

# Penn NET Center – Overview of Clinical and Basic Science Research

## Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)

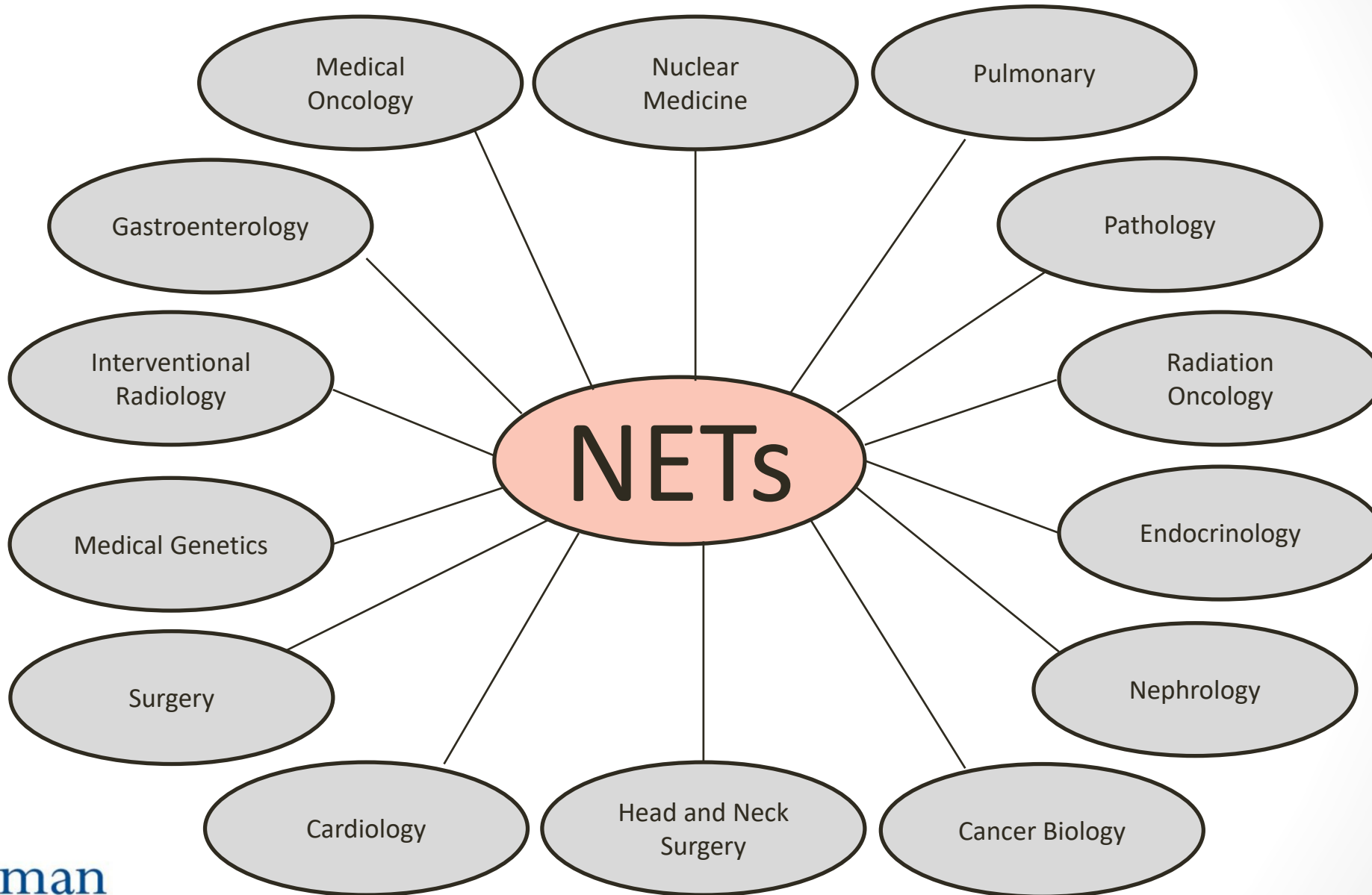
March 5<sup>th</sup>, 2021

Bryson W. Katona, MD, PhD  
Director, Gastrointestinal Cancer Genetics Program  
Division of Gastroenterology

# Disclosures

- Consulting: Exact Sciences
- Paid travel: Janssen
- Clinical trial/study funding: Janssen, Immunovia, Epigenomics, Guardant, Freenome

# PENN NET Center Overview



# Challenges associated with research in NETs

- Rarity and heterogeneity of NETs
- Few researchers compared to other fields
- Limited funding
- Limited/poor models for studying NETs in the lab

# Additional challenges in NET research due to the COVID-19 pandemic

- Increased use of telehealth → great for patient care, but difficult for research
- Workplace staffing restrictions → less research staff on site

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- Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)
  - Database and tumor collection
  - Basic science and translational laboratory research
  - Clinical studies and trials

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# Database and tumor collection

- GEP-NETs
  - Patients consented in the database  
> 400
  - Banked blood samples  
> 200
  - Tumor samples  
> 100



