A Survey Of Active Clinical Trials Using SPECT Imaging

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Imaging Applications in Drug Development

Biomarker enabled early decision opportunity window

- Target expressed and functional

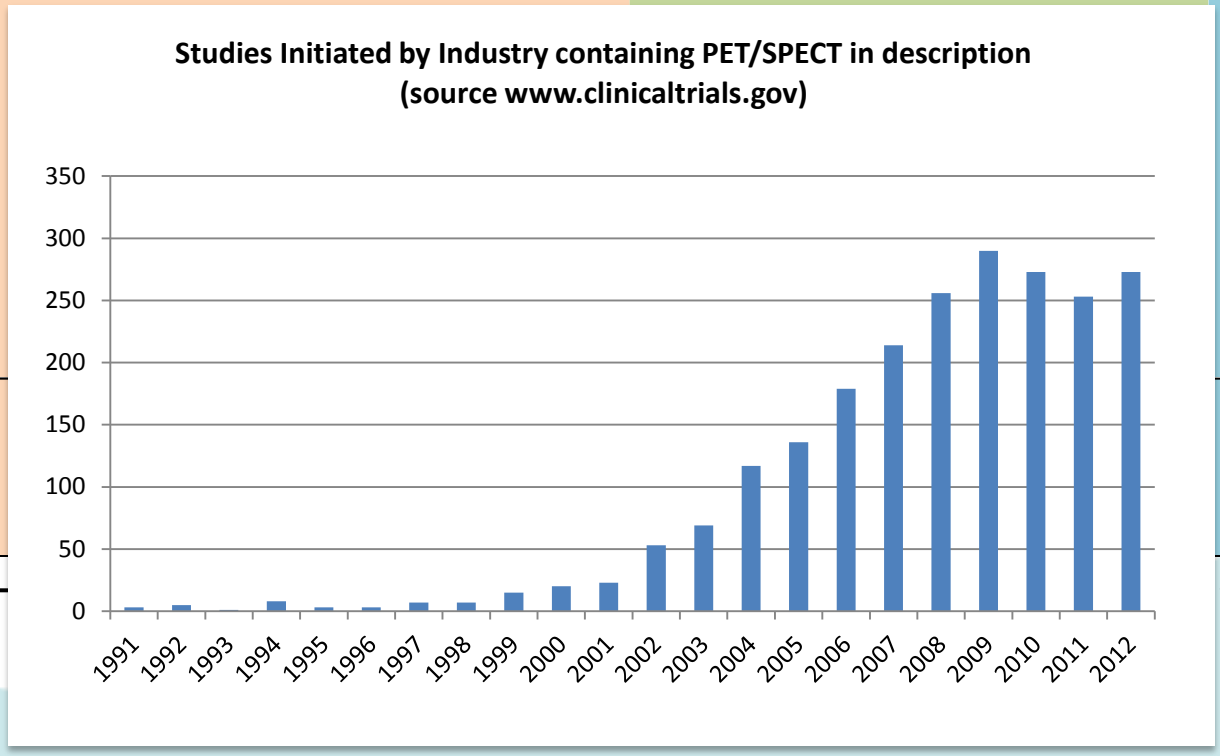
- Patient ID
- Response monitoring
- Dose adjustment
- Product differentiation
- Life Cycle management

