The PET-NET Study

2016 CNETS Grant Award

CANM Meeting
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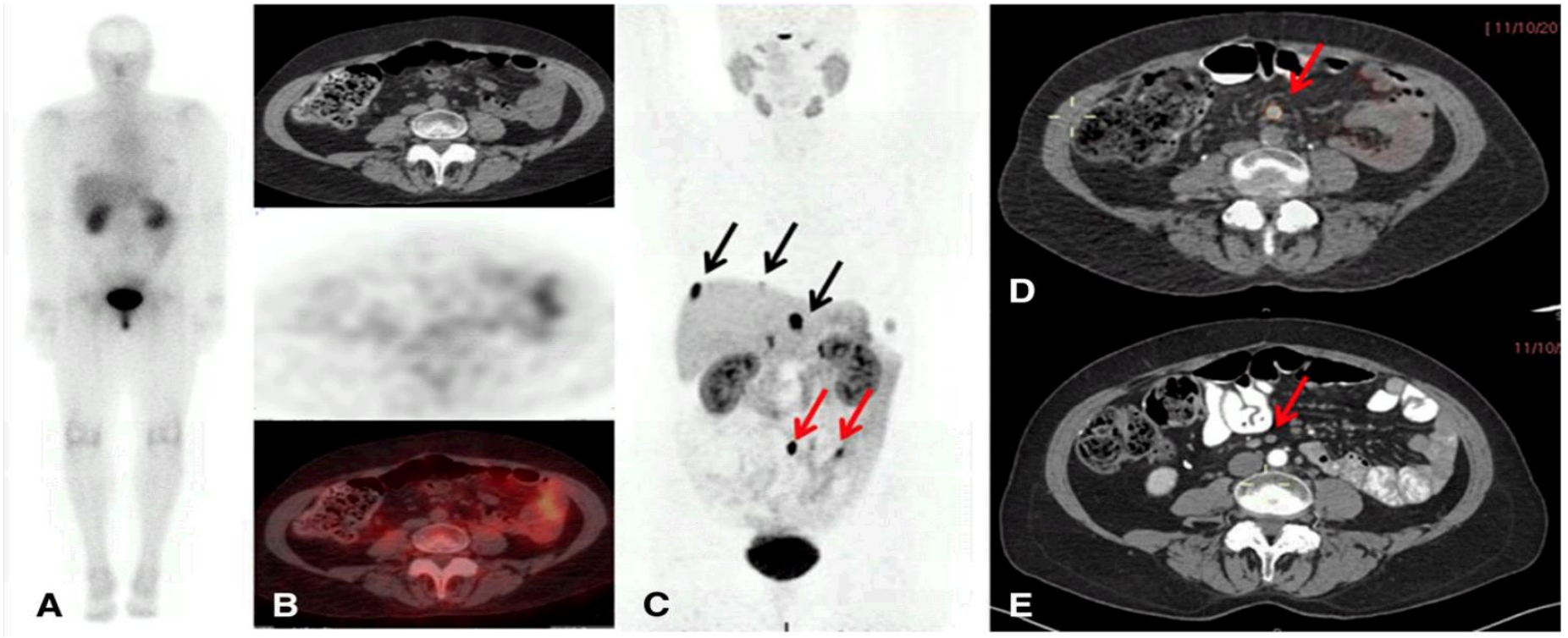
Objectives

- Define role of functional imaging in NETs
- Overview of study
- Timelines and milestones

Established role in NETs

Octroscan	**CT** **Octreoscan** **Octrescan/CT**	**Ga-68** **DOTATATE** **PET**	**Ga-68** **DOTATATE** **PET/CT**



JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Prospective Study of ^{68}Ga-DOTATATE Positron Emission Tomography/Computed Tomography for Detecting Gastro-Entero-Pancreatic Neuroendocrine Tumors and Unknown Primary Sites