# Use of database information

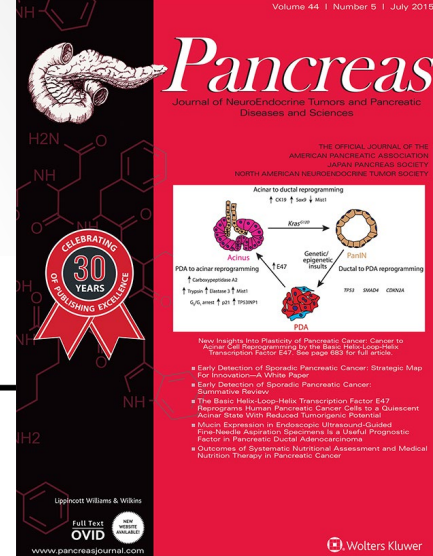
## ORIGINAL ARTICLE

### Predictors of Recurrence and Survival in Patients With Surgically Resected Pancreatic Neuroendocrine Tumors

*Rachel E. Rosenblum, MD,\* Cynthia K. Harris, MD,\* Kiwoon Joshua Baeg, BS,\* Julie A. Starr, BS,† Lauren K. Brais, MPH,‡ Kristen M. Stashek, MD,§ Stephen C. Ward, MD, PhD,|| Bryson W. Katona, MD, PhD,† Thomas E. Clancy, MD,¶ Juan P. Wisnivesky, MD, DrPh,\* Matthew H. Kulke, MD,‡ David C. Metz, MBBCh,† Michelle Kang Kim, MD, PhD,# and Jennifer A. Chan, MD, MPH‡*

*Pancreas* • Volume 49, Number 2, February 2020

Collaboration between Penn, Dana Farber, and Mount Sinai  
Examined 501 patients with surgically resected pancreatic NETs



# Use of tissue samples are critical for research

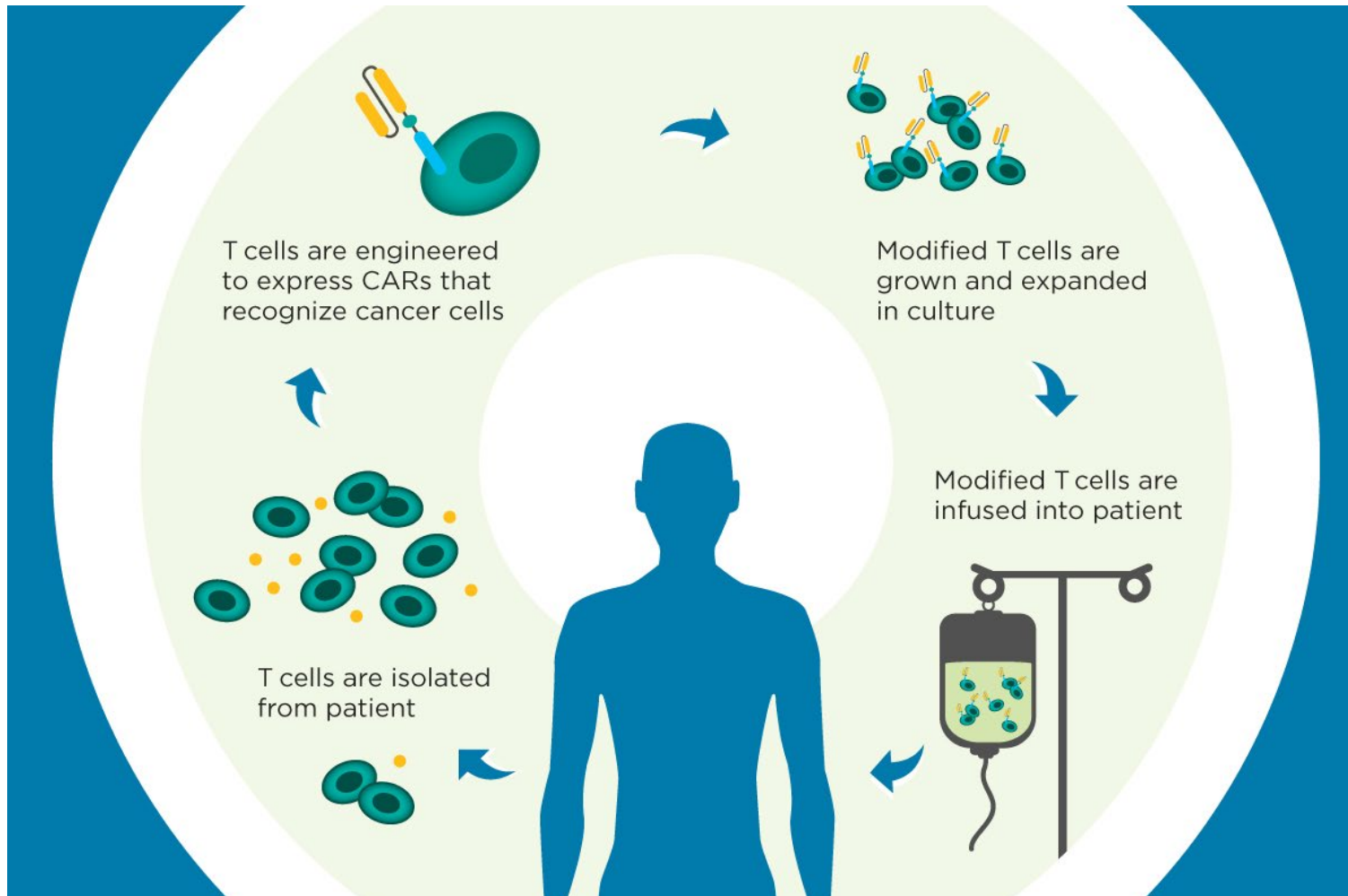
- Tissue sharing collaborations outside of Penn:
  - Dr. Juanita Merchant (University of Arizona)
  - Dr. Scott Oakes (UCSF → University of Chicago)
  - Dr. Neil Renwick (Queens University)
- Tissue use within Penn:
  - Dr. Xianxin Hua (Department of Cancer Biology)
  - Dr. Xiaolu Yang (Department of Cancer Biology)

