

# Active studies by Cooperative Group



Alliance  
Thoracic Group  
Co-Chairs:  
Linda Martin and Dennis Wigle



# Disclosures – L Martin

<b>Commercial Interest</b>	<b>Relationship(s)</b>
Astra Zeneca	Advisory Board for Aduara Trial dissemination
Pacira Pharmaceuticals	Advisory Board
On Target Laboratories	Steering Committee for ELUCIDATE trial



# Alliance Trials

- ALCHEMIST – Dennis Wigle – updates and new arm
- Varenicline Pre-Surgery - *CLOSED*
- CHIO3 (AFT 46)
  - What's next – concepts for Phase 3 study
- In Development:
  - AFT 51 Intraoperative Molecular Imaging for Metastatic Disease
  - C-PROTECT – Adjuvant Colchicine for Stage 1A-1B NSCLC
  - Phase3 trial for stage 3A/B lung cancer



# Alliance Foundation Trial-46 CHIO3 Trial: CHemotherapy Combined with Immune Checkpoint Inhibitor for Operable Stage 3A/B Non- Small Cell Lung Cancer

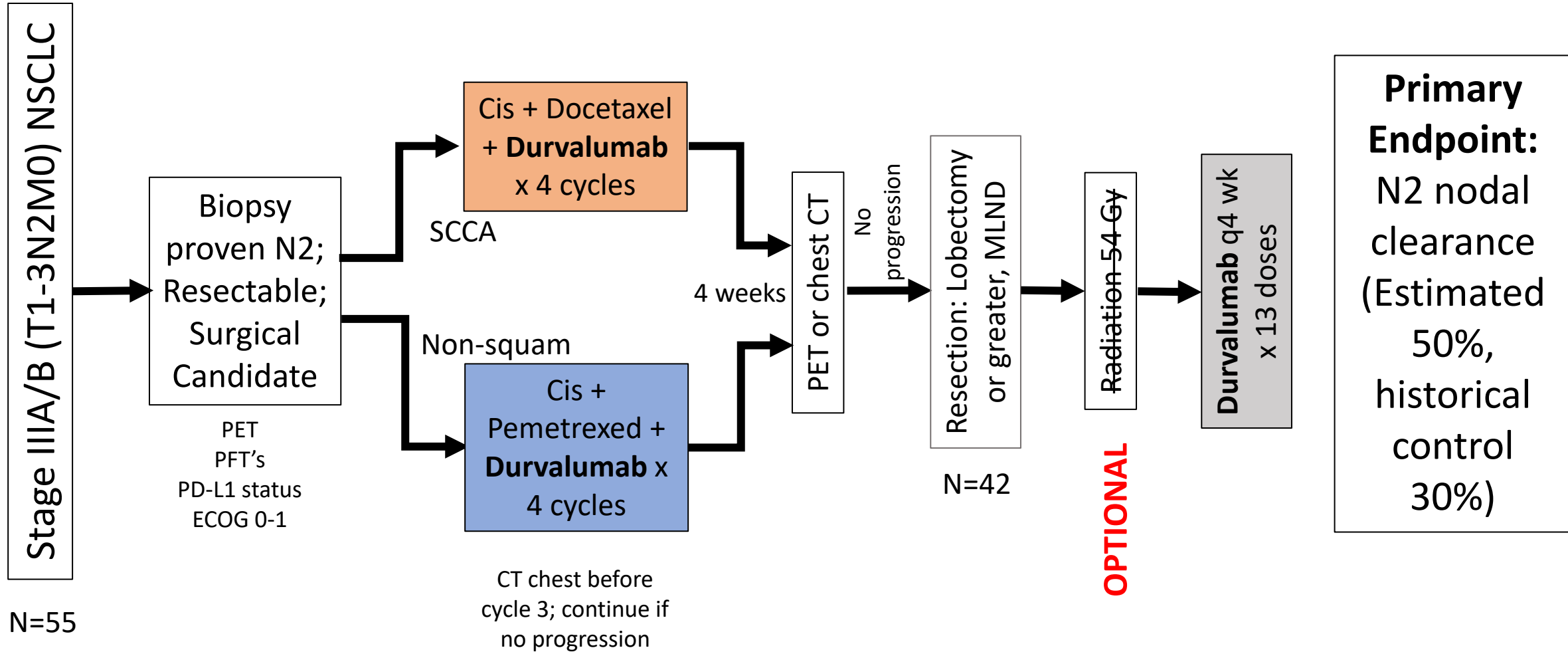
Linda W Martin, MD, MPH - Thoracic Surgery, University of Virginia

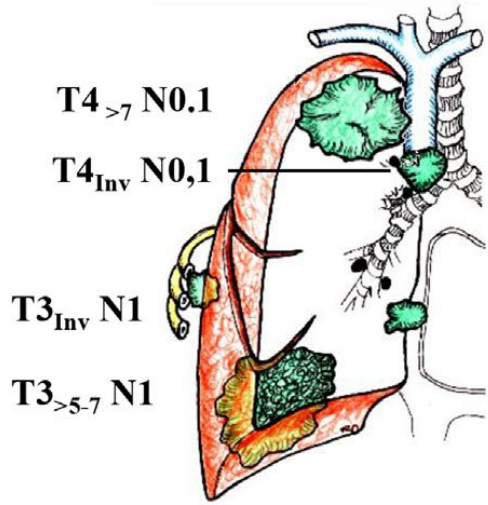
Jyoti Patel, MD - Medical Oncology, University of Chicago

