

GIST for Beginners

a guide for patients by patients



You do not have to be alone!



Gastrointestinal Stromal Tumour

This is the name of a rare form of cancer which one usually never hears about. This Guide is for all GIST patients, their relatives and for others who may be interested. It is a short explanation of GIST and how it is treated.

This booklet was inspired by a booklet produced for the Stichting Contactgroep GIST Nederland-België. It was adapted by Judith Robinson for the first UK edition. This is the second edition (2014) bringing the GIST community up to date.

DISCLAIMER

This booklet has mostly been written by patients, except where otherwise stated.

The information is not intended to replace expert medical advice that you may be given. We do our best to ensure that any information we publish is accurate, but any decisions about your treatment should be made after discussions with your consultant, (preferably a GIST expert).

CONTENTS

Introduction	2
What is cancer and what is GIST?	4
What causes GIST cancer?	6
Possible symptoms of GISTcancer	7
Diagnostic tests	8
Diagnosis of GISTcancer	11
Risk of Recurrence	12
Mutation analysis	13
Tissue Bank.....	14
Special rare types of GISTcancer	16
Treatment of GIST cancer	17
What if imatinib does not work or stops working?.....	19
How targeted drugs work.....	22
Side effects.....	23
Nutrition.....	23
Guidelines for treating GIST	26
Compliance.....	26
Preparing for your next visit to the oncologist.....	27
Life with GISTcancer	28
Finding other GIST patients.....	29
About GIST Support UK.....	30
PAWS-GIST Alliance (paediatric and wild type GIST)	32
Funding and Fundraising	33
Specialist GISTcancer centres in the UK.....	34
Speakers at recent GSUK Patient Meetings.....	34
Pathology Laboratories.....	35
Useful Links	36

Introduction

Gastrointestinal Stromal Tumour, or GIST for short, is a very rare cancer, a kind of sarcoma.

So people who get this diagnosis not only face the shock and fear experienced by all patients who get a cancer diagnosis, but also a feeling of isolation, as no-one (even many medical professionals), will have heard of it.

However, since the year 2000 massive strides have been made in the understanding and treatment of GIST, and the future for GIST patients now looks much brighter than it did back then.

GIST Support UK is a patient support group started and run by patients and their carers, to provide information and mutual support. Much information is now available for GIST patients and their families, provided by various support groups around the world like our own website and the excellent website by GSI – (www.gistsupport.org).

This booklet is aimed at newly diagnosed GIST patients, and their friends and families in the UK.

Since GIST is rare, the chances of meeting another GIST patient are very small. We hope you will join our community and our Listserve. You are also most welcome to come to our twice yearly meetings. We all remember very well the relief at meeting other patients at our first GIST Support UK meetings. We were no longer so alone, and could talk to others who really understood.

The Trustees of GIST Support UK

When my 15 year old daughter was diagnosed with the Paediatric/wild-type form of GIST it was undoubtedly the worst news our family had ever received. Very little was known or available to patients with this diagnosis in the UK.



Encouraged by the Trustees of GIST Support UK, with fundraising from our supporters and the dedication of Dr Ramesh Bulusu, we have now opened a specialist clinic for Paediatric, Adolescent, Wild-type and Syndromic GIST patients. This is called the PAWS-GIST Clinic and takes place at Addenbrooke's Hospital in Cambridge. If you have been diagnosed with one of these types of GIST, this clinic is for you!

Applications to participate in the clinic are made via our website (www.pawsgistclinic.org.uk) and further information can be obtained from me.

We are a centre of expertise working to understand the causes and mechanisms of Gastrointestinal Stromal Tumour in children, young people and all with wild-type GIST. Our work is aiming to improve treatment, provide highly specialised care plans and find a cure for this rare form of cancer. Our team will work with you to make life as normal as possible for you.

In the longer term we believe that seeing more wild-type and paediatric GIST patients will help us to improve our understanding of this disease and identify specific and effective treatments.

Jayne Bressington

GIST patient carer, Patient Director of the PAWS-GIST Alliance and Trustee GIST Support UK

What is cancer and what is GIST?

The human body is made up of countless cells. Each cell contains information which is copied during cell division. The stomach or intestines are made up of special cells which help them to do their job. Most organs remain healthy by getting rid of old cells that no longer work. These are replaced by new cells and this process takes place in the body all the time.

Cancer occurs when there is a breakdown in the natural genetic process. This process makes a cell grow and divide when it is not supposed to. When this happens it becomes a cancer cell and when a mass of these cells develop it becomes a tumour.

Some tumours are harmless and these are called **benign tumours**. However when your health is threatened these are called **malignant tumours**.

GIST (Gastro Intestinal Stromal Tumour) is a soft tissue sarcoma.

This means that it grows in the gastrointestinal or digestive system. It is classified as a stromal tumour because the cancer starts in the stroma, which is a type of tissue in the walls of the stomach or intestine. A GIST can occur in almost any part of the digestive tract but it usually is found in the stomach or small intestine.

GIST's often occur as a single tumour, however some of the cancer cells may enter the bloodstream. This can result in new tumours forming in other organs of the body. These are called metastases.

If this happens in the liver, for example, it is still called GIST because cancers are named by where they first appeared and by the kind of cancer cells they are.

The treatment of sarcomas is a speciality. Sarcomas are rare, so there are relatively few doctors who specialise in sarcomas. There are a

number of hospitals which have a specialist team that manage GIST patients and these are based throughout the UK. The hospital in which you are being treated will have discussed your case at a Multi Disciplinary Team (MDT) meeting which is made up of specialists of all medical disciplines and your treatment will be agreed by the whole team.

GISTs can vary greatly in size and in the ease with which they can be treated. They may be very small, 1-2 cms in diameter, or they can be large, up to 20 or more cms in diameter, with their own blood supply. They can also appear in a single easily removable capsule, or be wrapped round internal organs. Secondary tumours, called metastases, can also develop in a different place from the original primary tumour, usually in the liver. This is because blood goes directly from the stomach and intestines to the liver. This is not liver cancer, but GIST in the liver.

It is important that the primary GIST is found early and treated, to reduce the risk of it metastasizing, or spreading. Although large fast-growing GISTs are the most likely to return, even small tumours may metastasize eventually.

GIST is most commonly found in the stomach (40%), followed by the small intestine (30%), the rectum (10%). and colon (5%). GIST is also very rarely found in the oesophagus.