Target identification

Sales

Validation

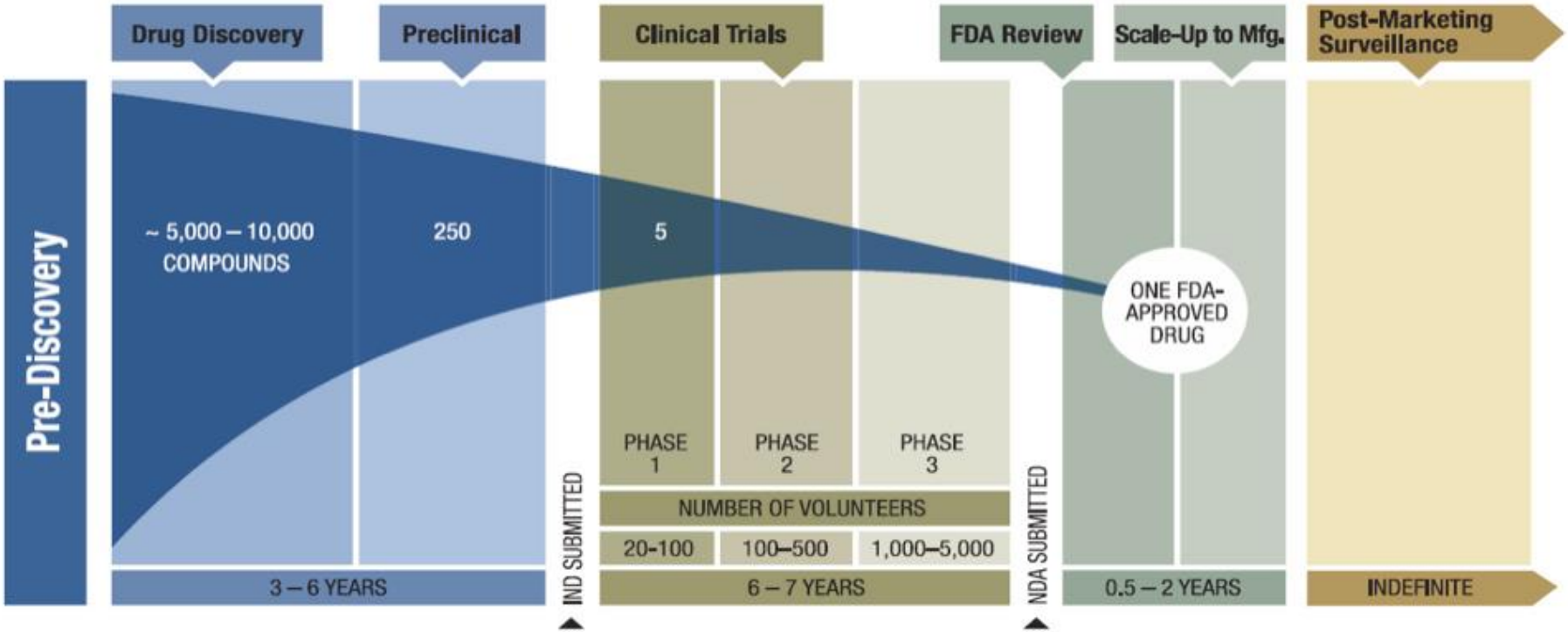
Clinical use



Biomarker vs. Biodistribution

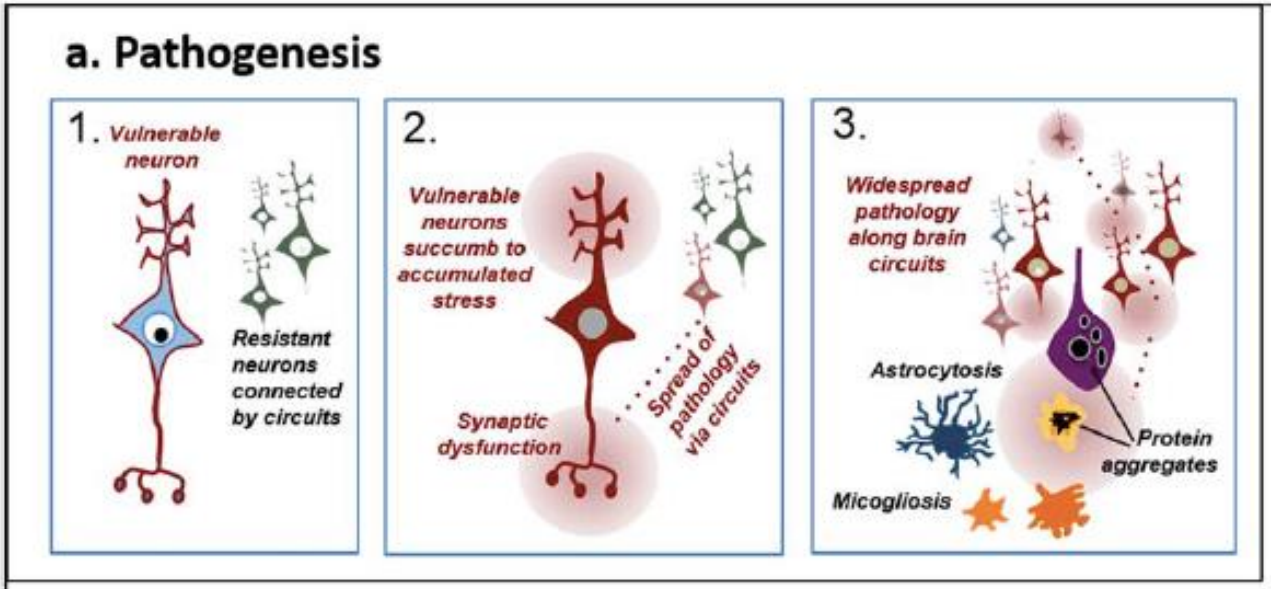
Hargreaves, et al.; CPT 2015

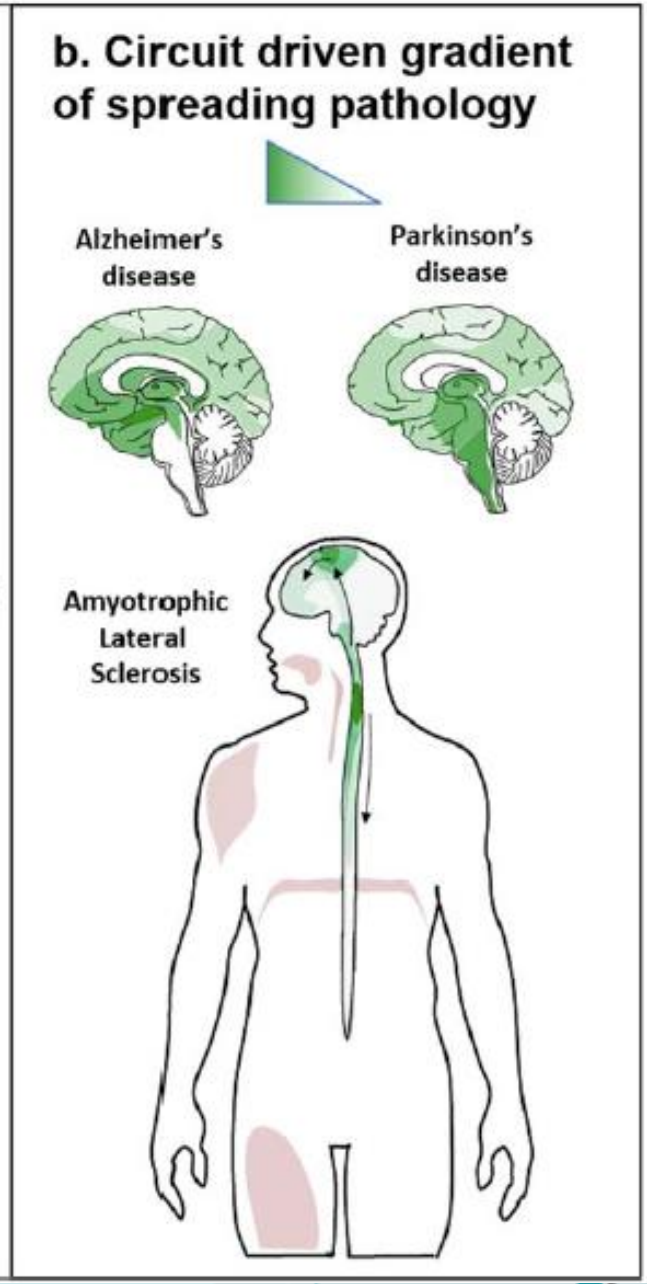
Drug Discovery and Development Timeline

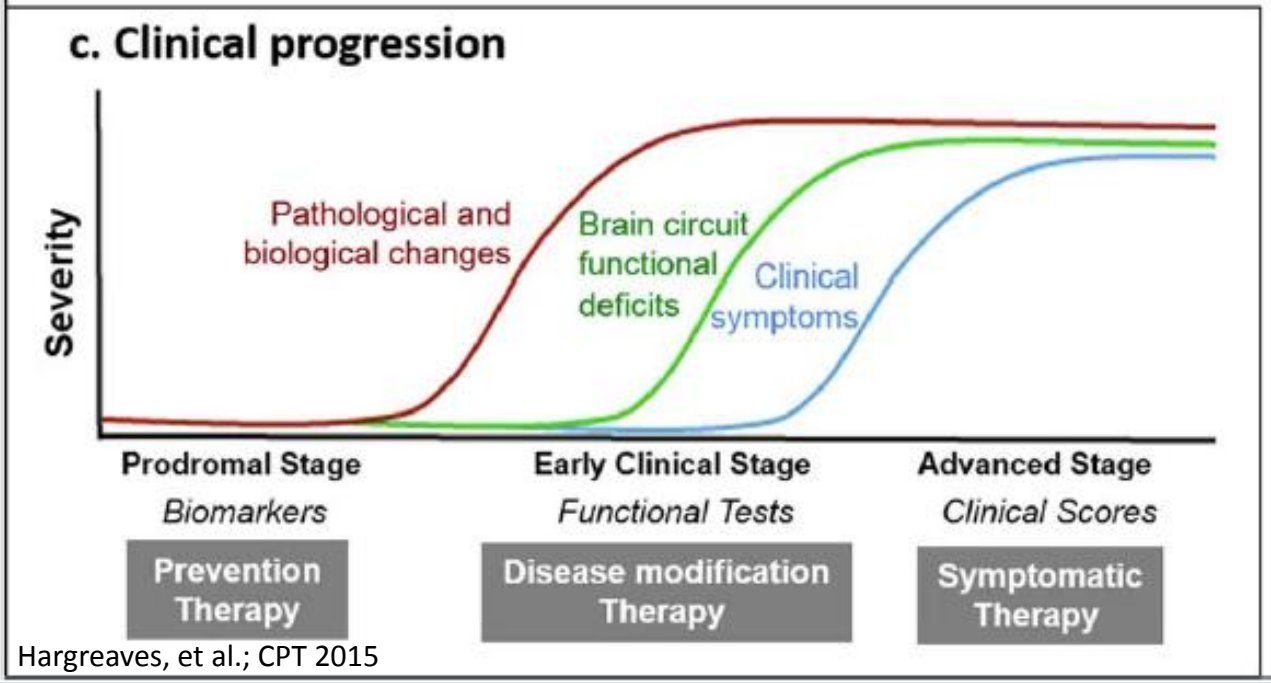


Source: American Association of Cancer Research 2011 Cancer Progress Report

- It takes 12-15 years on average for an experimental drug to go from lab to patients
- Only 5 of 5,000-10,000 compounds that enter preclinical testing reach human testing
- 1 in 5 of investigational drugs in clinical trials reach approval

