CNETS Patient Conference April 21 – 22/17, TO, ONT.

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Medical Therapy Options in NETS. The Somatostatin Analogues

Where we have come from?
Where are we going?

History of Somatostatin Analogues

- 1973 –Somatostatin isolated from sheep brain.
  - t1/2 < 2 minutes. Not useful clinically in its native form.
- 1980 – Octreotide. (Somatostatin Analogue) First stable synthetic form. Binds somatostatin receptors on neuroendocrine cells and inhibits secretion of hormones. (Most NET cells bear somatostatin receptors on their surface).
- 1986- Octreotide administered subcutaneously with excellent results in control of "carcinoid" related symptoms. (Introduction into clinical practice 1987).

Carcinoid Syndrome

- Somatostatin Analogues
  - Improved control of carcinoid syndrome and changed the natural history of NETs.
    - Carcinoid crisis – severe flushing, diarrhea, and hemodynamic instability was a common cause of death in the past and occurs rarely with use of SSA's today.
    - Appropriate use of the somatostatin analogues over the last 30 years has improved patient quality of life and contributed, along with other treatment advances to improved survival.

Somatostatin Analogues (SSA's)

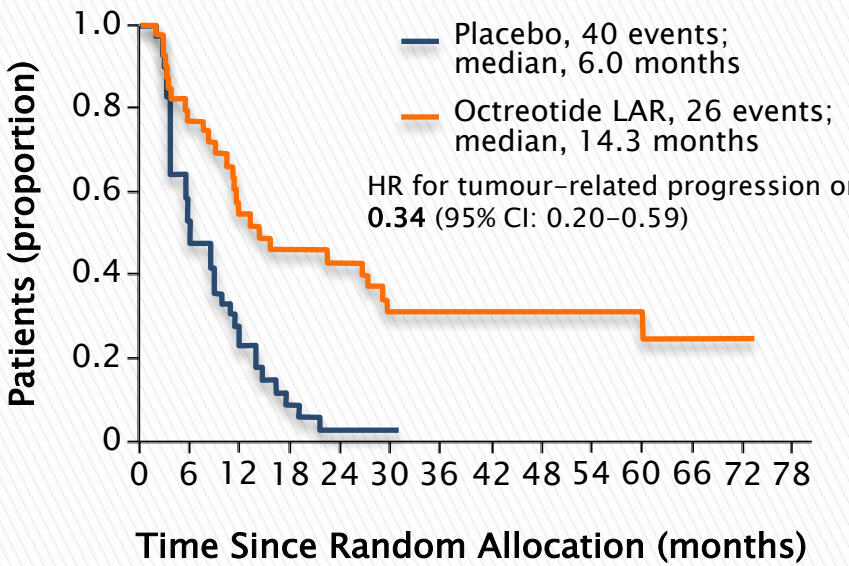
- Long acting SSA's
  - Octreotide LAR, Lanreotide
    - Consistent therapeutic levels.
  - Significant symptom relief in majority of patients with "functional" tumors.
  - Regular (often monthly) administration has dramatically improved patient care and patients QOL.

Somatostatin Analogues (SSA's)

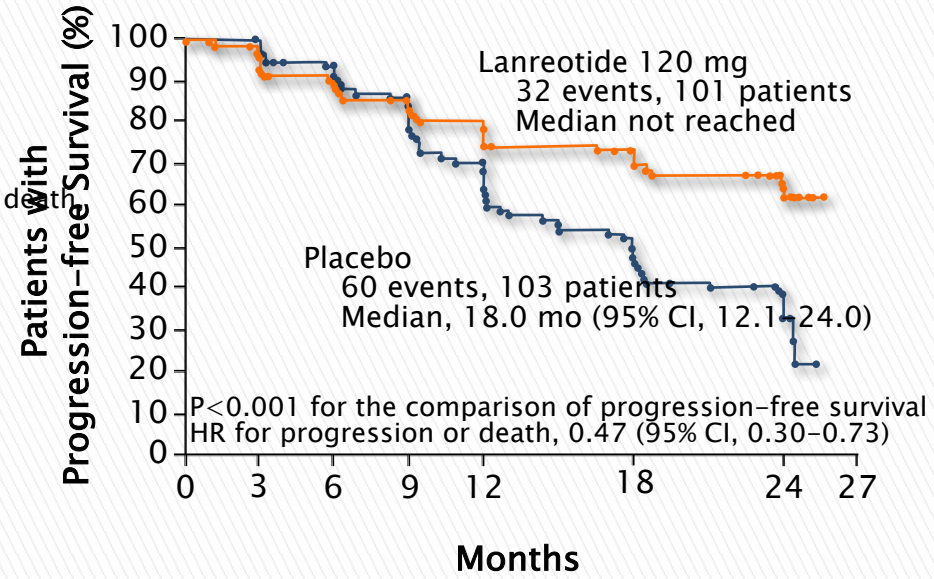
- Importantly for many patients with NETS, Octreotide and Lanreotide are also effective in slowing growth of tumors and progression of disease (whether the tumor is functional or not).
  - PROMID
  - CLARINET

Evidence Demonstrating Anti-Tumour Effect of Somatostatin Analogues in NETs

Long-acting octreotide vs. placebo: Time to progression or tumour- related death (PROMID)[1]



Prolonged-release lanreotide vs. placebo: Progression-free survival (CLARINET study)



HR: hazard ratio

Adapted from: 1. Rinke A, *et al*. J Clin Oncol 2009;27(28):4656-63.
2. Caplin M, *et al*. N Engl J Med 2014 Jul 17;371(3):224-33.

Systemic therapy in NET'S

- Targeting the somatostatin receptor is foundational to the care of patients with NETS.
- Modification of the somatostatin molecule has led to:
  - Improvements in diagnostic imaging & staging (Octreotide scans).
  - Systemic Therapy
    - Somatostatin Analogues
    - Peptide Receptor Radionuclide Therapy (PRRT).

Systemic therapy in NET'S

- Targeting the somatostatin receptor is foundational to the care of patients with NETS.
- Appropriate access to somatostatin analogues is problematic in Canada.
- We need your help!
  - Varying accessibility across the country for treatment of endocrine syndromes caused by NETS
  - Inconsistent access to SSA's for their benefits in tumor control
  -
- Access to new systemic therapy
  - Canadian approval processes are slow
  - Costly treatments

Systemic Treatment – Sequencing?

TKI	mTOR	Chemo	PRRT
mTOR	TKI	PRRT	Chemo
Chemo	PRRT	TKI	mTOR
PRRT	Chemo	mTOR	TKI

SSA's

Questions remain

- When to start treatment? When to stop?
- Sequencing of treatment?
  - Is there a best option?
- Treatment combinations?
  - SSA's + PRRT
  - SSA's + Targeted therapy
  - PRRT + Targeted therapy
  - Better treatment or more toxic?

Questions remain

- We need access to large data bases that will help us to learn from “real world” experience.
  - The data from clinical trials does not always reflect what happens in the day to day clinical environment.