Occasionally GISTs may be discovered outside the gastrointestinal tract. This can be in the omentum (a large fatty structure covering the intestines inside the abdomen), in the peritoneum (a thin membrane that forms the lining of the abdominal cavity), or in the retroperitoneum (the space in the abdominal cavity behind the peritoneum).

When a GIST is found, metastases may already have grown in other organs. Metastases are found in about half of newly-diagnosed GIST patients.

If the tumour bleeds into the abdomen or ruptures during surgery, cells may get into the blood stream, and the GIST can then spread into the abdominal cavity.

GISTs in the stomach or liver should be treated quite differently from the much more common stomach or liver cancers and need the attention of surgeons and oncologists who specialise in the treatment of GIST.

What causes GIST?

GIST was only classified in its own right in 2001

It arises from the ‘interstitial cells of Cajal’. These are small cells in the outer wall of the digestive tract, commonly called the gut. GISTs can grow from this wall into the abdominal cavity, and sometimes grow very large before causing problems and being discovered.

All the cells in the body have KIT and PDGFRA genes. If either of these genes changes (mutates), there is a risk of GIST developing. In most cases of GIST, it is the KIT gene that mutates. In about 10%-15% of cases it is the PDGFRA gene that mutates. In a further 10% of cases, neither of these genes has mutated, but a GIST develops anyway. These are called “Wild type” GISTs.

Although GIST is diagnosed mainly in people aged between 40 and 60, it can occur in people much younger than this and even (although not often) in children. In younger people it is usually called paediatric GIST and it differs in some ways from the types of GIST found in older people. About 54% of GIST patients are male, 46% are female.

GIST is hardly ever hereditary, so there is little likelihood of you passing it to your children.

It is estimated that there about 900 new cases of GIST diagnosed each year in the UK. Accurate data is now being collected. Sometimes in the past GIST was mistaken for another type of cancer.

Possible symptoms of GIST

GISTs often show no symptoms for a long time. The first symptoms are often caused by the tumour pressing on some other organ. Sometimes the GIST may bleed into the abdominal cavity or the gut. This causes anaemia. If the GIST is large, the doctor may be able to feel a swelling in the abdomen. GISTs, particularly in the liver, can also cause night-sweats.

- **GIST in the oesophagus** can cause difficulty with swallowing (dysphagia).
- **GIST In the stomach** can cause pain or discomfort, indigestion, nausea, vomiting, feeling of fullness, bleeding into the gastrointestinal tract causing black coloured stools, or any combination of these.
- **GIST in the intestine** can cause bleeding, pain, constipation, diarrhoea, pain, or just vague abdominal discomfort.

All these symptoms can be caused by common problems. However if they haven't responded to simple treatments, or got better on their own, your GP will then have referred you to a gastroenterologist. Some of the following tests will then be done.



COULD IT BE GIST? CANCER

<http://www.g1stsupportuk.com>

GIST = Gastro-Intestinal Stromal Tumour

How common is GIST?

- 600-1,000 new cases yearly in the UK
- mostly diagnosed: age group 40 - 60
- 60 - 100 children and younger adults affected each year

Possible symptoms

- Abdominal swelling / bloating / lump
- Persistent / Unexplained Indigestion
- Persistent / Unexplained Nausea
- Discomfort or pain in the stomach
- Bleeding from the stomach
- Weight gain / Weight loss
- Fever / Night sweats
- High blood pressure
- Anaemia

What we do:

- Provide information for patients/doctors
- Improve the treatment of GIST
- Support research
- Represent patients' interests

GIST is rare, but you are not alone

info@g1stsupportuk.com
 0300 400 0000
www.g1stsupportuk.com
www.facebook.com/GISTsupportuk
www.tumblr.com/GISTsupportuk
www.youtube.com/channel/UC...

g1st support uk
Helping you thrive

Diagnostic tests

CT scan (Computed Tomography)

This is the commonest diagnostic tool. It uses X-rays to build up a three-dimensional picture of your inside. It is painless and uses a small amount of radiation. You will usually be asked to drink some water and be given an injection of a contrast medium into a vein. If for some reason you cannot take the contrast medium, you will be given a special liquid to drink before you have the scan.

Ultrasound

This is a painless and harmless procedure using no X-rays. It is used all the time for looking at unborn babies, but is also good for finding tumours.

Endoscopy

A tube with a tiny camera is passed into the stomach. You will be sedated for this procedure. GISTs growing on the outside of the stomach cannot be seen. Sometimes ultrasound is done from inside the stomach to give a clearer picture than would be possible with ordinary ultra-sound. This is called endoscopic ultrasound (EUS). This will show tumours both inside and outside the stomach. During an endoscopy, small pieces of the tumour can sometimes be removed for examination. This is called an endoscopic biopsy.

MRI-scan (Magnetic Resonance Imaging)

This is a technique for measuring the activity of cells and their blood supply by using a magnetic field and radio waves. It uses no radiation, is painless, but noisy, and takes quite a long time.

PET scan (Positron Emission Tomography)

This is rather like a CT scan but you have to take a drink containing a kind of glucose which is slightly radio-active. Any very actively growing cells will absorb more of this glucose than other cells and are then highlighted on the scan. A PET scan is usually used either before

This is Pippa, one of our younger patients, who was selected to carry the Olympic torch. She is a fantastic ambassador for young GIST patients. Pippa has been living with Paediatric Wild-type GIST since October 2009. After two operations to remove tumours, Pippa enjoys life as a normal young woman but also with the uncertainties that go with having such a rare form of cancer.



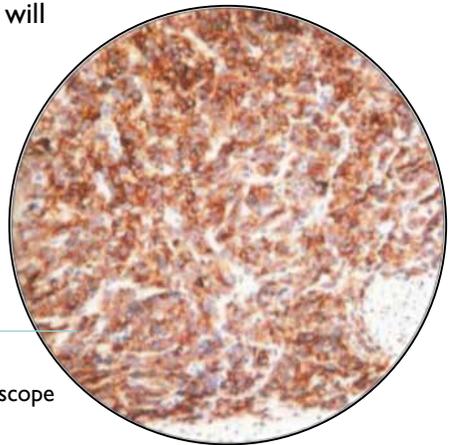
surgery if the doctor thinks there may be more than one tumour, or to see how your tumour(s) is responding to treatment.

Blood tests

Your blood will be tested to see whether you are anaemic, and to check whether your liver and kidneys are working well.