Lesions detected in 131 NETs, 45% PNETs

Ga-68 DOTATATE PETCT	CT/MRI	Octreoscan
95%	**45%**	**31%**

Management recommendations changed in 33%

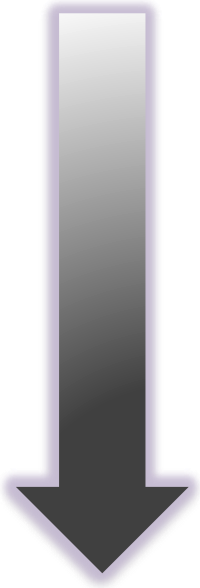
Found primary in 4/14 PU NET patients

Sadowski JCO 2016

Low Ki-67, Mitotic Rate

Well Differentiation

Gallium-68 SSTR PET



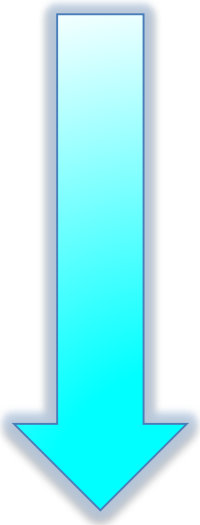
G1

G2

G3

NET

PNET



G3 NEC Neuroendocrine Ca

Small Cell Carcinoma

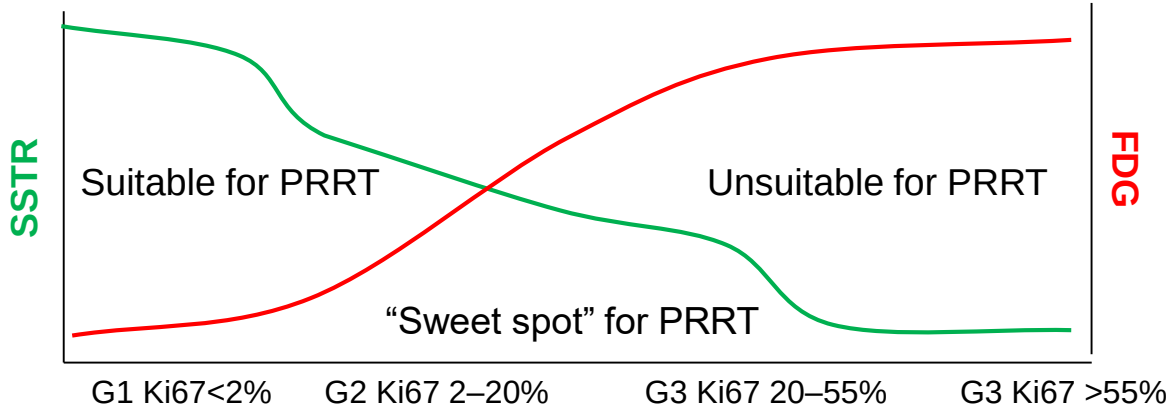
High Ki-67, Mitotic Rate

Poor Differentiation

FDG-18 PET

