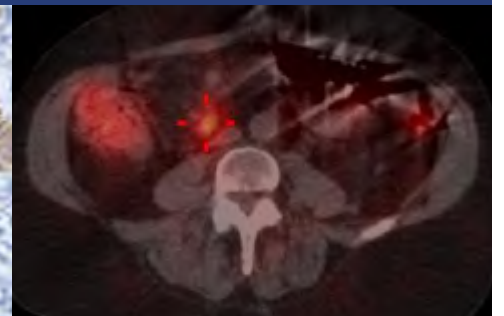
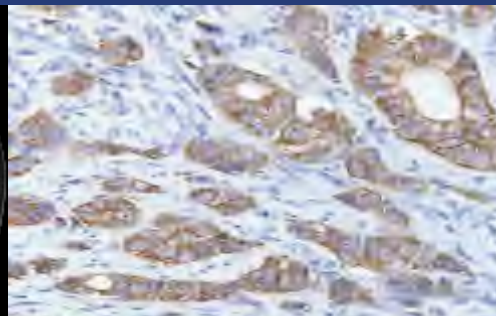
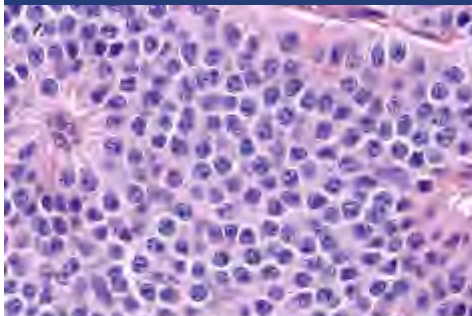


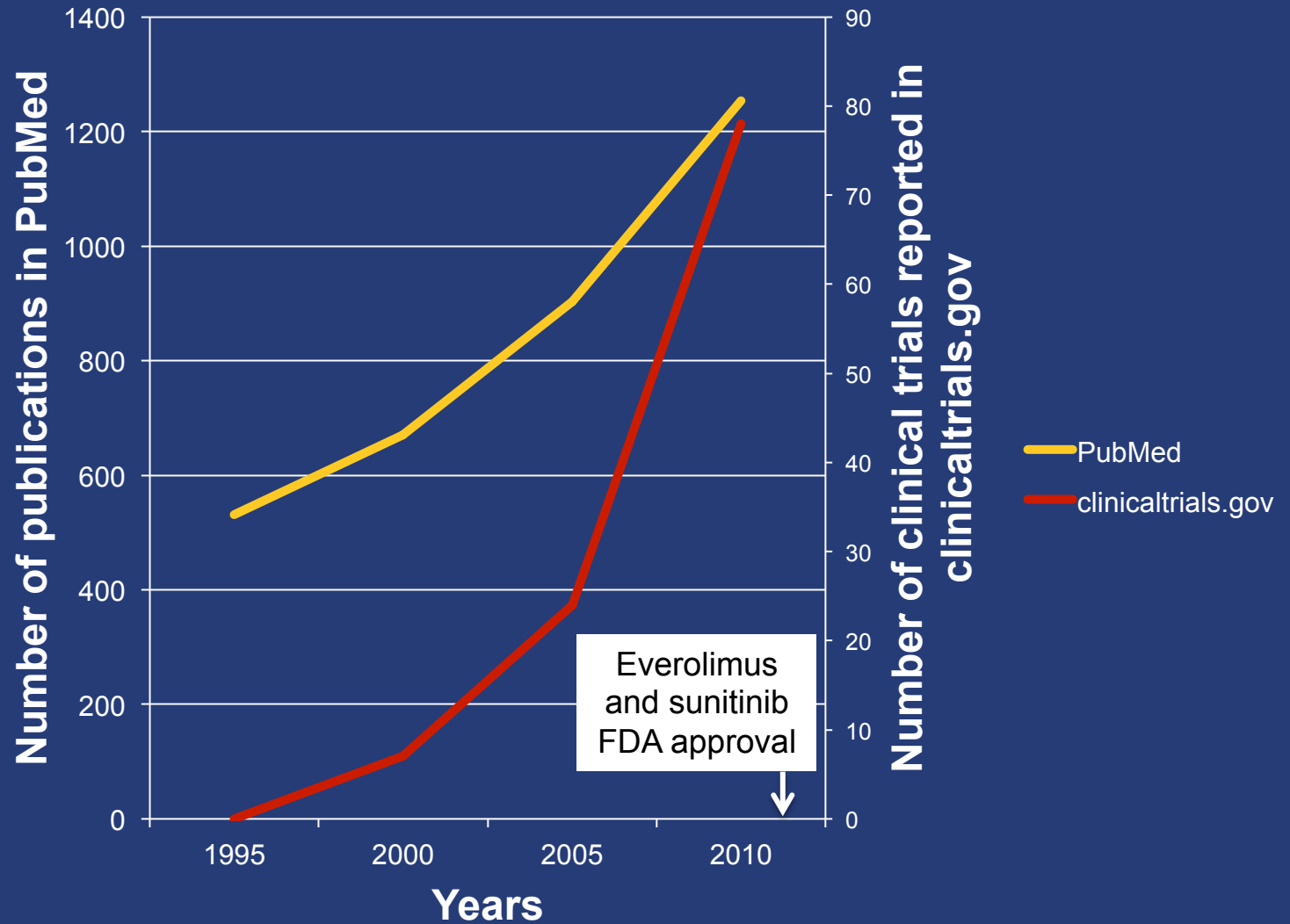
Clinical Trials 101 and Current Clinical Trials

Pamela L. Kunz, MD
Assistant Professor of Medicine / Oncology
Stanford Cancer Institute

Member, NCCN NET Guidelines Committee
Member, National Cancer Institute NET Taskforce
Co-Chair, NANETS Guidelines Committee



The state of NET research



Outline

- Clinical Trials 101
- What have we learned from recent trials?
- What trials are on the horizon?
- How can you learn about clinical trials?