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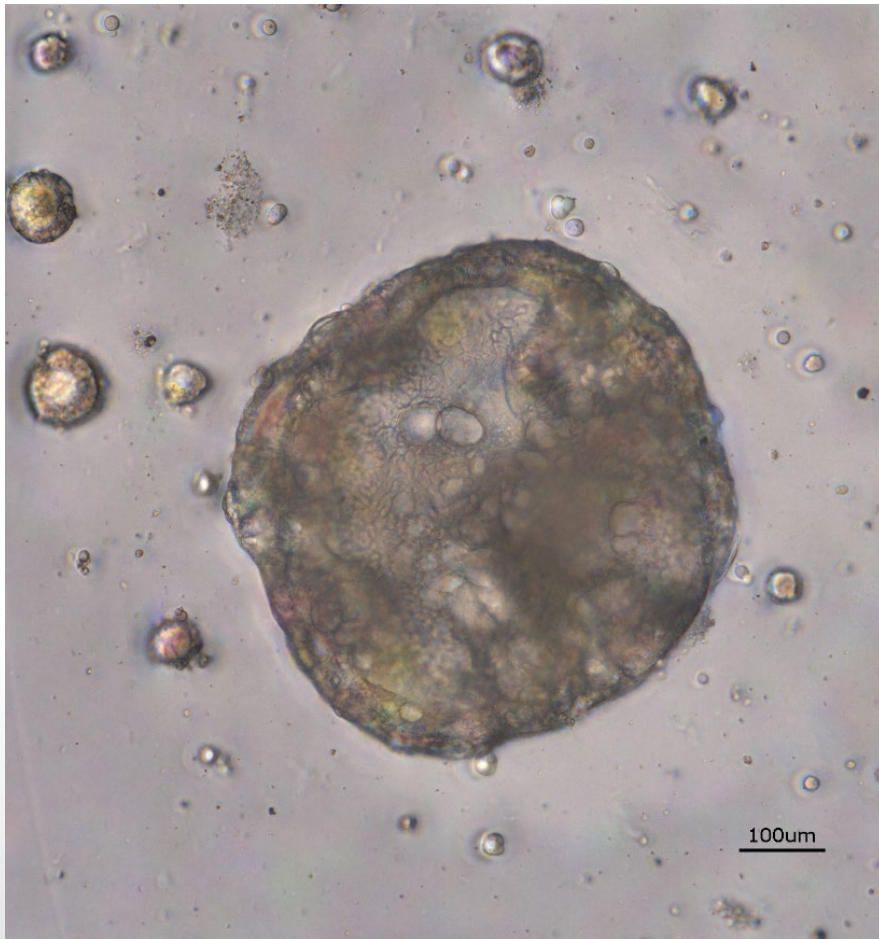
# Advances in NET CAR-T therapy

- Dr. Xianxin Hua's talk will go into this in detail!