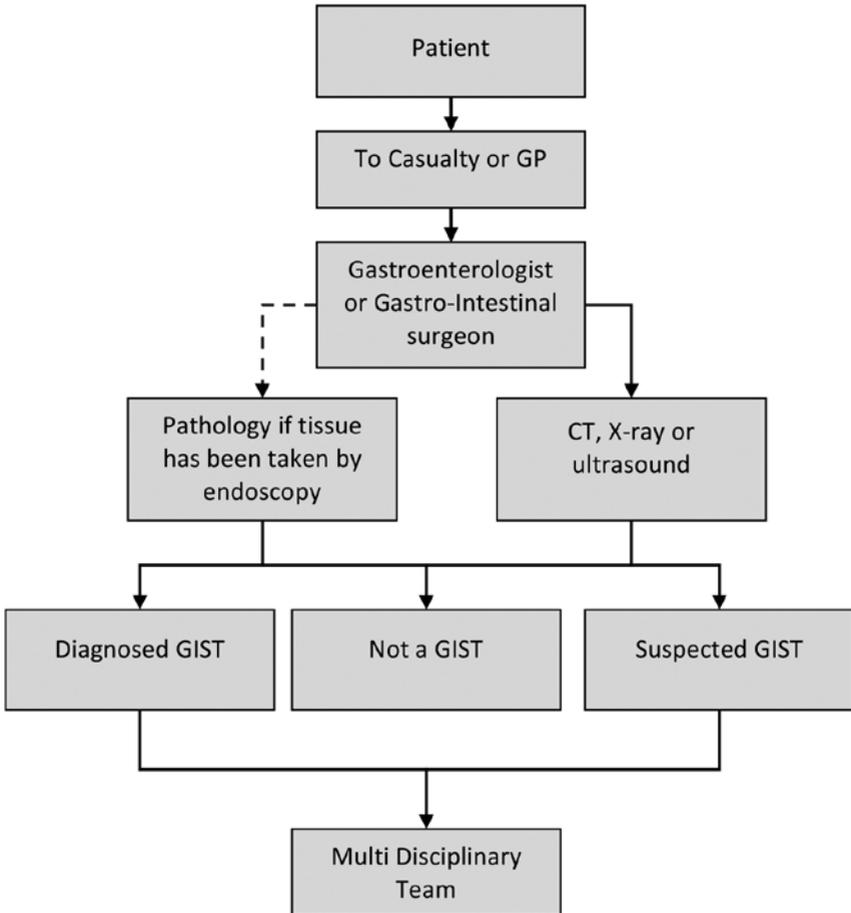
Histology

This means looking at the cells from your tumour under a microscope. If a biopsy is taken before you have any surgery, this biopsy sample will be examined and this will help to confirm the diagnosis. If your tumour is removed, it will be looked at by the pathologist. The diagnosis of GIST can then be confirmed. The edges of the tissues removed will be very carefully examined to make sure that all the tumour has been removed.



This is what GIST cells look like under the microscope when they have been stained by the pathologist

The diagram below shows the steps that you may have been through before it is suspected that you have a GIST.



NB Please confirm that the MDT working on your case includes or seeks an opinion from an Oncologist and Surgeon who specialise in GIST.

Diagnosis of GIST

Although the site of a tumour may suggest that it is a GIST, GISTs can only be definitely diagnosed after the pathologist has looked at the cells under his microscope. This may be done before any treatment if a tissue sample has been removed by a biopsy. Otherwise a firm diagnosis will be made after the tumour has been removed

The pathologist will also estimate the rate at which the tumour is growing. This is done by counting the number of cells which are in the process of dividing (undergoing mitosis) in 50 high-power fields of his microscope. This is the “mitotic count per 50 HPF”. The higher this is, the faster the tumour is growing. There are six accredited GIST pathology laboratories in the UK – please request mutational analysis at one of these. (See page 35).

Risk of Recurrence

The risk of a GIST coming back after surgery depends on three things:

- How big it is
- Its mitotic count (ie how fast the tumour cells are multiplying)
- Where it is growing

See the table overleaf for details of risk occurrence.

The best GIST to have (apart from none!) is a small one on the stomach, growing very slowly.

I may have been lucky but I have found life on imatinib quite bearable. It has not stopped me from doing anything. And it seems to have been effective in shrinking my tumour. So I am grateful for imatinib and for an NHS which is ready to pay for it.

Hugh GIST SUPPORT Member

Risk of Recurrence Table

Risk category	Tumour size (cms)	Mitotic count per 50HPFs	Place of primary tumour
Very low	Less than 2	5 or less	Anywhere
Low	Between 2 and 5	5 or less	Anywhere
	Between 2 and 5	More than 5	Stomach
Intermediate	More than 5	Between 6 and 10	Anywhere
	Between 5 and 10	More than 5	Stomach
	Any size	Any	The tumour has ruptured before or during surgery
High	More than 10	Any	Anywhere
	Any size	More than 10	Anywhere
	More than 5	More than 5	Anywhere
	Between 2 and 5	More than 5	Not in the stomach
	Between 5 and 10	5 or less	Not in the stomach
	Between 5 and 10	5 or less	Not in the stomach

Note: This table is proposed by a British group of GIST experts, adapted from a table produced by H Joensuu in 2008. It has not yet been validated.

Mutation analysis

Mutation analysis is probably a key predictor for the course of the disease, and may determine treatment options in the future.

If GIST is diagnosed, there is usually a mutation discovered in the KIT or PDGFRA genes. This change takes place at a particular place in the chromosome, called an exon.

KIT mutations occur in about 80% of GISTs:

- Exon 9: mostly in tumours in the small intestine
- Exon 11: the commonest mutation, which can occur anywhere in the gut
- Exon 13: rare
- Exon 17: rare

PDGFRA mutations occur in about 10% of GISTs:

- Exon 12
- Exon 14 is very rare
- Exon 18 is the most common

We recommend that all patients with GIST should ask to have mutational testing performed, and we are lobbying to make this standard within the UK. Mutational testing is particularly important in the case of tumours in the high risk group.

There is now a Tissue Bank for GIST cancer samples where fresh tumour or wax blocks of tissue can be stored. Please ask your surgeon to ensure that a sample is sent to the Tissue Bank in Newcastle.

Tissue Bank

There is now a Tissue Bank for GIST cancer samples where fresh tumour or wax blocks of tissue can be stored. Please ask your surgeon to ensure that a sample is sent to the Tissue Bank in Newcastle.