What are clinical trials?

- *“Clinical trials are research studies that explore whether a medical strategy, treatment, or device is safe and effective for humans.”*

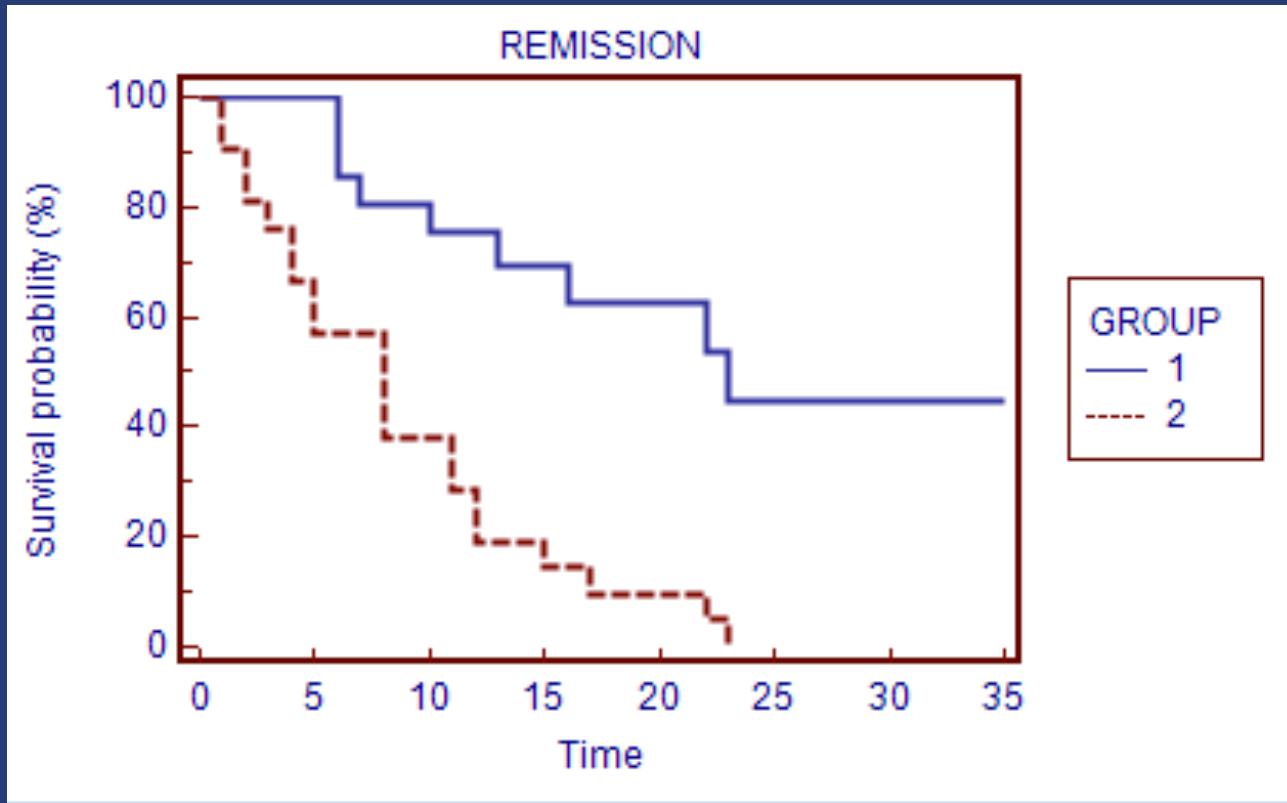
Types of clinical trials

- Preclinical: Works in mouse tumors...
- Phase I = tests safety (hope for efficacy)
 - Often any type of tumor eligible
 - Usually 15-25 patients
 - Defines sides effects; “best” dose
- Phase II = preliminary test of efficacy
 - Limited to specific tumor type
 - Usually 25-50 patients
- Phase III = tests efficacy compared to “standard”
 - Limited to specific tumor type; sometimes placebo “control”
 - Usually 200-500 patients
 - Essential to assess survival differences

Design and interpretation of clinical trials

- Eligibility Criteria
 - Which NETs?
 - Well vs. poorly differentiated?
 - Site of origin?
 - Growing (or not)
 - Prior treatment (or not)
- Measures of Success
 - Response Rate (RR)
 - How much does the tumor shrink?
 - Progression Free Survival (PFS)
 - How long does it take for the tumor to grow?
 - Overall Survival (OS)
 - How long do patients live?

How do we define success of a trial?