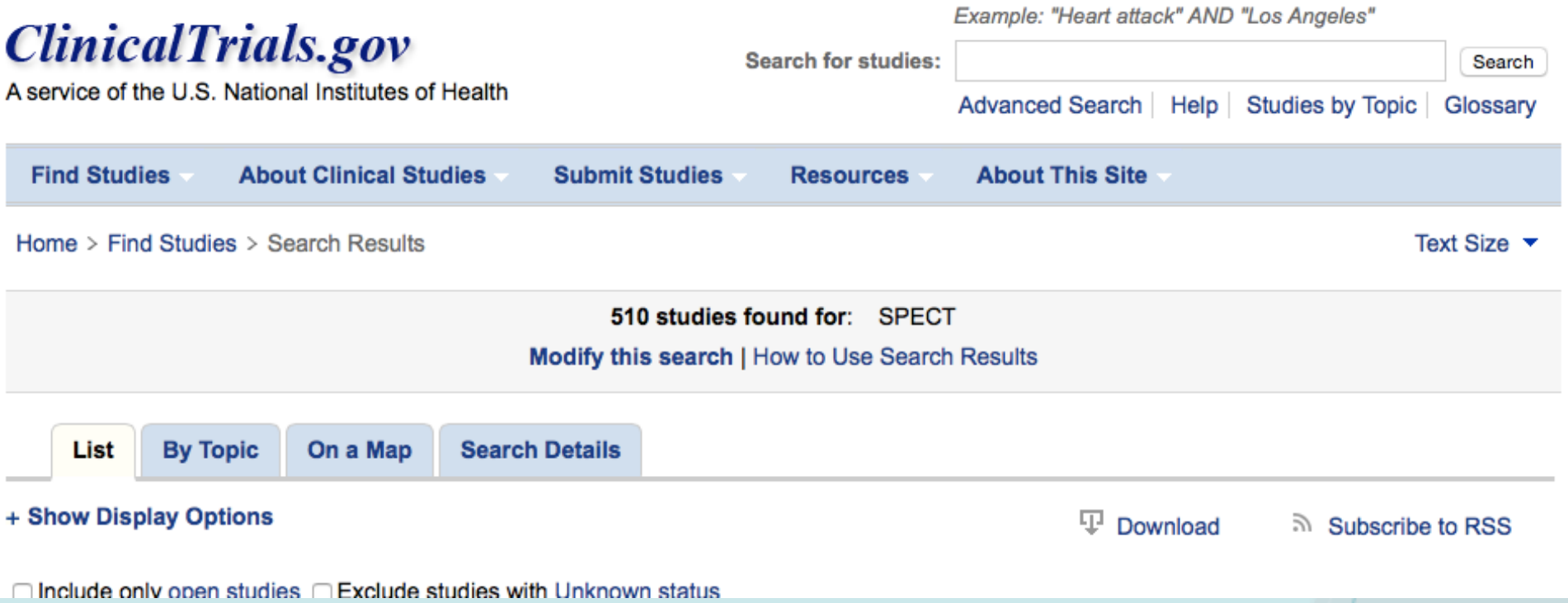




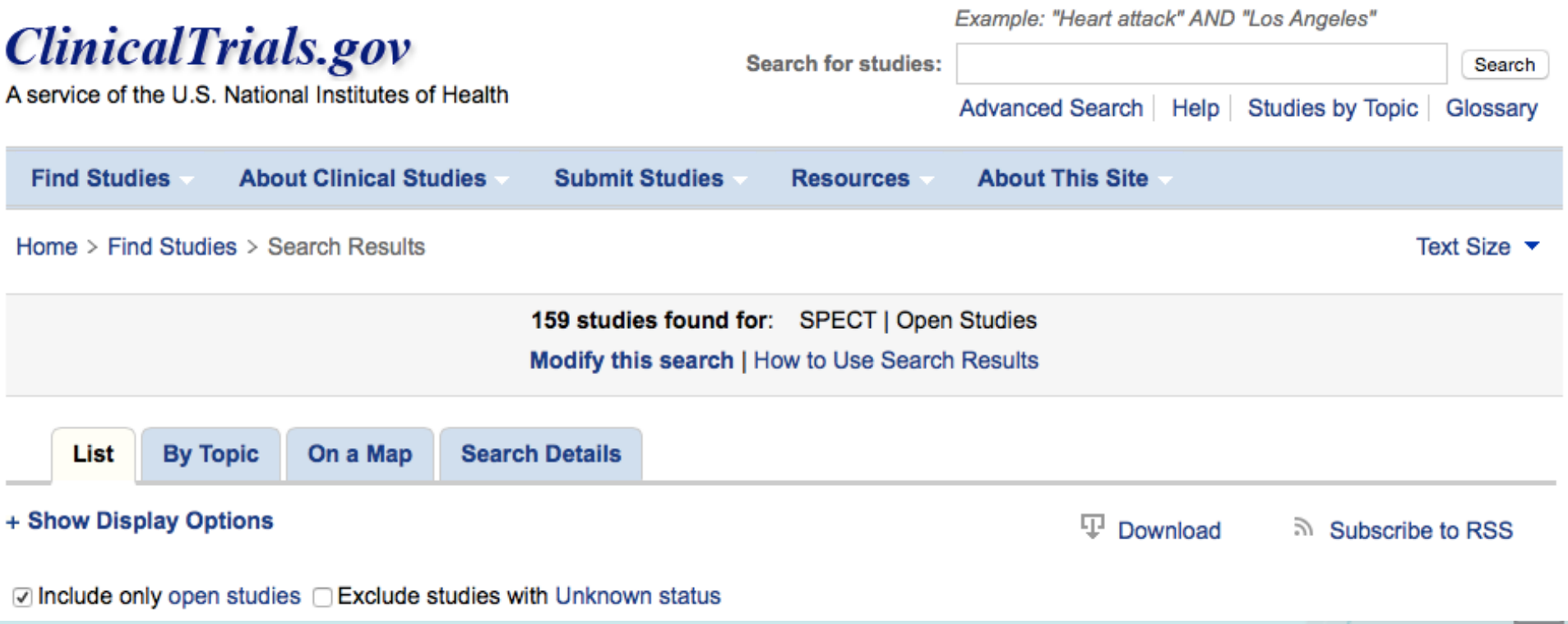


Hargreaves, et al.; CPT 2015

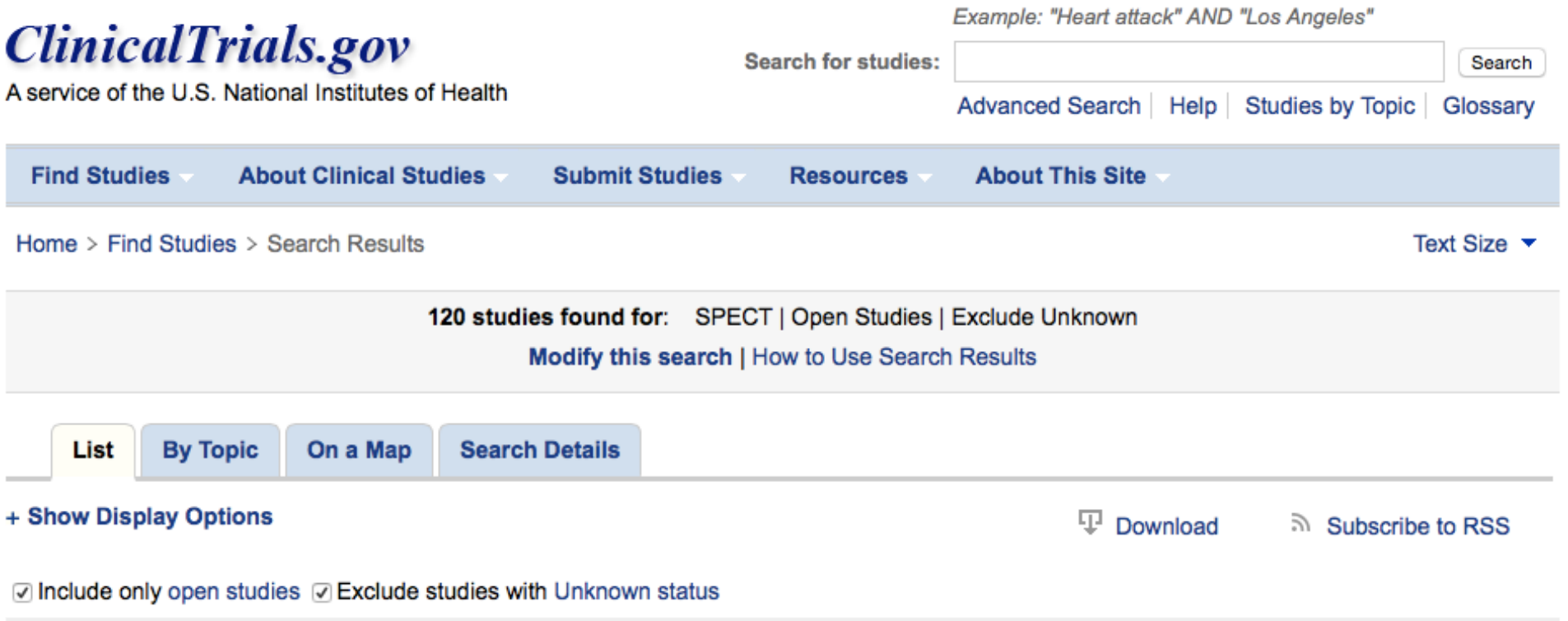
Clinical Trials Using SPECT Imaging



