Diagnosis and Treatment of Neuroendocrine Disease: From $^{79}\text{Au}$ to $^{40}\text{Zr}$

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Objectives

- Briefly discuss functional imaging tools available for staging neuroendocrine disease
- Describe the role functional imaging plays in guiding radioisotope therapy
- Discuss current Lu-177 therapy program in London
- Update on the proposed provincial Lu-177 Phase III trial
Diagnosis of Neuroendocrine Disease

• Apart from anatomical imaging (CT, MRI), neuroendocrine disease is staged using tracers which bind to specific tumoral markers

• Currently in Ontario we can use In-111 Octreotide and I-123 or I-131 MIBG
Treatment Options for Neuroendocrine Disease

- Surgery
- Chemotherapy
- Biologic drugs
- Targeted liver-directed therapy

Radioisotope therapy/PRRT
Principles of Radioisotope Therapy

- Primary principle of radioisotope therapy is **theranostics**
- Basic principle of **theranostics** is using diagnostic agent to guide a targeted therapy
- The mechanism by which most Nuclear Medicine isotope treatments work is via binding to tumor receptors
  - The term peptide receptor radionuclide therapy (**PRRT**) is often used
  - NET tumors express an abundance of somatostatin receptors
History of Radioisotope Therapy in London

- Long history of radioisotope therapy in London for neuroendocrine disease
- High dose Indium-111 Octreotide was used starting in ~1999
- Often In-111 therapies were offered in combination with chemotherapy
- Lutetium-177 therapy in London started around 2011
Lu-177 PRRT

- Been offered in London Ontario for a number of years under the Special Access Program (SAP)

- Health Canada discontinued the SAP program in 2013

- London and Edmonton both started Safety Registry Studies
  - An Open Label Phase II, Registry Study of Lutetium-177 (DOTA0,Tyr3] Octreotate (Lu-DOT-TATE) Treatment in Patients with Somatostatin Receptor Positive Tumours
What is Lu-177?

- Isotope which emits multiple forms of radiation
  - Gamma radiation which is useful for imaging
  - B-particles (or high energy electrons) which are responsible for tumor cell death
Patient Selection for Lu-177

- NET tumor G1 or G2
  - Ki-67 < 20%
- Tumor uptake on In-111 Octreotide scan = or > liver
- No significant renal impairment
Efficacy of Lu-177 Dotatate

N = 229 (ITT)
Number of events: 90
- $^{177}$Lu-Dotatate: 23
- Oct 60 mg LAR: 67

Hazard Ratio [95% CI]
0.209 [0.129 – 0.338]
p < 0.0001

$^{177}$Lu-Dotatate
Median PFS: Not reached

Octreotide LAR 60 mg
Median PFS: 8.4 months

All progressions centrally confirmed and independently reviewed for eligibility (SAP)

Presentation Presidential Session II of the 18th ECCO – 40th ESMO – European Cancer Congress 2015, 27 September 2015, abstract 6LBA, Vienna
N = 229 (ITT)
Number of deaths: 35

- $^{177}$Lu-Dotatate: 13
- Octreotide 60 mg LAR: 22

$P < 0.0186$
Moving Forward

• Provincial Lu-177 therapy trial involving:
  – Princess Margaret Hospital (Toronto)
  – Sunnybrook (Toronto)
  – Juravinski (Hamilton)
  – London Health Sciences

• Start date of provincial trial 2016(?)

Schulich Medicine & Dentistry
Provincial Lu-177 Trial

- Patient specific dosimetry

- Ga-68 Dotatate PET-CT imaging at both Princess Margaret and London Health Sciences
  - Used for staging and evaluation of interim therapy
Ga-68 Dotatate

vs

In-111 Octreotide
Questions?