Information for healthcare professionals

EWING SARCOMA

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Patient Information Forum

BONE CANCER RESEARCH TRUST

This information has been written for healthcare professionals to help raise awareness of Ewing sarcoma, its diagnosis and treatment.

The following Bone Cancer Research Trust (BCRT) resources about Ewing sarcoma are available to patients:

- Your guide to Ewing sarcoma (A5 booklet).
- Key points about Ewing sarcoma (leaflet providing a summary of key information).
- Our Ewing sarcoma webpage: **bcrt.org.uk/ewingsarcoma**

To request copies of the above, please:
Call: 0800 111 4855
Visit: bcrt.org.uk/requestinformation

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What Ewing sarcoma is and who it affects

What Ewing sarcoma is

Ewing sarcoma is a type of primary bone cancer that most commonly affects children and young adults. It is a rare cancer that can start in the bones or in soft tissue, like the muscles. It belongs to a group of tumours called 'undifferentiated small round cell sarcomas of the bone and soft tissue'.

88% of Ewing sarcoma tumours develop in the bones. They can develop anywhere in the skeleton, but more commonly start in the growth plate and central part of the long bones as well as the flat bones. In particular, the:

- pelvis
- thigh bone (femur)
- ribs

Who Ewing sarcoma affects

After osteosarcoma, Ewing sarcoma is the second most common type of primary bone cancer found in young people. It accounts for 1.6% of all childhood cancers and 1.4% of all cancers affecting teenagers and young adults in the UK.

Many cases of Ewing sarcoma are found in people between the ages of 10 to 24 years. However, it can also affect older adults and younger children.

- Each year in the UK, around 90 people are diagnosed with Ewing sarcoma.
- Most people are under 30 years old when they are diagnosed with Ewing sarcoma.

Symptoms of Ewing sarcoma

The symptoms of Ewing sarcoma are general and can be similar to sports injuries, growing pains and some other conditions (see 'Alternative diagnoses' section below). Symptoms may:

- be mild at first and slowly progress, or they may suddenly appear
- vary for every patient and can present alone or in combination with other symptoms
- differ depending on the location of the tumour in the body

The most common symptoms of Ewing sarcoma are:

- Bone pain, which may:
  - be worse at night
  - be constant or intermittent
  - be resistant to analgesia
  - increase in intensity over time
- Bony or soft tissue swelling / masses
- Pathological fractures
- Mobility issues such as an unexplained limp, joint stiffness or reduced range of motion (ROM)
- Tenderness over the bone

Less common symptoms include:

- Fever (high temperature)
- Lethargy or fatigue (feeling tired or weary)
- Pain, numbness and weakness in affected area, which may present as pins and needles
- Weight loss and loss of appetite
- Feeling breathless

Causes of Ewing sarcoma

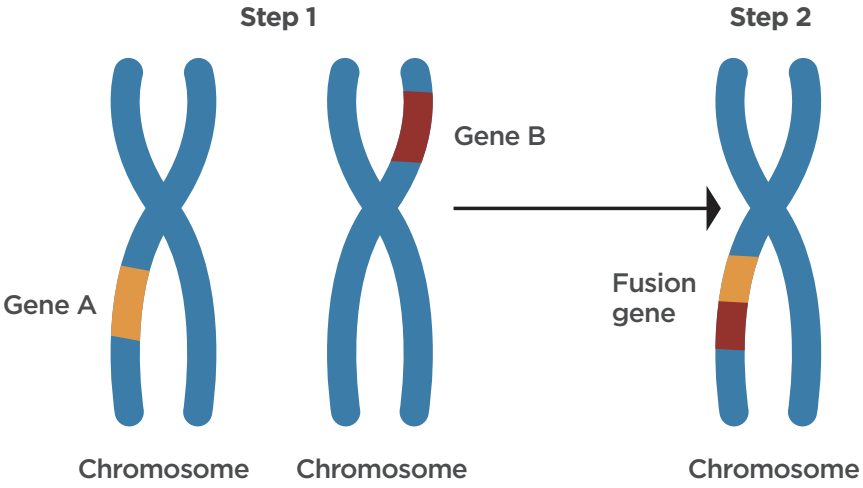
A large proportion of Ewing sarcoma tumours share the same kind of gene damage. However, it is not yet known what causes this damage to occur.

In Ewing sarcoma tumours, there is a 'chromosomal translocation'. This means that part of a chromosome breaks off and sticks to the wrong chromosome.

In 95% of Ewing sarcoma tumours, a chromosomal translocation happens where 2 genes stick together incorrectly to make a 'fusion gene'. The most common fusion gene in Ewing sarcoma is called '*EWS-FLI1*'.

