

What are NETs?

An overview of treatment

Judith Cave November 2020

Overview

1. What are NETs – types and subgroups
2. How do we start treatment planning?
3. What are the treatment options?

It's challenging to present an overview which doesn't tell you things you know already... many of you are experts.

But please type a question in the chat or save it for the end if you want more detail or anything isn't clear

What are NETs?

Neuroendocrine tumours (NETs)

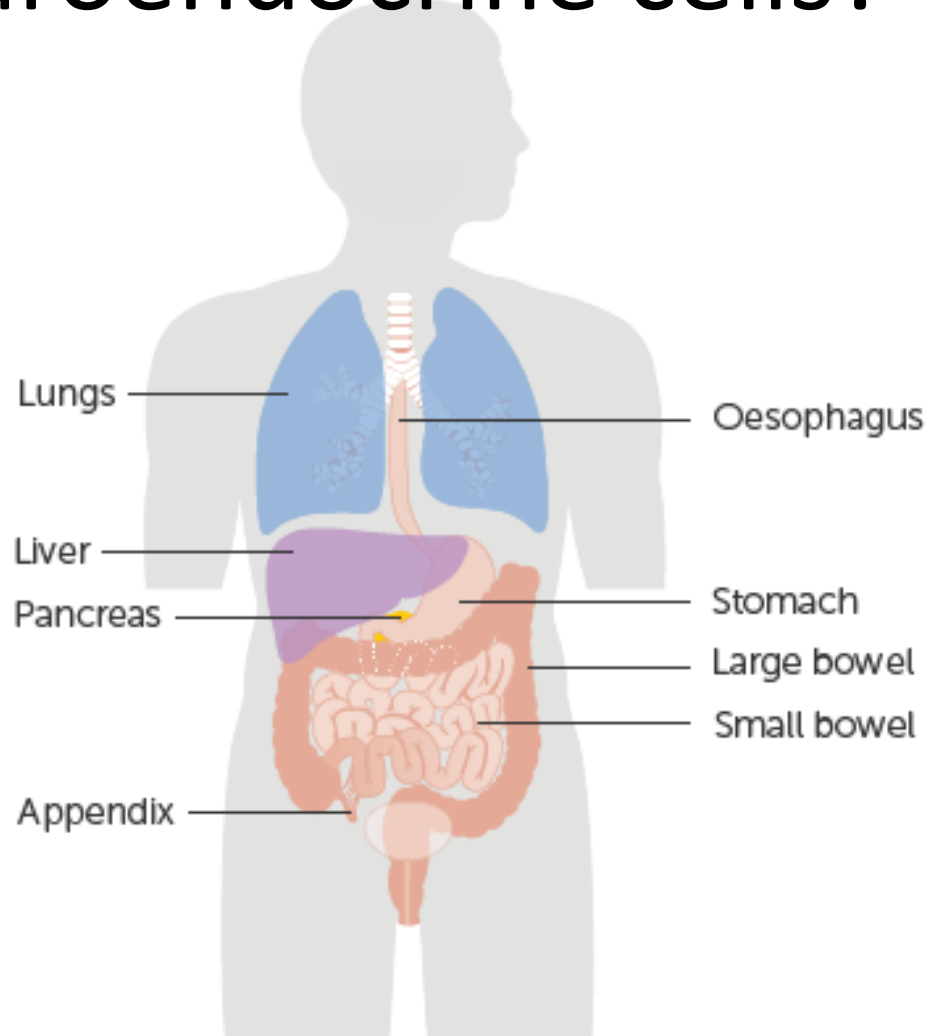
NETs are tumours that start in neuroendocrine cells*. Most develop slowly over several years.

Tumours are lumps of cells which are growing inappropriately, and can spread and grow in new places.

*Neuroendocrine cells make hormones and release them into the blood stream.

Where are neuroendocrine cells?

Neuroendocrine cells make hormones which control the flow of air and blood into the lungs, or the production of digestive juices, or the muscles that move food through the bowel.



