

Information for people affected by High-Grade Neuroendocrine Carcinomas

The NET Patient Foundation:
supporting the neuroendocrine cancer community.

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

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**Proud to be part of the International Neuroendocrine
Cancer Community (INCA)**

www.netcancerday.org

What are neuroendocrine tumours (NETs)?

Neuroendocrine tumours (NETs) are a complex group of tumours that develop predominantly in the digestive or respiratory tracts, but can occur in many areas of the body. These tumours arise from cells called neuroendocrine cells.

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 in medical literature, as we now know that these tumours can be malignant. Current terminology is either simply neuroendocrine tumours (or NETs) or your NET will be named dependent on the site of your primary tumour, for example a bronchial (lung) NET, a bowel NET or a pancreatic NET.

What are neuroendocrine carcinomas?

High-grade neuroendocrine carcinomas are a faster growing and more aggressive type of NET.

Unlike some other types of NET, high-grade neuroendocrine carcinomas are always malignant and metastatic (i.e can spread to other organs in the body).

A high grade NET may be described as a neuroendocrine carcinoma (NEC).

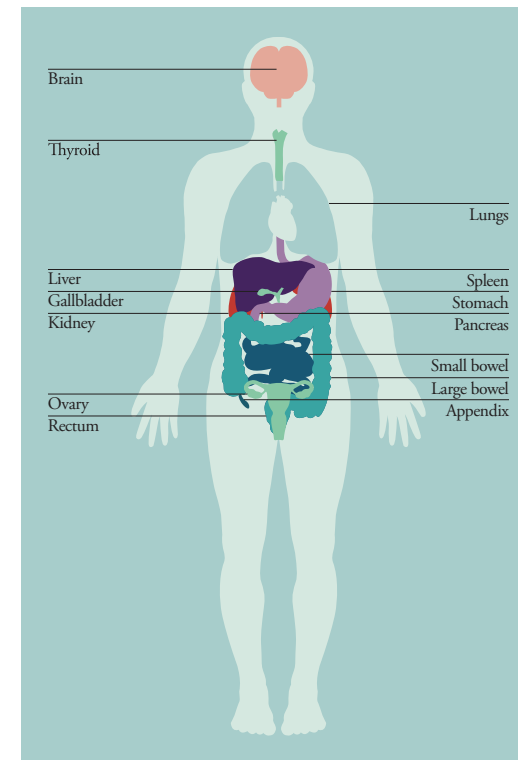
Neuroendocrine tumours and carcinomas are classified using four terms:

- stage
- differentiation
- functionality
- grade

Where do neuroendocrine tumours or carcinomas occur?

For information about other types of NETs, please visit our website at www.netpatientfoundation.org

Examples of where NETs can occur as primary sites or as metastases (spread)



High-Grade Neuroendocrine Carcinomas

The World Health Organisation (WHO) classification scheme puts neuroendocrine tumours into three categories:

- Well-differentiated neuroendocrine tumours, further subdivided into tumours with benign and those with uncertain behaviours
- Well-differentiated (low grade) neuroendocrine tumours with low-grade malignant behaviour
- Poorly-differentiated (high grade) neuroendocrine carcinomas

It is to this last group that neuroendocrine carcinomas belong. They arise most commonly in the intestine, lung and pancreas, but can also occur in other parts of the body.

Stage: the extent of disease

Stage is a measure of how far a tumour has spread. Health organisations around the world use slightly different classification systems for NET staging. The WHO classification uses 4 stages (I through IV), with a higher number indicating more widespread disease.

The following example shows the stage descriptions for a NET of the small intestine:

- **Stage I** tumour is less than 1 cm in size and has not spread to the lymph nodes or other parts of the body.
- **Stage II** tumour is greater than 1 cm in size and has started to spread beyond the original location, but has not spread to the lymph nodes or other parts of the body.
- **Stage III** is any size tumour that has spread to nearby areas of the body and also to one lymph node.
- **Stage IV** is any size tumour that has spread to one or more lymph nodes and has also spread to other, more distant areas of the body (for example, to the liver).

