

## NET web chat: outstanding questions

**Karen:** Is tumour size sufficient for effective diagnosis of where an advanced NET began? Or could size be misleading?

**Dr Christos Toumpanakis:** Hi Karen. Not always. Small NETs either in the lungs, small bowel or pancreas can all be associated with advanced disease.

**Ronny Allan:** The output from the NETTER-1 trial indicates patients can go straight to PRRT as a first line choice of treatment. What is the RF NET CoE view on this?

**Dr Christos Toumpanakis:** Hi Ronny. Not exactly, no. The NETTER-1 trial results indicate that advanced small bowel NETs which are progressing on regular doses of somatostatin analogues should be treated with PRRT. We have already been doing this in our NET unit for the last few years.

**Ali:** Is it just increasing awareness of NET that is responsible for the increase in numbers or do you think environmental factors are at play?

**Dr Christos Toumpanakis:** Thanks for your question Ali. At present we feel that increased incidence is due to increased awareness as well as easier access to modern imaging techniques.

**Alan:** With regard to flu vaccines, why are we not informed that the live vaccines are not suitable? I have just had my jabs and do not know what form it took.

**Dr Christos Toumpanakis:** Hello Alan, flu vaccine is not a live vaccine, so NET patients are advised to have it. With regards to live vaccines, we would suggest that you liaise with your oncologist.

**Anon:** Were different somatostatins used with these radionuclides in the past?

**Dr Christos Toumpanakis:** In the past some centres were using octreotide in the radionuclide treatments, but now the majority use octreotate that binds better to the somatostatin receptors in the tumours.

**Kenneth Ezerioha:** How effective is the molecular targeted therapy for bronchial carcinoid tumours now that the funding of the radio-targeted therapy has been discontinued?

**Dr Christos Toumpanakis:** Hi Kenneth, we are waiting for the results of a large trial called "LUNA".

**Anon:** Is the cyber knife ever considered when treating NET patients with liver mets?

**Dr Christos Toumpanakis:** There is no established evidence, but it could be considered in individual basis and following discussion in the tumour board meeting.

**Anon:** The video mentioned that trials were held in Rotterdam. What was the % success rate and did any patients experience total remission?

**Dr Christos Toumpanakis:** Complete remission with PRRT is extremely rare and has been noted in <5% of patients. Tumour shrinkage can be noted in 15-20% of patients.

**Ronny Allan:** If a secondary tumour is graded Ki-67 5%+ and the primary is graded later at Ki-67 1%, what is the NET grading of this patient (both well differentiated)?

**Dr Christos Toumpanakis:** Always the higher one (5%+).

**Karen:** Sorry, Karen again, following up about identification of primary sites. So far CT/pet scans have identified a 2cm high grade oesophageal tumour with 'spread' to two lymph

nodes and spot on liver. From what you said, this is likely to be correct diagnosis? If so, what are the (best) treatment options?

**Dr Christos Toumpanakis:** Hi again Karen, thanks for all your questions! Most likely, systemic chemotherapy. However, please follow the advice of your local oncologist who, I am sure, has discussed the case in the tumour board meeting.

**Ali:** Is it possible to have a mixed population of aggressive and less aggressive nets at the same time?

**Dr Christos Toumpanakis:** Hi Ali, it is possible to have a mix, as NETs are very heterogeneous tumours.

**Dinky B:** Hi Dr T when you mentioned carcinoid syndrome on the video, non-functioning pancreatic tumours weren't mentioned, just ovarian, bronchial and advanced small bowel. If someone with a small pancreatic tumour has carcinoid syndrome, including the wheezing, is the syndrome because they have metastatic disease (eg liver) or would you suspect another tumour lurking elsewhere that hasn't been found yet?

**Dr Christos Toumpanakis:** Hello Dinky. I did not mention pancreatic tumours, because <1% of pancreatic NETs secrete serotonin and are therefore associated with carcinoid syndrome. In those cases, the patients have liver metastases.

**Zebra:** My vitamin D keeps dropping even with treatment, what is the likely cause? Is it the shot?

**Dr Christos Toumpanakis:** Hi Zebra, there is no definite answer here. You may have other causes of vitamin D deficiency.