**NOBODY WANTS GIST TUMOURS
WE DO...**

NATIONAL GIST TISSUE BANK

**THE NATIONAL GIST TISSUE BANK
LAUNCHED AT NCR - NEWCASTLE**

**Rare and Incurable Stomach Tumours (GIST) are more
Prevalent than you think. Are you diagnosed with GIST
living in the UK watch out.**

**A national GIST tissue bank now exists
in Newcastle.**

What does this mean for you?

- This bank is a valuable resource that will support GIST cancer research locally, nationally and internationally.
- It will provide researchers with a diverse selection of high quality GIST tumour specimens and clinical data obtained by dedicated tissue bank staff who follow strict procedures and ethical guidelines.
- Research will progress faster if there is a good supply of GIST tissue upon which to base potential treatments and develop new diagnostic tests.

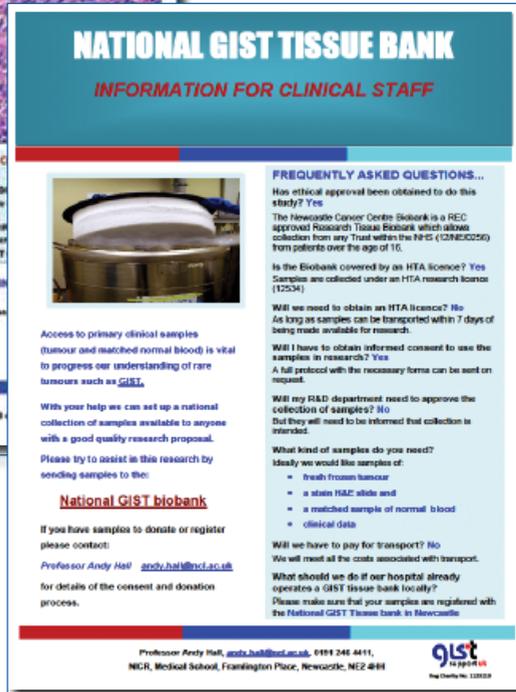
How will the Tissue Bank Operate?

Operating within the NCR in Newcastle, the GIST Tissue Bank will coordinate the collection, storage and distribution of a variety of gastric and duodenal biopsies including fresh, frozen and paraffin blocks in addition to blood samples and clinical data.

Working in collaboration with pathologists, medical oncologists, surgeons and other hospital personnel, specially trained staff will obtain patient consent, collect samples and assemble clinical information about each donor and their corresponding specimens.

**HOW YOU CAN
BANK...
If you are a GIST
about to have
Please request
tissue to visit
National GIST
CONTRACT IN
write
email
phone
small**

**National GIST Tissue Bank
Sincere thanks to Professor Andrew Hall
GIST Support UK**



NATIONAL GIST TISSUE BANK

INFORMATION FOR CLINICAL STAFF



**Access to primary clinical samples
(tumour and matched normal blood) is vital
to progress our understanding of rare
tumours such as GIST.**

**With your help we can set up a national
collection of samples available to anyone
with a good quality research proposal.**

**Please try to assist in this research by
sending samples to the:**

National GIST biobank

**If you have samples to donate or register
please contact:**

Professor Andy Hall andy.hall@ncl.ac.uk
for details of the consent and donation
process.

FREQUENTLY ASKED QUESTIONS...

**Has ethical approval been obtained to do this
study? Yes**

The Newcastle Cancer Centre Biobank is a REC-
approved Research Tissue Biobank which allows
collection from any Trust within the NHS (GMEK0202)
from patients over the age of 16.

Is the Biobank covered by an HTA licence? Yes
Samples are collected under an HTA research licence
(12534)

Will I need to obtain an HTA licence? No
As long as samples can be transported within 7 days of
being made available for research.

**Will I have to obtain informed consent to use the
samples in research? Yes**

A full protocol with the necessary forms can be sent on
request.

**Will my R&D department need to approve the
collection of samples? No**
But they will need to be informed that collection is
intended.

What kind of samples do you need?
Ideally we would like samples of:

- fresh frozen tumour
- a stain H&E slide and
- a matched sample of normal blood
- clinical data

Will we have to pay for transport? No
We will meet all the costs associated with transport.

**What should we do if our hospital already
operates a GIST tissue bank locally?**
Please make sure that your samples are registered with
the National GIST Tissue bank in Newcastle

**Professor Andy Hall, andy.hall@ncl.ac.uk, 0191 246 4411,
NCR, Medical School, Framlington Place, Newcastle, NE2 4BQ**



glist
to join UK
Reg Charity No. 1100218

Letter template to request that tissue samples are sent to the National GIST Tissue Bank.

Dear Dr

Re transfer / registration of my GIST tumour samples with the National GIST Tissue Bank (NGTB) in Newcastle

In advance of / further to (**please delete as appropriate*) my operation to remove my Gastro Intestinal Stromal Tumour, I am writing to request that my tumour sample, is transferred to / or registered with* (**please delete as appropriate*) the **National GIST Tissue Bank in Newcastle.**

The National GIST Tissue Bank is collecting, fresh, frozen and paraffin embedded tumour tissue and serum samples from GIST patients throughout the UK who have undergone or who are about to undergo surgery where GIST is diagnosed.

The National GIST Tissue Bank has Research Ethics Committee approval and a Human Tissue Act research licence to make these materials available to researchers in academia or industry for projects concerned with GIST cancer research.

I am very keen to support this work and therefore request that my samples are transferred to or at least registered with the bank.

I have enclosed a copy of the information sheet providing more information about the bank and a link to the details online (<http://www.pawgistclinic.org.uk/updates.htm>)

Please can you confirm when the transfer has taken place.

Yours sincerely

Special rare types of GIST

Wild-type GIST

If none of the normal mutations already described is found, nor any other mutations in KIT or PDGFRA, then the tumour is called “Wild-type”. This can be found in patients of any age but is commonest in younger patients.



Paediatric GIST

Paediatric/adolescent GISTS occur in patients under the age of 25 years. They are often located in the stomach, can be multifocal and are mostly wild type i.e. do not have any mutations in KIT or PDGFRA genes. Some of these can be associated with certain syndromes (see below). It is usual for PAWS-GIST tumours to be slow growing so with specialist management the outlook is generally a positive one. See PAWS-GIST Alliance on page 32.

Syndromic GIST

GIST may occur as what is called Carney's Triad, which is a combination of GIST, lung chondroma and paraganglioma. Two or three of these may occur together. It may also occur in the Carney-Stratakis dyad Syndrome. Both of these syndromes are extremely rare. GISTs may also occur as part of the neurofibromatosis syndrome (NF1).