Please note that the stage descriptions may also vary depending on the type of NET you have. For example, stages for a NET of the lung can differ from stages for a NET of the pancreas.

The European Neuroendocrine Tumour Society (ENETS) have recently proposed a new classification called the TNM staging.

- T - primary tumour (this is split into 5 main areas: stomach, small intestine, pancreas, appendix and colon/rectum)
- N - disease in the lymph nodes
- M - metastatic spread

They also proposed looking at the speed in which the tumours are growing.

These different ways of staging NETs are used in conjunction with one another in order to gain a full picture.

Differentiation: what NET cells look like

Differentiation is the word used to describe a NET or other cancer in terms of how it looks under a microscope. This includes how different the NET cells look compared to the healthy cells around it.

A NET can be described as being “well-differentiated”, meaning it looks similar to surrounding tissue.

Well-differentiated NETs are considered to be either grade 1 or grade 2. These NETs may be called “low grade” or “intermediate grade.” A “poorly differentiated” neuroendocrine carcinoma means that the cells look very abnormal - that is, very different to the surrounding tissue.

These neuroendocrine carcinomas are faster growing and are categorised as grade 3, or “high grade”.

High-Grade Neuroendocrine Carcinomas

(continued)

Grade

The “grade” of a NET is an estimation of how fast the cells are dividing to form new cells. The grade of a NET is related to its differentiation. There are several systems for grading NETs, including a new WHO system introduced in 2010, which is shown here.

Grade	Differentiation
NET Grade 1	Well-differentiated tumour with a low number of cells actively dividing
NET Grade 2	Well-differentiated tumour, but with a higher number of cells actively dividing
Neuroendocrine carcinoma Grade 3	Poorly differentiated, malignant carcinoma (most aggressive form of NET)

By using information about stage, differentiation, and grade together, your doctor can decide how best to manage your NET.

Although your doctor may not talk about grade and differentiation with you, he or she may talk about how serious or aggressive your NET is, which refers to how quickly or how much it may grow or spread. Be sure to ask questions if you are unsure about something or want to better understand your disease.

Treatments

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.

The treatment you get is more likely to be a chemotherapy based treatment as chemotherapy is known to act well on faster growing cells.

There are however other treatment options now available.

The decision about treatment is determined by your own particular disease and needs, so the options described below provide an outline of possible treatments, but your specialist will discuss your own individual plan with you.

Decisions about treatment will depend on:

- Where the neuroendocrine carcinoma has spread to
- Speed of cell growth
- Results of other diagnostic tests
- General health
- Quality of life
- Your feelings towards your treatment options

The initial goal maybe to stabilise the disease.

To accomplish the treatment goal, it is important for the doctor to consider each individual’s health and treatment history.

Treatment *(continued)*

Surgery

If the carcinoma 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 carcinoma completely, no other treatment may be necessary.

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

Palliative surgery

When the carcinomas have already spread or become too large to remove completely, then surgery may be considered. If the carcinomas are causing symptoms by pressing on other organs or by releasing hormones then surgery may be 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 an area of carcinoma is critically placed close to an important structure such as a blood vessel or the bile duct or bowel. Even if the disease cannot be cured, removing the tumour may prevent problems in the future by removing disease from key areas before the vital structure has been damaged or blocked.

Cyto-reductive surgery

All of the many medical treatments for NET cancers aim to reduce symptoms and prolong survival by cyto reduction.

This means reducing the number of living carcinoma cells inside the patient. Operations can also be used to achieve this when the disease has already spread, by surgically removing bulky areas of disease to reduce the total number of cells inside the patient. Cyto-reduction often involves other treatments used in combination with surgery.

Chemotherapy

This is a drug treatment which acts by attacking the cells and trying to shrink the carcinoma.

There are various types of drugs which may be used according to the type of carcinoma 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.

For high-grade NETs, combined chemotherapy treatments are likely to be used.