Clinical Trials Using SPECT Imaging



Clinical Trials Using SPECT Imaging

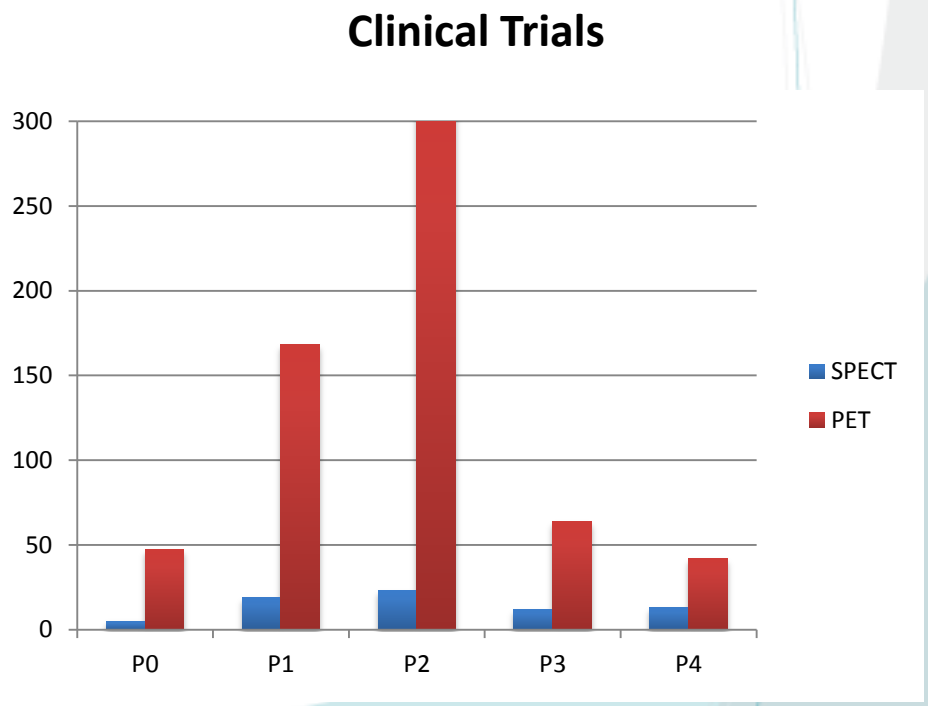


- 120 CT using SPECT open to accrual and active
- 1036 CT using PET open to accrual and active