Damage to specific genes and the presence of *EWS-FLI1* causes cells to behave differently and grow abnormally, leading to cancer. The presence of the *EWS-FLI1* gene or other fusions are used to help confirm a diagnosis of Ewing sarcoma.

Gene fusion



Diagnosing Ewing sarcoma

Since the symptoms of Ewing sarcoma are general, this means there is no one clear sign that doctors can easily look for to make a diagnosis. Primary bone cancers are rare, and many GPs will have no experience of them. If a GP is worried about a person's symptoms, they should follow the National Institute for Clinical Excellence (NICE) guidelines for suspected bone cancer and other sarcomas: **cks.nice.org.uk/topics/bone-soft-tissue-sarcoma-recognition-referral/management/** and also arrange for an x-ray of the patient in 2 planes.

The first step in diagnosis will usually involve a clinical examination and an X-ray. Further tests will then be carried out to confirm a diagnosis of Ewing sarcoma. These may include:

- Biopsy of the tumour
- Blood tests
- Bone marrow biopsy
- CT scan
- MRI scan
- PET scan

Imaging helps doctors to see the size of the tumour and exactly where in the body it is. Scans also check if the cancer has spread to any other parts of the body. This is known as 'staging'. Taking a biopsy involves taking a small sample of the tumour or bone marrow and examining it under a microscope. Results from a biopsy can take up to 2 weeks to analyse. Doctors use the results to confirm a diagnosis of Ewing sarcoma and decide on a treatment plan.

Patients may be asked to donate a tissue sample for whole genome sequencing, to contribute to the National Genomic Research Library. By taking part, it may help:

- the patient's clinical team get answers which could lead to a diagnosis, access to a different treatment, or an opportunity to participate in clinical trials
- other sarcoma patients and more widely, other cancer patients in the future
- researchers to understand sarcomas better, to improve things for patients now or, more likely, in the future

To find out more, visit Genomics England's webpage: **genomicsengland.co.uk**

Alternative diagnoses

When diagnosing Ewing sarcoma, it is important to consider other health conditions or more common illnesses which present in a similar way. These conditions include:

- **Osgood-Schlatter disease:** Usually occurs in physically active adolescents and is caused by stress on the tendons that connect to the knee cap.
- **Slipped epiphysis or slipped capital femoral epiphysis (SCFE):** The growing section of bone, present at the end of the long bone, slips and moves on the bone which can cause bone pain.
- **Eosinophilic granuloma:** A non-cancerous (benign) tumour-like growth that is found mainly in children and adolescents.
- **Osteomyelitis:** An infection of the bone.
- **Osteosarcoma:** Another type of primary bone cancer. Visit **bcrt.org.uk/osteosarcoma** for more information
- **Chondrosarcoma:** Another type of primary bone cancer. Visit **bcrt.org.uk/chondrosarcoma** for more information
- **Benign bone growths**
- **Tendonitis:** Inflammation of a tendon, usually causing pain and stiffness.
- **Trauma:** A physical injury, often caused by force, which may result in broken bones and wounds, such as a sports injury.
- **Growing pains**

Holistic Needs Assessment

Patients, their family or friends may benefit from discussing any feelings of anxiety or their concerns. Some hospitals offer a 'Holistic Needs Assessment' for patients. This is where they can have a chat with someone in their medical team who will ask questions about their worries and concerns. It covers all parts of life, not just how the cancer and treatments affect the body. A support plan will be made to help the patient manage their worries and concerns.

Patients can ask their medical team for more information about this. They may be offered an assessment around the time of diagnosis, during treatment or after treatment has ended.

Prognosis

60 out of every 100 people with Ewing sarcoma are alive 5 years after their diagnosis. This number is lower if the cancer is metastatic (has spread) at diagnosis. Some people may not be cured 5 years after diagnosis but may still be having treatment.

Healthcare professionals will consider the following when making a prognosis for Ewing sarcoma:

- where in the body the tumour is, since this can affect which treatments will work best
- the size of the tumour
- the age and general health of the person
- if the Ewing sarcoma is at the original (primary) site (is local), or has spread (is metastatic)
- how the tumour responds to treatment

Because everyone is different, doctors can never be sure how Ewing sarcoma will affect each individual patient.

Treatments for Ewing sarcoma

Most patients will usually be diagnosed and usually have surgery at a bone cancer centre. These are special centres where a group of experts in bone cancer will discuss and manage patient care together.

Treatments for Ewing sarcoma may include:

- chemotherapy (before and after surgery)
- surgery
- radiotherapy
- Proton Beam Therapy (a type of radiotherapy)

Chemotherapy

Chemotherapy is a type of medicine used to treat cancer, that travels around the whole body in the bloodstream. In most cases, chemotherapy is given both before surgery (neoadjuvant chemotherapy) and after surgery (adjuvant chemotherapy).