For example:

- Cisplatin + etoposide
- Carboplatin + etoposide
- Temozolomide + capecitabine
- Temozolomide + bevacizumab

For neuroendocrine carcinomas of the lung, available chemotherapy regimens include combination of 5-FU and Interferon A, streptozotocin-based combinations, the etoposide–cisplatin regimen or chemotherapy combining cyclophosphamide, doxorubicin and vincristine.

Somatostatin Analogues

Daily or monthly injections of somatostatin analogues are available to control some of the unpleasant symptoms caused by the carcinomas. 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.

Injections of these analogues can stop the overproduction of hormones that cause symptoms such as flushing and diarrhoea.

Targeted Peptide Receptor Radionuclide Therapy PRRT

These treatments are sometimes referred to as 'magic bullet' therapies. The treatments are based on using different radiolabelled peptides which target receptors on the carcinoma surface. In PRRT for neuroendocrine carcinomas, the radionuclides commonly used are indium - 111, lutetium-177 and yttrium-90. The basis for which treatment is suitable for which patient is the diagnostic tracer imaging. To decide whether this therapy is suitable, you will be asked to take an Octreotide, PET or MIBG scan as described in the diagnosis section. The results of these scans will indicate whether or not you have the correct receptors present and whether this sort of therapy would be an option.

Treatment *(continued)*

SIRT

SIRT stands for Selective Internal Radiation Therapy. It is a new way of using radiotherapy to treat liver metastases which cannot be removed with surgery.

The doctor inserts a thin tube called a catheter into the hepatic artery. This is the main artery which supplies blood to the liver. They then send tiny beads called microspheres down the catheter and these get stuck in the small blood vessels around the carcinoma. The microspheres contain a radioactive substance which give a dose of radiation to the carcinoma. The microspheres are also called SIR-spheres and the radioactive substance is called yttrium 90.

Embolisation

If the carcinoma has spread to the liver, you may be offered hepatic artery embolisation (HAE). In this procedure, a catheter is placed in the groin and then threaded up to the hepatic artery that supplies blood to the carcinomas in the liver. Tiny particles called embospheres (or microspheres) are injected through the catheter into the artery.

These particles swell and block the blood supply to the carcinoma, which can cause the carcinoma to shrink or even die. This treatment can also be combined with systemic treatments in some patients where the carcinoma has spread. It is a procedure that would be carried out by a specialist called an interventional radiologist. The patient would be sedated for the treatment.

Sometimes this embolisation process is combined with chemotherapy (called HACE (Hepatic Artery Chemoembolisation) or TACE (Transcatheter Arterial Chemoembolisation) or radiotherapy (RMT or SIRT).

Sutent (Sunitinib)

Sutent is a medication that comes in capsule form. It is mainly used in patients with pancreatic neuroendocrine tumours.

It works mainly by blocking a process called angiogenesis. Angiogenesis is the process of making new blood vessels.

Tumours need a good blood supply to grow and Sutent helps stop that process. The drug comes under an umbrella group of drugs known as tyrosine kinase inhibitors.

Affinitor (Everolimus)

Affinitor is another medication for patients with pancreatic neuroendocrine carcinomas.

It also comes in a capsule form and is a type of drug that interferes with the process of new cancer growth. The drug comes under an umbrella group of drugs known as mTOR inhibitors.

Clinical trials are running to look at the effectiveness of this medication in other NET types either alone or in combination with other NET medications.

Clinical Trials

Clinical trials are medical research trials involving patients. They are carried out to try to find new and better treatments.

Carrying out clinical trials is the only sure way to find out if a new approach to cancer care is better than the standard treatments currently available.

You can find out more about current NET trials at: www.netpatientfoundation.org/category/patient-resources/research/

Follow up

The follow-up intervals are highly variable depending on the clinical situation, functionality (whether any syndrome is present), stage, grade and time since diagnosis.

Multidisciplinary teams

The care of NETs 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 between 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 NETs and other adrenal tumours. This specialist is commonly an endocrinologist or oncologist.