Functional imaging for the management of NETs

NETPET may be useful for predicting response to PRRT

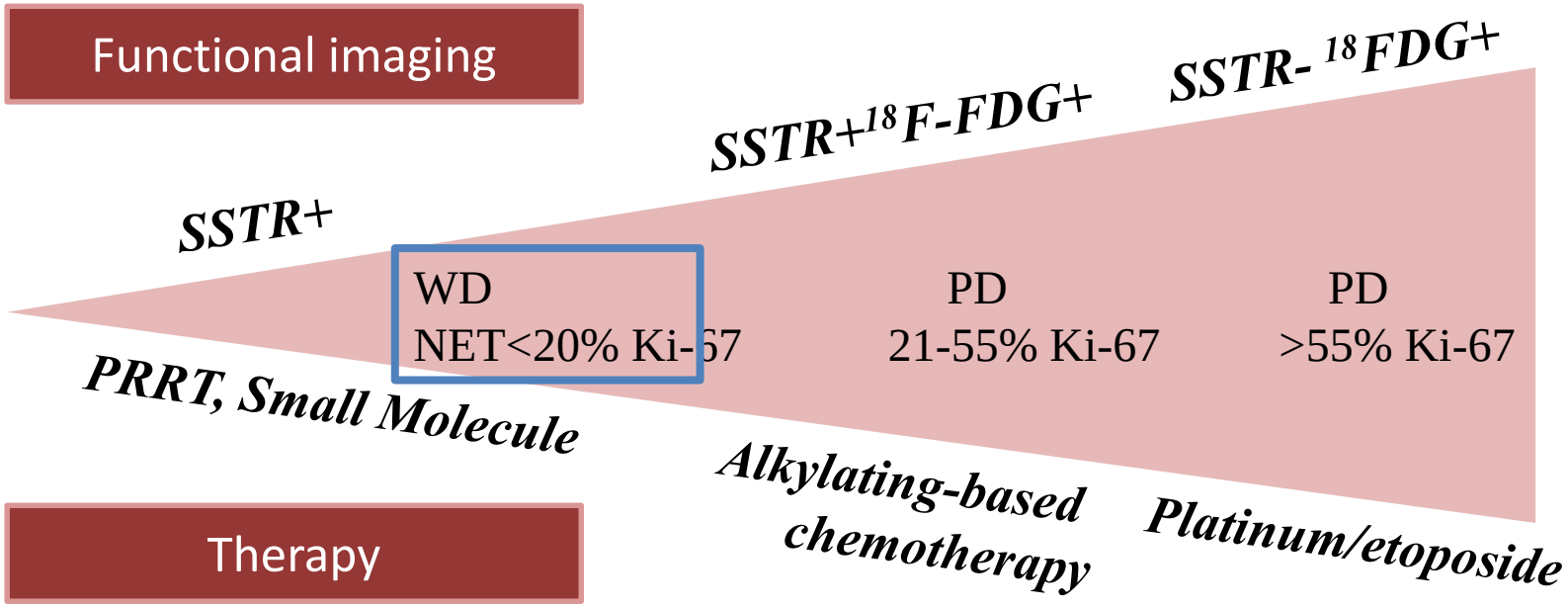


- Patients with lesions showing high SSTRI uptake are obvious candidates for PRRT
- Lesion(s) showing *both* FDG and SSTRI avidity, suggesting intermediate-grade clinical behaviour, may also benefit from PRRT
- Further validation is needed

R. Hicks. Workshop: Imaging Update, March 10, 2017.

PRRT, peptide receptor radionuclide therapy; SSTRI, somatostatin receptor imaging