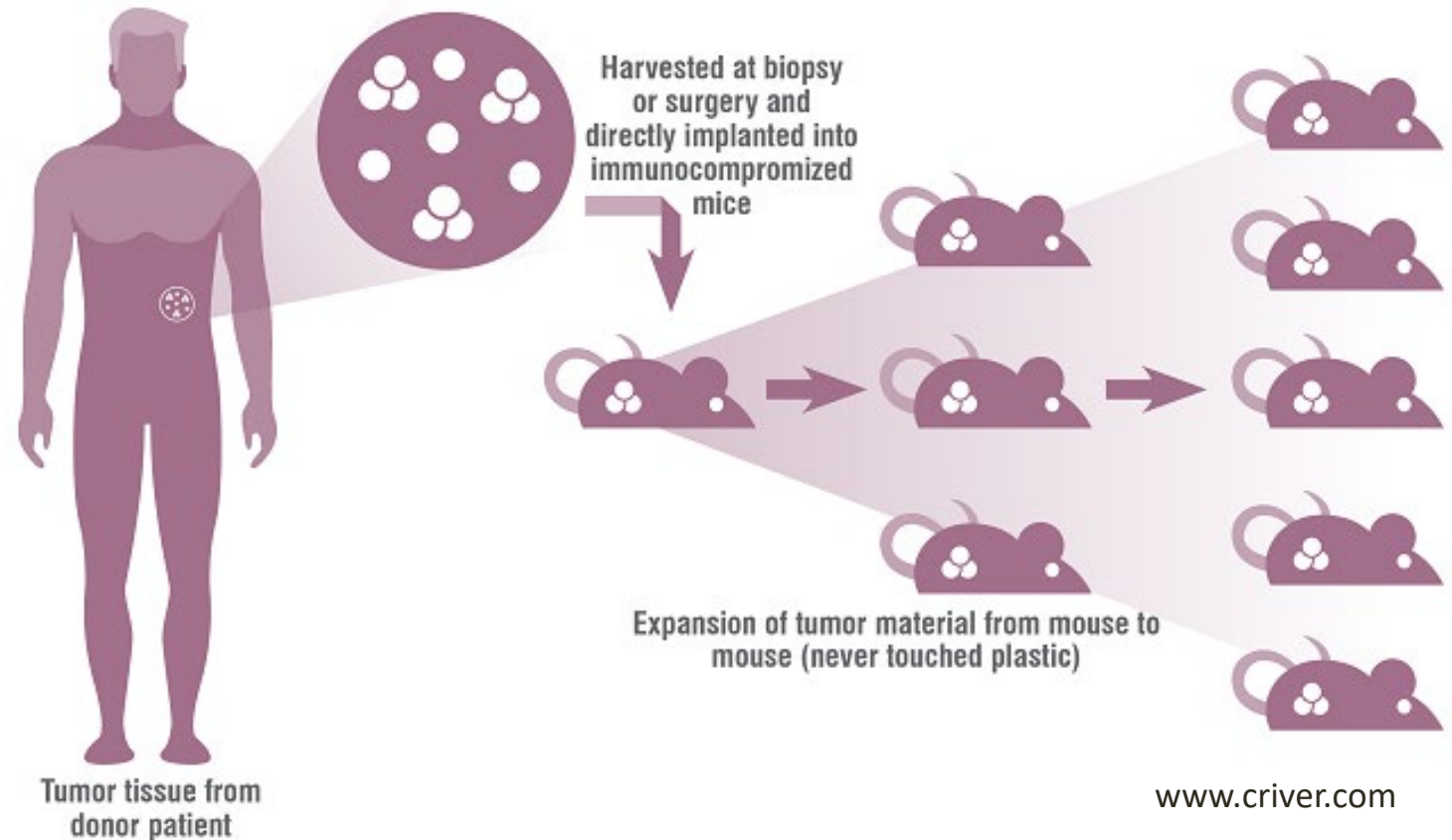


# Study of NET liver metastases

- Dr. Terence Gade's talk will go into this in more detail