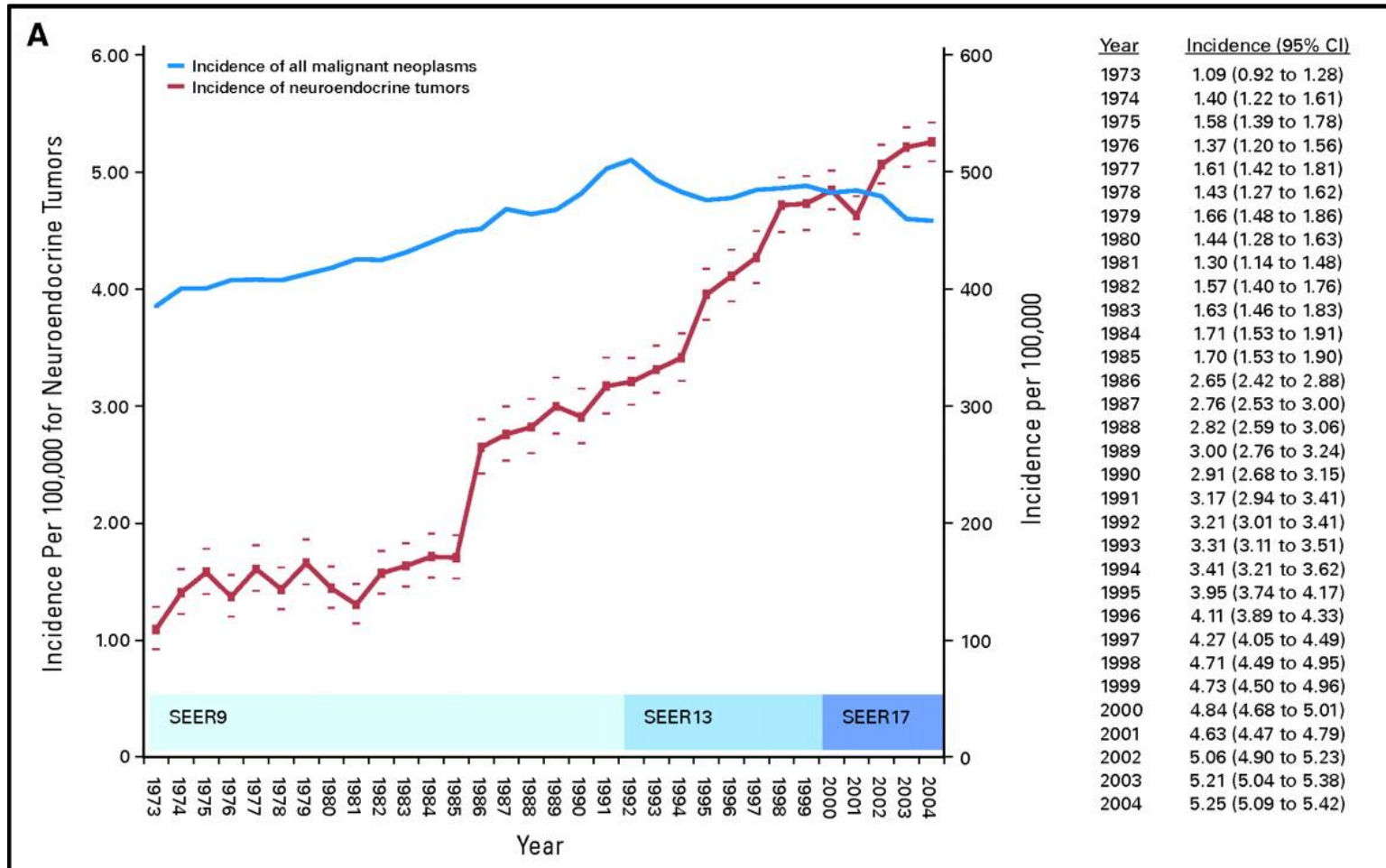
Different types of NETs

There are many types of NETs. They are categorized according to

- Where they started
- Where they have spread to
- Grade (how similar they are to normal tissue)
- Whether they produce hormones

