SPOTLIGHT ON
NEUROENDOCRINE
CANCER

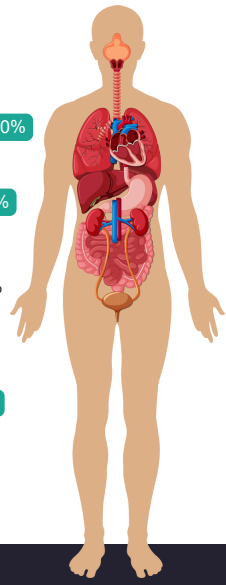
Neuroendocrine Cancer UK
Incorporating The Ann Edgar Trust

NEUROENDOCRINE CANCER

An overview for Oncologists

KEY FACTS

- **Neuroendocrine cancers, often referred to as neuroendocrine neoplasms (NENs), are now the second most prevalent GI cancers and the 10th most prevalent cancers in England.**(1)
- These tumours will, not infrequently, be presented at MDTs. **Being aware of some of the challenges in diagnosing NENs, variation in NEN biology and treatment pathways is therefore important for Oncologists.**
- **These tumours are diverse and range from slow growing grade 1 lesions to highly aggressive lesions with rapid proliferation** as such stage and grading are of the utmost importance in defining treatment strategies. Due to their complex nature referral to a local expert MDT or CoE is advised.
- **There are challenges to diagnosing NENs** because individual symptoms may mimic or be masked by more common conditions such as IBS. This can also be exacerbated by a perceived pressure to discharge patients with these symptoms who have had a normal gastroscopy and / or colonoscopy. (2)
- **CT and/or MR imaging can assist in detecting NENs in symptomatic patients where a diagnosis has not been established by endoscopic or other means.** Clinical features that may suggest a need for further investigations such as contrast-enhanced abdominal CT scan may include persistent symptoms (e.g., diarrhoea or abdominal pain), new onset of symptoms in older patients in whom a new diagnosis of IBS is less likely, the presence of one or more carcinoid syndrome symptoms (facial flushing, diarrhoea, bronchospasm), weight loss or bowel obstructive symptoms. (2)
- **The diagnosis of a neuroendocrine cancer can result in a significant and negative impact on quality of life for patients** (and their families). This is due to multiple factors including the impact of a new cancer diagnosis, potential tumour-associated hormonal symptoms, information and diagnostic barriers and delays, alongside an often incurable and uncertain prognosis. (3)
- **Diagnosing patients earlier is life-changing because there are treatments that can improve the prognosis as well as symptoms even in the presence of metastatic disease.**



The diagram above shows the likely locations of Neuroendocrine neoplasms (5)

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DEFINITION

DEFINITION OF NEUROENDOCRINE CANCER

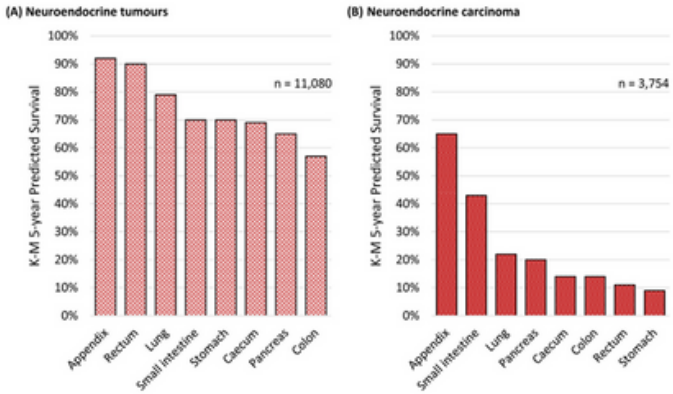
Neuroendocrine neoplasms (NENs) are a heterogeneous group of cancers, which arise in the neuroendocrine cells. The WHO has defined two principal subtypes – neuroendocrine tumours (NETs) and neuroendocrine carcinomas (NECs):

Neuroendocrine Tumours (NETs) and Neuroendocrine Carcinomas (NECs).
Both subtypes are considered as malignant tumours.

Neuroendocrine tumours (NETs)	Neuroendocrine carcinomas (NECs)
• Two-thirds of NENs are NETs ~70% • Well-differentiated • Slow to rapid growth - Graded 1-3 • Relatively good prognosis • May present/develop site- associated hormone syndrome	• One-third of NENs are NECs ~30% • Poorly differentiated • Rapid growth - Grade 3 • Poor prognosis • May present/develop paraneoplastic syndrome

- NENs are complex with aspects of both a cancer and a chronic disease and may develop almost anywhere in the body, most commonly within the respiratory or digestive tracts (GI tract /pancreas).
- Neuroendocrine neoplasms arising from the digestive tract are referred to as gastro-entero-pancreatic NENs (GEP-NENs), and these account for over 60% of NENs (4). The respiratory system represents the site of disease in 20-30% of patients, and less commonly affected sites include skin, thymus, and reproductive system structures, such as the ovaries.