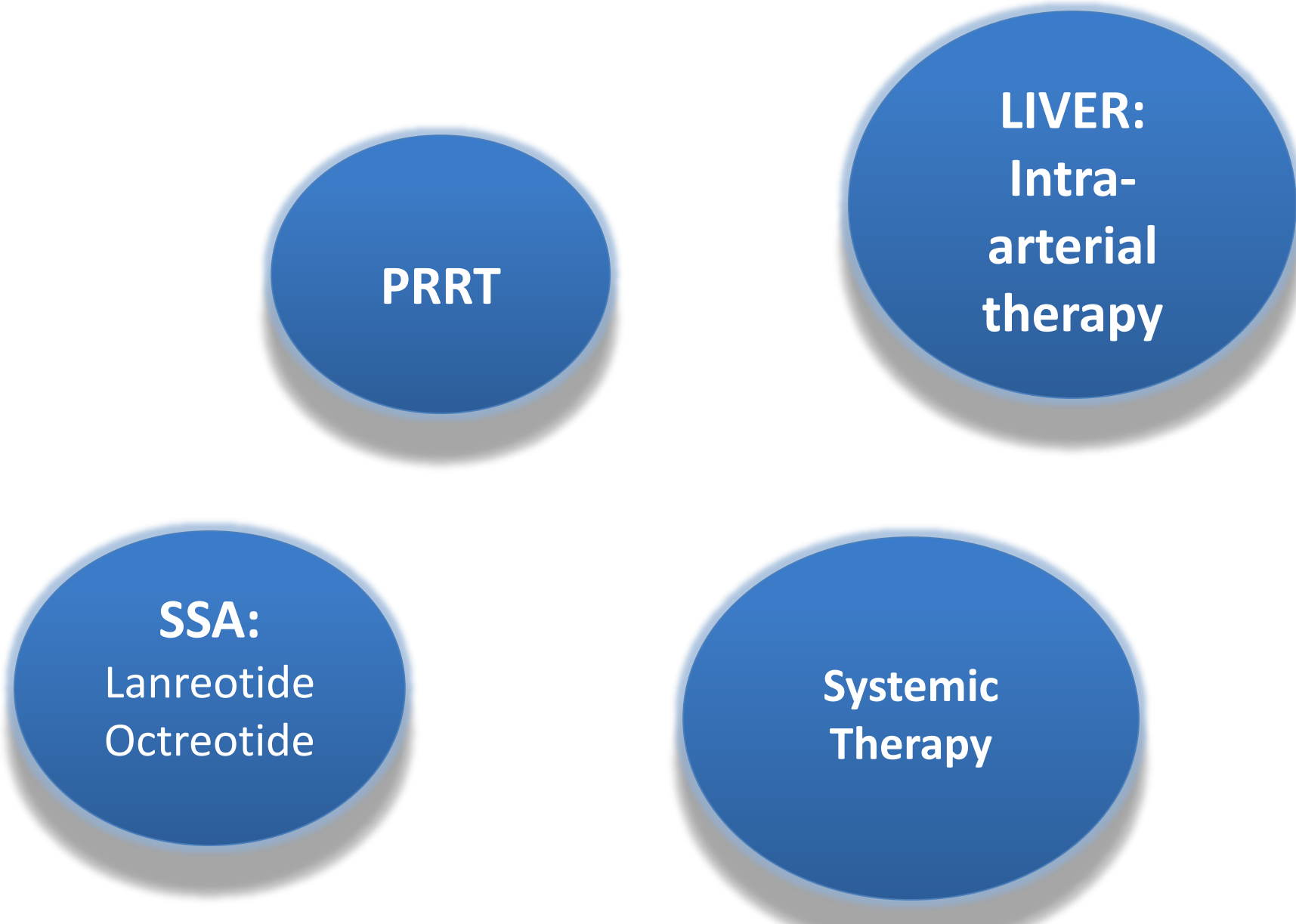
NET-NEC heterogeneity: possible treatment implications



Adapted from Fazio N and Milione M. Cancer Treat Review 2016: 50: 61-67.

GEP NEC – Gastroenteropancreatic neuroendocrine neoplasms; **SSTR** – somatostatin receptor; **FDG** – fluorodeoxyglucose; **G-** grade; **WD** – well differentiated; **PD** – progressive disease; **NET** –neuroendocrine tumour.

NET Treatment Options



PET-NET Study Aims

1. To measure the change in treatment recommendations after DUAL 18F-FDG and 68Ga-DOTATOC PET in NET patients

2. Determine the association between change in 12 week PET SUVmax and CT response at 40 weeks in patients initiating therapy.

3. Conduct genomic correlative studies

PET-NET Study: What is the effect of DUAL 18F-FDG and 68Ga-DOTATOC PET on NET treatment decisions?

NET
-G1
-G2
-G3

PET-CT

18F-FDG-PET
68Ga- DOTA-TOC PET

Pre-PET survey and stage

Investigator choice

- Surgery
  Liver Directed Tx
- Cytotoxic:
  Cap-TMZ *or*
  Streptozotocin
  doublet *or*
  Cis-Etoposide
- Somatostatin Analogue
- Small molecule:
  Sunitinib *or*
  Everolimus
- PRRT: Peptide Receptor Radiotherapy
- Observation