e.g. Grade 1 pancreatic NET with liver metastases

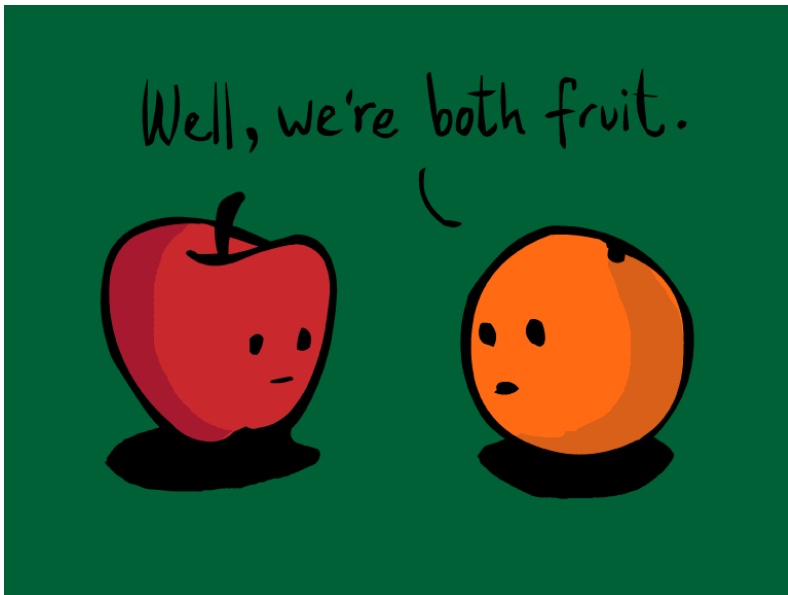
How common are NETs?



James C. Yao et al. JCO 2008;26:3063-3072

How do we start planning
treatment?

What is different about NETS?



Because they are different to other tumours....

When I first meet the patient:

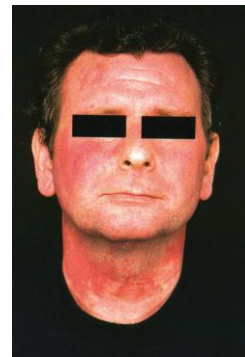
Much more to do than with other patients!

M MDT

U Urinary 5-HIAA, Chr A/B

C Carcinoid syndrome?

H History past/family?



Functioning tumours

Carcinoid syndrome is caused by hormones that the tumour produces. Symptoms include

- Flushing,
- Diarrhoea
- Weight loss, abdominal pain
- Syncope and in rare cases low blood sugars

Small bowel NETs usually cause classical carcinoid syndrome due to a hormone called serotonin. Pancreatic NETs present with a wider variety of hormone symptoms including low or high blood sugar, excess stomach acid, etc.

The first thing is to control carcinoid syndrome if possible

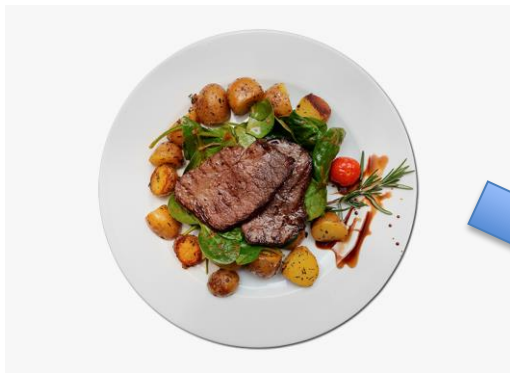
Sometimes carcinoid syndrome is the main risk to a patient!! It can be unpleasant, but also cause heart disease or weight loss. Heart disease is due to serotonin causing scarring on the heart valves. We check all our patients for this.

To control carcinoid syndrome we can block the hormones with somatostatin analogues or similar drugs, or use surgery or ablation to reduce the amount of hormone being produced.