Survival curves

Sources of clinical trials

Investigator Initiated	Industry Initiated	Cooperative Group
<ul style="list-style-type: none">• Often smaller Ph I/II• Usually available at a single academic institution• Idea is initiated by academic MD• Funding and/or drug supply from industry	<ul style="list-style-type: none">• Ph I, II or III• Usually involves many sites and sometimes international• Idea is initiated by industry• Funding from pharmaceutical company	<ul style="list-style-type: none">• Ph I, II or III• Sponsored by NIH / National Cancer Institute• Open at centers participating in a cooperative group (i.e. ECOG, SWOG, ALLIANCE)• Funding is federal

Why are clinical trials important?

- Clinical trials are a key research tool for advancing medical knowledge and patient care.
- Clinical research is done to learn:
 - Whether a new approach works well and is safe
 - Which treatments or strategies work best for certain illnesses or groups of people
- Yet...only 3% of U.S. adults with cancer participate in clinical trials!

Outline

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Somatostatin Analogues: Ph III PROMID

85 patients with well-differentiated metastatic midgut NETs

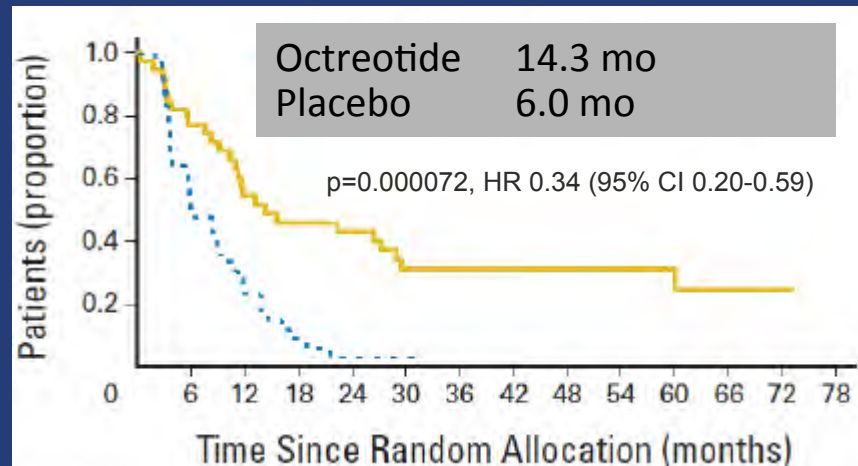


Octreotide LAR
30 mg IM q4wks
N=42

Placebo IM q4wks
N=43

- Primary Endpoint
 - TTP
- Secondary Endpoints
 - OS
 - RR

Time to Progression



mTOR Inhibitors: Ph III Everolimus (RADIANT 3)

Advanced
pancreatic NETs
n=410

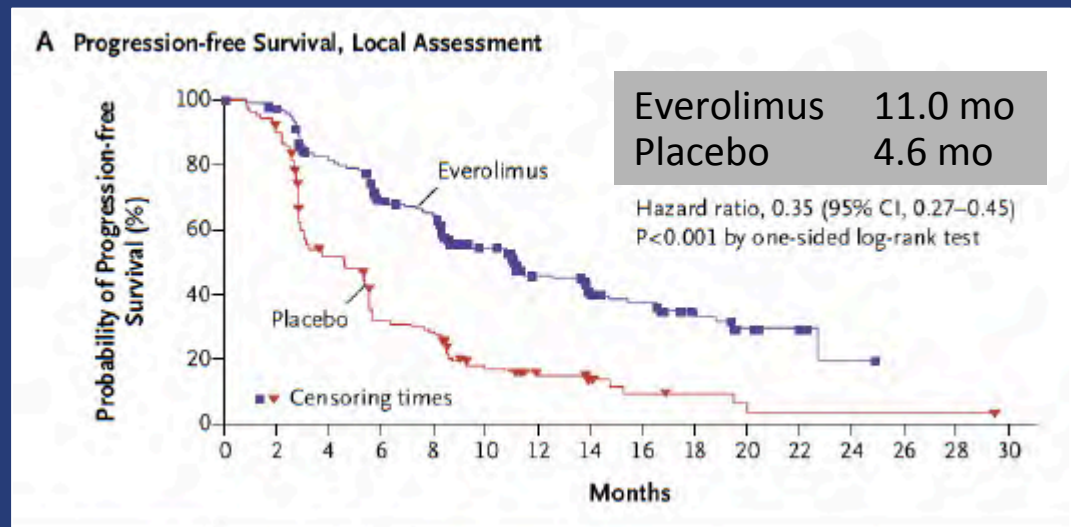


R



Everolimus 10 mg
N=207

Placebo
N=203



FDA approved for
Pancreatic NET

mTOR Inhibitors: Ph III Everolimus (RADIANT 2)