120 Clinical Trials Using SPECT

- 67 Instrumentation
- 47 Cancer
- 47 Cardiac
- 37 Others
- 50/120 Safety

- 1036 CT using PET



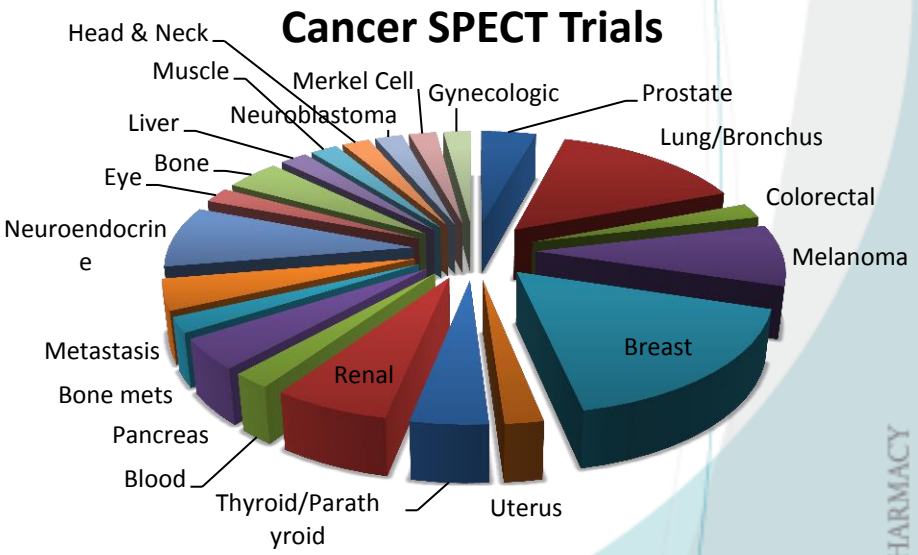
SPECT Trials in Cancer

Seeking NDA

- Diagnosis
- Staging/Restaging
- Monitoring response
- Monitor safety

As CT tools

- Accrual
- Multifocal disease
- Monitoring response
- Longitudinal assessment

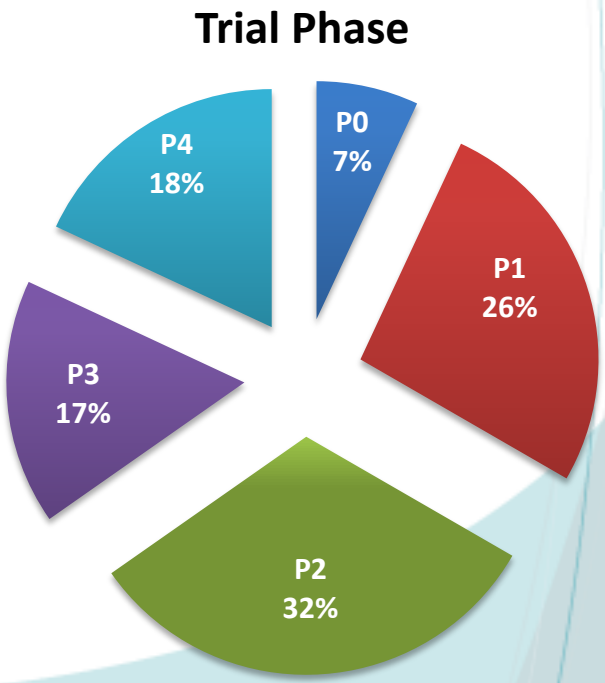


Clinical Trials – Phase 0 (n=5)

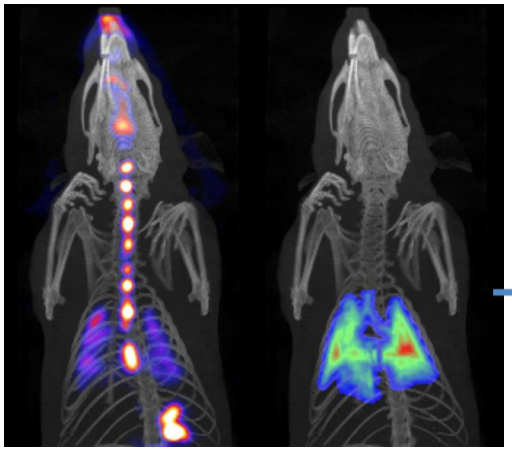
Phase 0 Studies n≤15

- *Proof-of-Concept*
- Exploratory, Small doses
- No benefit to patients
- Aims:
  - Drug distribution/PK
  - Action of drug in human/PD
  - Tissue/Cell response to drug
- Extra biopsies, scans, and blood samples
- Lower risk than P1
- 5 Novel radioligands
  - 2 Cancer
  - 1 Cardiac
  - 1 Nuero
  - 1 Metabolic