The aim of chemotherapy is to:

- shrink the tumour before surgery
- destroy any cancer cells that could have spread from the original (primary) site to other areas of the body

The standard chemotherapy regime given to treat Ewing sarcoma before and after surgery is now internationally recognised as VDC/IE, as determined by the Euro Ewings 2012 trial (EE2012). The 5 medicines given are called vincristine, doxorubicin, cyclophosphamide, ifosfamide and etoposide.

The medicines are given in combination to maximise their effect. This means that if the cancer does not respond or stops responding to one of the medicines, the others will still be effective.

Chemotherapy is given in 'cycles.' A cycle is the treatment time plus resting time. The resting time helps the healthy cells to recover before the next cycle starts. Each 'cycle' of chemotherapy is usually 2 weeks (14 days).

Patients will be given a cycle of vincristine, doxorubicin and cyclophosphamide (VDC), followed by a cycle of ifosfamide and etoposide (IE). They will switch like this until the end of treatment. Patients usually have 9 cycles, after which the doctor will check how well the chemotherapy is working. They may then receive a further 5 cycles.

Before chemotherapy, patients will have blood tests to check neutrophil levels. They will also have tests to check kidney, heart and ear function, as some chemotherapy medicines can affect these organs. Patients will also have regular tests during treatment to check for side effects.

In rare cases, a patient may be offered a 'stem cell transplant' alongside high-dose chemotherapy. However, this is not common practice in the UK. Patients are given a hormone which instructs the stem cells to leave the bone and enter the bloodstream. The stem cells are then collected from the blood before high-dose chemotherapy starts. This is called 'stem cell harvesting'. Once removed, the stem cells are stored and frozen. After chemotherapy, they are transplanted back into the patient using a drip. These stem cells help replace blood cells that have been destroyed by the high-dose chemotherapy.

Surgery

Patients may have surgery after chemotherapy and, or radiotherapy, with the aim of completely removing the primary tumour and keeping the body working as normally as possible.

Most people have surgery after cycle 9 of chemotherapy. The patient's surgeon and oncologist will talk to them about when surgery will be carried out. It is very difficult to remove the tumour in some people. For example, if the tumour is in the pelvis or the spine.

The surgical removal of Ewing sarcoma requires 'wide surgical margins'. This means that some healthy tissue is removed alongside the tumour to ensure that all tumour cells are removed and there is a lower risk of the tumour returning.

If the tumour has spread to other parts of the body, the oncologist and surgeon may want to think about removing these secondary tumours by surgery.

If the Ewing sarcoma is in a limb, the medical team will do their best to save the limb by doing 'limb-sparing surgery'. This is not always possible, and they may need to remove the limb. This is called an 'amputation'. Patients should be involved in these treatment decisions.

Surgical procedures that Ewing sarcoma patients may undergo are:

- **Resection:** The affected area of bone is removed along with some healthy bone and tissue around the tumour to ensure complete removal.
- **Autograft:** The affected area of bone is removed and reconstructed using bone and tissue from another area of the patient's body.
- **Allograft:** The affected area of bone is removed and reconstructed using bone and tissue donated by another person.
- **Metallic replacement:** Once the tumour is removed, the area of damaged bone is replaced with a metal implant (an 'endoprosthesis'). After surgery, rehabilitation therapy is usually needed.
- **Irradiation or reimplantation:** Damaged bone is removed and treated with radiation to destroy the cancer cells. The bone is then put back into the body.
- **Amputation:** On occasion, removal of the whole limb is needed due to the size or location of the tumour. If possible, a prosthetic limb will be made for the patient. Further resources can be found on the BCRT's website at: **bcrt.org.uk/amputation**

Radiotherapy

Radiotherapy means treating the tumour with high doses of concentrated radiation. It is usually given as a single dose each day for about 5 to 6 weeks. However, the exact dose and length of time patients will be treated for will vary.

In comparison with other forms of primary bone cancer, Ewing sarcoma responds well to radiotherapy treatment. The NHS website shows a video of what happens during radiotherapy: **nhs.uk/conditions/radiotherapy**

Radiotherapy may be used:

- before surgery to shrink the cancer
- after surgery to destroy any cancer cells that remain in the area
- instead of surgery if the tumour cannot be removed by surgery
- in combination with surgery and chemotherapy if the tumour cannot be fully removed or if full removal would limit how well the body works

Proton Beam Therapy (PBT)

Some patients with Ewing sarcoma may be eligible for Proton Beam Therapy (PBT). It is a type of focused radiotherapy that delivers a radiation dose directly to the tumour. This means healthy tissue around the tumour is less likely to be affected by radiotherapy.

