Non Functioning Pancreatic Neuroendocrine Tumours (PNETS)

NET Patient Foundation
What are neuroendocrine tumours?

Neuroendocrine tumours (NETs) arise from neuroendocrine cells, also called neurosecretory cells. These are specialised cells, which release hormones and peptides into the bloodstream when required to affect the function of different organs in the body. Neuroendocrine cells can be found in many areas of the body.

Like all cancers, NETs develop when the specialised cells undergo changes causing them to divide uncontrollably and grow into an abnormal tissue mass (tumour).

Neuroendocrine tumours can be benign or malignant. Back in 1907, when neuroendocrine tumours were first classified, they were named ‘carcinoid’ (meaning ‘cancer-like’) as they seemed to grow slowly and were therefore not thought to be truly cancerous. The use of the term ‘carcinoid’ is being phased out, as we know that these tumours can be malignant. Now these cancers are called either simply ‘neuroendocrine tumours’ (or NETs); or tumours found in the GI tract may be called ‘gastrointestinal neuroendocrine tumours’ (or GI NETs).

Another term you may hear is GEP NETs, (gastroenteropancreatic) and this includes all NETs of the gastrointestinal tract, stomach and pancreas.

*For the purpose of this booklet, we will focus only on the malignant type.*
Where do neuroendocrine tumours occur?

Neuroendocrine cells are found in endocrine glands, and also in the mucosa of the lungs and the gastrointestinal tract. It is in these two regions that neuroendocrine tumours usually arise. When neuroendocrine cells are working well, they release a number of hormones, which do various important jobs in the body. For example, in the lungs they regulate the air and blood flow, and in the gastrointestinal tract the cells can help to produce stomach acid, and control blood sugar levels.

Tumours most commonly grow in the areas listed below, but other rarer sites include ovaries, testes, skin, adrenal glands, thyroid and pituitary glands.

Figure 1: Common sites for NET cancers in the gastrointestinal system (digestive system)? (Source CNETS Canada)

This booklet will focus on neuroendocrine tumours which begin in the pancreas – a PNET. For information about other types of NET cancer, please visit our website at www.netpatientfoundation.org
How common are neuroendocrine tumours?

At the moment, we don’t have the data available to tell us exactly how many people are diagnosed with NETs each year in the UK, or how many people are living with the condition. Early data from the UK, Switzerland and Sweden shows that 2 to 3 people per 100,000 are diagnosed with a NET each year. What is known is that the number of people being diagnosed is reported to be rising significantly. The reasons for this increase is unknown, although it is likely to be related to improvements in scanning techniques, and to an increase awareness and understanding of NETs.

The prevalence of NETs (i.e. the number of people living with the condition at any time) is remarkably high. This is due to various factors, including the slow-growing nature of many types of NET cancer, and the availability of an increasing number of successful treatment options.
What are non-functioning pancreatic neuroendocrine cancers (PNETS)?

There are two main groups of neuroendocrine cancers which start in the pancreas (PNETs).

One group is called ‘functioning’ PNETs. These cancers, such as insulinomas and gastrinomas, cause the pancreas to produce abnormal amounts of certain hormones, which produce a ‘syndrome’ or set of symptoms in the patient.

The other group is known as ‘non-functioning’ PNETs. These cancers also begin in the pancreas, and may cause certain hormones and chemicals to be released. However, in these cases, the release of the chemicals does not cause a special set of symptoms in the patient.

We will be looking at non-functioning PNETs in this booklet. For information about functioning PNETs, please see our website. Examples of these are:

- Gastrinomas
- Insulinomas
- Somatostatinomas
- VIPomas
- Glucagonomas
What is known about these cancers?

These are rare NETs but are the most common of the PNETs. They are often discovered between the ages of 40 and 60 but can occur in younger patients.

Quite a high number of patients diagnosed with non-functioning pancreatic NETs (between 60-80%) will also have disease which has spread (metastases), possibly to the liver. However, as cancer cells can spread via the bloodstream and lymphatic system, there can be metastases to other areas of the body such as lymph nodes and bones.

Between 20-40% of patients diagnosed with this condition have a genetically inherited condition called MEN 1. (See the NET Patient Foundation booklet on MEN 1).

