Non-Functioning Pancreatic Neuroendocrine Tumours

NET Patient Foundation
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This booklet is intended to provide patients and their carers with information relating to the diagnosis, treatment and management of non-functioning pancreatic neuroendocrine tumours. A glossary of terms has been provided at the back of the booklet to provide additional information and explanation of some of the terms used.

What are Neuroendocrine Tumours?

Neuroendocrine Tumours (NETs) are relatively uncommon, usually slow growing cancers. You may hear them referred to as GEP NETs, because they often arise in the cells of the stomach (gastro), intestines (entero) and the pancreas (pancreatic). There are a number of different types of NET. These are examples of the more common NETs:

- Carcinoids
- Functioning and Non-Functioning Pancreatic Tumours
- Multiple Endocrine Neoplasias
- Gastrinomas
- Insulinomas
- Glucagonomas
- Phaeochromocytomas
- Vipomas
- Goblet Cell Carcinoids
What is Cancer?

The body is made up of hundreds of millions of living cells. Normal body cells grow, divide, and die in an orderly way. During the early years of a person’s life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out, damaged, or dying cells.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of this out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells keep on growing and form new cancer cells. These cancer cells can grow into (invade) other tissues, something that normal cells cannot do. Being able to grow out of control and invade other tissues is what makes a cell a cancer cell.

In most cases the cancer cells form a tumour. But some cancers, like leukaemia, rarely form tumours. Instead, these cancer cells are in the blood and bone marrow. Tumours can be benign or malignant. In this booklet ‘tumour’ refers to a malignant non-functioning pancreatic neuroendocrine cancer.

When cancer cells get into the bloodstream or lymph vessels, they can travel to other parts of the body. There they begin to grow and form new tumours that replace normal tissue. This process is called metastasis.

No matter where a cancer may spread, it is always named for the place where it started. For instance, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is called metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their own kind of cancer.
What are Non-Functioning Pancreatic Neuroendocrine Tumours?

These are cancers (tumours) that may secrete certain hormones and peptides, but the release of these chemicals do not cause an identifiable ‘syndrome’ or collection of symptoms. It may not be until a blood test is performed that elevated levels of tumour markers and peptides are discovered. This can lead to suspicion that a tumour is present and patients will undergo further tests to ascertain a diagnosis.

Patients with a non-functioning NET may not be aware of any symptoms, particularly during the early stages of the disease. This means that they may not be aware of their illness or go to their doctor until quite late in the disease process. It explains why many cases are picked up ‘incidentally’, perhaps as a result of tests and scans for another problem. Sometimes patients may experience pain, possibly as a result of a tumour within the pancreas or there may be pain at other sites if the tumour has already metastasised (spread) to another organ such as the liver.

What is known about these tumours?

Non-functioning pancreatic neuroendocrine tumours are the more common type of pancreatic NET, however they are still rare even amongst NET cancers. They are often discovered between the ages of 40 and 60 and are usually slow growing. However they have the capacity to ‘change’ and become more aggressive, or sometimes to start producing hormones that create noticeable symptoms.

Quite a high proportion of patients diagnosed with non-functioning pancreatic NETs (between 60 - 80%) will also have disease spread (metastases), possibly to the liver. However, as tumour 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. (Visit www.amend.org.uk for more information on MEN 1).
**Signs of disease**

As explained, these tumours do not create a particular set of symptoms as they develop, unlike other pancreatic NET cancers that are described as ‘functioning’. These functioning tumours are so named because they produce large levels of identifiable hormones that cause a recognisable syndrome, or collection of symptoms.

Patients with non-functioning pancreatic NETs are often first alerted to disease because of symptoms caused by the growth of their tumours. These symptoms may 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 gastro-intestinal symptoms such as loss of appetite or indigestion
How are the tumours diagnosed?

If a non-functioning pancreatic neuroendocrine tumour 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 tumour 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 prior to the test. Blood will be tested for certain tumour markers, particularly chromogranin A and B (nearly all NETs express abnormally high levels of chromogranin A). The tests will also find out if you have high levels of other hormones and peptides (Pancreatic Polypeptide, Gastrin, Vaso Intestinal Peptide, Neurotensin, Somatostatin and Glucagon).