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

Gastroenterologist
Oncologist
Surgeon
Endocrinologist
Cardiologist
Radiology staff
Nuclear medicine physician
Dietician
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 patients.

Being diagnosed with cancer can be a confusing and frightening time for you and your loved ones. Although your healthcare team will do their best to support you, medical appointments can be stressful and it is worthwhile to be reminded of ways to get the most out of each appointment.

A few things to keep in mind:

- The most important member of the healthcare team is YOU
- YOU know more about YOU than anyone else does
- Your doctor can help you more if you are an active partner in your treatment
- If you are dissatisfied with the care that you receive, and discussion with your doctor does not resolve the situation, you can ask for a second opinion - how you feel about the care you receive is the most important thing.

Tips:

Bring a trusted friend or family member with you to the appointment if you can. If you are feeling anxious, you may not hear everything that's said, or ask all the questions you wanted to. It helps to have additional ears there to listen, and your guest may help to make sure your concerns are brought up. Try to get into the practice of taking notes on how you are feeling, and take these notes into your appointments.

Write down a list of questions you want to ask. If you don't understand the answers to any of your questions, don't be embarrassed to ask for the answer to be repeated or rephrased. Make sure you know who your point of contact is and how to get hold of them in case you have questions later.

Deciding on a treatment strategy can be difficult so choosing to get a second opinion is quite common. Physicians are usually very open to this because they appreciate the fact that making an effective treatment choice can be very challenging.

If getting a second opinion through your specialist is not possible, you can get a referral from any of your physicians, including your general practitioner.

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 are not successful in stabilising your disease.

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

Further Support

NET Patient Foundation

From diagnosis and throughout treatment and beyond our services are here every step of the way. Below is an overview of all the services we offer to people living with and beyond NETs.

Helpline – 0800 434 6476

Our free, confidential helpline is for anyone who has questions about NETs (neuroendocrine tumours). Your call will be answered by one of our nurses or trained staff members with experience of NETs. Whatever your concern, you can be confident we will understand the issues you might be facing, and that the information you receive will be 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 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. Our website is here round-the-clock giving you instant access to information when you need it. As well as clinical information, you will find real life experiences and access to the largest online NET 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.

Information and support sessions

We run information and support sessions for people living with NETs. These meetings include talks from some of the country's top NET specialists plus invaluable Question & Answer sessions and an opportunity to meet other NET patients. For information about meetings in your area, please see our website or call our helpline.

NET Natter groups

These are informal groups which meet locally on a regular basis. To find out if there is a NET Natter group in your area, or if you'd like to set one up, please visit our website.

Information resources

Our free information resources are for anyone affected by NETs. 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 NETs, 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

NHS Choices

Information on clinical trials and treatment centres, including reviews and ratings.

www.nhs.uk

Cancer Research UK

Trusted information on all cancer types.

www.cancerresearchuk.org

Macmillan Cancer Support

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.

www.macmillan.org.uk

General enquiries: 020 7840 7840

Helpline: 0808 808 0000

Textphone: 0808 808 0121 or Text Relay

Have you visited us online?



Our website is packed full of information that will help you find out more about the NET Patient Foundation and stay up-to-date with our services, campaigning and fundraising.

We provide high quality information and support for NET patients, their families and carers.

Visit our website for...

- Information on NETs
- Support in your area
- Patient meetings and events
- NET clinics and research

...or get Social!

 @netpatientfound

 www.facebook.com/NetPatientFoundation

www.netpatientfoundation.org



Did you know?

- Over 50% of patients are diagnosed when the cancer has already spread
- Early diagnosis significantly improves outcomes for patients
- There are dedicated NET clinics around the UK. Find out where 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 Foundation has the following aims:

- To provide support, education and information to anyone affected by neuroendocrine cancers
- To advocate for neuroendocrine cancer patients so that they may achieve the best possible outcomes
- To encourage standardised care for all NET patients
- To provide community supportive care to patients and their carers or family members
- To raise awareness of NETs throughout the UK
- To raise funds for clinical research projects.

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