Signs of disease

As previously explained, these cancers may not create particular ‘symptoms’ as they develop, and patients only become aware of a problem if and when they have symptoms caused by the growth of a cancer.

These might include:

- Jaundice
- Abdominal pain
- Recurrent pancreatitis (inflammation of the pancreas causing abdominal pain)
- Weight loss
- A type of diarrhoea called ‘steatorrhoea’ that produces light, foul-smelling stools that are difficult to flush
- Bleeding in the gastrointestinal (GI) tract leading to anaemia
- Unexplained tiredness
- General non-specific gastrointestinal symptoms such as loss of appetite or indigestion
How are the cancers diagnosed?

Patients with a non-functioning PNET may not be aware of any symptoms, particularly during the early stages of the disease. This means that they may not go to their GP until quite late in the disease process and which can make investigation and diagnosis difficult. It may not be until a blood test is performed that higher levels of cancer markers and peptides are discovered. This can lead to suspicion that a cancer is present and patients will undergo further tests to ascertain a diagnosis of a PNET.

Many cases are picked up ‘incidentally’, perhaps as a result of tests and scans for another problem. Sometimes patients may complain of pain, possibly as a result of a cancer within the pancreas or there may be pain at other sites if the cancer has already metastasised (spread) to another organ such as the liver.

If a PNET is suspected you can expect to face numerous, regular tests and scans that will provide your doctor with important information about your disease.

**These can include:**

**Biopsy** - this involves taking a piece of tissue from a suspected cancer and having it analysed in the laboratory by a histopathologist.

**Blood tests** - you will be asked to have a fasting gut hormone blood test. This will involve you fasting for six hours before the test. Blood will also be tested for certain tumour markers, particularly chromogranin A and B. The tests will also find out if you have high levels of other hormones and peptides.

**Other biochemical tests may include:**

- Full blood count
- Kidney function tests (urea and electrolytes)
- Liver function tests
- Thyroid function tests
- Pituitary hormone screen e.g. adrenocorticotropic hormone (ACTH), prolactin, growth hormones and cortisol
- Serum calcium, parathyroid hormone levels (in all pancreatic NET patients, as a simple screening test for MEN-1 syndrome)
**Ultrasound scan** - Ultrasound uses high-frequency sound waves to produce images of organs and structures inside the body such as the liver and pancreas. This is an easy scan to perform and it may detect abnormalities in the liver or other organs but other types of scan would also need to be done to confirm the results.

**Endoscopic ultrasound** - Endoscopic ultrasound (EUS) is a technique that uses a special endoscope that has an ultrasound probe attached. Endoscopy refers to the procedure of inserting a long flexible tube via the mouth or the rectum to see the digestive tract. Using the EUS scope, doctors can get a very detailed image of the deeper layers of the GI tract, surrounding lymph nodes, blood vessels, and organs. Biopsies can also be taken at the same time. EUS is performed under sedation in the endoscopy unit.

**CT scan** - A computerised tomography (CT) scan provides a three-dimensional picture of the inside of the body. It can be used to determine the position and size of the cancers, and regular scans are useful to find out more about the rate of cancer growth and how your cancer is responding to treatment. When you arrive at the clinic you will probably be asked to drink a litre of fluid that contains a contrast agent that helps to highlight cancers, and you may also have a cannula inserted in your arm, through which a special contrast dye is administered during the scan. These both help your specialists to ‘read’ the scans more clearly as the cancers are highlighted.

**MRI scan** - Magnetic resonance imaging (MRI) scans can help reveal where cancers are positioned. They use magnetism rather than X-rays to take pictures of inside the body. Scans can take up to one hour to complete and you have to lie very still inside the scanner lying on a couch. These scans are often used in addition to CT scans.

**Octreotide scan** (Octreoscan) - This is a common scan for NET patients. It can help to detect cancers that might be not be seen on other conventional scans. Some non-functioning pancreatic NETs have special receptors on their surfaces called somatostatin receptors. Octreotide is a somatostatin analogue, a substance that mimics the action of naturally occurring somatostatin. When octreotide is combined with a mildly radioactive agent and then injected via a vein in the arm, it sticks to somatostatin receptors on the cancer surface and the cancers ‘light up’ on the screen as hot spots. This is a useful test to find out more about your cancer, where the tumours are positioned, and also whether you would be suitable for certain treatments known as peptide receptor radionuclide therapy (PRRT).