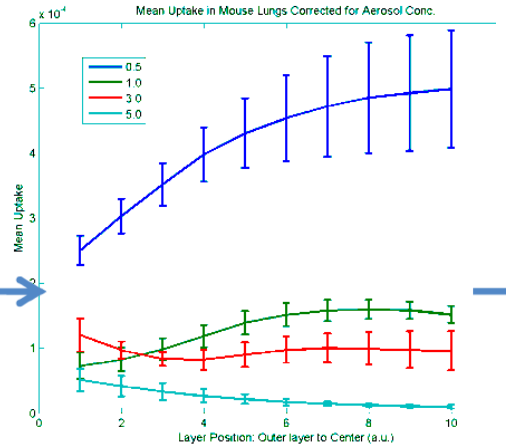
Distribution



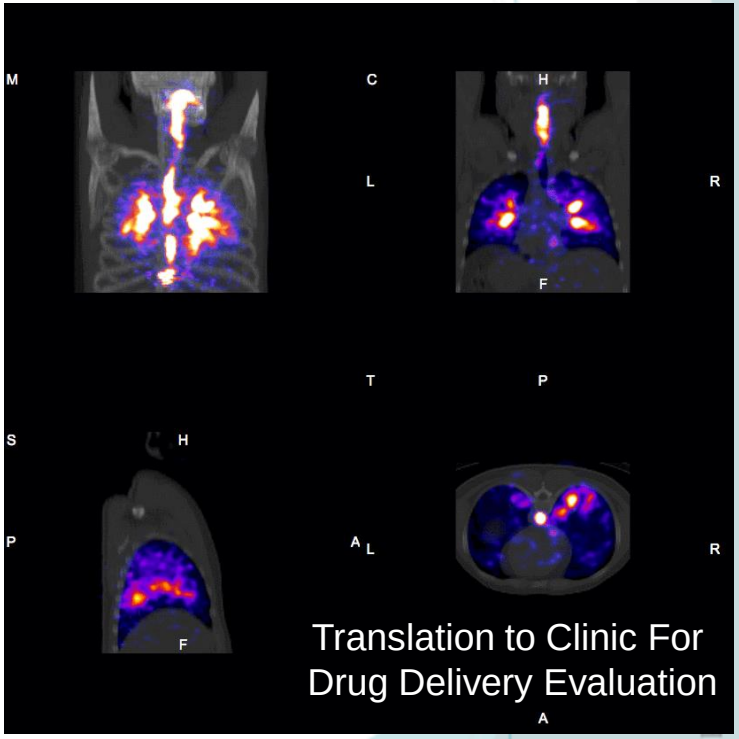
Translational Imaging Drug Delivery



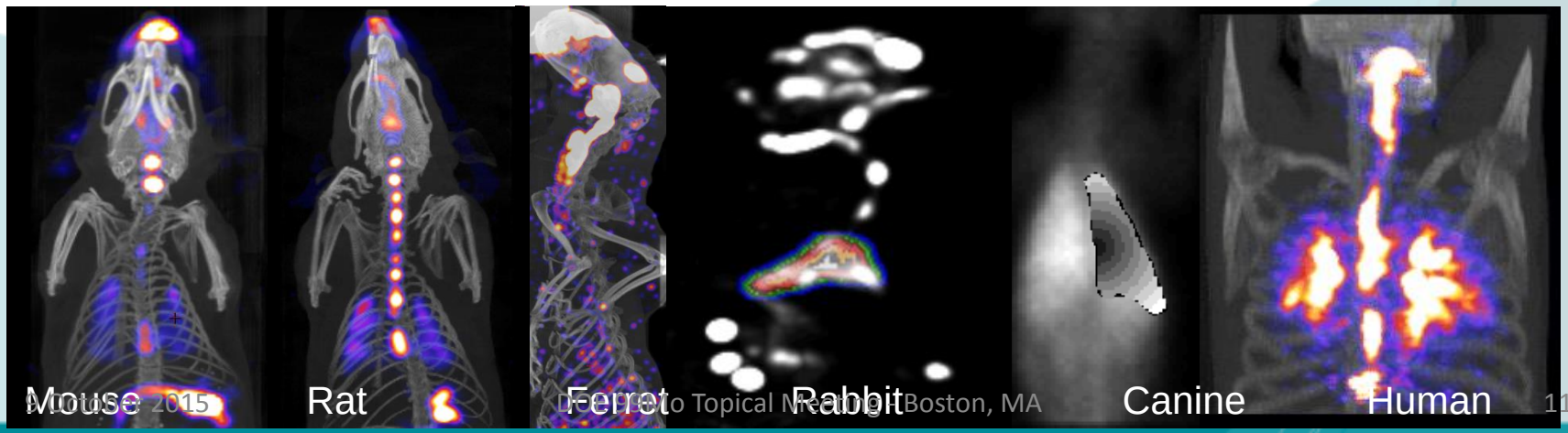
Rodent: Topographic Thinning or "Onion" Model of the lung



"Onion" Deposition Plots for Varying Particle Sizes



Translation to Clinic For Drug Delivery Evaluation

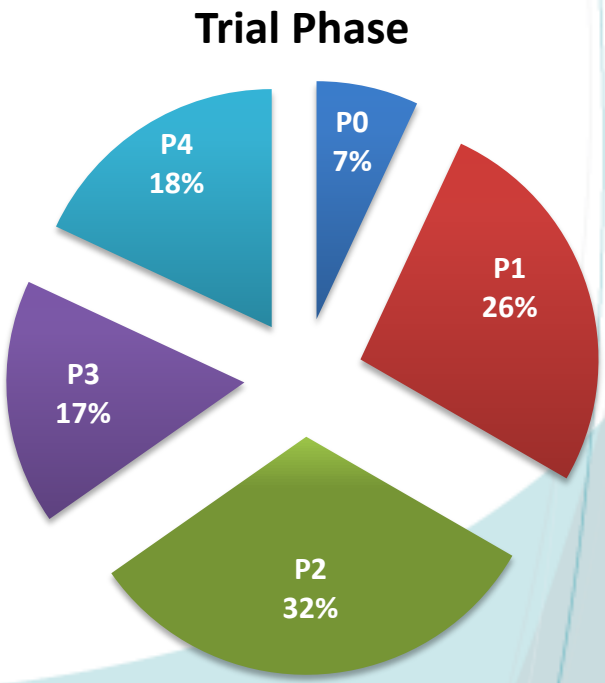


Clinical Trials – Phase 1 (n=19)

Phase 1 Studies n=10-20

- *First-in-Man*
- Safety in humans
- Dose escalation
  - *Maximum Tolerated Dose* (MTD)
- Dose to toxicity
- Establish safety parameters
- PK/PD, Metabolism/Clearance
- 10-20 subjects
- 7 Novel radioligands
  - 2 Cancer
  - 1 Cardiac
  - 1 Nuero
  - 1 Metabolic

Distribution



SPECT/CT in Measuring Lung Function in Patients With Lung Cancer Undergoing Radiation Therapy

This study is currently recruiting participants. (see Contacts and Locations)

Verified August 2015 by University of Washington

Sponsor:
University of Washington

Collaborator:
National Cancer Institute (NCI)

ClinicalTrials.gov Identifier:
NCT01982123

First received: October 22, 2013
Last updated: August 10, 2015
Last verified: August 2015
History of Changes

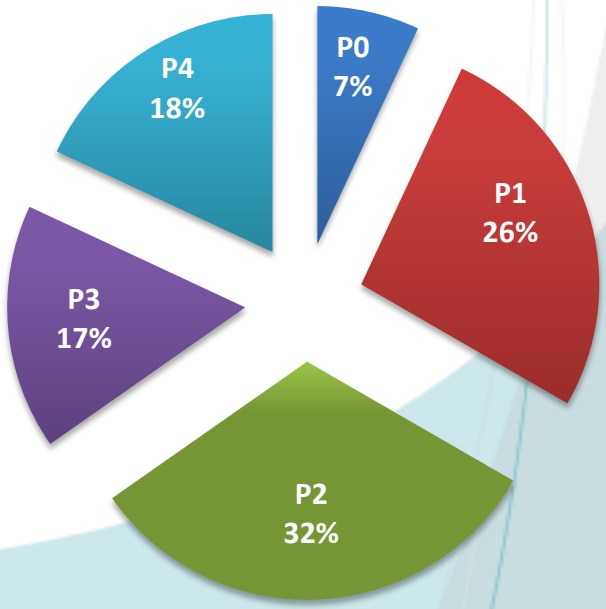
Condition	Intervention
Extensive Stage Small Cell Lung Cancer	Radiation: technetium Tc 99m-labeled macroaggregated albumin
Limited Stage Small Cell Lung Cancer	Drug: technetium Tc 99m DTPA
Occult Non-small Cell Lung Cancer	Procedure: **single photon emission computed tomography**
Recurrent Non-small Cell Lung Cancer	Procedure: computed tomography
Recurrent Small Cell Lung Cancer	Radiation: fludeoxyglucose F 18
Stage IA Non-small Cell Lung Cancer	Procedure: positron emission tomography
Stage IB Non-small Cell Lung Cancer	
Stage IIA Non-small Cell Lung Cancer	
Stage IIB Non-small Cell Lung Cancer	
Stage IIIA Non-small Cell Lung Cancer	
Stage IIIB Non-small Cell Lung Cancer	
Stage IV Non-small Cell Lung Cancer	