Advanced carcinoid
n=429



R

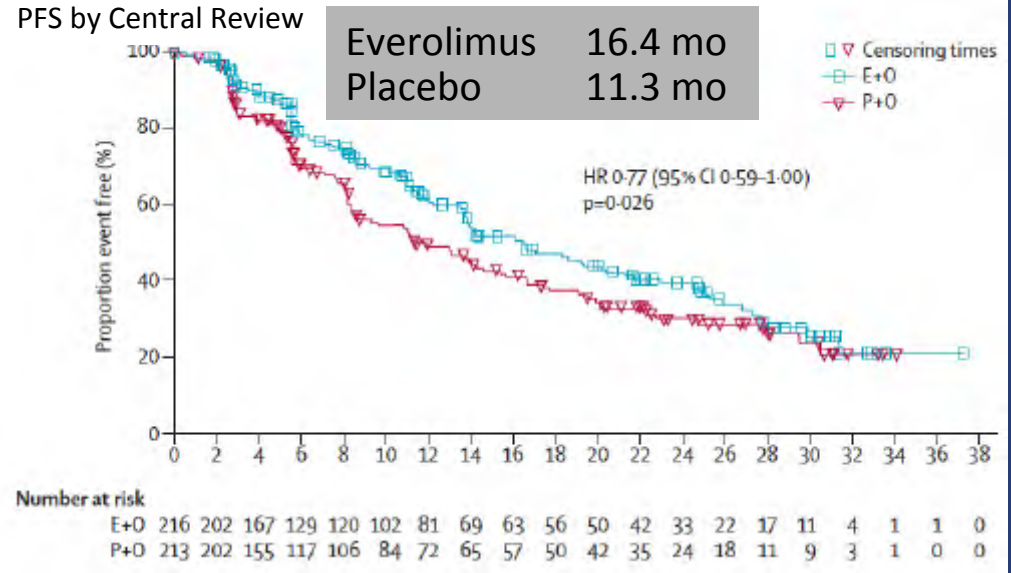


Everolimus 10 mg
+ Octreotide LAR
N=216

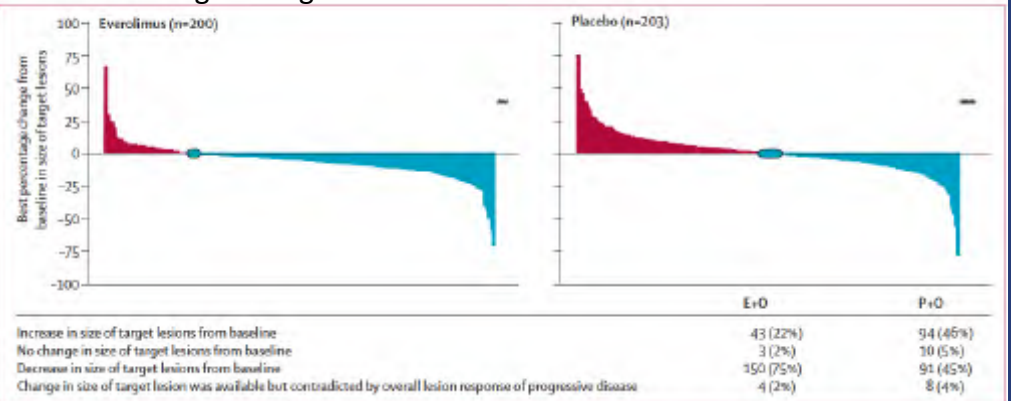
Placebo +
Octreotide LAR
N=213

**RADIANT 4 is
ongoing**

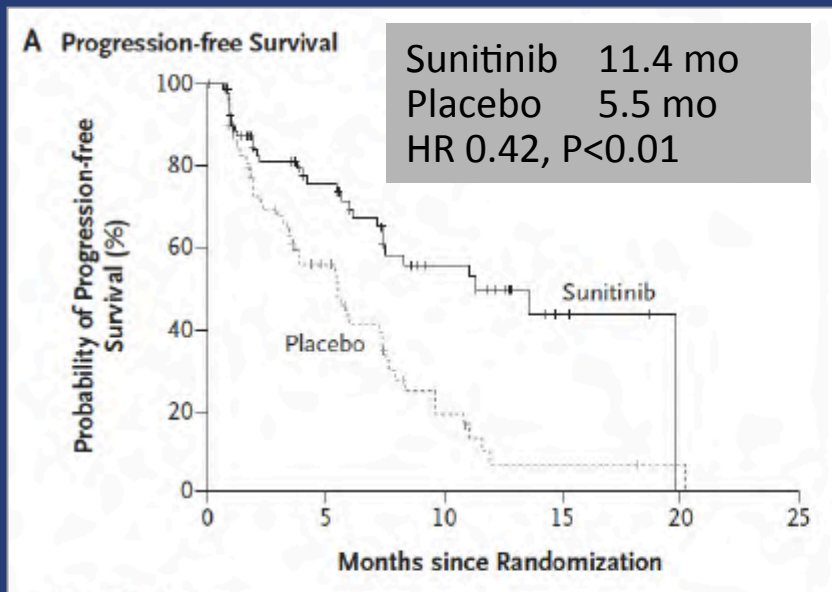
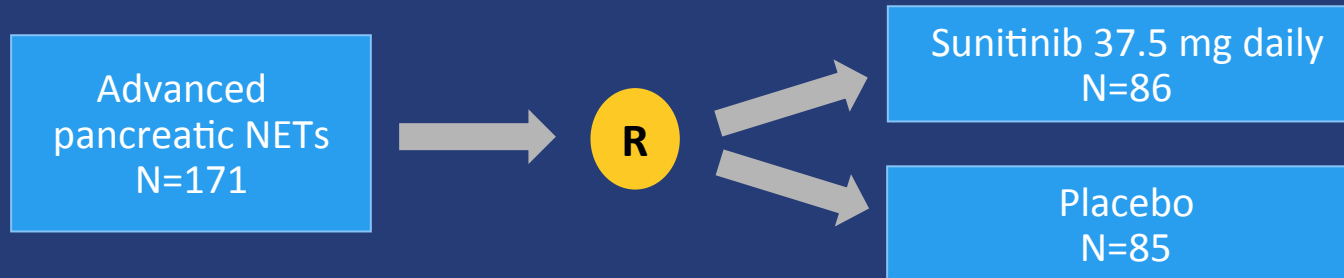
PFS by Central Review