**Positron emission tomography (PET) and/or PET CT**

Standard fluorodeoxyglucose (FDG) PET imaging is not good at detecting non-functioning pancreatic NETs. Researchers are currently working on new types of radiotracers that are effective in detecting these tumours.
Treatment
The decision about treatment is determined by your own particular disease and needs, so the treatments described below provide an outline of possible options but your specialist will discuss your own individual treatment plan with you before you start treatment.

Patients should ideally be treated within a specialist multidisciplinary team (MDT). Each patient will have an individualised treatment plan: there are a number of options available, depending on the type and location of the tumour, and the general well-being of the patient.

Surgery
If the tumour is contained in one area (localised), or if there has been only limited spread, surgery is usually the first choice of treatment. If it is possible to remove the tumour completely, no other treatment may be necessary.

If the tumour has spread to other parts of the body (metastasised), surgery may still be possible to remove the part of the tumour that is producing too many hormones. This is often referred to as tumour debulking.

Curative surgery – This is when the cancer has not spread outside the organ or area where it first started. If the tumour can be removed whole and intact with a surrounding margin of clear, healthy tissue then the surgery is potentially curative and no other treatment may be necessary. A follow-up plan will need to be put into place after surgery.

Palliative surgery – When the tumour or tumours have already spread or become too large to remove completely, then surgery may be considered. If the tumours are causing symptoms by pressing on other organs or by releasing hormones then surgery maybe performed to reduce the symptoms by removing or bypassing the part of the disease that is causing the problems.

Pre-emptive surgery – This is when we can see that an area of tumour is critically placed close to an important structure such as a blood vessel or the bile duct or bowel. Even if we can’t cure the disease by removing it all we can prevent future problems by removing disease from key areas, before the vital structure has been damaged or blocked.

Cyto-reductive surgery – All of the many medical treatments (e.g. chemotherapy) for NET cancers aim to reduce symptoms and prolong survival by cyto reduction. This means reducing the number of living tumour cells inside the patient. Operations can also be used to achieve this when the disease has already spread, by surgically removing bulky areas of tumour to reduce the total number of cancer cells inside the patient. Cyto-reduction often involves other treatments used in combination with surgery.
Somatostatin analogue injections

Somatostatin analogues are man-made drugs that copy the role of natural somatostatin that is found in the body. In our bodies somatostatin is a protein made by:

1. A gland in the brain (hypothalamus)
2. The stomach
3. The pancreas
4. The bowel

Somatostatin does several things:

1. It slows down hormone production, including many of the gut hormones
2. It slows down the emptying of the stomach and bowel
3. It controls the release of hormones made by the pancreas, including insulin
4. It slows down or stops the release of growth hormones

There are at present two forms of these somatostatin analogue that are given in an injection form. 1-Sandostatin LAR and 2-Lanreotide Autogel. These medications are predominately used to control symptoms that are caused by too many hormones circulating in the blood stream, but they may help to stabilise the tumour or even reduce tumour growth. They are usually administered monthly (every 28 days) usually by a health professional and are available in different dosages.

**Sandosatain LAR** - 10mg, 20mg, 30mg

**Somatuline Autogel** - 60mg, 90mg, 120mg, and this can be self administered.

New somatostatin analogues such as pasireteotide are currently in clinical trials to determine their role in treating syndromes from neuroendocrine tumours and/or for antitumour effects.

Chemotherapy

This is a drug treatment which acts by attacking the cancer cells and trying to shrink the tumour. There are various types of drugs which may be used according to the type of tumour you have, and how aggressive this is. Chemotherapy can either be given intravenously (through a drip) or in tablet form which you can take at home. Once your specialist has decided the most appropriate treatment for you, you will be given detailed information.