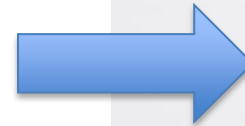
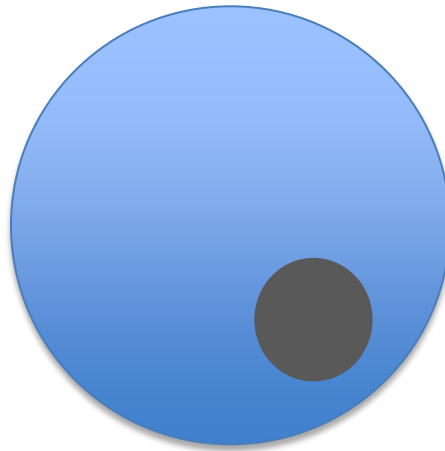
For complex syndromes, the MDT might involve specialist from other teams e.g. endocrinology or gastroenterology.

What are somatostatin analogues?

Usually our guts are controlled by hormones



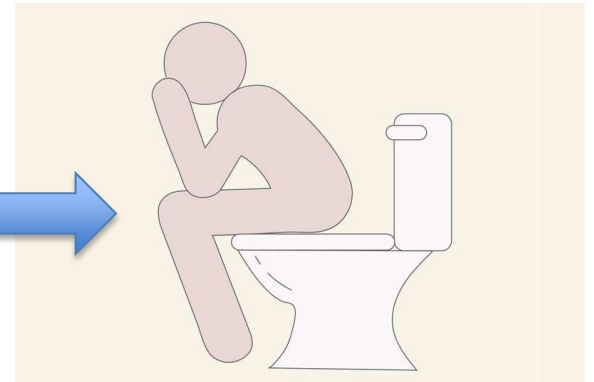
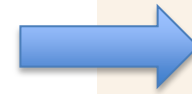
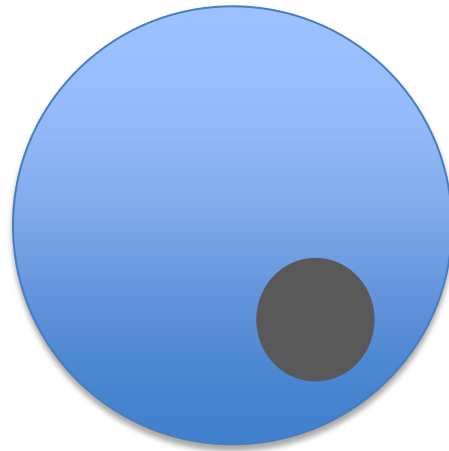
Neuroendocrine cell