Best Percentage Change from Baseline

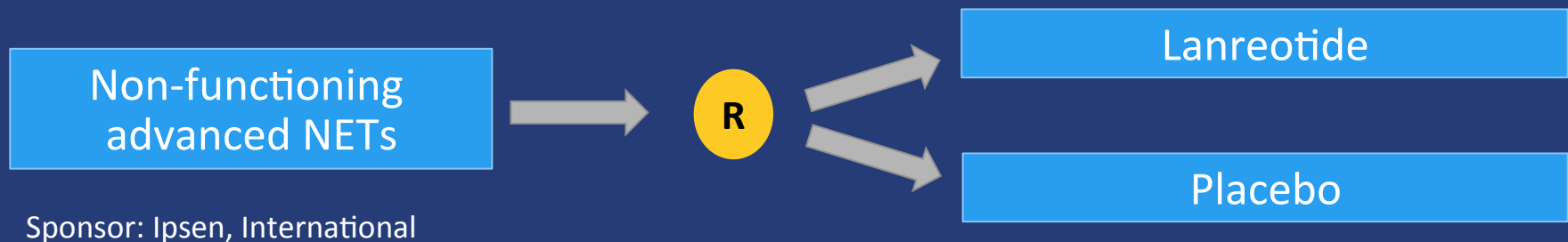


Angiogenesis Inhibitors: Ph III Sunitinib



FDA approved for
Pancreatic NET

Somatostatin Analogues: Ph III CLARINET

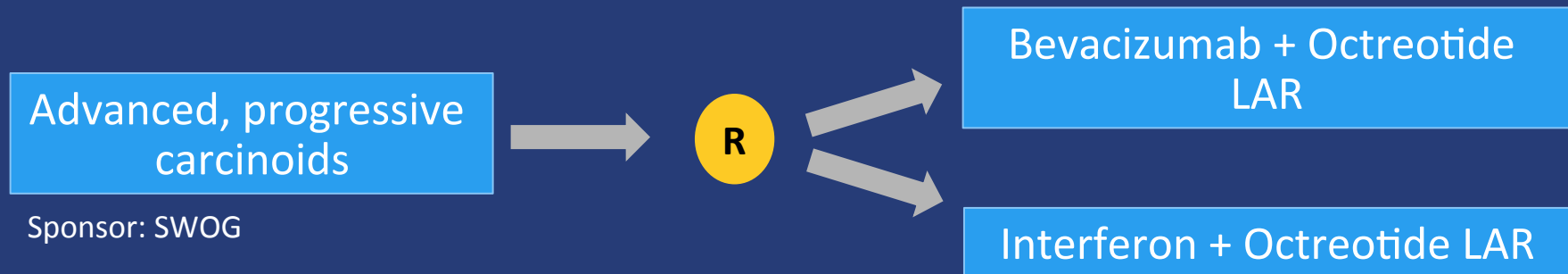


Primary site	%
Pancreas	45
Midgut	36
Hindgut	7
Unknown	13

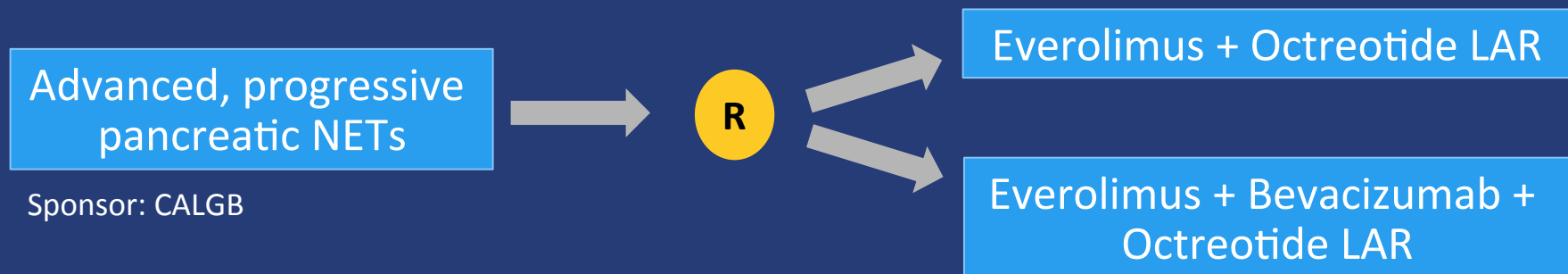
PFS	months
Lanreotide	>24 mo (and counting...)
Placebo	18 mo
Hazard ratio = 0.47 (CI 0.3 – 0.73)	

Recently completed trials (eagerly awaiting results!)