**The most commonly used chemotherapy agents used are:**

- 5-fluorouracil (5-FU) used in combination with streptozotocin
- Cisplatin in combination with etoposide
- Temozolomide
- Embolisation or chemo-embolisation for liver metasatases

All cells require an adequate blood supply to survive. The human liver has two main
sources of blood: the portal vein and hepatic artery. The portal vein supplies blood to most liver cells while tumour cells mostly depend on the hepatic artery for their blood supply. A hepatic embolisation is a non-surgical procedure which involves the blockage of selective branches of the hepatic artery that supply tumour cells with blood. This blockage is made possible by the injection of embolic particles (specialised particles that cause a blockage) which travel to and cut off tumour blood supply. There are two types of embolisation of the hepatic arteries: 1) embolisation – the injection of just embolic particles, and 2) chemoembolisation – the injection of embolic particles and chemotherapy.

Individuals with liver metastases may be considered candidates for hepatic embolisation or hepatic chemoembolisation if they have non-resectable liver metastases, uncontrolled growth of liver metastases and/or uncontrolled symptoms.

These procedures are carried out by a specialist radiologist.

You will need to be admitted into hospital for this treatment.

**Peptide Receptor Radionuclide Therapy (PRRT)**

This is a special treatment that uses radioactive substances to target tumour cells. It is like a localised radiotherapy inside your body.

PRRT combines octreotide with a radionuclide (a radioactive substance) to form highly specialised molecules called radiolabeled somatostatin analogues or radiopeptides. These radiopeptides can be injected into a patient and will travel throughout the body binding to tumour cells that have receptors for them. Once bound, these radiopeptides emit radiation and kill the tumour cells they are bound to.

In PRRT for neuroendocrine cancers, the radionuclides commonly used are indium-111, lutetium-177 and yttrium-90.

You will need to be admitted into hospital for this treatment.

**Sunitinib and Everolimus**

These are two new drugs which have recently been shown to be beneficial for patients with certain types of PNETs. These drugs are given in tablet form. They are not chemotherapy and they work by disrupting the blood supply to the tumour with the aim to slow down the tumour growth and sometimes even tumour shrinkage. Your consultant will advise whether these drugs may be suitable for you.

**Drug Trials**

Research is carried out to try to improve understanding of the management of neuroendocrine tumours and to improve treatments. This involves research both in the laboratory (on blood and samples of tumour) and also in the clinic. Your consultant will discuss this with you and you may be invited to participate in a clinical trial of a new drug therapy.
You have the right to know as much about your own prognosis as you wish and you have the right to know the overall treatment strategy, including what options are available to you if initial treatments do not work to stabilise your disease.

You have the right to make decisions for yourself, even if the decision is against medical treatment or the decision is to end medical treatment.

You can find out more about current trials at:

**Current Controlled Trials**
This website allows users to search, register and share information about randomised controlled trials. Covers multiple registers, including England, Scotland and the US.

http://www.controlled-trials.com/

**ClinicalTrials.gov**
This is a register of federally and privately supported clinical trials conducted in the United States and around the world.

clinicaltrials.gov

You can also search for research trials available to patients in the UK and Europe on these websites:

www.macmillan.org.uk

www.cancerhelp.org.uk

www.ctu.mrc.ac.uk (The Medical Research Council Clinical Trials Unit)

www.ncrn.org.uk (National Cancer Research Network)

www.eortc.be/ (European Organisation for Research and Treatment of Cancer)
Further support

NET Patient Foundation
From diagnosis, throughout treatment and beyond, our services are here every step of the way. Here is an overview of all the services we offer to people living with and beyond NET cancer.

Helpline – 0800 434 6476
Our free, confidential helpline is here for anyone who has questions about NET cancers (neuroendocrine tumours). Your call will be answered by one of our nurses or trained staff members with experience of NET cancer. Whatever your concern, you can be confident we will understand the issues you might be facing, and that the information you receive is clear and up-to-date. We will also let you know where else you can go for further support. The helpline is open 10am-2pm Monday to Friday. We also operate a call-back service for those who wish to leave a message out of hours.