**Tracey:** What is the average timescale for diagnosis of a net?

**Dr Christos Toumpanakis:** Hello Tracey. There is always a gap between symptoms' onset and diagnosis. There aren't many studies identifying this, but to our experience, it is around two years.

**Ronny Allan:** How important is a pathologist to a NET diagnosis and can any pathologist hit the ground running when analysing NET tumour samples even for the first time?

**Dr Christos Toumpanakis:** Pathologists are very important, but they should be experienced in NETs.

**Wendy:** Is there a way of distinguishing what are NET flushes and what are menopausal flushes?

**Dr Christos Toumpanakis:** Hi Wendy, carcinoid syndrome flushing is usually red and dry and menopausal flushes are usually white and wet.

**Jennie:** What triggers NET to activate? Does it relate to changes in hormones throughout a person's life span? Do malignant tumours start off as benign tumours?

**Dr Christos Toumpanakis:** Hi Jennie, there is no clear answer to your first two questions. In answer to your third question, this is rarely the case.

**Jacqueline:** Is there any evidence to suggest elevated adrenaline and cortisol levels could be implicated in the development of NETs?

**Dr Christos Toumpanakis:** Hi Jacqueline, there is no evidence for this.

**Paul:** Is there a treatment apart from surgery for parago?

**Dr Christos Toumpanakis:** Hi Paul, if you mean paragangliomas, the answer is yes. Patients with advanced disease may be suitable for radionuclide treatment.

**Sam:** Why are some NET tumours not suitable for surgery?

**Dr Christos Toumpanakis:** Hello Sam. Some tumours are not suitable for surgery either because they are advanced (the disease is in multiple sites throughout the body) or because they are invading large vessels and there is an increased risk of mortality during surgery.

**Anon:** Do PNETS that have metastasised in the liver produce more hormone than the primary? Is there a risk of carcinoid heart disease from non-functioning PNETS in the liver?

**Dr Christos Toumpanakis:** Question 1: Most times, yes. Question 2: No.

**Anon:** Prof Meyer mentioned that the proliferation of tumours can be sustained by Everolimus - does he mean reduced or sustained?

**Dr Christos Toumpanakis:** Prof Meyer was referring to the fact that tumours may remain stable.

**Anon:** Both Lutetium and Yttrium have been used in radiotherapy treatment for NETs in the past. If PRRT uses both these radioactive elements, in what way is this treatment new?

**Dr Christos Toumpanakis:** This treatment is considered new as it is the first time that we have obtained evidence about its efficacy through a large phase III clinical trial.

**Ronny Allan:** I heard anecdotally that the NHS is not very efficient at capturing NET cancers using the correct ICD codes and that this is the key reason why decent statistics are not available. Is the RF confident about any UK statistics regarding NET cancer incidence rates?

**Dr Christos Toumpanakis:** There is no national UK NET registry yet.

**Dinah Ballance:** I have read that carcinoid syndrome begins when a NET has spread to the liver. I still have no disease in the liver eight years on from diagnosis with a small bowel tumour that had spread to the mesentery. How unusual is this and can you explain how it has happened with a fully functioning liver. I also want to sing the praises of the team at the Royal Free and thank you for your wonderful care and research.

**Dr Christos Toumpanakis:** Thanks for your kind words, Dinah. This happens rarely (5%) in patients with carcinoid syndrome, the vasoactive substances produced by the tumour are bypassing a fully functioning liver and are secreted directly in the systemic circulation.

**Paula:** Is it still recommended to take large amounts of vitamin C with an insulinoma. Thank you all for doing such an amazing job in keeping us all alive.

**Dr Christos Toumpanakis:** Thanks Paula. Keep on taking vitamins, but not in large amounts.

**Karen:** I read (abstract of a paper) that there may be a correlation between taking Rosuvastatin and NETs. Is there any real evidence of this link?

**Dr Christos Toumpanakis:** There is no convincing evidence.

**CS:** I am very grateful for the Royal Free for taking me on as a patient although I do not live in London. Is the Royal Free still able to take referrals irrespective of where people live in the UK?

**Dr Christos Toumpanakis:** Yes, patients are advised to contact their GPs and ask to be referred to RFH for a second opinion.