## Patient Derived Xenografts (PDX)



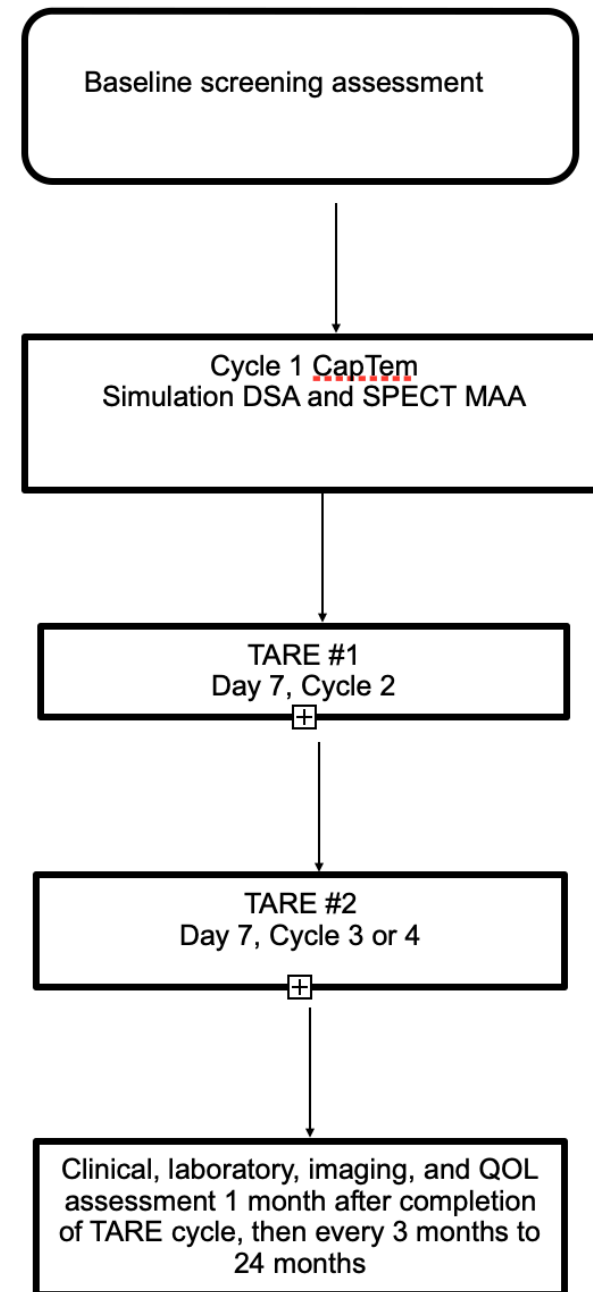
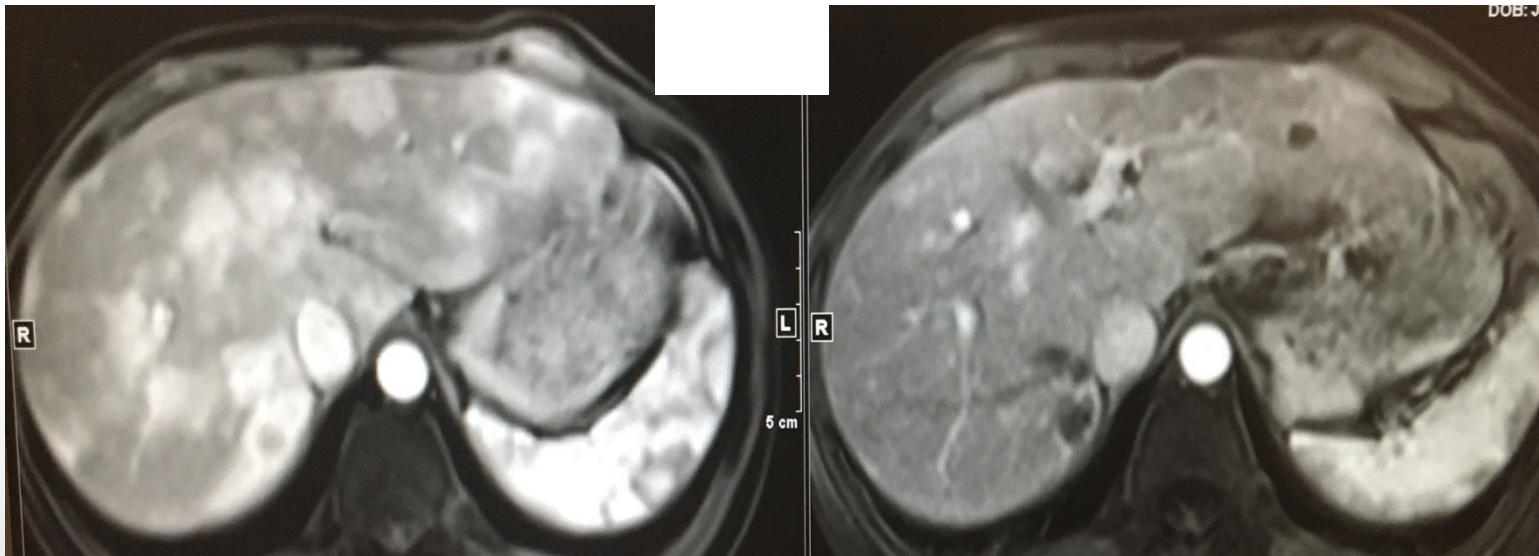


