



Addendum to Webcast Recordings

## CNETS Winnipeg Conference Questions

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### 1. A family has members with Melanoma, mid-gut Carcinoid and Paraganglioneuroema. Is there a genetic basis of these diseases?

#### Response from Dr Tom O'Dorisio

I have seen Paraganglioneuroema in relatives of [patients with] mid-gut Carcinoid and neuroblastoma. There are at least three centers in the U.S. presently trying to identify a common gene, first in tumour tissue and then hopefully [we] will be able to measure it in peripheral blood of members at risk.

[With a few notable exceptions,] familial neuroendocrine tumour associations are at present relatively uncommon. [The exceptions include:] Familial Multiple Endocrine Neoplasia type 1 (ie- pituitary tumours, parathyroid hyperplasia, and pancreatic Neuroendocrine tumours associated with a MENIN Gene - a tumour suppressor Gene), and Multiple Endocrine Neoplasia type 2 (ie- Medullary thyroid cancer - a neuroendocrine tumour - parathyroid hyperplasia in 95% of Familial MTC, termed MEN type 2B, and pheochromocytoma also a neuroendocrine tumour). One other Familial inherited neuroendocrine tumour set is Von-Hippel-Lindau (VHL) which is also associated with pancreatic Neuroendocrine pancreatic tumours and pheochromocytoma. [It is] also a neuroendocrine tumour that can occur in 10% of the Familial syndrome. VHL is associated with retinal and cerebellar hemangioblastoma and a VHL Gene has been identified.

Carcinoids of the intestine can be found in both the MEN 1 & 2 Familial kindreds, and paraganglioneuromas can be co-associated in MEN type 1 Families.

Hopefully over the next several years, we will be able to pinpoint a gene or genes that may predict susceptibility [to] developing Carcinoid tumours. But the science is just not here at the moment.

#### Response from Maureen Coleman

This is fascinating and [was] one of my own questions in Winnipeg.

My mother had a melanoma 30 years before she developed kidney cancer. The melanoma had been removed 30 years before and she had not followed it up, as she tended to be hospital phobic. Then, within three weeks of diagnosis of her kidney cancer, she passed away suddenly.

The kidney cancer was an unusual one in that it had a primary tumour that did not remain in the kidney but had migrated up the [inferior] vena cava and [lodged] at the entrance of the [right] atrium of the heart.

I [recently attended] a meeting of the Canadian Organization of Rare Disorders. At that meeting the Pfizer [representative] spoke of a (neuroendocrine) paraganglioma patient who had been diagnosed with a kidney cancer who had a very rare manifestation in which it had been observed that the tumour had moved up the vena cava. Sutent was administered in this case and the patient's tumour shrank.

It was a Eureka moment for me. Later the [Pfizer representative] and I talked as we were both fascinated by the fact that this rare instance had been the case with my mother as well and that her kidney cancer may well have been neuroendocrine in origin.

Perhaps I should connect with this gene study as I am a mid-gut Carcinoid patient.

**2. What is the effectiveness of anti-angiogenic drugs on aggressive neuroendocrine tumour behavior?**

**Response from Dr Tom O’Dorisio**

Most clinical trials [testing the efficacy of anti-angiogenic compounds against neuroendocrine disease] have examined the effectiveness of [these] drugs for the well-differentiated [neuroendocrine] tumours or carcinomas. [Some trials have included] moderately well-differentiated tumours - [those with] WICK Classification type 1 or type 2 (out of 3).

I am sure clinical trials for the more aggressive type Carcinoids (poorly differentiated or WICK type 3, are presently being designed, but to my knowledge, none have been FDA-approved for indication in [neuroendocrine] tumours.

**3. Is Pancreastatin [testing] available in Canada?**

**Response from Dr Shereen Ezzat**

[Pancreastatin is an amino acid peptide produced by degradation of Chromogranin-A which inhibits release of Somatostatin. The level of Pancreastatin in a patient's blood is measured by direct radioimmunoassay.] This measurement is not available in Canada. In fact, it's available in only a few centres throughout the U.S. [Here in Canada] we're still having difficulty getting Chromogranin-A done. Ideally, both measurements should be made available to patients with NETs.

**4. Is diabetes a common occurrence with [patients taking] Sandostatin?**

**Response from Dr Shereen Ezzat**

Diabetes is distinctly uncommon, developing in only 10-20% of [NETs] patients. Most of those who develop this have an underlying pre-disposition or family history of diabetes.

**5. How can we facilitate earlier diagnosis?**

**Response from Dr Shereen Ezzat**

Increased patient and physician awareness of NETs and their varied presentations will prove to be a critical step in earlier diagnosis.