SWOG 0518 (Yao PI): Phase III, opened 12/07, 1° endpoint PFS



CALGB 80701 (Kulke PI): Phase II, opened 10/10, 1° endpoint PFS



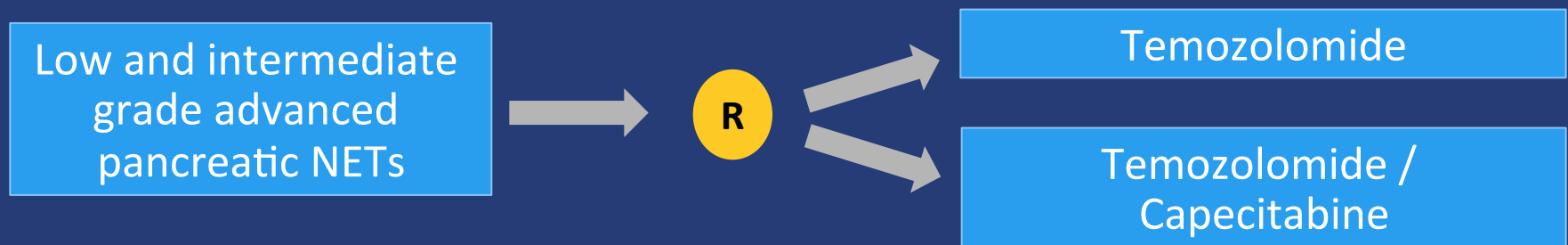
Outline

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New trials (1)

Can we define a standard cytotoxic chemotherapy for pNETs?

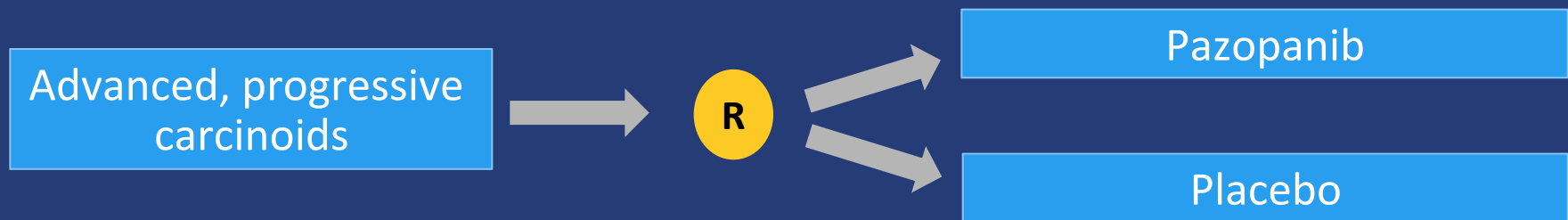
ECOG 2211 (Kunz PI): Phase II, 1° endpoint PFS



New trials (2)

What's next for carcinoid tumors?

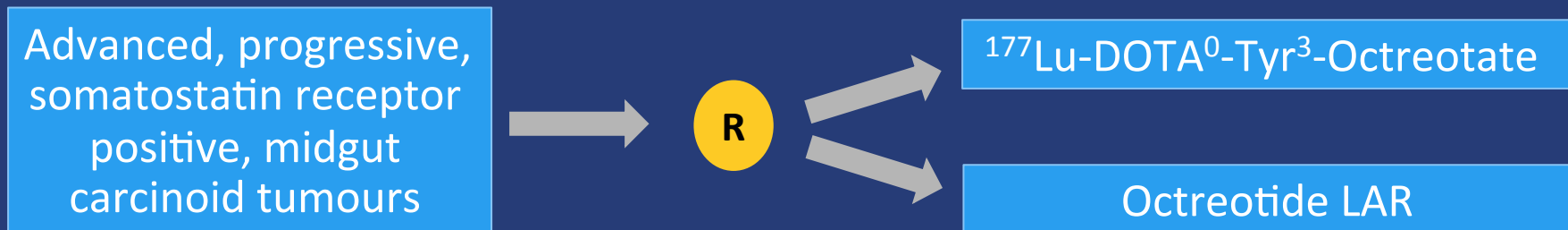
CALGB 81103 (Bergsland PI): Phase II, 1° endpoint PFS



New trials (3)

Is PRRT ever going to be available in the US?

AAA-III-01: Phase III, 1° endpoint PFS

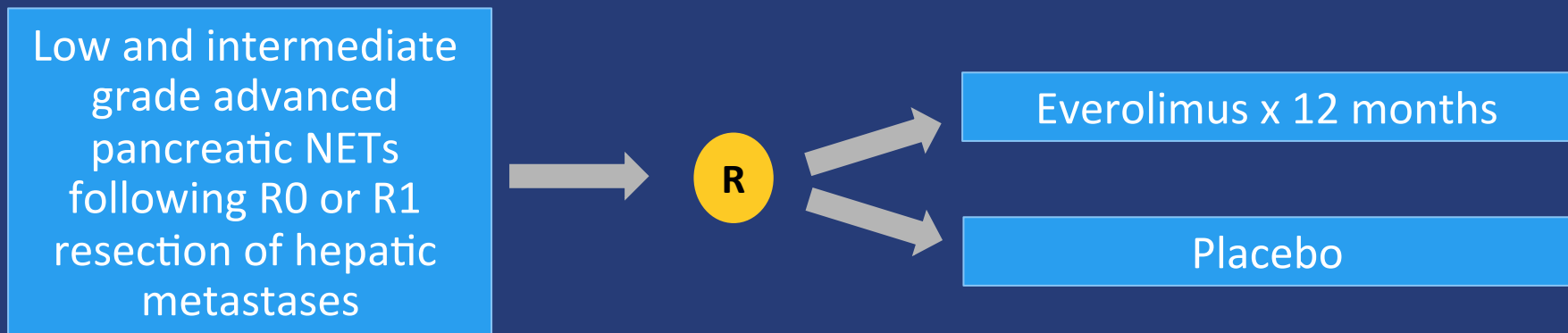


Sponsor: Advanced Accelerator Applications, France

Trials in development

What is the role of post-operative therapy in pNETs?