James Urbanic, MD - Radiation Oncology, UC San Diego

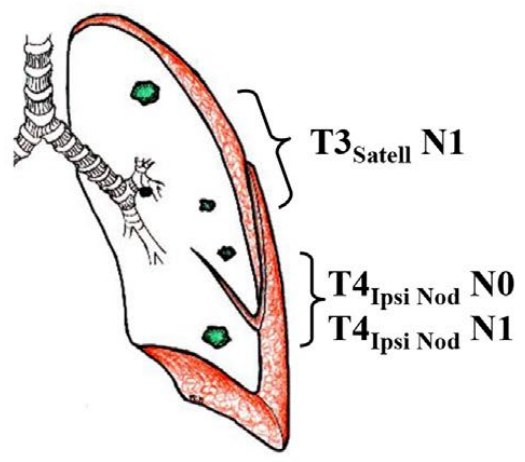
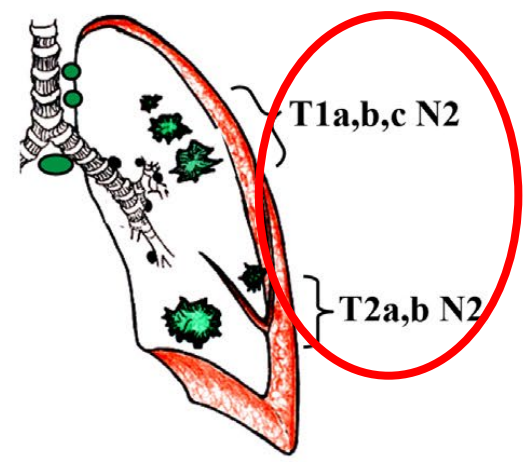
# AFT 46 Phase II Single Arm Trial

CHIO 3: Chemotherapy Combined with Immune Checkpoint Inhibitor for Operable Stage III NSCLC



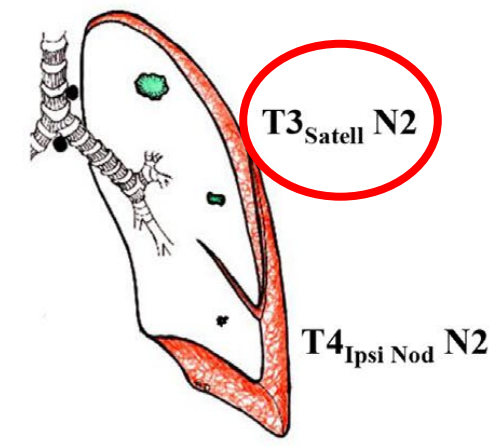
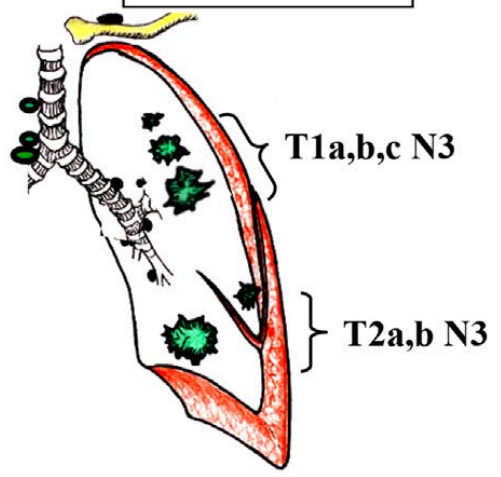
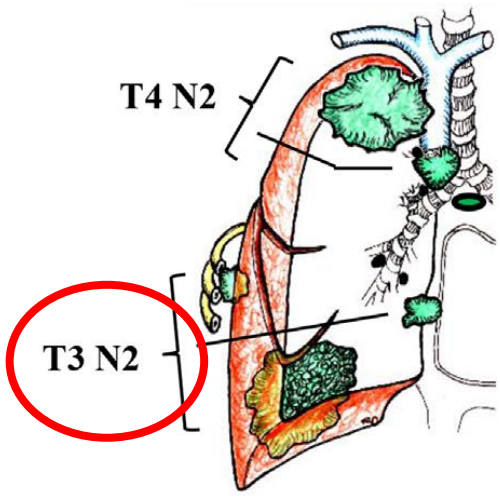


### Stage IIIA

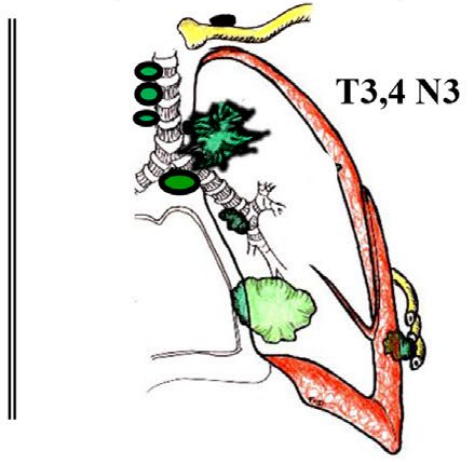


Specific Notes:  
 Tumor size defined as largest dimension of the solid (imaging, c-stage) or invasive (p-stage) component  
 Direct extension of the primary tumor into an adjacent node counts as nodal involvement  
 Extension of a nodal metastasis into a T structure does not count for the T category  
 The highest T category is used when there is a discrepancy between T by size or by other factors