Website - www.netpatientfoundation.org
We know how important it is to understand as much as possible about your NET cancer. Our website is here round-the-clock giving you instant access to information when you need it. As well as clinical information, you’ll find real life experiences and access to the largest online NET cancer community in the UK, so you can share your questions or concerns with other people in a similar situation.

Discussion forums
Through our discussion forums you can exchange tips on coping with the side effects of treatment, ask questions, share experiences and talk through concerns online. Our dedicated areas for popular topics should make it easy for you to find the information you’re looking for. The discussion forums are easy-to-use. If you’re feeling anxious or just need to hear from someone else who’s been there, they offer a way to gain support and reassurance from others in a similar situation to you.

Ask the nurse
If you find it difficult to talk about your cancer, we can answer your questions by email instead. Our ‘ask the nurse’ service is available on the website - complete a short form that includes your question and we’ll get back to you with a confidential, personal response.

Information and support sessions
We run information and support sessions for people living with NET cancer. These meetings include talks from some of the country’s top NET specialists, invaluable Question & Answer sessions, as well as an opportunity to meet other NET patients. For information about meetings in your area, please see our website or call our helpline.
Information resources
Our free information resources are for anyone affected by NET cancer. They are here to answer your questions, help you make informed decisions and ensure you know what to expect. All of our information is written and reviewed regularly by healthcare professionals and people affected by NET cancer, so you can trust the information is up-to-date, clear and accurate. You can order our publications by sending us an email or calling the helpline. All our publications can also be downloaded from our website.

Other organisations

Macmillan Cancer Support
89 Albert Embankment London SE1 7UQ
General enquiries: 020 7840 7840
Helpline: 0808 808 0000
Website: www.macmillan.org.uk
Textphone: 0808 808 0121 or Text Relay
Macmillan Cancer Support provides practical, medical, emotional and financial support to people living with cancer and their carers and families. Over the phone, its cancer support specialists can answer questions about cancer types and treatments, provide practical and financial support to help people live with cancer, and are there if someone just wants to talk. Its website features expert, high-quality information on cancer types and treatments, emotional, financial and practical help, and an online community where people can share information and support. Macmillan also funds expert health and social care professionals such as nurses, doctors and benefits advisers.

The Foundation has the following aims:

- To provide accurate and up-to-date information for people living with, or affected by, NET cancers
- To provide support for patients and others affected by NET cancers
- To provide education for healthcare professionals in the treatment and care of NET patients
- To raise awareness of NET cancers within the medical community, and amongst the general public
- To improve access to care for NET patients
- To raise funds, which will help to support research around the UK & Ireland

Did you know?
- 50% of patients are diagnosed when the cancer has already spread
- Early diagnosis significantly improves outcomes for patients
- Help us to make a difference. Donate now at www.netpatientfoundation.org

Why the moth?
We have chosen the moth as our logo to symbolise this ‘camouflaged’ condition. We aim to encourage medical professionals to consider an uncommon alternative when symptoms persist (i.e. a NET rather than IBS).

“When you see an insect beating its brightly patterned wings against your window, don’t assume it’s a butterfly. It could be a moth.”
About Us

The NET Patient Foundation incorporating Living with Carcinoid was formed at the start of 2006 and has Charity Commission status. The collaboration with Living with Carcinoid meant that the charity could spread its wings to include patients with all types of neuroendocrine tumour.

The Foundation has 5 main aims:

1. To provide accurate and up-to-date information for people living with, or affected by, neuroendocrine tumours. We do this through information and forums provided on the website (and links to other sources of information on the web).

2. To provide support for patients and others affected by neuroendocrine tumours. We offer a support line which is manned by an experienced healthcare professional; and organise patient support groups around the UK and Ireland.

3. To improve the quality of life for patients and their families. We can do this by providing support and information about services and treatments available, as well as by funding and publicising research and existing medical initiatives.

4. To raise funds, which will help to support research around the UK.

5. To raise awareness of neuroendocrine tumours throughout the UK and Ireland, within the medical community and the general public.

There is much campaigning work to be done. We don’t have the funding that breast or bowel cancer attracts, but our patients deserve exactly the same attention and research support.

IF you found this booklet useful and would like to make a donation to the NET Patient Foundation, please contact us.
Edited by:
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NET Patient Foundation