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# CapTem+Y90

- Treatment with combined capecitabine/temozolomide (CapTem) in combination with Y90 transarterial radioembolization
- Grade 2 NETs



# CapTem+Y90

- Multicenter phase 2 trial of CapTem plus Y90 TARE for liver-dominant G2 NETS is funded and will be beginning 2021
- Recruitment goal is 55 patients



# RETNET Trial


Chen et al. *Trials* (2018) 19:390  
<https://doi.org/10.1186/s13063-018-2782-5>

Trials

## STUDY PROTOCOL

## Open Access

Randomized Embolization Trial for NeuroEndocrine Tumor Metastases to the Liver (RETNET): study protocol for a randomized controlled trial

James X. Chen<sup>1</sup>, E. Paul Wileyto<sup>2,3</sup> and Michael C. Soulen<sup>1,3,4\*</sup> 

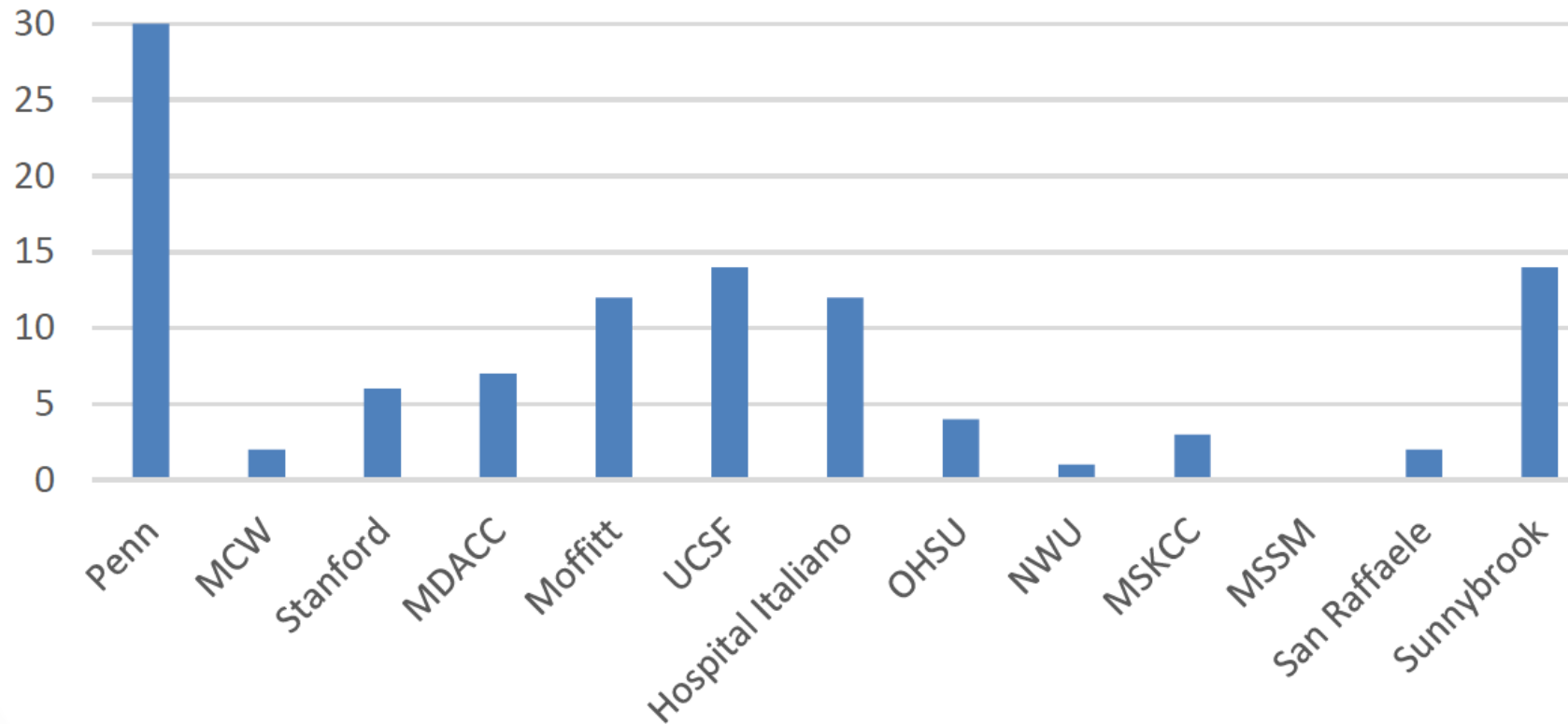


The RETNET trial is a prospective, multicenter randomized controlled trial designed to determine the optimal embolotherapy technique for NET liver metastases.




# RETNET Trial

- 13 sites
- Closed to enrollment now at Penn
- Results will be coming soon



# Abnormal Pretreatment Liver Function Tests Are Associated with Discontinuation of Peptide Receptor Radionuclide Therapy in a U.S.-Based Neuroendocrine Tumor Cohort

JASON M. HECKERT,<sup>a</sup> SARIT T. KIPNIS,<sup>a</sup> SHRIA KUMAR,<sup>b</sup> SAMUEL BOTTERBUSCH,<sup>b</sup> ALICE ALDERSON,<sup>b</sup> BONITA BENNETT,<sup>b</sup> CAROLINE CREAMER,<sup>b</sup> JENNIFER R. EADS,<sup>c</sup> MICHAEL C. SOULEN,<sup>d</sup> DANIEL A. PRYMA,<sup>d</sup> DAVID A. MANKOFF,<sup>d</sup> DAVID C. METZ,<sup>b</sup> BRYSON W. KATONA <sup>b</sup>

<sup>a</sup>Division of Internal Medicine, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA; <sup>b</sup>Division of Gastroenterology, <sup>c</sup>Division of Hematology and Oncology, and <sup>d</sup>Department of Radiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

2020;25:572–578

- PRRT can be administered to a diverse NET population
- Baseline liver function test abnormality increases the likelihood of PRRT discontinuation



## Laboratory, Clinical, and Survival Outcomes Associated With Peptide Receptor Radionuclide Therapy in Patients With Gastroenteropancreatic Neuroendocrine Tumors

Sarit T. Kipnis<sup>1</sup>, Matthew Hung<sup>2</sup>, Shria Kumar<sup>3</sup>, Jason M. Heckert<sup>1</sup>, Hwan Lee<sup>2</sup>, Bonita Bennett<sup>3</sup>, Michael C. Soulen<sup>2</sup>, Daniel A. Pryma<sup>2</sup>, David A. Mankoff<sup>2</sup>, David C. Metz<sup>3</sup>, Jennifer R. Eads<sup>4</sup>, Bryson W. Katona<sup>3</sup>

<sup>1</sup>Division of Internal Medicine, Hospital of the University of Pennsylvania, Philadelphia, PA