### Stage IIIB



### Stage IIIC



# Surgery

- Lobectomy or greater
- Mediastinal Lymph Node Dissection
- Per Operative Standards for Cancer Surgery “rules”





# Adjuvant radiation – “PORT” criteria

- OPTIONAL – per treating team
- Positive margins must get it
- Use treatment planning guidelines from Lung ART trial



# Endpoints

## Primary:

- To increase N2 nodal clearance rate from 30% (with platinum doublet alone as induction therapy) to 50% (with combined platinum doublet with durvalumab) in patients with potentially resectable stage IIIA (N2) NSCLC

## Secondary:

- To assess the radiographic response rate of the combination of chemotherapy and durvalumab in patients with potentially resectable stage III (N2) NSCLC



# Progress

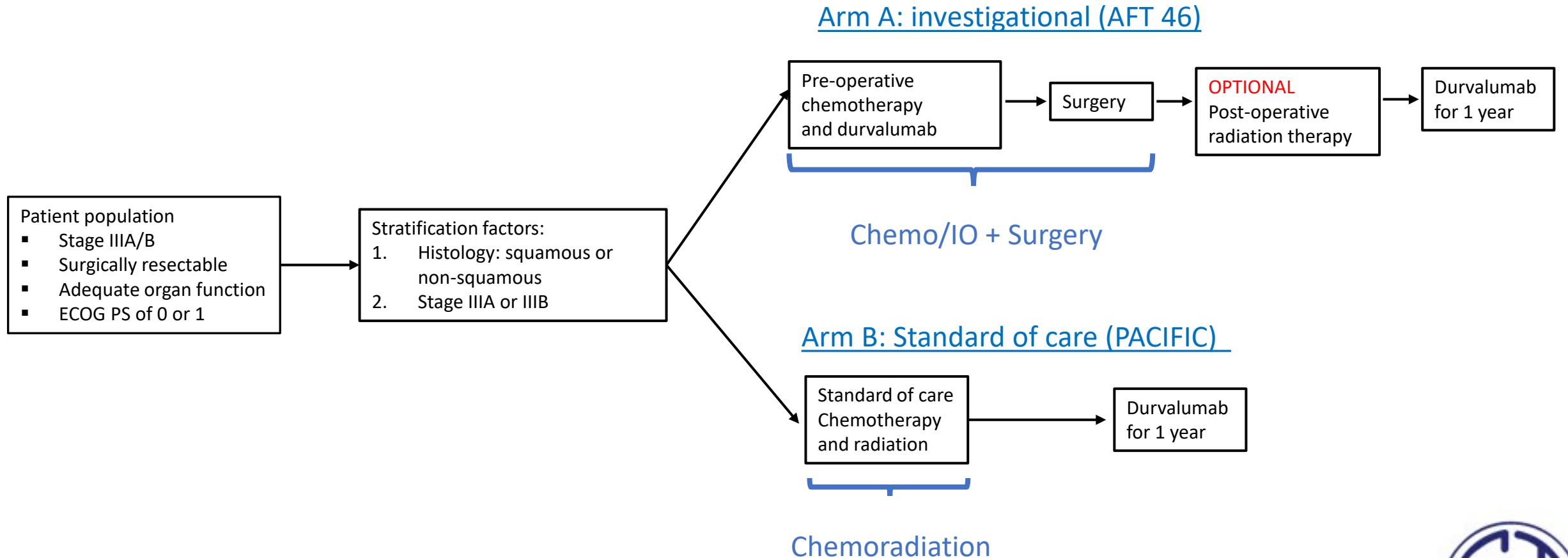
- LOI submitted April 2017
- Final proposal submitted 7/31/18, revisions reviewed 10/30/18
- Approved by Alliance Foundation and Astra Zeneca Dec 2018
- Alliance Foundation Trial, using the Alliance trial mechanism and resources
- CIRB approval underway Feb 2020
- Covid.... Contracts... Delays...
- First patient in this month, opening at 16 sites



# Trials in Development



# Phase 3 follow up to AFT 46 – *OPERABLE* stage III



# AFT 51

Linda Martin, MD  
and Sunil Singhal, MD



# Pulmonary Metastasectomy

SURGEONS GOAL:

COMPLETE DISEASE CLEARANCE

Problem

Identification of all disease

# Hypothesis

**Near infrared imaging can improve detection of metastases missed by**

**(a) preoperative CT imaging**

**(b) intraoperative inspection**



# NIR Imaging—TumorGlow®

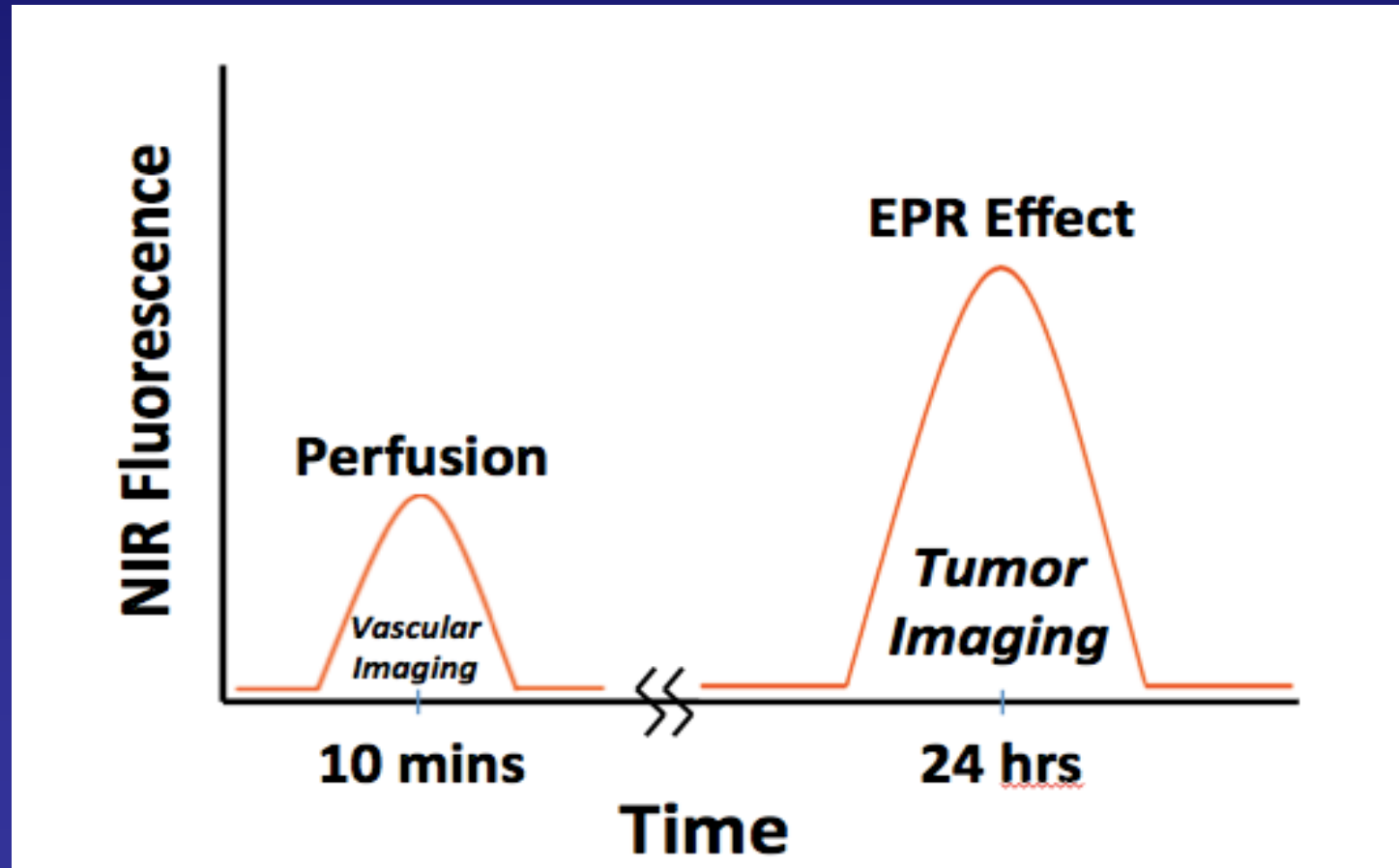
ICG GIVEN SYSTEMICALLY (NOT INTRATUMORAL)