ECOG 2212 concept (Libutti PI): Phase II, 1° endpoint RFS



Outline

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How can you learn about clinical trials?

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world. Learn more [about clinical studies](#) and [about this site](#), including relevant [history](#), [policies](#), and [laws](#).

[Find Studies](#) [About Clinical Studies](#) [Submit Studies](#) [Resources](#) [About This Site](#)

ClinicalTrials.gov currently lists **153,457 studies** with locations in all 50 states and in **185 countries**.

Text Size ▾

Search for Studies

Example: "Heart attack" AND "Los Angeles"

[Advanced Search](#) | [See Studies by Topic](#)
[See Studies on a Map](#)

Search Help

- [How to search](#)
- [How to find results of studies](#)
- [How to read a study record](#)

Locations of Recruiting Studies



Total N = 31,113 studies
Data as of October 10, 2013

- [See more trends, charts, and maps](#)

For Patients & Families

- [How to find studies](#)
- [See studies by topic](#)
- [Learn about clinical studies](#)
- [Learn more...](#)

For Researchers

- [How to submit studies](#)
- [Download content for analysis](#)
- [About the results database](#)
- [Learn more...](#)

For Study Record Managers

- [Why register?](#)
- [How to register study records](#)
- [FDAAA 801 Requirements](#)
- [Learn more...](#)

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How can you learn about clinical trials?

Clinical Trials Finder | Carcinoid and Pancreatic Neuroendocrine Cancer Research | CFCF

YAHOO!

www.caringforcarcinoid.com/clinical_trials

Most Visited | Getting Started | Latest Headlines

Caring for Carcinoid FOUNDATION

Dedicated to Discovering Cures for Carcinoid and Pancreatic Neuroendocrine Cancers

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NEUROENDOCRINE CANCER | RESOURCES | JOIN US FOR A CURE | RESEARCH | ABOUT US

Home » Resources » Clinical Trials » Clinical Trials Finder

Clinical Trials Finder

The Caring for Carcinoid Foundation offers its Clinical Trials Finder and Patient Resource. This resource will provide the neuroendocrine tumor community with the most up-to-date and comprehensive information on relevant clinical trials in the United States.

With this resource, patients and caregivers may learn about the availability and purpose of existing clinical trials, and access supplemental resources from the Food and Drug Administration, the American Cancer Society and the National Cancer Institute.

By using CFCF's Clinical Trials Finder, patients and caregivers can search our comprehensive neuroendocrine tumor database of clinical trials, which consists of all active clinical trials being conducted in the US for carcinoid, pancreatic neuroendocrine tumors and pheochromocytoma.

Visit our [About Clinical Trials](#) page to learn more. For additional information on clinical trials or help using this site, please contact CFCF at 617-948-2514 or info@caringforcarcinoid.org.

Conditions <Any> **Status** <Any> **Phase** <Any>

State (abbreviation) Apply

Title	Phase	Status	Conditions	State
131I-Metiodobenzylguanidine (131I-MIBG) Therapy for Refractory Neuroblastoma and Pheochromocytoma		Not Yet Recruiting	Pheochromocytoma	MN
			Carcinoid Tumor	
			Neuroendocrine Tumor	
177Lutetium-DOTA-Octreotate Therapy in Somatostatin Receptor-Expressing	II	Enrolling	Pancreatic	TX

Make a Difference **DONATE NOW**



Newly Diagnosed

Carcinoid & Neuroendocrine Tumor Patient Community

Doctor Database

Clinical Trials

- Clinical Trials Finder
- About Clinical Trials
- Clinical Trials Updates

Educational Resources

News

Additional Resources

Get the Facts on Pancreatic Neuroendocrine Cancer
Check out Lauren's Blog

NET Survivors Tell your story
Submit and read other survivors stories.

Sign-up for our e-Newsletter:
Enter email to sign up **SUBMIT**

Latest Video
Check out the CFCF video library.

Lauren's Blog
Read the latest blog from CFCF's Director of Research.

Connect with CFCF online:
Facebook | Twitter | YouTube | RSS

How can you learn about clinical trials?

The screenshot shows the Stanford Cancer Institute website. At the top, there is a navigation bar with links for 'Patient Resources', 'Diseases & Treatments', 'Understanding Cancer', 'Clinical Trials', 'Research', 'Training', 'Outreach', and 'About Us'. The main heading is 'Find Cancer Clinical Trials'. Below this, there is a paragraph stating: 'The clinician scientists of the Stanford Cancer Institute are engaged in more than 300 clinical trials, investigating a broad spectrum of new diagnostic, prevention and treatment strategies. If you would like assistance searching for trials please contact the Stanford Cancer Clinical Trials Office at 855-498-7061 or ccco-office@stanford.edu.' There are three tabs: 'Search Trials', 'Browse Conditions', and 'Eligibility Flowcharts'. A 'Filter by One or More Trial Details' section contains several input fields: 'Keyword', 'Adult/Pediatric' (set to 'All'), 'Condition' (set to 'All'), 'Drug Used', 'Dexter', 'Trial ID', and 'Status' (set to 'Accepting Patients'). A 'Search' button is located at the bottom of the filter section. On the left side, there is a sidebar with various links including 'Find Active Clinical Trials', 'Basics for Patients', 'Patient Stories', 'MD Community Newsletter', 'Información en español', 'Cooperative Groups', 'Cancer Clinical Trials Education & Outreach', 'Cancer Clinical Trials Office', 'Scientific Review Committee', 'Clinical Research Groups', and 'Data and Safety Monitoring Committee'.