Familial GIST

In an extremely small number of families in the world, there appears to be an inherited form of GIST. Much more detail about all of these special forms of GIST can be found on the PAWS-GIST clinic website www.pawsgistclinic.org.uk

Treatment of GIST

GIST requires a multi-disciplinary approach, which means that a group of experts should be involved, probably including:

- A surgeon
- A gastroenterologist (a specialist in the gastrointestinal tract ie the gut)
- An oncologist (a doctor who specialises in treating cancers)
- A pathologist
- A radiologist
- A specialist nurse

They form the Multi-Disciplinary Team, (MDT), and decide together on the best treatment for each patient.

It is really important that a relationship of trust is established between you and your doctors. If for any reason you feel uncomfortable about the way you are being treated, **do ask for a second opinion**. This is particularly important if you are facing major surgery. Your GP can arrange for a second opinion, and you may be able to find suitable GIST experts from our website or from the lists on page 35.

What are the options?

I Surgery

If the tumour is small and easy to get at, and has not spread, surgery is the usual treatment. This may be possible laparoscopically, (by key-hole surgery), but open surgery may be needed. You may like to get a copy of our booklet, “Eating after Surgery for GIST”.

2 Adjuvant treatment with imatinib (Glivec®) after surgery

If the tumour has a high risk of recurrence, trial data shows that taking imatinib after surgery statistically increases the time to recurrence. It also increases overall survival, and more data is being collected to confirm these findings. Imatinib has now been approved in the UK as a standard treatment for between 3 and 5 years following surgery.

3 Treatment with imatinib before surgery

This is the usual first-line treatment in the UK if there is more than one GIST, or when the hospital team decide that the tumour or tumours are too difficult to remove surgically. Imatinib usually stops the tumour or tumours growing. It may even cause tumours to shrink, occasionally to the point when they *can* be removed surgically. However funding is not normally available for a *primary* tumour to be shrunk in this way, unless it is too difficult to be removed surgically.

Imatinib does not have the same side effects as normal chemotherapy, used for many other cancers. Normal chemotherapy affects all growing cells, and causes healthy cells to be destroyed. This leads to a number of difficult side effects like the loss of all body hair. Imatinib works differently and is one of a group of drugs called **targeted drugs** (see page 22). These act mainly on the GIST cells, so they cause far fewer side effects than the usual drugs used to treat cancer. Targeted drugs are taken every day as a pill.

While you are taking imatinib you should have regular blood tests to make sure that you are not anaemic and that your liver and kidneys are working well. You should also have CT or MRI scans every three months.

What if imatinib does not work or stops working?

1 Change to sunitinib (Sutent®)

Because of the problem of resistance, other drugs are available to use when imatinib stops or does not work. The usual drug prescribed is sunitinib. This drug blocks the signalling pathway in a different place from imatinib, and it also helps to stop new blood vessels from growing. This is a second factor in stopping the GIST from growing, but because it is a general effect, rather than just affecting the GIST cells, sunitinib can have more side effects than imatinib.

Before you are given sunitinib, you should be given the patient booklet published by Pfizer. This gives you hints about how to prepare, how to take the pills and what to do about any side effects you may have. If the normal regime doesn't suit you it may be possible to change the dose or the pattern of the way you take the drug. Talk to your doctor if you want to change the way you take sunitinib, or the dose you take.

2 Increase the dose of imatinib to 800 mgs a day

Funding for this is not generally available under the NHS, but some NHS Clinical Commissioning Groups will fund it from the Cancer Drug Fund. If you know you have an exon 9 mutation, this would probably be the best course to take if you can get the drug, since it has been proved to work better than 400 mgs for exon 9 mutation GISTs.

3 Regorafenib (Stivarga®) This Drug has now been approved in the European Union and is available for oncologists to prescribe after patients have progressed or are intolerant to imatinib and/or sunitinib.

4 Enter a clinical trial

There are often new drugs becoming available which are currently under trial. For example, recent published reports indicate that masitinib (Masican®) may be useful for GIST patients. Ask your oncologist about whether you might be eligible for entry into a trial. Trials usually have very strict entry criteria which depend on what treatments you have already had, so eligibility will not be a foregone conclusion.

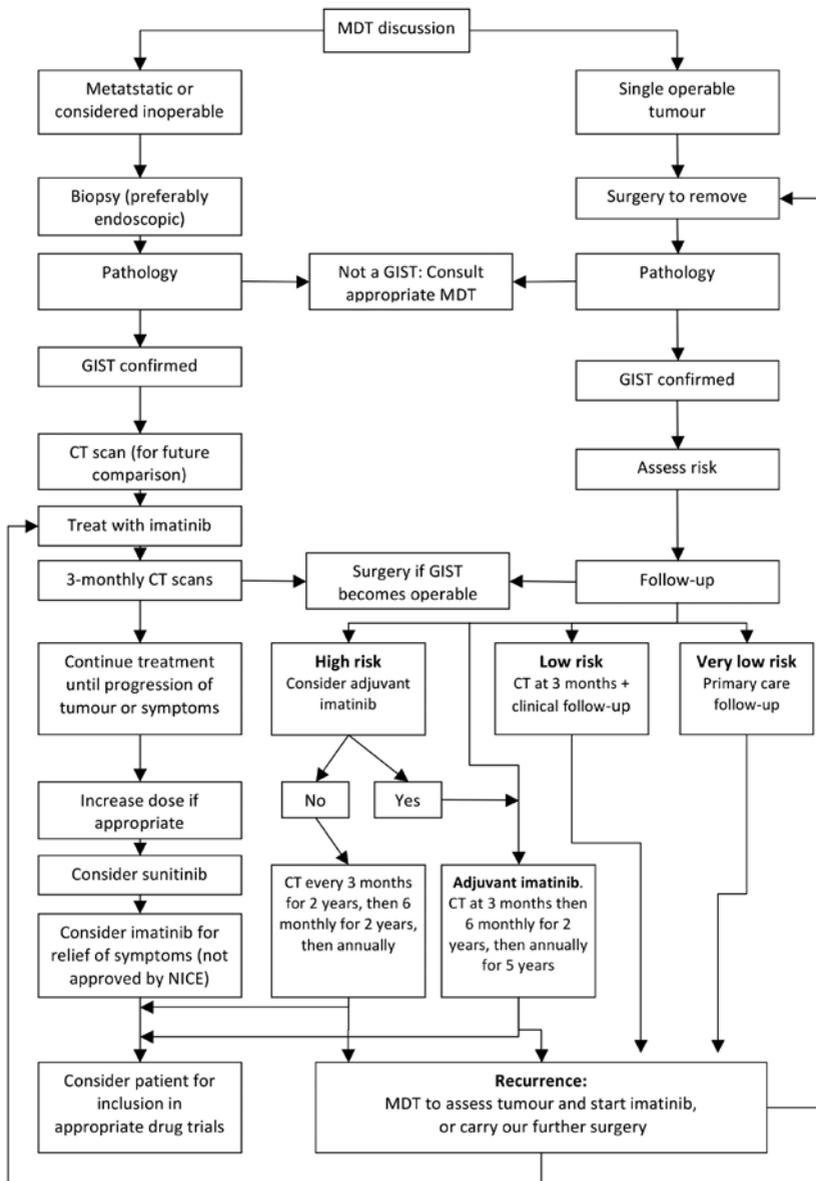
5 Have more surgery

This could be open or laparoscopic.

