumab is being used. If it is being used to allow less aggressive surgery to be performed then most patients receive treatment for 3 months. The Denosumab is then stopped and your operation performed. If the Denosumab is being used because surgery is not possible or because your GCT has returned then you may need to be on Denosumab for a prolonged period but your doctor will talk to you about how the dosing or timing of your Denosumab may change over time.

What Are The Side Effects of Denosumab?

Denosumab is known to cause a number of side effects. You may experience all, some, or none of the side effects listed below. Rare or unforeseen side effects can occur and it is important that you inform your doctor of any change in your medical condition, or develop any symptoms associated with the side effects detailed below.

Common

- Joint aches and pains following injection with Denosumab. This usually happens within 24-48 hours of an injection. It is minor and often becomes less of a problem once you have had 3 or 4 doses.

Uncommon

- Long term treatment with Denosumab has been associated with an increase in cholesterol.
- Patients receiving Denosumab for a long period of time also describe symptoms of dizziness, cough, altered skin sensation and

difficulty emptying the bladder.

Very uncommon (rare)

- A small number of patients report eczema type skin irritation while receiving Denosumab; this clears when treatment stops.
- Denosumab can lower the levels of calcium in the blood. The signs and symptoms of a low level of calcium include a tingling sensation in the fingertips, muscle cramps or an abnormal heart rate. If you develop any of these symptoms you should seek medical advice as soon as possible.
- A rare but significant side effect of Denosumab treatment is the development of osteonecrosis of the jaw. This rare condition is caused by reduced blood flow to the jawbone. It initially presents as a sore in the mouth or tooth and can be precipitated by dental surgery (eg root canal surgery). It is important that you maintain good dental hygiene whilst receiving Denosumab and avoid dental surgery if possible. If dental surgery is absolutely necessary you must tell your dentist before treatment that you are receiving Denosumab.
- A small number of patients have experienced pains in their thigh bones (femur), which have been characterised as an atypical stress reaction thought to be caused by very small fractures of the femur, which do not heal whilst on Denosumab. In rare circumstances, this can cause a complete fracture of the femur requiring an operation to stabilise the bone. Patients are also required to stop their Denosumab for a period, usually around 3 months, during which time the thigh pain in the majority of cases, resolves. Similar atypical stress reactions may also occur in other bones, including the ribs. In such cases, the



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pain often settles with a short period off Denosumab.

- A small number of patients have experienced an uncontrolled rise in blood calcium levels (hypercalcaemia) having stopped Denosumab. This typically occurs 4 to 6 months after stopping Denosumab. Symptoms of hypercalcaemia include difficulty in passing urine, passing large volumes of urine, continuous nausea and vomiting, constipation, loss of appetite, dry mouth, increased thirst, muscle weakness or excessive tiredness, headache, drowsiness, depression, confusion and irritation. If you develop any of these symptoms during treatment or after Denosumab has stopped, you should seek medical advice as soon as possible.

What if I Have Any Concerns During My Treatment?

If you have any concerns or questions about your treatment with Denosumab, or your GCT, you should contact the specialist nursing team who work alongside the consultants. They will often be able to answer your query or they will be able to ask the consultant so that you can get the help you need.

Contacts

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