Determining whether patients have NETs or NECs is of vital importance, as this can have a significant impact on prognosis as well as treatment planning. (6) There are significant differences in 5-year survival of NETs and NECs. (7)



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PRESENTATION

NENs are not as rare as you may think

Between 1995-2018 the incidence of NENs has risen 371%: age-adjusted incidence increases from 2.35 to 8.61 per 100,000. (1)

Neuroendocrine neoplasms have a higher prevalence than incidence: incidence ~ 9 per 100,000(1), prevalence ~ 35 per 100,000. (8)

WHEN TO SUSPECT NET AT THE MDT

- Can present incidentally during routine CT scanning or Endoscopy.
- GEP-NETs and their metastases are often hypervascular, usually appearing more conspicuous in the early arterial phase of the CT acquisition.
- The primary tumour in the small bowel is often too small to be identified on CT and so secondary features, such as liver metastasis or tumour associated desmoplastic fibrosis are more commonly appreciated.
- Gastric and Hindgut NETs are often diagnosed at endoscopy.

USEFUL INVESTIGATIONS FOR DIAGNOSING NEUROENDOCRINE NEOPLASMS

- For people with persistent, troublesome, particularly watery diarrhoea, consider a functional NET and arrange a Gut Hormone Profile and measurement of plasma/urinary 5-HIAA. (11)
- Chromogranin A is the most useful general biomarker for NENs but is not completely sensitive or specific. It is helpful for patients with confirmed NEN but shouldn't be used as a screening test.
- Unusual looking polyps in the stomach, duodenum or rectum that could potentially be NENs should initially be biopsied rather than being removed at the time of the initial endoscopy. If a NEN is histologically confirmed, full tumour characterisation and staging is required to determine the optimal treatment plan.
- CT and MR imaging are useful for patients with persistent abdominal pain and diarrhoea and will often detect previously undiagnosed NENs. However, they will not necessarily demonstrate the full extent of disease.
- Nuclear medicine scans (e.g. Tektrotyd scan, 68Ga DOTATATE PET/CT and FDG-PET/CT), whilst not available in every hospital, can be very useful for determining the full extent of the disease and the optimal treatment plan and these should be considered before proceeding to treatment, unless it is an emergency.

Refer patients with a confirmed or highly suspected diagnosis of NEN on to your local expert MDT or Centre of Excellence.

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TREATMENT

- Treatments will vary depending on stage and grade of NEN, but include Somatostatin analogues, targeted agents such as Everolimus or Sunitinib, Chemotherapy and PRRT.
- Often surgical resection is considered for localised disease.
- For Low grade metastatic NETs, somatostatin analogues are often the first line treatment which offer both tumour control and improvement in carcinoid syndrome.
- Guidelines for the management of NENs exist and can be found on the ENETs website.
- Patients should be managed by expert MDTs and specialist teams.

PROGNOSIS

- Prognosis will vary depending on both stage and grade. It is important to note that patients with low grade disease can still live for many years even in the face of metastatic disease.

SPOTLIGHT ON NEUROENDOCRINE CANCER IS A COLLABORATION BETWEEN UKINETS & NEUROENDOCRINE CANCER UK

UKI NETS

Clinical guidelines are available - alongside expert advice from any one of 14 UK accredited European Centres for Neuroendocrine Cancer - should NENs be suspected/diagnosed: UKINETs: www.ukinets.org ENETs: www.enets.org

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Patient-facing and HCP information, education and support is available from Neuroendocrine Cancer UK Office: 01926 883487 I Helpline: 0800 434 6476 Registered charity number: 1092386

THE LACK OF A NATIONAL PATHWAY AND NON-INCLUSION IN NG12 DIFFERENTIALS HAS HAMPERED THE DIAGNOSIS OF NENS, HOWEVER, A COLLABORATIVE MULTI-STAKEHOLDER WORKING GROUP – INCLUDING NHS EARLY DIAGNOSTIC LEADS – HAS ADDRESSED THIS DISPARITY. THE **NEUROENDOCRINE CANCER PATIENT CARE PATHWAY** WAS LAUNCHED MAY 2023. IT IS AVAILABLE TO VIEW HERE: WWW.NEUROENDOCRINECANCER.ORG.UK

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