**DIFFERENT DOSE—5 mg/kg**

# NIR Imaging—TumorGlow®

Imaging 24h later



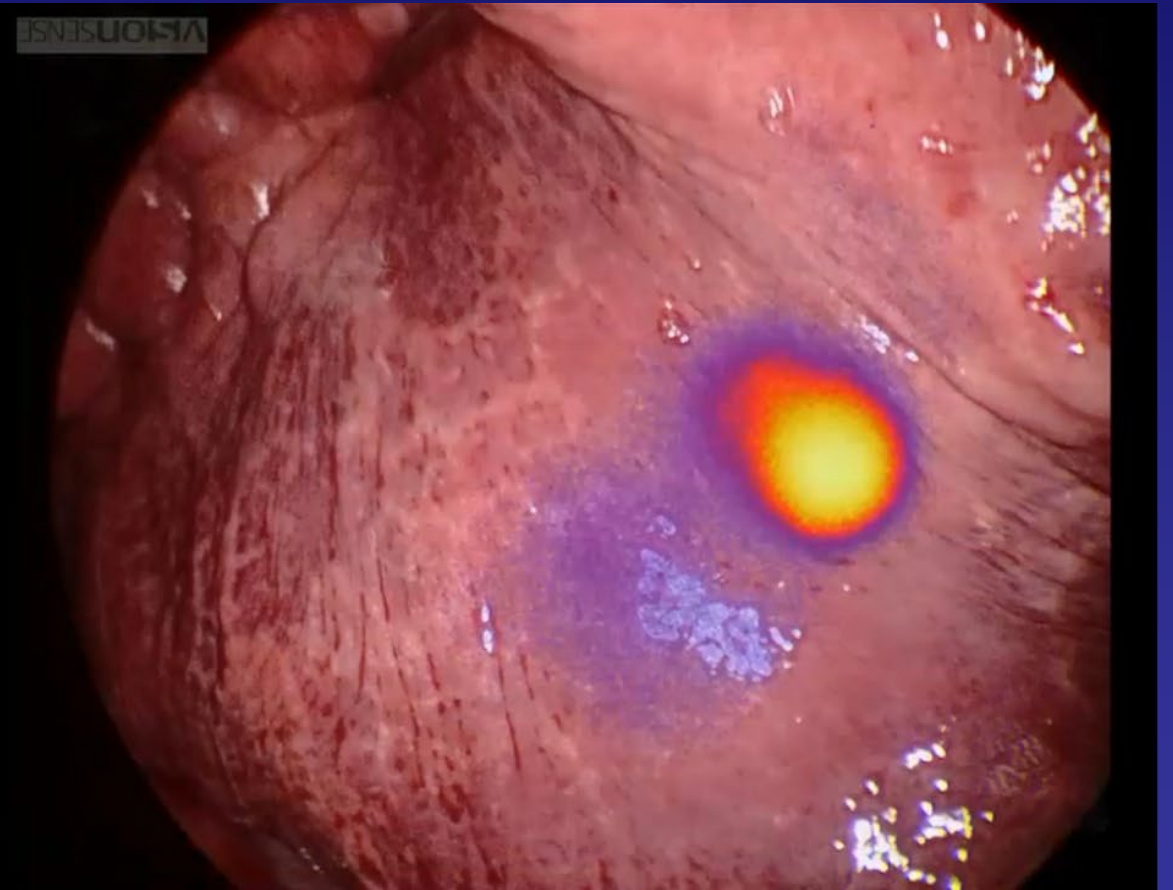
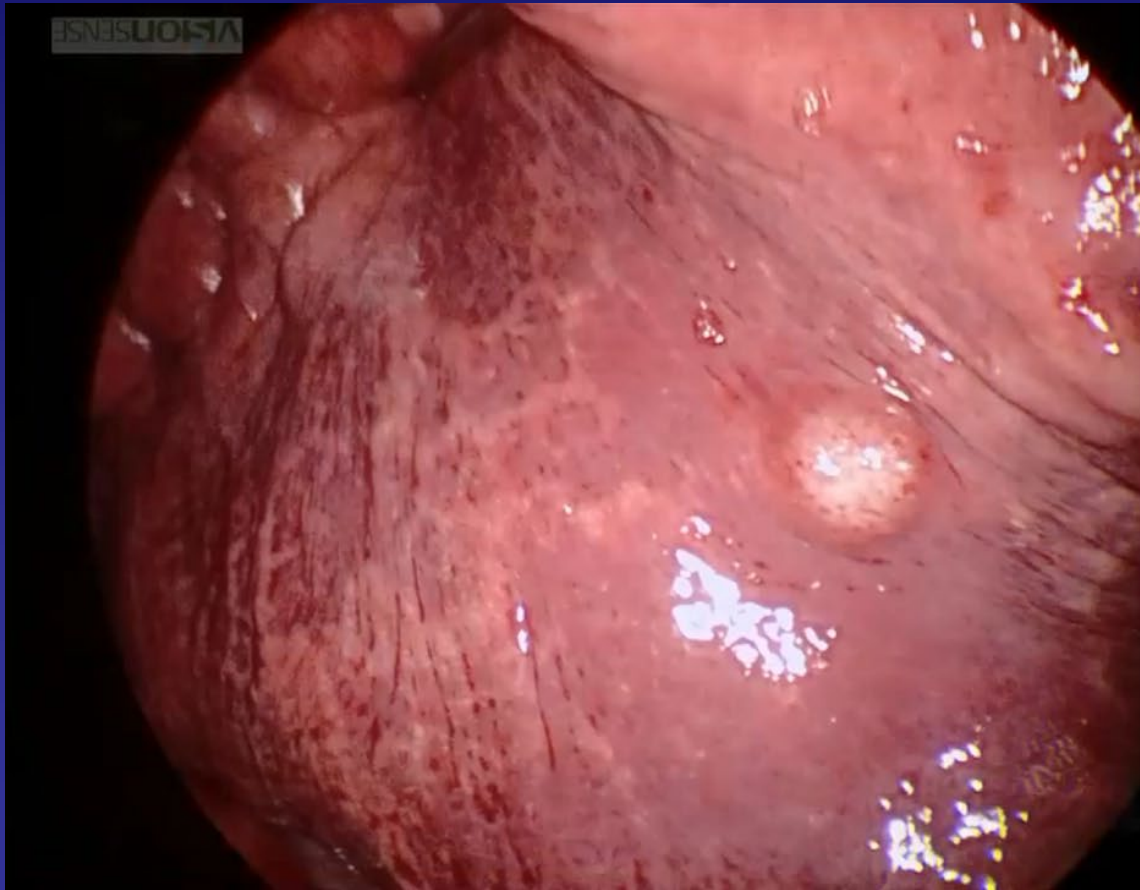
# Clinical Trial