Cases will need to go to a PBT panel, which will decide if a patient is eligible. Applications for PBT must be made using the NHS Proton Beam Therapy Referral Portal: **protons.protontherapyreferrals.nhs.uk/login**

If patients are eligible for PBT, the BCRT offer financial assistance to support the extra costs associated with travel and hospital stays. You can find out more about our Financial Assistance Grants here: **bcrt.org.uk/support**

After treatment

Follow-up care

When treatment is finished, doctors will monitor patients for a long time. This is called 'follow-up care'. Outpatient hospital visits will be needed on a regular basis. The frequency of visits will depend on the patient. It might be every 3 months for the first 2 years, every 6 months for the 3 to 5 years after that and then once a year after that.

At these visits, doctors check a patient's general health, discuss concerns and run some important tests to:

- check for relapse or recurrence (if the cancer has come back)
- check for any 'late effects' from the cancer treatment. This includes longer-term effects on kidney function, fertility and risk of developing a secondary cancer

Patients may also have follow-up care, where their surgical team will look out for any surgery-related problems.

Follow-up visits can be useful for patients to talk about any emotional or practical worries, or any problems they may have. In-between visits, it is important that patients report any problems or concerns they experience to their medical team.

Rehabilitation

During and after treatment, many patients benefit from rehabilitation, a therapy that helps them regain strength and tackle day-to-day activities.

Rehabilitation services include:

- **Physiotherapists:** Help patients return to an active lifestyle, restoring strength, movement and function.
- **Occupational therapists:** Help improve patients' ability to do everyday tasks.
- **Dieticians:** Offer advice on suitable nutrition for patients during and after treatment.
- **Prosthetists:** Design and create prostheses for patients who have had amputations, matching as closely as possible to the patient's affected limb.
- **Orthotists:** Provide aids for patients who have had surgery, such as splints or special footwear.

The BCRT has a selection of Support and Information Webinars which might be helpful for patients to watch during rehabilitation. You can find them here: **bcrt.org.uk/support/webinars**

Advanced Ewing sarcoma

Your patient's cancer may have come back (recurred). At which point, their medical team will decide on the best course of action. This might include more treatment, or deciding whether a clinical trial may be beneficial.

The patient may have been told that the cancer can no longer be cured, and the focus now is to make them comfortable and give them as much time as possible with their loved ones.

The hospital team may talk to the patient about palliative care and ways to ensure their pain is managed. They may also talk to them about hospice care. The team could help direct patients to a local hospice or patients might like to search for one themselves.

Support after treatment

Patients may be worried about their cancer coming back. They may also feel lost and alone or worried about leaving behind the medical team and support network at the hospital. Parents or carers may also feel like this.

Services are available which offer support. These include:

- **Psychological support and services:** Psychologists will support patients with any concerns, feelings of anxiety or depression.
- **Local support groups:** Many support groups are organised and run locally. Clinical nurse specialists can usually provide information on local services.
- **The Bone Cancer Research Trust (BCRT):** Provides support and information for people affected by primary bone cancer. The BCRT can connect patients with others who have experience of primary bone cancer.
- **The Children's Cancer and Leukaemia Group (CCLG):** Provide useful information for children, teens and their parents about what to expect once treatment is finished.
  Visit **cclg.org.uk**
  Call **0333 050 7654**

- **Macmillan Cancer Care:** Provide useful information for adults who have had treatment for cancer, and who are living with and beyond cancer.
  Visit **macmillan.org.uk/cancer-information-and-support**
  Call **0808 808 0000**

The Bone Cancer Research Trust (BCRT)

The BCRT is the leading charity dedicated to fighting primary bone cancer. We are here for anyone who needs information on, or support with, primary bone cancer.

As well as producing information for patients, we offer a range of primary bone cancer information resources and training for healthcare professionals. Visit our website to find out more: **bcrt.org.uk/information/for-healthcare-professionals/**

You can also visit **bcrt.org.uk/ourhealthinformation** to find out how we produce our health information resources.

Contact our Support and Information Service:

Call: **0800 111 4855**
(Monday to Friday, 9am to 5pm)
Email: **support@bcrt.org.uk**
Visit: **bcrt.org.uk/support**

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Email: support@bcrt.org.uk
Call: 0800 111 4855

References

The Bone Cancer Research Trust's information has been created using peer-reviewed clinical and scientific publications, reviews, case studies and reference books. If you are interested in reading more, below is a list of key references used to compile our information about Ewing sarcoma.

For a full list of references and further reading, or for more information, contact our Support and Information Service. You can also visit our Request Information Materials page to order printed resources for patients: **bcrt.org.uk/requestinformation**

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Also available:
Leaflets and booklets about Ewing sarcoma.

Please contact us to request a free copy or visit our website to view our printable/downloadable resources.

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