Chromogranin A is a useful marker: doctors will be interested in seeing the trend over a period of time to see whether the levels are rising or falling. Other blood tests will look at the functioning of your liver and kidneys and other organs such as the thyroid. A full blood count will provide information on various components in the blood such as red and white cells, and platelets.

**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.

**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 obtain 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 tumours, and regular scans are useful to find out more about the rate of tumour growth and how your tumour is responding to treatment. When you arrive at the clinic you will probably be asked to drink a litre of fluid containing a contrast agent that helps to highlight tumours, and you may also have a cannula inserted through which a special contrast dye is administered during the scan. These both help your specialists to ‘read’ the scans more clearly as the tumours are highlighted.

MRI scan - Magnetic resonance imaging (MRI) scans can help reveal where tumours are positioned. It uses 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 - this is a common scan for NET patients. It can help to detect tumours that might be not be seen on other conventional scans. A high proportion (but not all) of 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 tumour surface and the tumours ‘light up’ on the screen as hot spots. This is a useful test to find out more about your tumours, where they are positioned, and also whether you would be suitable for certain treatments that use octreotide or another chemical called lanreotide as a ‘carrier agent’.

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 novel types of radiotracers that are effective in detecting these tumours.

Urine tests (5HIAA)
You may hear that some NET patients have regular urine tests. In the case of non-functioning pancreatic NETs this test is not useful as the hormones expressed are not revealed through the urine test known as 5HIAA.
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 prior to starting treatment.

Somatostatin analogue injections

Daily, fortnightly or monthly injections of somatostatin analogues are available, which may help to control the growth of the tumours. Somatostatin analogues are synthetic versions of somatostatin, a naturally occurring hormone produced in the brain and digestive tract that inhibits the release of several other hormones and chemicals from our internal organs.

Surgery

There are many different types of surgical procedures which can be carried out when treating this type of tumour. The surgeon will base their decision on many factors such as the size and site of the tumour, the intent of treatment (whether it is to try to cure the cancer, or improve symptoms and quality of life) and also on the medical condition of the patient. Once the surgeon has made the decision about the appropriate operation they will provide detailed information.

For more information on any of these treatments, or those listed on the facing page, please contact us at the NET Patient Foundation.
What if the tumour has spread?

If the tumour has spread from the original site then it is not possible to cure the disease and treatment is aimed at controlling the tumour and improving any symptoms. The following treatments are often used:

**Liver resection** - if the tumour is present in a limited area it is sometimes possible to remove part of the liver to try to control symptoms. The remaining normal liver gradually grows back to replace the portion that has been removed.

**Liver ablation** - this means treating the liver with specific methods that directly treat tumours in the liver. There are several methods available and if your consultant feels that this is suitable for you they will discuss the specific treatment and provide written information.

**Embolisation or chemo-embolisation** - this is carried out by a specialist radiologist. The aim is to block the blood supply to the part of the liver containing tumour; This cuts off the oxygen and nutrient supply, and the tumour may stop growing or even shrink for a period of time.

**Radionuclide targeted therapy** - Also called peptide receptor radionuclide therapy (PRRT) or hormone-delivered radiotherapy. This treatment involves a similar strategy as that applied in an octreotide scan, but the dose of radiation is high enough to stabilise the tumour and potentially to shrink the tumour. Radioactive substances are chemically combined with hormones that are known to accumulate in a NET. This combination is injected into the patient: the hormones will enter the tumour, and the attached radiation will kill the tumour cells. The benefits of this treatment are the ability to deliver radiotherapy directly to the cancer tissue with minimal damage to normal tissue and it is extremely well tolerated with only minor side effects for the majority of patients.

There are a number of different radioactive agents available.

**Chemotherapy** - this is a drug treatment which acts by attacking the tumour 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 upon the most appropriate treatment for you, you will be given more detailed information.