Clinical Trials – Phase 2 (n=23)

Phase 2 Studies n=20-500

- *Head-to-Head, Pivotal Study*
- Establish effect on specific disease
  - e.g. Reduce tumor size
- Must show likely to work and safe
- Compared to standard treatment
- ≥2 years
- Sometimes randomized
- Continue to assess safety
- 8 New radioligands/indications
  - 5 Cancer
  - 3 Other

Distribution



Study of 99mTc-Sestamibi SPECT/CT Imaging for the Preoperative Diagnosis of Renal Oncocytoma

This study is currently recruiting participants. (see Contacts and Locations)

Verified March 2015 by Johns Hopkins University

Sponsor:
Johns Hopkins University

Information provided by (Responsible Party):
Mohamad E. Allaf, Johns Hopkins University

ClinicalTrials.gov Identifier:
NCT02160925

First received: June 6, 2014
Last updated: March 31, 2015
Last verified: March 2015
History of Changes

Purpose

The objective of this study is to investigate the utility of 99mTc-sestamibi SPECT/CT imaging for the diagnosis of renal oncocytomas.

Primary Outcome Measures:

- Correlation of preoperative 99mTc-sestamibi SPECT/CT findings with tumor histology following surgical resection. [Time Frame: Within 2 weeks of surgery]
  [Designated as safety issue: No]

Estimated Enrollment:	100
Study Start Date:	May 2014
Estimated Primary Completion Date:	July 2015 (Final data collection date for primary outcome measure)

Diagnostic Accuracy of Gallium-68-DOTATATE PET/CT Compared to Indium-111-pentetreotide Scintigraphy (SPECT/CT) for Gastroenteropancreatic Neuroendocrine Tumors (GaIN)

This study is currently recruiting participants. (see Contacts and Locations)

Verified July 2015 by University Hospital Inselspital, Berne

Sponsor:
University Hospital Inselspital, Berne

ClinicalTrials.gov Identifier:
NCT02078843

First received: February 26, 2014
Last updated: July 16, 2015
Last verified: July 2015

Purpose

The investigators hypothesize that the new imaging method Gallium-68-DOTATATE has a higher diagnostic value in the detection of neuroendocrine tumors than the established imaging method Indium-111-Octreoscan. Therefore, the investigators will perform both imaging procedures in patients with suspected or confirmed neuroendocrine tumors. Subsequently, the investigators will compare the diagnostic performance of both methods.

Condition	Intervention	Phase
Gastroenteropancreatic Neuroendocrine Tumors	Drug: Gallium-68-DOTATATE PET/CT (index test) Drug: Indium-111-Octreoscan (standard test)	Phase 1 Phase 2

Study Type: Interventional
Study Design: Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Diagnostic

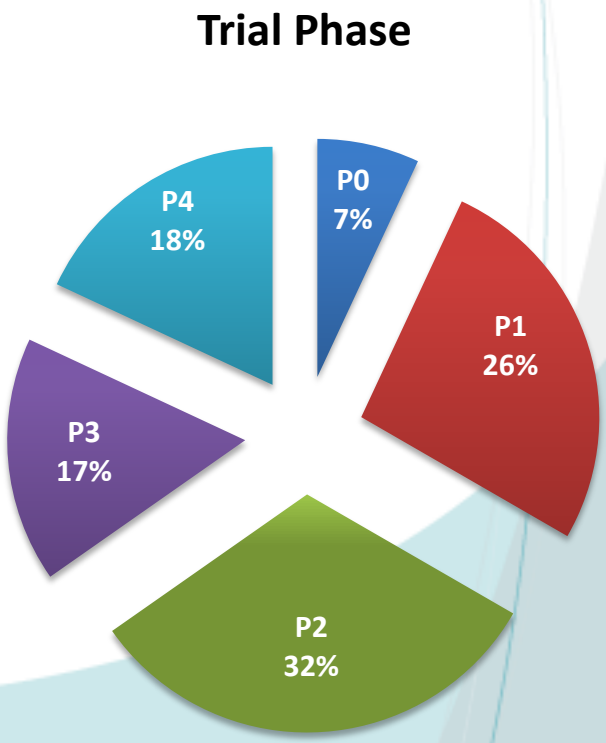
Official Title: Diagnostic Accuracy of Gallium-68-DOTATATE PET/CT Compared to Indium-111-pentetreotide Scintigraphy (**SPECT**/CT) for Gastroenteropancreatic Neuroendocrine Tumors

Clinical Trials – Phase 3 (n=12)

Phase 3 Studies n=1000-5000

- Establish efficacy in specific disease
- Compare to standard-of-care
- Larger number of patients
- Usually randomized
- Compare 2 or more treatments
- Include patients of various ages, ethnicities, and both genders
- Many years to complete
- Favorable results submitted to FDA as new drug Application (NDA)
- 6 New radioligands/indications
  - 3 Cancer
  - 2 Cardiac
  - 1 Neuro

Distribution



A Cross-Over, Multi-Center Trial to Evaluate the Diagnostic Efficacy and Safety of [123I]NAV5001 as an Imaging Agent to Aid in the Diagnosis of Parkinsonian Syndromes

This study is not yet open for participant recruitment. (see Contacts and Locations)

Verified September 2014 by Navidea Biopharmaceuticals

Sponsor:
Navidea Biopharmaceuticals

Information provided by (Responsible Party):
Further study details as provided by Navidea Biopharmaceuticals:

ClinicalTrials.gov Identifier:
NCT01950468

First received: September 23, 2013
Last updated: September 23, 2014
Last verified: September 2014
History of Changes

Primary Outcome Measures:

- The incidence of Parkinson' Syndrome based on the Movement Disorder Specialist Consensus Panel [Time Frame: One Year] [Designated as safety issue: No]
- The incidence of positve [123I]NAV5001 **SPECT** brain scans [Time Frame: Baseline] [Designated as safety issue: No]
- The incidence of Parkinson' Syndrome based on the on-site neurologist assessment [Time Frame: Baseline] [Designated as safety issue: No]