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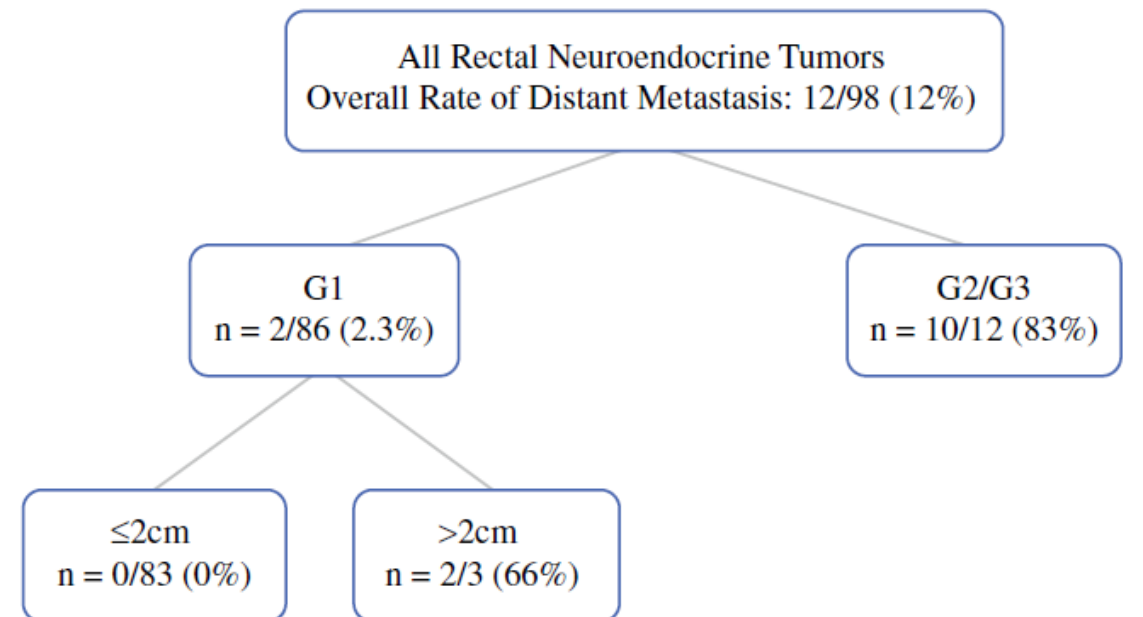
<sup>4</sup>Division of Hematology and Oncology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

ORIGINAL ARTICLE – ENDOCRINE TUMORS


## Grade is a Dominant Risk Factor for Metastasis in Patients with Rectal Neuroendocrine Tumors

Ian W. Folkert, MD<sup>1</sup>, Andrew J. Sinnamon, MD<sup>1</sup>, Seth J. Concors, MD<sup>1</sup>, Bonita J. Bennett, BSN RN<sup>2</sup>, Douglas L. Fraker, MD<sup>3</sup>, Najjia N. Mahmoud, MD<sup>4</sup>, David C. Metz, MD<sup>2</sup>, Kristen M. Stashek, MD<sup>5</sup>, and Robert E. Roses, MD<sup>3</sup>

- Patients with diminutive and small rectal NETs (< 2cm) are at risk of metastatic disease, especially if grade 2 or grade 3
- Tumor grade is a dominant predictor of dissemination



# **$^{68}\text{Ga}$ -DOTATATE Positron Emission Tomography-Computed Tomography Quantification Predicts Response to Somatostatin Analog Therapy in Gastroenteropancreatic Neuroendocrine Tumors**

HWAN LEE <sup>a</sup>, JENNIFER R. EADS,<sup>b</sup> DANIEL A. PRYMA<sup>a</sup>

Departments of <sup>a</sup>Radiology and <sup>b</sup>Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA


2021;26:21–29

- Goal: To determine if gallium scans can predict response to somatostatin analogs
- Showed that low tumor uptake on gallium scans predicted failure of somatostatin analogs in well-differentiated GEP-NETs
- Gallium scans may allow for prediction of who will not benefit from somatostatin analog use

# Antiproliferative Effects of Telotristat Ethyl in Patients with Neuroendocrine Tumors: The TELEACE Real-World Chart Review Study


Michael A Morse<sup>1</sup>

Eric Liu<sup>2</sup>

Vijay N Joish <sup>3</sup>

Lynn Huynh<sup>4</sup>

Mu Cheng<sup>4</sup>

Mei Sheng Duh <sup>4</sup>

Kiernan Seth<sup>3</sup>

Pablo Lapuerta<sup>3</sup>

David C Metz<sup>5</sup>

2020:12 6607–6614

- 200 patients with NETs who received telotristat ethyl for at least 6 months
- 8.5% reduction in tumor size
- Telotristat ethyl may have antitumor effects

<sup>1</sup>Duke Cancer Institute, School of Medicine, Duke University, Durham, NC, USA; <sup>2</sup>The Neuroendocrine Institute at Rocky Mountain Cancer Centers, Denver, CO, USA; <sup>3</sup>Lexicon Pharmaceuticals, Inc., The Woodlands, TX, USA; <sup>4</sup>Analysis Group, Boston, MA, USA; <sup>5</sup>Neuroendocrine Tumor Program at Penn Medicine, Philadelphia, PA, USA