<http://cancer.stanford.edu/trials/>

The screenshot shows the UCSF Helen Diller Family Comprehensive Cancer Center website. At the top, there is a navigation bar with links for 'PATIENT CARE', 'CLINICAL TRIALS', and 'RESEARCH'. The main heading is 'Clinical Trials (List View)'. Below this, there is a 'Thank you for your interest in clinical trials at UCSF.' section with a small image of people and text: 'Research studies conducted with cancer patients are called clinical trials. As a cancer patient, you may take part in a clinical trial. Please see the links below for current open trials at UC San Francisco.' There are three links: '> More information about participating in a trial', '> A PDF of current open Adult Interventional Trials can be downloaded [here](#)', and '> For questions call us at 877-827-3222 or [email](#)'. Below this, there is a section for 'Pediatric Cancers are listed here: [Visual View](#) | [List View](#)'. Another section is titled 'Adult Cancers by Disease Site:' with a list: 'Blood' (Malignant Hematology/Leukemias) including 'Lymphoid Leukemia' and 'Leukemia, other'. On the right side, there is a 'CONTACT US' section with a phone icon and text: 'Clinical trial availability changes frequently. For information about any of our studies, contact us: Call us at 877-827-3222 or [email us](#)'. At the bottom right, there is a small note: 'For other types of clinical trials at UCSF'.

<http://cancer.ucsf.edu/clinical-trials>

UCSF NET Trials

- CARC: Ph II Axitinib
- CARC: Ph II Pazopanib vs. placebo
- CARC SYNDROME: Ph III Telotristat vs. placebo
- MIXED: Ph 1/2 study of CC-223 (mTOR kinase inhibitor)
- MIXED: Safety profile assessment of theraspheres for treatment of metastatic liver disease from primary NET

Stanford NET Trials


- PNET: Ph II Temozolomide, Cape, Bevacizumab
- PNET: Ph II Temozolomide vs. Temozolomide + Cape
- CARC: Ph III ^{177}Lu -DOTA⁰-Tyr³-Octreotate vs. Octreotide
- CARC SYNDROME: Ph III Telotristat vs. Placebo
- NET Registry database

NET Registry

- A NET Registry will allow researchers to identify connections between the molecular characteristics of tissue samples and the patient data associated with individual disease progression, and to test and validate correlation hypotheses.

The logistics

NET Registry discussed with patient during regular clinic visit; meet with research coordinator.



STANFORD UNIVERSITY – RESEARCH CONSENT FORM
Protocol Title: A registry of clinical information for patients with neuroendocrine tumors
Version number: v1.0
Principal Investigator: Thomas M. Kelly, MD
IRB Approval Date: 10/2/10
Protocol for Director: Thomas M. Kelly, MD
IRB Approval Date: 10/2/10

Are you participating in any other research studies? yes no

INTRODUCTION TO RESEARCH STUDIES

A research study is designed to answer specific questions, sometimes about a drug or a different type of treatment. The study is run by a doctor or research staff. When you participate in a study, you will follow the instructions of the research staff. You will complete a questionnaire and provide a blood sample.


Consent form reviewed and signed



Blood drawn



Survey completed



Neuroendocrine Tumor Registry Patient Questionnaire Page 1 of 21

Dear patient - We hope you will complete the questions on the following pages. Please try to complete all of the questions. If there are any questions that you do not understand or do not feel comfortable answering, please feel free to ask for assistance or to leave them blank. Thank you in advance for your participation. Sincerely, Your physician, nurses and research staff in the Stanford Gastrointestinal Oncology Clinic

Patient demographic information

Study ID: _____

Medical Record Number:
This is an 8 digit number that may start with one or more 0s.
For example: 01234567 _____

Last name: _____

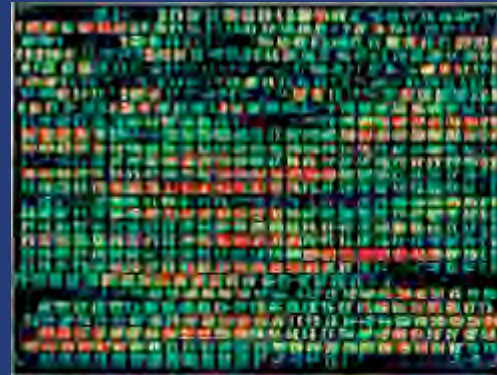
First name: _____

Timeline

- September 2009: Institutions granted funds from Caring for Carcinoid Foundation
- Sept 2009-Sept 2010: Database development and optimization of data collection
- Currently over 200 patients enrolled
- January 2012: Data presented at ASCO GI; 1st publication in preparation

Future directions

- The NET Registry will connect the tumor tissue bank, databases containing clinical and epidemiologic data, clinical outcome data, and archived blood specimens.
- The NET Registry is a tool that will lead to improved understanding of neuroendocrine tumor prevention, pathogenesis, and treatment.



Take home points

- There has been a renaissance of research in the field of NETs
- There are numerous active and developing clinical trials
- Participation in clinical trials is essential to advance the field
- Thank you to all clinical trial participants!