**Interferon** - this drug can stimulate the body’s immune system to fight cancer cells. It is given by injection three times a week. As with all drugs, there are potential side effects and if your specialist recommends treatment with interferon you will be given further information.
What if the disease has spread to the bones?

If there is tumour in the bone, patients may experience pain and external radiation therapy may be considered as a therapy for this. Radiotherapy or orthopaedic surgery may also be considered if there is involvement in a weight-bearing bone such as the femur (thigh bone) in order to stabilise the bone and prevent fractures.

New anti-cancer drugs

Sunitinib and everolimus are two drugs which have recently been shown to be beneficial for patients with certain types of pancreatic neuroendocrine tumours. These drugs are given in tablet form. They work by interfering with the development of blood vessels to the tumour and they also disrupt the ability of the tumour cells to grow. 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.
Glossary of terms

**Cannula** - a thin tube inserted into a vein or body cavity to administer medicine, drain off fluid, or insert a surgical instrument.

**Endocrine system** - the system in your body that produces hormones

**Endocrinologist** - a doctor who specialises in treating patients with illnesses caused by the system that produces hormones

**Fasting gut hormones** - a blood test taken when you have had nothing to eat or drink for 6 hours

**Gastroenterologist** - a doctor who specialises in treating patients with illnesses which affect the gastrointestinal tract

**Gastrointestinal tract** - the stomach and intestines (gut)

**Genetic** - inherited, or passed down, from parents

**GEP NETS** - gastroenteropancreatic (stomach, gut and pancreas) neuroendocrine tumours

**Histopathologist** - histopathologists are medical specialists who work to analyse human tissue in order to diagnose diseases

**Hormone** - a chemical messenger which travels in the blood stream and helps to control bodily functions

**Metastases** - the spread of tumour cells to another part of the body

**Oncologist** - a doctor who specializes in the treatment of cancer. They may be a Clinical Oncologist (who can give radiotherapy) or a Medical Oncologist (who provides drug therapy)

**Pancreas** - a gland which lies behind the stomach and produces hormones and enzymes which help to maintain functioning of the human body

**Radioisotope** - a way of giving a small amount (for diagnosis) or larger amount (for treatment) of a radioactive drug by injection

**Somatostatin** - a substance produced naturally in many parts of the body which can stop the over-production of certain hormones

**Somatostatin analogue** - drugs such as lanreotide and octreotide which may have an anti-tumour effect

**Specialist nurse** - a nurse with expertise in the treatment and management of a particular type of condition

**Tumour** - an abnormal growth or swelling on, or in, the body. In this booklet, ‘tumour’ refers to cancerous growth
Multidisciplinary teams

The care of NET cancers can be complex, and for the patient the journey can encompass not only a whole host of emotions, but also a whole range of investigations, treatments and healthcare professionals. The very fact that there is often not just one treatment option at diagnosis and throughout the patient journey, means that there has to be a collaboration among all key healthcare professional groups, who are making clinical decisions for individual patients.

This collaboration has been termed an MDT (multidisciplinary team). This is a formula that is now being used across the world in the care of cancer patients.

An MDT will usually be formed by a particular specialist with expertise and interest in NET cancers and other adrenal tumours. This specialist is commonly an endocrinologist or oncologist.

A patient may see some or all of the following people:

- Oncologist
- Surgeon
- Endocrinologist
- Radiology staff
- Dietitian
- Nurse Specialist
- Palliative Care Team
- Pain Team
- General Practitioner/Practice Nurse
- Counselling Staff
- Various Technicians
- Clinic Staff
- Hospital Staff
- Hospice Team

Patients can feel more confident in the knowledge that all aspects of their care have been discussed and that the best possible treatment plan will be formulated. A well coordinated and disciplined MDT is a very important aspect for care when striving to achieve the best quality of life and the best outcome for NET cancer patients.
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)
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NET Patient Foundation

The NET Patient Foundation supports people diagnosed with
euroendocrine tumours and their families.

For further information and to make contact telephone 0800 434 6476
or visit our website:
www.netpatientfoundation.com

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