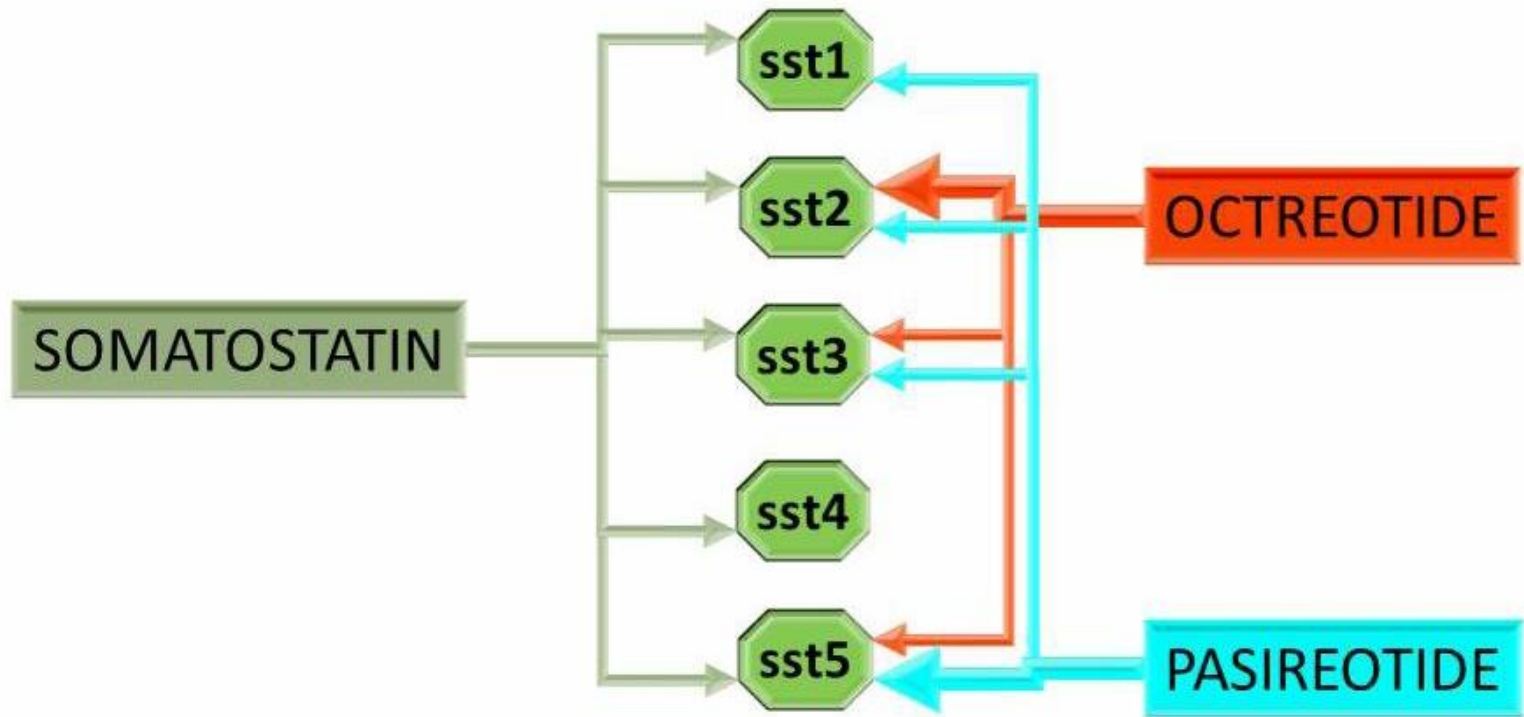
What are somatostatin analogues?

The problem with NETs is that they produce hormones randomly!

Neuroendocrine cell



Somatostatin is the 'empty plate' hormone.



Somatostatin analogues are synthetic versions of this useful hormone

What are the treatment options?

What is the goal of treatment?

There are different reasons we treat patients

1. To cure it so it never comes back
2. If this is not possible then the goal is to prolong life and control symptoms

N.B. sometimes control of symptoms and observation is all the right thing to do.

Surgery/ablation

First ask whether it is possible to remove or destroy the tumour, and hence potentially cure it. This should be decided by an experienced MDT. The next talk goes into detail about surgery.

If surgery is not possible either due to location of disease, or patient factors including preference, then we next consider systemic treatment.

Systemic options – treatment that goes to the whole body

- Somatostatin analogues
- Chemotherapy
- Targeted treatment (tablets)
- Targeted radiotherapy (PRRT)

The choice of which is best depends on a detailed and individual assessment, as described above