Secondary Outcome Measures:

- The incidence of Parkinson' Syndrome based on the on-site neurologist assessment at 6 months [Time Frame: 6 months] [Designated as safety issue: No]
- The incidence of Parkinson' Syndrome based on the on-site neurologist assessment at 1 year [Time Frame: 1 Year] [Designated as safety issue: No]
- Incidence of adverse events post baseline [Time Frame: 1 year] [Designated as safety issue: Yes]

Other Outcome Measures:

- The incidence of positve DaTscan SPECT brain scans [Time Frame: Baseline] [Designated as safety issue: No]

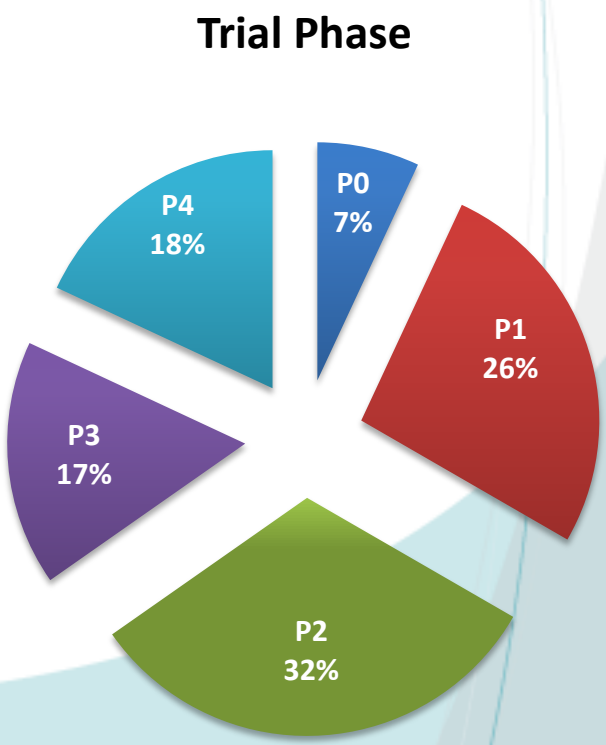
Estimated Enrollment:	275
Study Start Date:	April 2015
Estimated Study Completion Date:	March 2016
Estimated Primary Completion Date:	March 2016 (Final data collection date for primary outcome measure)

Clinical Trials – Phase 4 (n=13)

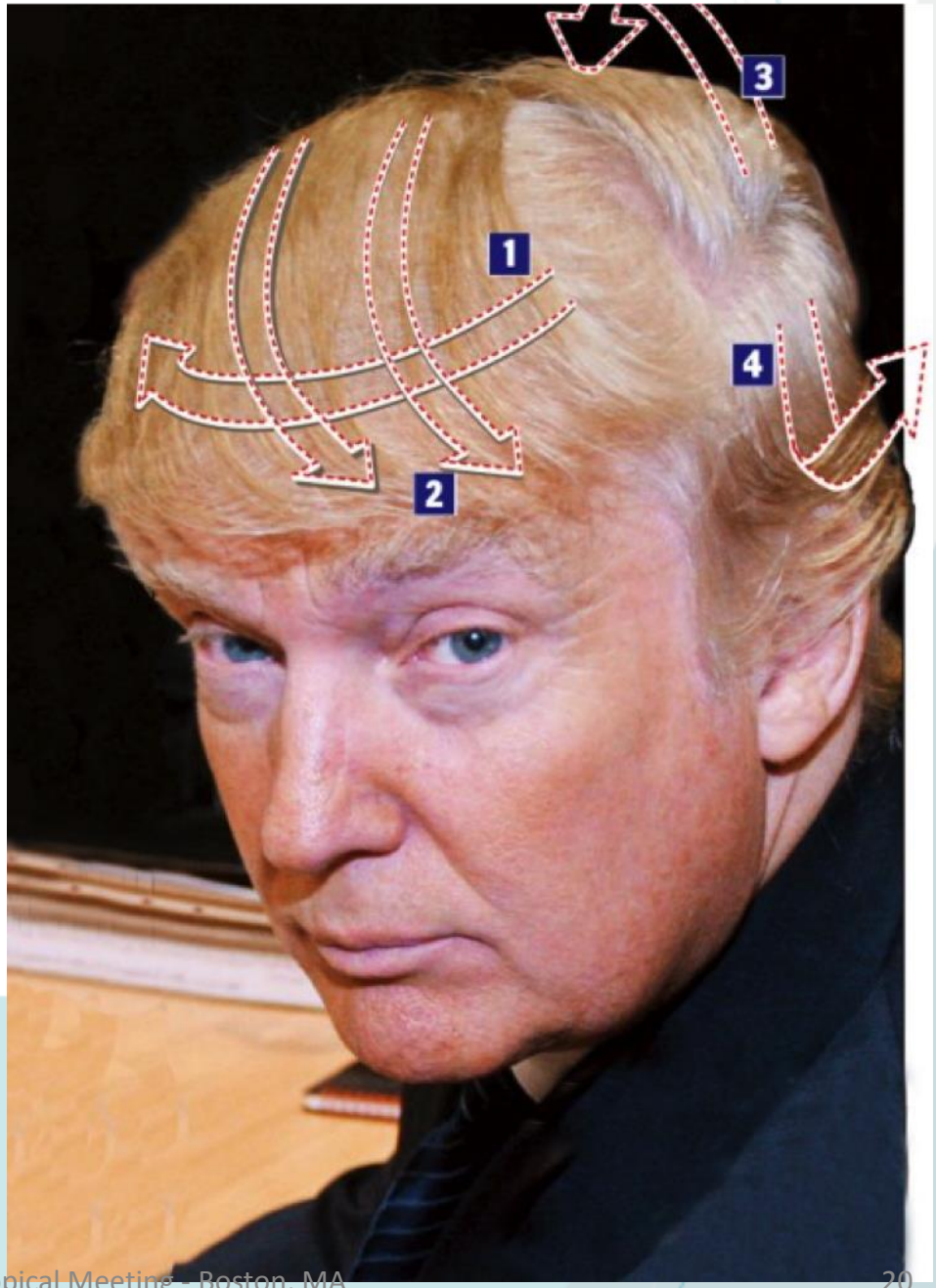
Phase 4 Studies n≥10,000,000

- *Post marketing surveillance*
- Pharmacovigilance = Drug Safety
- Ongoing technical support
- Maybe required by FDA
- Maker seeks new indications
- Evaluate drug interactions
- Test in new groups of patients
- Assess rare & long-term effects
- Many years…Ongoing…
- 4 New radioligands/indications
  - 1 Cancer
  - 2 Cardiac
  - 1 Neuro

Distribution



Thank you!!!



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