6 Less common treatments

- **Radio Frequency Ablation**, where the tumour is effectively cooked by focused microwaves. How appropriate this treatment is depends very much on where the tumour or tumours are, and on the risk to neighbouring organs.
- **Radiotherapy**. It had been thought that radiotherapy did not work for GIST. However there has recently been some experimental use of radiotherapy on GIST patients who have no other treatment left to try. It has been found to be quite successful in shrinking the tumours, so more work needs to be done to see how radiation can best be used for GIST patients.
The Cyberknife can irradiate the tumour from many directions by highly focused X-rays. Currently there are very few Cyberknife installations in the world, and the treatment is still experimental.
- **Embolisation**, where the blood supply to the tumour is choked off, so that the tumour dies.

If you like diagrams, the chart on the next page shows the possible steps in your treatment. This has been adapted from a chart in “Suggested Guidelines for the Management of GIST 2011”



How targeted drugs work.

The first and second line targeted drugs available in the UK are imatinib (Glivec®) and sunitinib (Sutent®) and we should have Stivarga® (regorafenib) for third line treatment very soon. Clinical trials are being performed across the world investigating other new targeted drugs.

Tumours form when a cell starts to grow in an uncontrolled way. It does this because there has been a change in the genes in the cell. We do not know why this happens in GIST. The genetic change means that the very complex system, which should tell the cell when to grow and when not to grow, stops working. The cell just goes on dividing, and a tumour grows. What the targeted drugs do is to block one of the essential steps in the growth-signalling system in these particular cells, without affecting the normal cells of the body.

Imatinib was the first targeted drug developed for GIST, and it is still the first choice because it is usually easy for patients to take and gives few side effects. Unfortunately, we now know that GIST cells quite often mutate again, and find a way round the block in the signalling pathway. This means that the tumour can start to grow again. In some patients this happens in a few months, but we know of some patients who have been taking imatinib for 10 + years, and it is still working. The average time is about three years. Why there is this difference is a question we cannot yet answer. Another question we don't know all of the answer to, is why there is a small percentage of patients who do not respond to imatinib at all. We know that Wild type and paediatric GISTs respond less well than other GISTs to imatinib, but there is much more we need to know about this. This is why the PAWS-GIST initiative has been started.

(See page 32 and www.pawsgistclinic.org.uk).

Side effects

If you read the leaflet which is enclosed with the pills of either imatinib or sunitinib, you could start feeling ill – before you have even taken a single pill! However, remember that the company which makes the pills has to mention every side effect ever known, and most of them are very rare. Some are fairly common, but most of these, at least for imatinib, are quite easy to cope with (see table on page 24). With both drugs, some patients have virtually no side effects, and many people find that the side effects they have at first get less of a problem after time.

Nutrition

Taking targeted medicines may cause a temporary loss of taste. Food and drink suddenly taste different. This does usually get better in time. In the meantime, try to keep up a healthy weight by eating all kinds of good food, and try to avoid eating a high-fat diet or too much sugar. Eat plenty of fresh fruit and vegetables.

If you feel sick, it may be helpful to eat small amounts of food and to drink plenty. If this doesn't help, your doctor may prescribe you a medicine to tackle the nausea. If you experience significant weight loss please ask your GP or oncologist to refer you to a consultant nutritionist who will help you to gain and stabilise your weight

The commonest side effects of imatinib noticed by patients	Patients' suggestions for dealing with them
Puffy eyelids	Put up with it: we all have this!
Swollen ankles	Put your feet up when you can
Indigestion or feeling sick	Take your pills with your main meal and with a large glass of water. Try peppermints, or if they don't work try Gaviscon.
Being sick	Ask your GP for help. There are various medicines which can help
Diarrhoea or abdominal pain	Ask your GP for help.
Rash	Ask your GP for help
Cramp, particularly at night.	Make sure your blood chemistry is fine. If it is, some patients find that quinine helps. Tonic Water contains small amounts of quinine, but if this is not enough, ask your GP.
Tiredness	The only answer is to get more rest.

Note: Grapefruit (juice) in combination with imatinib (Glivec®), and with sunitinib (Sutent®), is strongly discouraged, as grapefruit will interfere with the working of these drugs and may stimulate over-absorption.

There are other side effects that may show up when you have your blood tests at your hospital checks, and the hospital doctors will advise you about these. You will also have regular CT scans, usually every three months, to check that the treatment is working.

There are a few very rare and possibly serious side effects. These include, chest pain, sudden bleeding in the stomach or intestine producing black stools, sudden high fever or very sore throat, rapid swelling and weight gain, and sudden shortness of breath. If you have any of these, go to your nearest A&E department, and make sure the doctors there know that you are a GIST patient and taking imatinib or sunitinib.

If you are one of the very few unlucky people in whom the side effects become bad, and nothing seems to help, it may be sensible to lower the dose. This is something you must talk to your GIST specialist about. (We do know of a patient who remained stable on only 100mg imatinib per day.) It is your life, and only you can decide when something is too bad to live with.

There are some drugs which interact with imatinib, and should not be taken. GIST Support UK publishes a little pocket booklet called “I am a GIST Patient”, which lists the drugs you need to avoid, and in which you can record the details of your own treatment. If you need medicines for something other than GIST, you can always show your pocket booklet to your GP or to the hospital where you are being treated. Always carry the booklet with you. You should also remember that you must avoid some foods, and over-the-counter remedies, like grapefruit and St John’s Wort. It is a good idea to keep a list of everything you are taking, even vitamins, and show it to your hospital doctor.