Systemic options – treatment that goes to the whole body

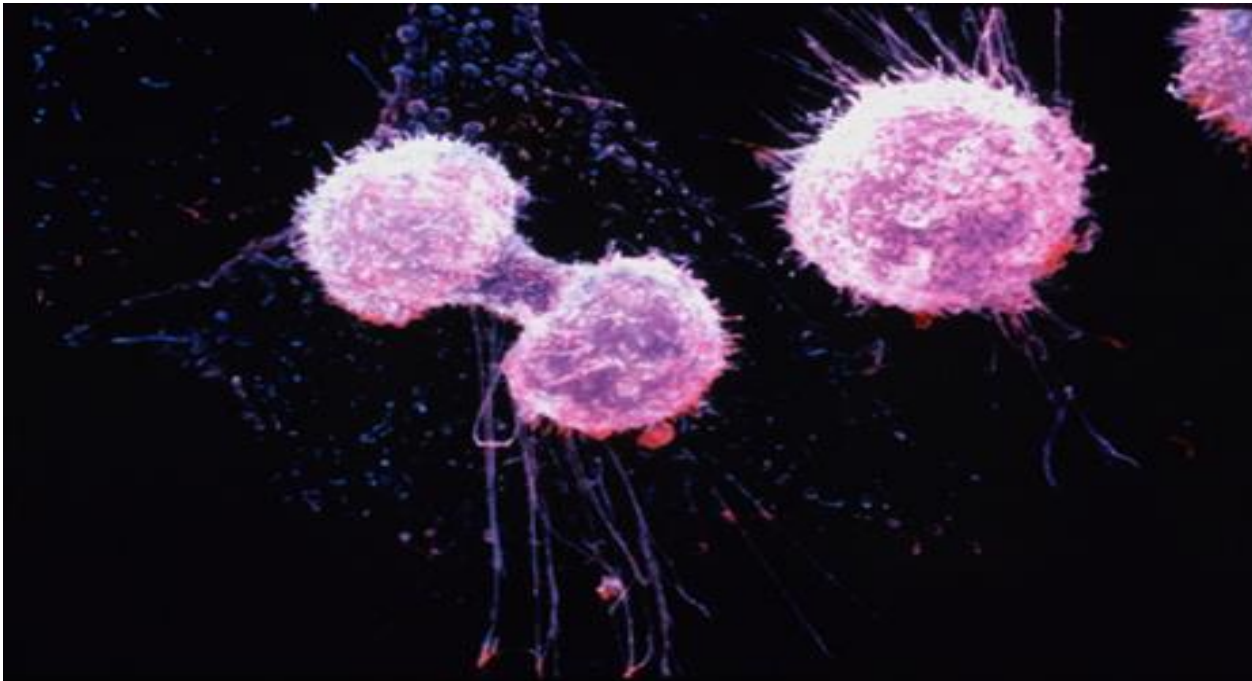
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Chemotherapy

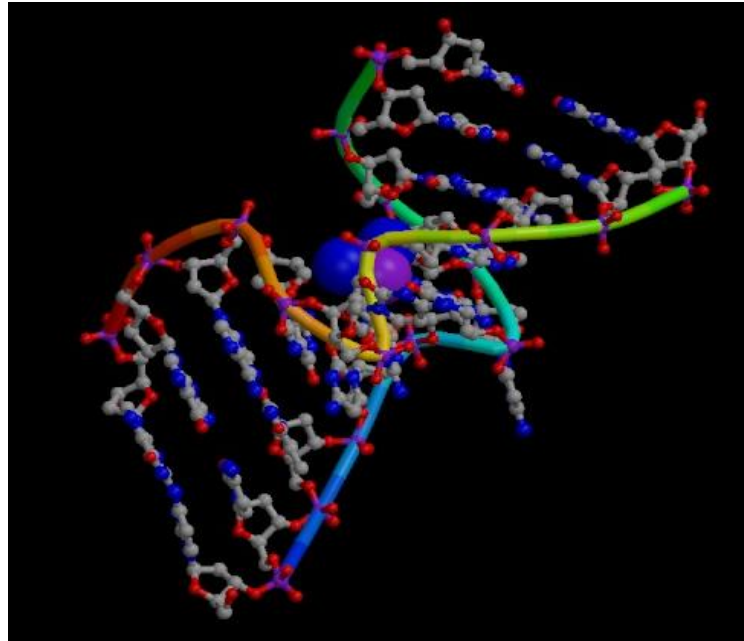


Chemo means drugs which kill dividing cells



How does chemo kill dividing cells?

The double helix of DNA needs to unwind during cell division. Alkylating agents and platinum drugs link the strands, resulting in double strand breaks on division.





Although chemotherapy attacks any cells which are dividing, some cells take longer than others to recover.