# Example 1

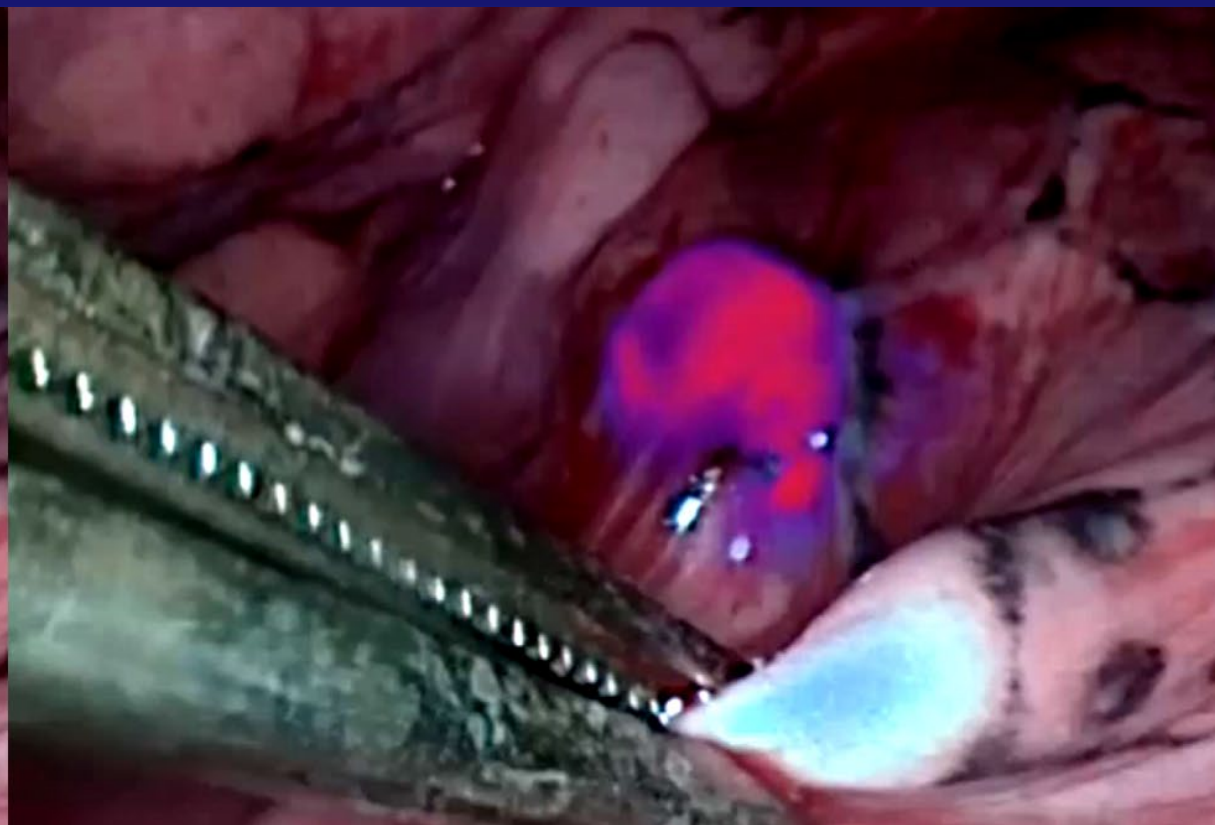
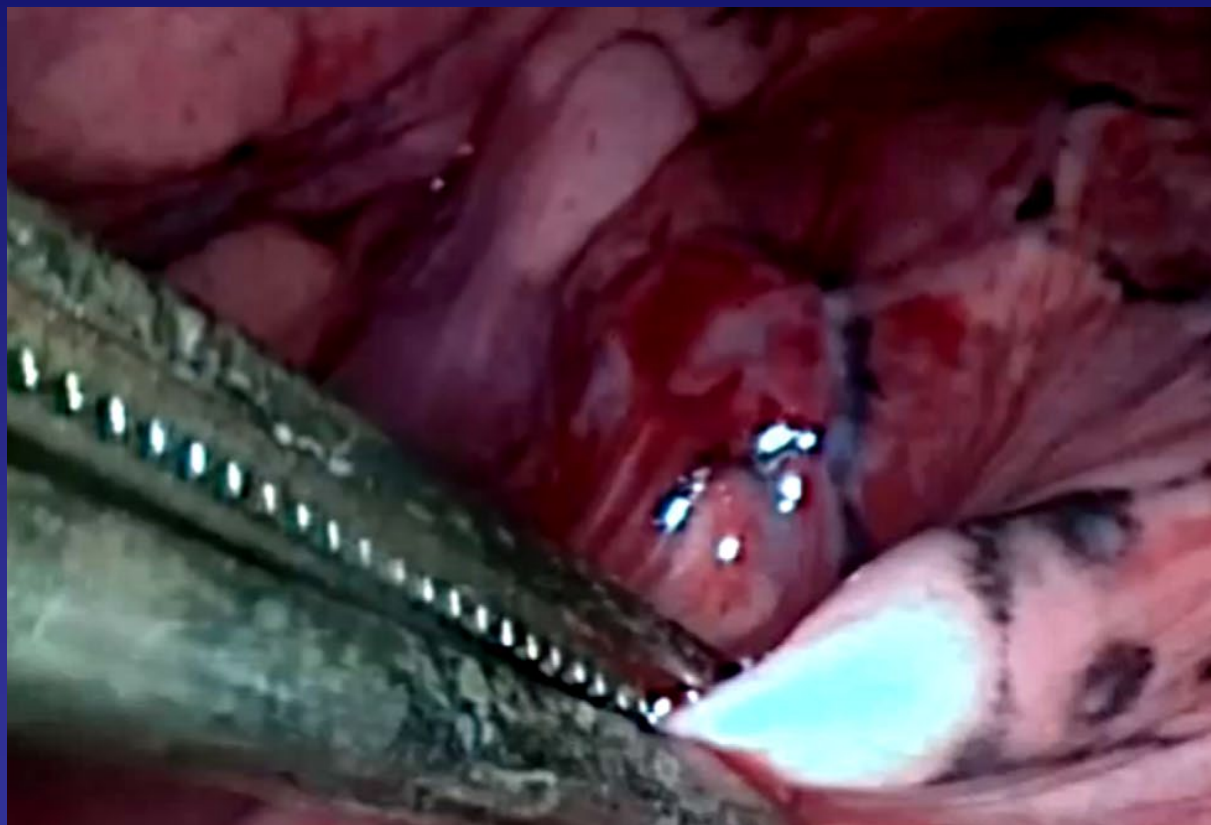
32M, femur osteosarcoma, RLL mets  
(known)