Guidelines for treating GIST

Teams of doctors have prepared guidelines for the best way of treating GIST. They have looked at all the known evidence from clinical trials. For example, there are the European ESMO guidelines, which are brought up to date as new evidence becomes available. There is also a version of this for use in the UK which takes into account the UK health system and the treatments permitted by NICE*. These Guidelines also recommend the best follow-up regime for patients with different risks of recurrence. See diagram on page 21.

Sometimes, there is no clear answer as to how you should be treated in a particular situation. The way forward should then be a matter for you and your close family to discuss with the oncologist and surgeon looking after you.

You have the right to be referred elsewhere if you are unsure or unhappy with your current physician or treatment.
See <http://www.esmo.org/Guidelines-Practice/Clinical-Practice-Guidelines/Sarcoma-and-GIST>

Compliance

This just means doing what your doctor has told you to do! In other words, take the pills. It is important for your care that you do your very best to remember to take them. If you don't then the tumour cells have a chance to start growing again. If you do miss a dose or two, do tell your doctor. Your care is a joint venture and you do need to have a doctor you trust, and he can only do his best for you if you are honest with him.

* NICE: National Institute for Health Clinical Excellence. This is the government body responsible for deciding which treatments can and cannot be paid for under the NHS in England, Wales and Northern Ireland. In Scotland the Scottish Medical Consortium has this role.

Preparing for your next visit to the oncologist

Make a list of all the medications you use, whether regularly or once in a while. Talk about any drugs and vitamins you take, both from the chemist's and from the supermarket. The best thing is to ask your oncologist or your family doctor what you are allowed to use.

Make written notes of all the questions you want to ask. It is very easy to forget something until you are on the way home. The time with your consultant goes very quickly, but the doctor will be happy to answer your questions.

It's a very good idea to take a family member or a friend with you. They will often remember things from the discussion that you don't.

Questions you might like to ask your oncologist about your treatment:

1. Where is the primary tumour?
2. Are there any metastases (secondary tumours)?
3. Do you know the mutation (Kit exon, PDGFRA exon, Wild-type etc)? (If not, please can I have mutational analysis?)
4. What treatment are you proposing?
5. What are the possible side-effects and risks?
6. What is the chance that the tumour will come back and that there will be metastases?
7. Can I take part in a trial, or are there any new approaches to treatment available?
8. How many GIST patients do you treat?
9. I would like my tissue to be stored in the National GIST Tissue Bank. Are you able to organise this for me?

Life with GIST

Hearing the news that you have a rare cancer, and having to face up to all the treatments and hospital appointments can put a huge strain on the life of a GIST patient. Feelings of panic and fear are almost inevitable. Your family and friends will be scared too. There may well be times when you feel depressed, and this is very understandable. Since it often takes years before a GIST is finally discovered, you may have experienced a long period of unexplained symptoms and the lonely feeling of not being understood.

Talking about your feelings helps. You may find it helpful to tell your story to the hospital oncology nurse, who may refer you to a specialist for counselling. Or you can go to your GP and ask him for support. In any case, do not keep these feelings to yourself, but get help somehow.

There are currently no official regional GIST groups in the UK. GIST Support UK has an online community of GIST patients from all over the UK and further afield. GIST patients and their relatives/carers who sign into our Listserve group often find other patients who live near to them and form useful friendships, sharing experience and supporting one another.

There are other more general cancer support groups available locally. Some towns have Sarcoma groups, and GIST is a sarcoma, so these groups would be open to you. There may be Macmillan Cancer Support facilities near you, or a Maggie's Centre. These provide general information about living with cancer, eating well, and offer complementary therapies which may make you feel better. They also offer a good cup of tea and understanding friendship.

I am a patient and a GP, and even with all the knowledge and resources that come with the profession, nothing came close to the help, information, advice and reassurances I received from the group. The group helped me ask the right questions at the right time, and so helped me steer my management in a positive and beneficial way. I am so grateful to everyone and yourselves for this invaluable group.



Amna GP and GIST SUPPORT Member

Finding other GIST patients

Because GIST is so rare, you are very unlikely to find another GIST patient by chance. You can find out more about GIST by going to our web site **www.gistsupportuk.com**, and if you want to, you can make contact with this group. Then you will be invited to the regular patient support meetings. You will also be invited to join our Listserve email group. This group is only for patients and their carers. You may just want to read the postings from others, or you may want to contribute with your story, or to ask questions about other patients' experiences or your own treatment. How you use the group is up to you. Many patients get huge support from this new group of friends, who really do understand what you are talking about.

About GIST Support UK

GIST Support UK has been a registered charity since 2008 and is run by a team of volunteer Trustees, many of whom are also GIST Cancer patients. **Our primary aim is to offer many kinds of support to patient and carer meetings.**

We provide:

- web sites
www.gistsupportuk.com
www.pawsgistclinic.org.uk
both packed with useful information and contacts
- a phone help line 0300 4000000
for patients and carers
- a private online GIST patient and carer discussion /question and answer group (Listserve)
- two annual regional patients and carer meetings, where you can meet each other and hear about the latest research and developments from the GIST specialists.
- Facebook and Twitter communities giving you the most up to date information on GIST cancer developments and what GIST Support UK is doing to improve services for GIST patients.

We can give you:

- This booklet. “*GIST for Beginners*” is for you and your family. You can also have more copies for hospitals to give to other patients
- A pocket-sized booklet to keep with you called “*I am a GIST Patient*”
- A booklet called “*Eating after GI Surgery for GIST*”
- A leaflet called “*Helps and tips for patients after removal of the stomach*”
- GIST ribbons so that you can recognise other GIST patients at hospital
- Posters raising awareness about GIST for your GP or hospital to display
- Advice about where to find GIST specialists for second opinions
- Information about how to give your tumour tissue to the tumour bank if you are going to have surgery.



We also:

- Represent patients’ interests at NICE appraisals of new treatments
- Represent patients’ interests at national and international meetings
- Work to support an infrastructure that supports research and improves patient care
- Lobby for the rights of rare GIST cancer patients
- Work with the pharmaceutical industry to support research and good patient information about their drugs
- Keep informed about the results of research world-wide.

PAWS-GIST Alliance

GSUK has promoted an alliance of specialist doctors and patients called the PAWS-GIST Alliance. This group concentrates on Paediatric/Adolescent/Wild-type/Syndromic



GIST, raising awareness, raising funds and being a catalyst for research to improve GIST treatments. Working with our clinical lead Dr Ramesh Bulusu we have established a PAWS-GIST clinic at the Addenbrooke's Hospital in the UK to complement the work being done in America and Dublin .

