Everything you always wanted to know about PRRT, but didn’t know whom to ask.

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Department of Surgery
Nashville, TN
November 2, 2013
Let me tell you a story...
My Story

• Grew up in Maryland
• College in Boston
• Medical School in New York
• Trained in ISLET CELL TRANPLANTATION
• Trained in general surgery at New York-Presbyterian Hospital
• Trained in Diabetes Research at the National Institutes of Health
• Studied novel imaging for diabetes
• Training in Research, GI, Endocrine, Cancer, Surgery, Imaging, Nuclear Medicine
Uppsala, Sweden

Uranium City

Nashville

Monte Carlo, Tunisia, Casablanca
Uppsala, Sweden
Why Uppsala?

>2500 patients
>1000 current patients
>150 new patients/year (203 new patients 2008)

20-30% from abroad
>90% from other parts of Sweden/abroad
**Why Uppsala?**

**In-patients - 13 Beds**
- 2800 hospital days
- 80% from other parts of Sweden
- 13% from abroad
- 1100 visits/year
- 87% from other parts of Sweden
- 12% from abroad
- 25–30 patients/week

**Out-patient-clinic**
- 973 visits/year
- 76% from other parts of Sweden
- 11% from abroad
PATIENT

Personalized Medicine

Endocrinologist

Gastroenterologist

Radiologist

Nuclear medicine

Surgeon

Pathologist

Oncologist

Pulmonary

Research

Nursing

Support Group

Primary Care

Primary Care
Another Story...
Another Story...
PRRT

Peptide Receptor Radionuclide Therapy
(a.k.a. PRRNT)
Outline

• What is it?
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Somatostatin

Somat = Body
Stat = Stop

Roger Guillemin
Andrew Schally
1977
Sandostatin LAR Depot Timeline

Sandoz forms Somatostatin project team, 1973

New analogue discovered, 1978

Sandoz abandons work and focuses on mini-SSAs, 1979

Wilfried Bauer synthesizes SMS 201-995, 1980
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Octreotide binding affinity

sst-1

+++ +

sst-2

sst-3

sst-4

sst-5

++

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What are SRS, PET and PRRT?

- SRS = Somatostatin Receptor Scintigraphy
- SPECT = Single Photon Emission Computed Tomography
- PET = Positron Emission Tomography
- PRRT = Peptide Receptor Radiotherapy
  – aka PRRNT (nuclide)

THERANOSTICS
Octreotide binding affinity

Somatostatin Receptor Scintigraphy

sst-1
sst-2
sst-3
sst-4
sst-5
Types of PRRT

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**Additional Elements**

- Ne: gas
- Ga: liquid
- Ge: solid
Beta and Gamma emitter
T1/2 6.73 days
Path length 0.04-1.8 mm
Toxicity: renal, bone marrow, liver

Beta emitter
T1/2 64 hr
Path length 2.7 mm
Toxicity: renal, bone marrow

Pagel et al, Principles of Cancer Biotherapy, Oldham and Dillman, 2009
Metastatic Insulinoma Treated with $^{177}$Lu-DOTA-Octreotate
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Survival With PRRT - Dutch

Predictors:
- Disease Stabilization
- Less Liver Involvement
- Good Performance
- No weight loss
- No Bone Mets
- Not gastrinoma/
  insulinoma/VIPoma

Kwekkeboom et al, JCO, 2009
- 504 patients
- PFS 40 mo
- Median OS from Tx 46 mo
- Median OS from Dx 128 mo

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Kwekkeboom et al, JCO, 2009
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Side Effects

• Bone marrow suppression
  – WBC (immune cells)
  – RBC (anemia)
  – Platelets (clotting)

• Kidney function
  – Lost 1-3% per year

• Nausea
  – Amino Acid Infusion

• LIMITED NUMBER OF TREATMENTS
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Candidates

✓ STRONG SSTR2 SIGNAL
  Octreoscan
  68Ga-DOTA-SSA PET/CT

✓ Strong kidneys

✓ Strong bone marrow

✓ Good nutrition
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• http://netter-1.com/

• “A multicenter, stratified, open, randomized, comparator-controlled, parallel-group phase III study comparing treatment with 177Lu-DOTA0-Tyr3-Octreotate to Octreotide LAR in patients with inoperable, progressive, somatostatin receptor positive, midgut carcinoid tumors”
USA

- Nashville, TN (Eric Liu)
- Los Angeles, CA (Ed Wolin)
- Palo Alto, CA (Erick Mittra)
- Tampa, FL (Jon Strosberg)
- Chicago, IL (Al Benson)
- Iowa (Dave Bushnell)
- Houston, TX (James Yao, Ebrahim Delpassand)
- New Orleans, LA (Richard Campeau)
- Boston, MA (Matt Kulke)*
- Rochester, MN (Anthony Hobday)
- New York, NY (Stan Goldsmith)
- Durham, NC (Michael Morse)*
- Philadelphia, PA (Dave Metz)

* NOT RECRUITING
Eligibility

- 18 y/o or greater
- MIDGUT carcinoid (lower duodenum through right colon)
- PROGRESSING through a stable dose of Sandostatin LAR 20 or 30 mg
- Off other systemic therapies for 4 weeks
- No procedures for 12 weeks
- RANDOMIZED 1:1 PRRT vs. Sandostatin LAR 60mg monthly
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A day in the life of PRRT...

• Land in Europe
• Evaluation (tests, ultrasound, kidney tests)
• IV – hydration and amino acids
• PRRT Infusion
• Nauseated overnight
• Mildly tired for about a week
• Fly home
• Repeat every 8 weeks, 4x
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• **What can I hope for?**
• When is it going to be here in the U.S.?
Hope...

- Stop the disease growth
- Slow the disease growth
- Improve the symptoms (hormones, pain, fatigue)
- Shrink the tumors
- Lasting effect
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The history of the FDA...

• NETTER-1: 3-5 years
• FDA review
• Other small trials

• NEXT GENERATION OF PRRT
• COMBINATION THERAPY
Thank You

At the Vanderbilt Neuroendocrine Center, we care for people with diseases of the neuroendocrine system including carcinoid tumors, pancreatic neuroendocrine tumors and adenocortical carcinoma. We offer a multidisciplinary team approach to patient care that is the standard of excellence throughout the Vanderbilt-Ingram Cancer Center and Vanderbilt University Medical Center.

www.vanderbiltneuroendocrine.com