White Light

NIR Imaging



# Additional lesion? (right middle lobe)



# Future Directions

**WELCOME A MULTI-INSTITUTIONAL CLINICAL TRIAL**

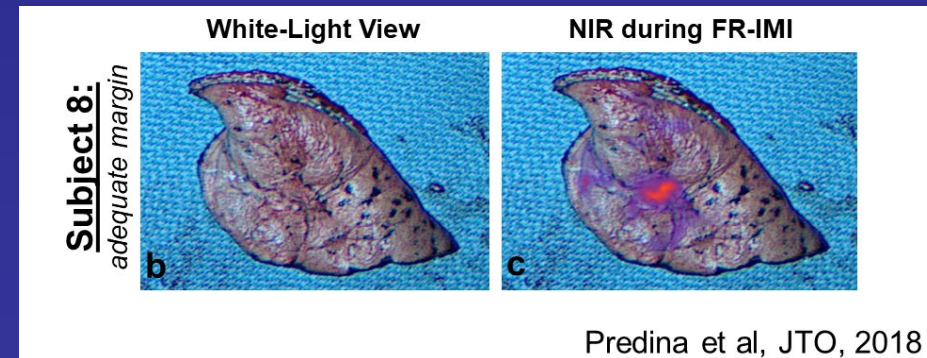
[sunil.singhal@uphs.upenn.edu](mailto:sunil.singhal@uphs.upenn.edu) (Sunil Singhal)

[lm6yb@virginia.edu](mailto:lm6yb@virginia.edu) (Linda Martin)

- AFT 51 in development
- 120 patients, 10-15 sites

## QUESTIONS TO ANSWER:

- Is this reproducible nationwide?
- Are particular histologies better at imaging?
- Ex vivo margin assessment (growing importance)?