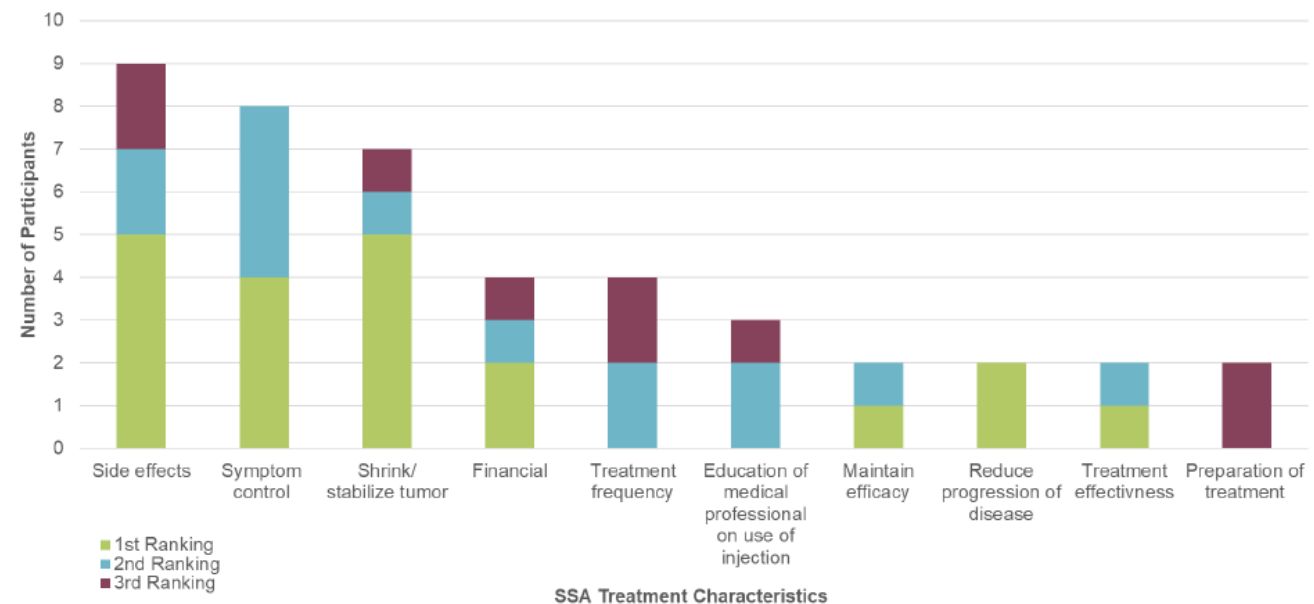
# Patient Experience with Somatostatin Analog Treatments for Neuroendocrine Tumors: Insight from Qualitative Interviews

Caroline Seo<sup>1</sup>, Erica Horodniceanu<sup>1</sup>, Rachel Shah<sup>1</sup>, Grace Goldstein<sup>2</sup>, David Ray<sup>3</sup>, Bonita Bennett<sup>4</sup>, Alexandria Phan<sup>5</sup>, Kelly McCarrier<sup>1</sup>

<sup>1</sup>Pharmerit International, Bethesda, MD, USA, <sup>2</sup>The Carcinoid Cancer Foundation, Mt. Kisco, NY, USA, <sup>3</sup>Ipsen Biopharmaceuticals, Cambridge, MA, USA, <sup>4</sup>Abramson Cancer Center, Philadelphia, PA, USA, <sup>5</sup>UT Health East Texas North Campus MD Anderson Cancer Center, Tyler, TX, USA

- Study aimed at exploring the somatostatin analog treatment experiences and preferences of patients with NETs
- Presented as a poster at NANETS in 2020

Figure 1. Top 10 Important SSA Treatment Characteristics





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# Thank you!

- **Our patients**
- **Co-Directors of Penn NET Center**
  - **Debbie Cohen**
  - **David Metz**
  - **Jennifer Eads**
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  - Anna Raper
  - Stephanie Asher
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  - Megan Lawrence
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  - Robert Roses
  - John Kucharczuk
  - Douglas Bigelow
  - Christopher Rassekh
  - M. Sean Grady
  - Heather Wachtel
  - Major Kenneth Lee
  - Charles Vollmer
  - Thomas Guzzo
  - Frank Venuto
  - Caitlin Perch
  - Pamela Sellers
  - Jason Brant
  - Paul Foley
  - Ara Chalian
  - Kelley Culley
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  - Nevena Damjanov
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  - Kim Reiss-Binder
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  - Thomas Karasic
  - Aditi Singh
  - Kathryn Green
  - Dana Weyrick
  - Adam Fredo
  - Abigail Smith
  - Suzanne McGettigan
  - Melissa Fritz
  - Elizabeth Prechtel Dunphy
  - Gamil Hanna
  - Courtney Gabriel
  - Theodore Laetsch
  - Marcia Brose
  - Ryan Massa
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  - Heather Sheaffer
  - Doris Piccinin
  - ACC Staff and Dieticians
- **Infusion Services**
  - Rob Tobin
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  - Michelle Alonso-Basanta

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  - Sara Attalla
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  - Samboun Bo-Khao
  - Trish Gambino
  - Diann Boyd
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  - Kathleen Montone
  - Beth Furth
  - Stuti Shroff
  - Rashmi Tondon
  - Danielle Fortuna
  - Zhaohai Yang
- **Radiology**
  - Joshua Cho
  - Sudhir Kunchala
  - Emmanuel Magara
  - Sophia O'Brien



[www.netrf.org](http://www.netrf.org)

- **Nuclear Medicine**
  - Daniel Pryma
  - David Mankoff
  - Hwan Lee
  - Ayana Smith
  - Glafirah Dumas
  - Mehran Makvandi
  - Ellie Mantel
- **Renal**
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  - Matthew Denker
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  - Caitlin White
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  - Benita Weathers
  - CHTN Staff
- **Pharmacy**
  - Anna Jung
- **Cardiology**
  - Victor Ferrari
  - Joseph Carver



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  - Michael Soulen
  - Mandeep Dagli
  - Jeffrey Mondschein
  - William Stravopoulos
  - Diana Van Houten
  - Laura Herron
  - Amanda Davis
  - Ginna Deitrick
  - Scott Trerotola
  - Deepak Sudheendra
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  - NET Research Foundation
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  - NANETS
  - Run for the Stripes