If you are a PAWS-GIST patient please contact Jayne Bressington jayne@pawsgistclinic.org.uk for more information and/or register for one of the clinics to receive the best advice, a personalised treatment plan and also help towards researching for a cure.

FaceBook www.facebook.com/pawsgist,
via Twitter at <http://twitter.com/pawsgist> or
via our website www.pawsgistclinic.org.uk

Funding and fundraising

GSUK is supported by unrestricted educational grants from Novartis and specific grants from Pfizer. These are principally to help finance our twice-yearly patient meetings and the production of information materials for patients. We continue to be very grateful for these grants.

However additional fund-raising is essential for the future of our charity. It allows GSUK to continue its work on behalf of the GIST patient community. In addition to supporting our core operation, it has helped us to undertake further work such as the opening of the PAWS-GIST clinic and the financing of some research.

We are very grateful to patients and other supporters who organise and participate in fund-raising events for us. We have tee-shirts and other items for use at fund-raising events, both for GIST Support UK and for the PAWS-GIST initiative. More information can be obtained from our websites.

www.gistsupportuk.com/fundraising.htm
www.pawsgistclinic.org.uk/donate.htm

Donations can be sent to:

The Treasurer GSUK
15 Somersby Avenue, Walton
Chesterfield, Derbyshire S42 7LY.

Cheques for GSUK funds to be made out to **GIST Support UK**.
Cheques for PAWS-GIST funds to be made out to
GIST Support UK/PAWS-GIST

You can give on line via Just Giving or Virgin Giving, and also on a mobile phone by texting "PAWS01 £xxxxx" to 70070.
See our website for details.

Specialist GIST centres in the UK

There are a number of hospitals in the UK with specialist clinics and physicians for GIST patients. It can be useful to be aware of these facilities and we will happily share details of your nearest specialist hospital on request.

This does not mean that your treatment at other hospitals is not good. However, the specialist hospitals see many more GIST patients than smaller ones, so they may have more up-to-date information. They are also the hospitals where clinical trials take place.

Speakers at recent GSUK Patient Meetings

Oncologists

Dr Charlotte Benson Consultant Oncologist Royal Marsden Hospital

Dr Ramesh Bulusu Consultant Clinical Oncologist, Addenbrookes Hospital

Dr Stephen Falk Consultant Oncologist Bristol Royal Infirmary

Dr Ian Geh Consultant Clinical Oncologist, Queen Elizabeth Hospital, Birmingham

Prof Bass Hassan Professor of Medical Oncology, University of Oxford

Prof Ian Judson Professor of Cancer Pharmacology, The Royal Marsden Hospital

Dr Mike Leahy Consultant Medical Oncologist, Christie Hospital, Manchester

Dr Maria Marples Consultant Oncologist St. James Leeds

Dr Michelle Scurr Consultant Oncologist, The Royal Marsden (Now living in Australia)

Dr Beatrice Seddon Consultant Clinical Oncologist, University College Hospital, London

Dr Mark Verrill Consultant Medical Oncologist, Northern Centre for Cancer Care, Newcastle

Prof Penella Woll Sarcoma Specialist Medical Oncologist, Sheffield

Surgeons

Mr Evangelos Efthimiou Consultant Surgeon, The Royal Marsden Hospital

Mr Long R Jiao Consultant Surgeon, Hammersmith Hospital

Mr Satvinder Mudan Consultant Surgeon, The Royal Marsden Hospital

Mr Simon Toh Consultant Surgeon Portsmouth

Mr Simon Wood Consultant Surgeon, Royal Gwent Hospital

Other experts

Dr Zahir Amin Consultant Radiologist, University College Hospital

Ms Jane Ballantyne Macmillan Benefits Advisor

Dr Dominic Bray Clinical Psychologist, Southport & Aintree Hospitals

Mr Nick Duncan Principal Pharmacist, Queen Elizabeth Hospital Birmingham

Prof Andy Hall Director of the National GIST Tissue Bank Newcastle

Dr David Hughes Consultant Histopathologist, Sheffield Teaching Hospitals

Dr Bill Newman Consultant Clinical Geneticist, Manchester University

Ms Sarah Newton Senior Dietician, The Royal Marsden Hospital

Mrs Cerys Propert-Lewis Clinical Nurse Specialist, The Royal Marsden Hospital

Dr Peter Stephens Clinical Research Associate, Newcastle Cancer Centre

Dr Phillippe Taniere Consultant Histopathologist, Queen Elizabeth Hospital, Birmingham

Mr Roger Wilson CBE Founder of Sarcoma UK and expert patient advocate

Pathology Laboratories with specialists in GIST

Royal Marsden Hospital, London

Bristol Royal Infirmary

Queen Elizabeth Hospital, Birmingham

The Christie Hospital, Manchester

Ninewells Hospital, Dundee

Cardiff Royal Infirmary

Useful Links

Sarcoma UK

An organisation dedicated to support and research on all kinds of sarcoma • www.sarcoma-uk.org

UK Clinical Trials

The NHS site giving details of UK trials

www.nhs.uk/Conditions/Clinical-trials/Pages/Introduction.aspx

Macmillan Cancer Support

Macmillan has many leaflets on all aspects of cancer including information on statutory UK benefits • www.macmillan.org.uk

Pediatric & Wild-Type GIST Clinic USA

www.pediatricgist.org

Maggie's Centres

These provide emotional and practical support for all cancer patients

www.maggiescentres.org

Carney's Triad Group

A site for Carney's Triad patients (in Dutch and English)

www.carneytriad.com/?lang=en

GIST Support International

An independent international US-based patient group. They have a Listserve group and have produced an excellent leaflet on understanding your pathology results. • www.gistsupport.org

SPAEN (Sarcoma PAtients EuroNet)

European organisation for support and advocacy on behalf of sarcoma patients and their carers. GSUK is a member.

www.sarcoma-patients.eu/index.php

Life Raft Group U.S.A.

A US patient group supported by Novartis • www.liferaftgroup.org

Consent for use of tissue samples

I

Date of Birth

Address

.....

Do give my consent for any tissue samples removed from my body at any time during my life or after my death, to be used for research, including genetic research.

Signed

Date

In the presence of a witness, who is not a relative or part of the medical team:

Name

Signature

Address

.....

When you have completed this form and had it witnessed, please ask your oncologist to have it filed with your medical records. It might also be helpful if you were to attach a copy to your Will.



www.gistsupportuk.com

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