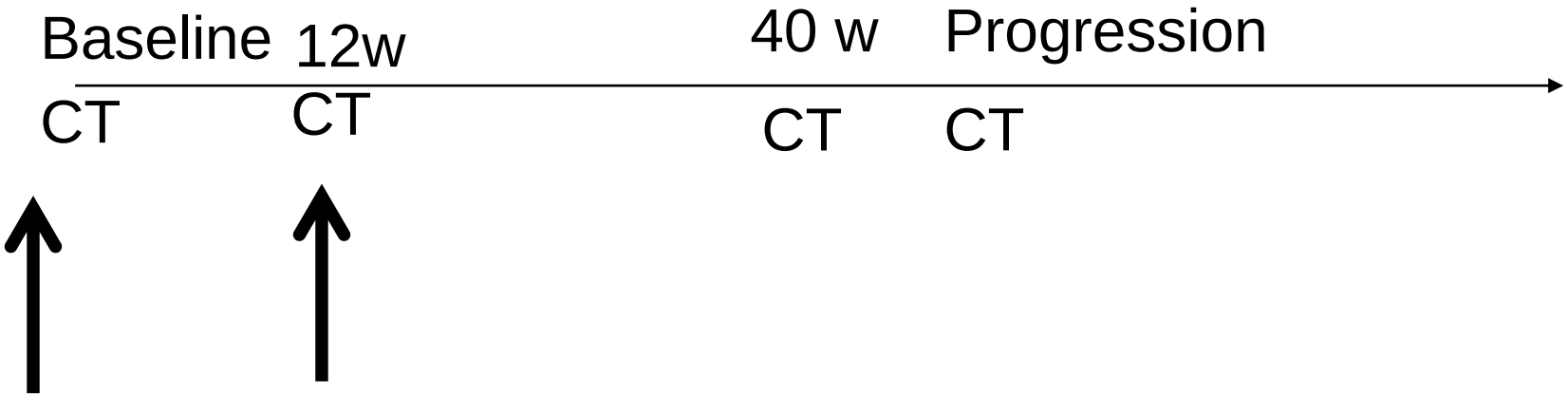
Post-PET survey and stage

Secondary Question: Can 12-week PET response predict 40 week CT response rate?

68 GA 18 FDG **68 GA 18 FDG**

Response:

-CR,PR,SD, PD



Relevant Question for slow-growing tumors: can 12 week change in SUVmax predict futile vs. effective therapy at 40 weeks.

Statistics

N= 46

87% probability of detecting a change in management of 30% or more (prior study with Ga68 DOTA alone= 33-54%)

SUVmax decrease >20% predicts PFS >40 wks
SUVmax decrease <20% predicts PFS < 40wks
86% Power to detect difference in response groups, two sided alpha 5%

Comprehensive Genomic Characterization of NETs is Lacking

- NET reports of limited to N=10-15 patients
- Only PNETs have been studied in a large series of over 100 patients (*Nature*, 2017)

- Common data sets available to compare mutation/copy number differences across different NET histology's or grades are required
- The utility of ctDNA in NETs has not been assessed

ARTICLE

doi:10.1038/nature21063

Whole-genome landscape of pancreatic neuroendocrine tumours

A list of authors and their affiliations appears at the end of the paper

LETTERS

nature genetics

Somatic mutation of *CDKN1B* in small intestine neuroendocrine tumors

***DAXX/ATRX*, *MEN1*, and mTOR Pathway Genes Are Frequently Altered in Pancreatic Neuroendocrine Tumors**

2 MARCH 2017 | VOL 543 | NATURE | 65

www.sciencemag.org SCIENCE VOL 331 4 MARCH 2011

NATURE GENETICS VOLUME 45 | NUMBER 12 | DECEMBER 2013

Correlative Aims and Objectives

- Explore genomic alterations that differentiate G1 vs G3 tumors
- Assess whether NETs from different histology's share genetic characteristics.
- Describe recurrent genomic alterations present in NETs to guide future research and suggest which pathways may be important drivers of NET biology.
- Correlate whole exome sequencing (WES) with 40-week PFS, ctDNA analysis, and PET scan results.

Milestones

Q2 2017
Study Activation

Q2 2019
Accrual Complete

Q3 2019
Primary Endpoint

Study Sites:
BC Cancer Agency, Vancouver
Virginia Mason Cancer Institute, Seattle

Principal Investigators:
Hagen Kennecke
Francois Benard

Co-Investigators:
Etienne Rousseau
Jonathan Loree

Manta Ray