**6. Do patients develop immunity to Octreotide-LAR?**

**Response from Dr Shereen Ezzat**

Patients rarely develop immunity to Octreotide [or Lanreotide]. However, tolerance to the medication is common. This usually occurs after several years of use as the disease itself progresses. Identification of this shift from sensitivity to tolerance is critical in determining the need for additional treatment(s).

**7. Should all patients with NETs [who are undergoing surgery] have pre-operative Sandostatin?**

**Response from Dr Shereen Ezzat**

Pre-op [Lanreotide or Octreotide, better known as Sandostatin] is critical in patients whose NETs are associated with increased hormone production such as Serotonin (evidence by increased urinary 5-HIAA), insulin, glucagon, or gastrin. Those whose tumours are hormonally inactive are less likely to benefit from short-term or pre-operative treatment [with Sandostatin].

**8. Which imaging test would be most helpful for diagnosing metastatic paraganglioma?**

**Response from Dr Shereen Ezzat**

Paragangliomas are tumours which arise from nerve cell bodies that can manufacture adrenalin-like substances. They frequently spread to other parts of the body requiring multi-modal therapy. Metastatic disease [arising from Paragangliomas] can be localized using the MIBG scan, providing evidence for hormonal activity.

**9. Canada produces Y-90 and ships it to the UK . Then the [Canadian] patient is shipped to the UK for treatment. Does this make sense?**

**Response from Dr John Buscombe**

[Y-90 or Yttrium is a radioisotope produced in Canada and used in Peptide Receptor Radiotherapy. This treatment is not currently available in Canada, and many patients travel at their own expense to receive this treatment at centres in Europe.] Clearly this is not ideal. CNETS is in an ideal position to help lobby the federal government to look at how unusual and experimental drugs which may benefit patients suffering from rare diseases can be used in Canada in a framework that protects the safety and legal rights of the patient.

**10. This question relates to treating lung metastases with Lu-177 DOTATATE. How small does the tumour need to be for Lu-177 DOTATATE to be effective and would there be collateral damage?**

**Response from Dr John Buscombe**

[Lu-177 or Lutetium is another radioisotope produced in Canada and used in Peptide Receptor Radiotherapy.] We do not use Lu-177 DOTATATE in our centre [at Nuclear Medicine Royal Free Hospital in London UK,] but we have used Y-90 DOTATATE in patients with lung metastases with good effect. The size does not matter. Other groups using Lu-177 DOTATATE report they have treated lung metastases as well. There does not appear to be any evidence of any subsequent damage to the normal lung with either agent. Theoretically it would be unlikely that either Lu-177 DOTATATE or Y-90 DOTATATE would cause damage to the normal lung.

**11. I am a patient with Carcinoid tumours within the liver but I have a strong sweet tooth. I often feel light-headed just like a diabetic with a hypoglycaemic attack but feel better after sweets or a full meal. I have had this problem for years, long before I knew about my carcinoid tumour. I am presently receiving chemotherapy and radiation therapy. If I eat sweets (such as candies) will I put extra strain on the pancreas and make the liver metastases worse?**

**Response from Dr John Buscombe**

I think it is unlikely that your need for frequent meals has anything to do with your carcinoid tumour. Some people just need to eat more frequently than other people. For all patients with NETs it is vital to maintain a good varied diet and it may be that more [frequent] smaller meals are better than a few large meals. If you have any other [dietary] concerns it may be worth discussing this with the nutritionist at your hospital.

- 12. Some patients may have to travel great distances from home to the hospital where they receive treatment. In Canada, is there any standardization of protocols for CT scans and MRI? Is it the norm to have one's scan done locally and then the patient themselves sends the images and report forward to a specialist?**

**Response from Professor Sylvia Asa**

There are no "standard protocols", but second opinions are the right of every patient, so anyone can ask to have their imaging reviewed. This is facilitated by the increasing use of digital imaging for many of these tests that can easily be sent for review electronically. As with any aspect of medicine, those who deal with a disease on a regular basis have more experience and can offer a more enlightened opinion, and no patient should be afraid to ask their local doctors for a second opinion.

- 13. We appear to face similar issues in research as those faced in the clinical approach to the disease: "benign neglect". How does one stimulate NET research in Canada or elsewhere?**

**Response from Professor Sylvia Asa**

In general rare diseases do not get as much attention as common ones, since researchers are dependent on funding and the funding is usually allocated to common illnesses. Unfortunately, rare diseases only get a "boost" when someone rich and famous offers to be a champion for fundraising! That said, Canada does have centres of excellence that have obtained funding for research on neuroendocrine carcinomas. Some [are] funded by CIHR [and] some by private foundations with an interest in this [illness]. Patients can encourage support by lobbying with CIHR, NCIC, the Cancer Research Society and other funding agencies.

Note: Square brackets with [enclosed text] denote changes or additions made by the editor. The questions have in many cases been paraphrased to improve readability or to combine similar questions submitted by more than one individual.