Chemotherapy can also be injected into the hepatic artery, the peritoneal cavity, or the CSF.

Also some drugs deliver chemotherapy selectively to the liver.



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Targeted treatments

The aim is to understand what makes the malignant cell different from the other cells, and target these differences.

It is known that:

- NETs are highly dependent on a rich supply of new blood vessels
- NETs often have defective genes in their internal growth control mechanism

Targeted drugs aim to exploit these differences by blocking new blood vessel formation, or internal messages which cause cell division.

Targeted treatments

Advantages	Disadvantages
<ol style="list-style-type: none">1. Tablets not injections2. Side effects are less than some other treatments3. The idea is very smart4. Can control disease for long periods of time	<ol style="list-style-type: none">1. Only funded for some subsets of patients2. Don't tend to shrink disease, just stabilize3. Don't always work

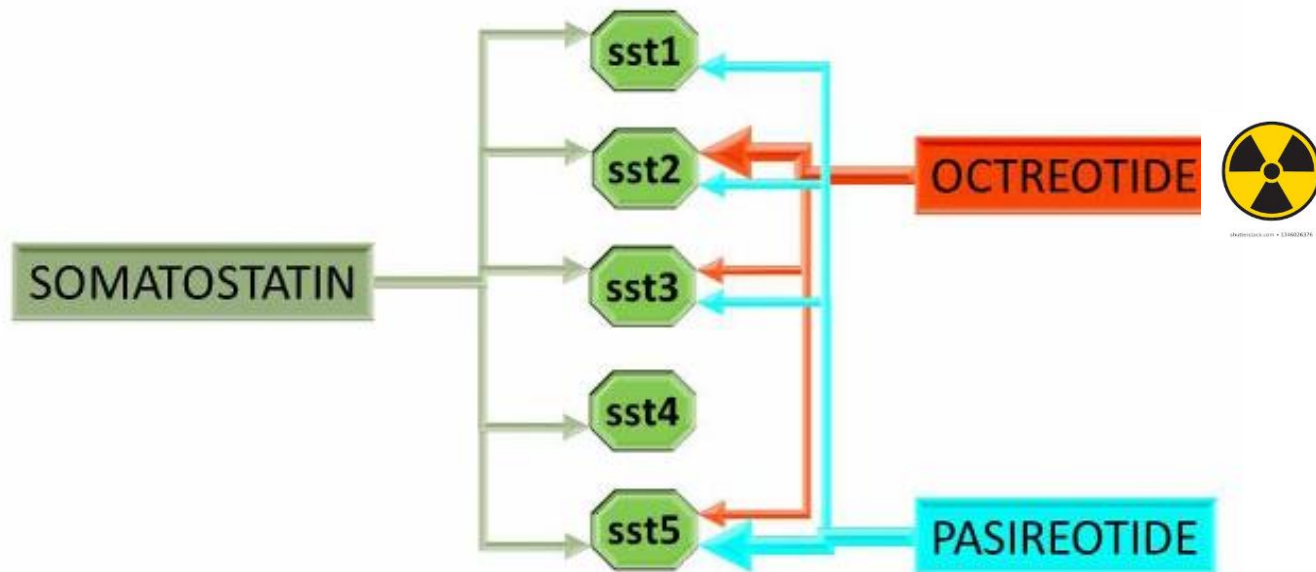
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Radiotherapy - PRRT

PRRT is an injection of somatostatin analogue, but there is a radioactive drug attached to the octreotide.



How will we know whether systemic therapy is working?

1. Monitor symptoms
2. Monitor bloods or urine 5-HIAA
3. Do a scan (CT/MRI). NB need to know what was happening before you started.

Summary

NETs are tumour arising from neuroendocrine cells.

A bespoke treatment plan is needed and thorough assessment should be done before making a plan.

The involvement of an experienced multidisciplinary team is essential.

Options for treatment include somatostatin analogues, surgery, ablation, chemo, tablets, and radiotherapy.