Lu-177 OPS-201 Trial for Metastatic Neuroendocrine Tumour

Dr Nat Lenzo, Dr Joe Cardaci, Dr Danielle Meyrick, Dr Andrew Henderson, Ms Julie Crouch, Dr Sharon Yeo, & Prof Harvey Turner

Oceanic Molecular Hollywood PET-CT Centre, Nedlands, Western Australia
Theranostics Australia, Hollywood Private Hospital, Nedlands Western Australia
School of Medicine and Pharmacology, The University of Western Australia
Disclosures

Founding Director:

- Theranostics Australia P/L
- Oceanic Molecular P/L
- Principal Investigator (Hollywood Private Hospital): Ipsen Lu-177 OPS-201 Trial
Introduction

• *The times they are a changin’* ..... 
• 2005:
  – Indium octreotide imaging 
  – Somatostatin receptor agonist treatment 
• 2016:
  – Ga-68 octreotate: state of the art imaging for NET (not Medicare) 
  – Lu-177 octreotate: most efficacious therapy for NET 
• 2020:
  – ? Ga-68 OPS 202 for NET imaging 
  – ? Lu-177 OPS 201 for NET therapy
Background

SOMATOSTATIN RECEPTOR AGONISTS VS ANTAGONISTS

• Somatostatin receptor (SSTR) targeting for imaging has been common for over 20 yrs and for therapy for over 10 yrs

• Conventional wisdom
  – binding of a SSTR agonist (e.g. octreotate) to G-protein activated receptor with subsequent internalisation into cell
  – More robust for imaging
  – Safety for therapy
Somatostatin Receptor Agonists Vs Antagonists
Somatostatin Receptor Agonists Vs Antagonists

- Ginz et al PNAS 2006 found a new class of antagonistic peptides
- Independent to receptor activation status therefore many more potential binding sites
- Despite lack of internalization did not show increased clearance – in fact appeared to be the opposite (Cescato 2011, Fani 2012, Wild 2014)
Somatostatin Receptor Antagonist

- Higher Bmax$^1$
- Higher Tumor Uptake$^2$
- Longer Tumor Retention Time$^3$
- Higher renal uptake

177Lu-DOTA-TATE 
Agonist

177Lu-DOTA-BASS 
Antagonist$^4$

Somatostatin Receptor Agonists Vs Antagonists
Further Development: Radiolabeled SST2 “Antagonist” for PET

$^{68}$Ga-DOTATATE  $^{68}$Ga-OPS202

**Fig. 1**
Micro-PET imaging of $^{68}$Ga-OPS202 in HEK-sst2 mice xenografts, compared to $^{68}$Ga-DOTATATE$^{1,2,3}$

In comparison to the agonist the antagonist:
- Higher number of binding site (Bmax)
- Higher tumour uptake

$^{68}$Ga-OPS202 = sstr antagonist

Gallium-68 OPS-202 in NET
Patient 3: 32-year old male with Ileum NET (G2, Ki67 2-5%) who has known liver and lymph-node metastases  

? Restaging

Octreoscan®
scintigraphy 24h p.i.
sst₂ receptor agonist
02.09.14

past

68Ga-DOTATOC
PET 1h p.i.
sst₂ receptor agonist
14.11.14

present

68Ga-OPS202
PET 1h p.i.
sst₂ receptor antagonist
18.11.14

future?
Somatostatin Receptor Antagonists in the Clinic

$^{177}$Lu-OPS201

$^{177}$Lu-DOTA-TATE

Pilot Study: SPECT imaging illustrating an increased tumor uptake of $^{177}$Lu with antagonist (OPS-201), implying potential for greater therapeutic efficacy.

PET scan demonstrates pelvic metastases. SPECT imaging post-$^{177}$Lu-agonist and antagonist, demonstrating increased (x4) tumour uptake of $^{177}$Lu with antagonist, implying potential for greater therapeutic efficacy; higher tumour / kidney ratio implies wider safety window.

68Ga-DOTATATE PET images of patient 2 before (A) and 3 mo after (B) treatment with 15.2 GBq of 177Lu-DOTA-JR11 and 68Ga-DOTATATE PET images of patient 3 before (C) and 12 mo after (D) treatment with 5.9 GBq of 177Lu-DOTA-JR11.

New agent trials

• Ipsen commenced phase III trial of In-111 octreotide vs Ga-68 OPS-202 (USA)

• Ipsen in recruitment/early phase I Lu-177 OPS-201 in NET (USA – New York) – dose finding/toxicity

• Ipsen chosen sites for phase II/III Lu-177 OPS-201 in metastatic NET:
  – 7 sites around the world - 1 in USA, 1 in UK, 4 in Europe, Theranostics Australia Hollywood Hospital Perth and Peter MacCallum Cancer Institute, VCCC Melbourne are Australian sites.
Phase II/III Lu-177 OPS 201 Trial

- Metastatic GPNET; low ki-67; No previous Lu-177 therapy; No significant renal disease; Progressive disease (imaging)
- Lutetium therapy alone – not with chemotherapy; 4 cycles 8 weeks apart
- Initial Gallium- octreotate scan
- 45 patients to be recruited worldwide
- Extensive follow up: clinical, imaging and blood tests over 2 years
- Initial application approved by Hollywood Ethics June 2016; awaiting revision of protocol (Ipsen); for recruitment likely October/November 2016
How Do I Contact Theranostics Australia?

• Administration:
  – Theranostics Australia
    Unit 106, 1 Silas Street
    Richmond Quarter Building East Fremantle WA 6158

• P| +61 8 9091 1081
  F| +61 8 9387 7866
  E| reception@theranostics.com.au