# I-PROTECT

Linda Martin, MD

David Kozono, MD

Thomas Stinchcombe, MD

Paul Ridker, MD



# New Study Concept

For Early Stage Lung Cancer

Stage IA-IB  $\leq$  4 cm node negative



# Inflammation and cancer

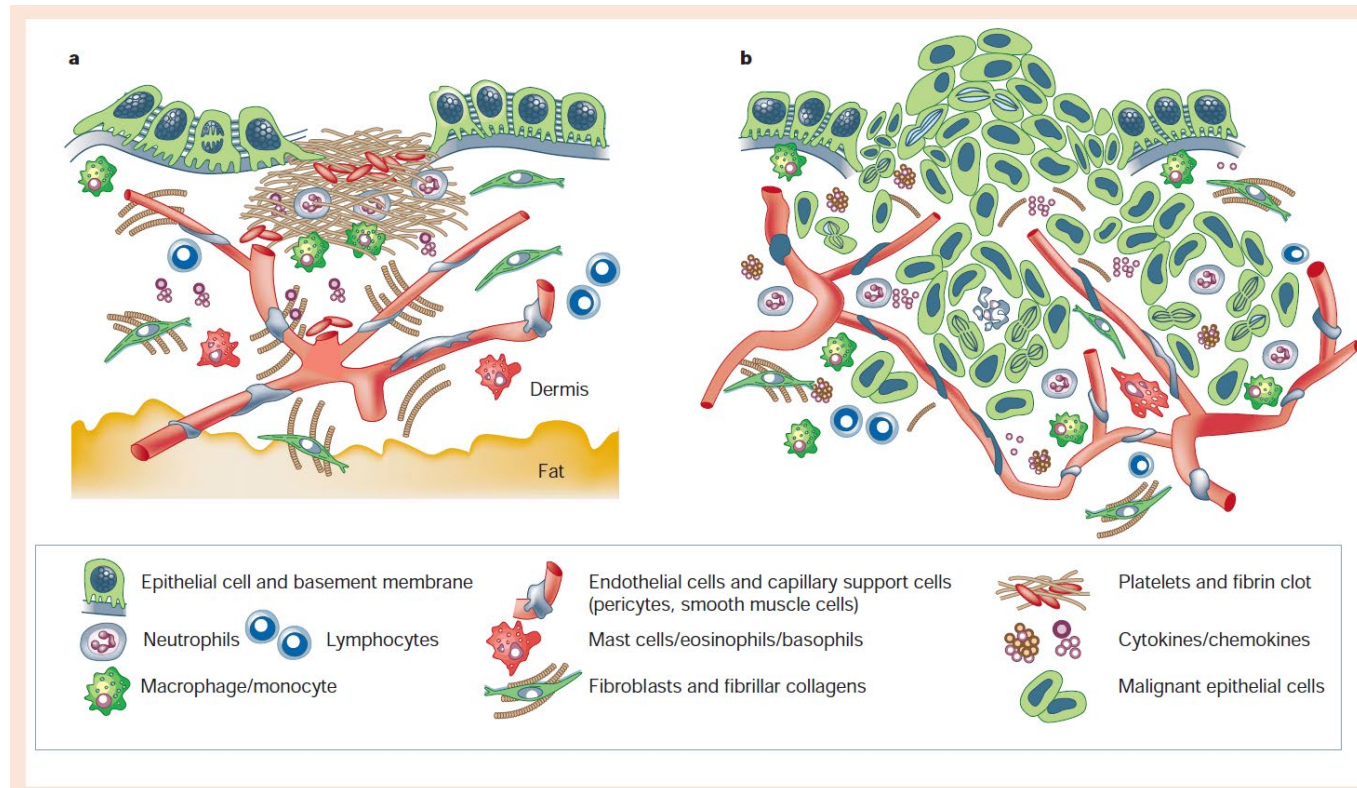
Lisa M. Coussens\*†§ & Zena Werb‡§

\*Cancer Research Institute, Departments of †Pathology and ‡Anatomy, and the §UCSF Comprehensive Cancer Center, University of California, San Francisco, California 94143 USA (e-mail: coussens@cc.ucsf.edu; zena@itsa.ucsf.edu)

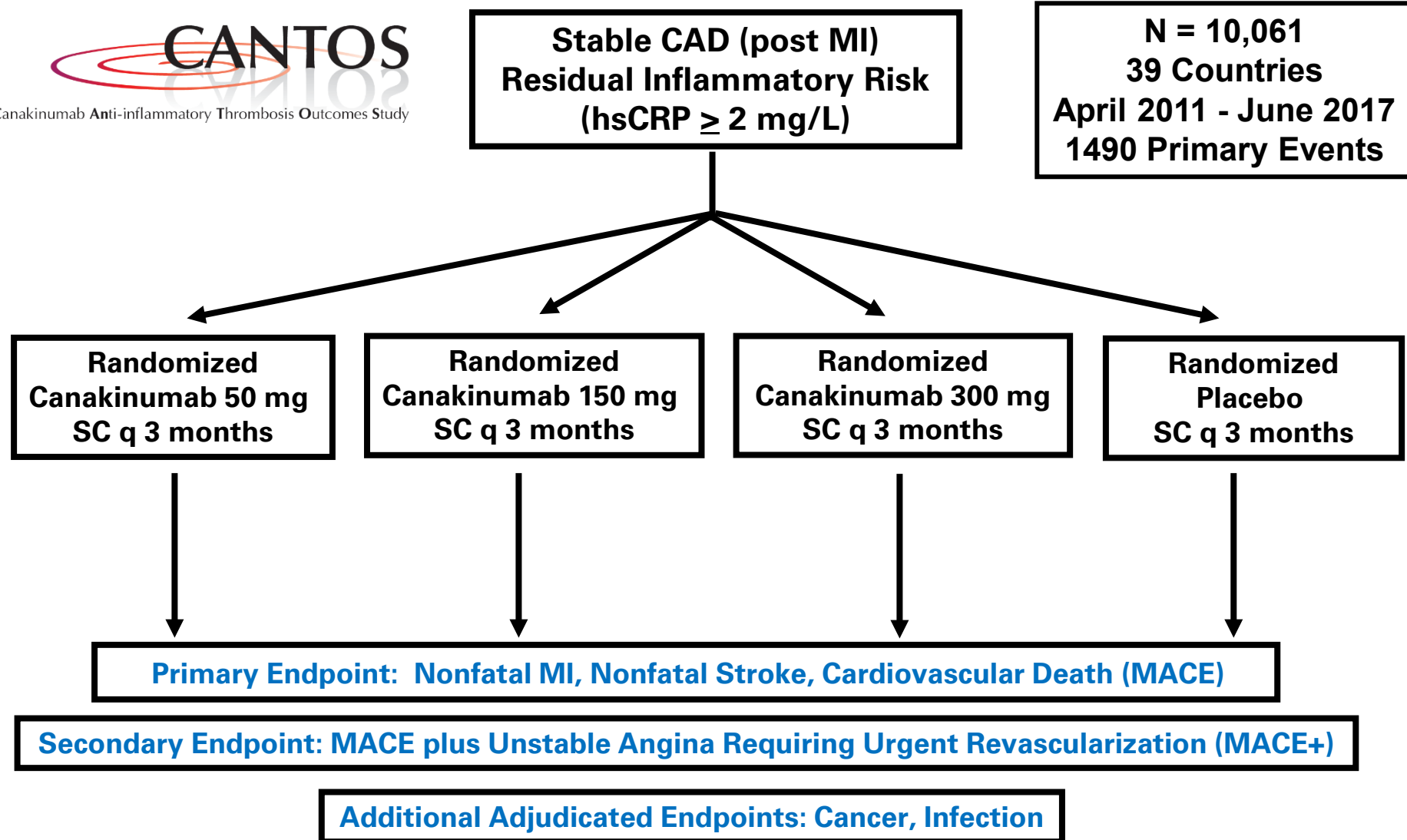
“Inflammation is a critical component of tumour progression (and) it is now becoming clear that the tumour microenvironment, which is largely orchestrated by inflammatory cells, is an indispensable participant in the neoplastic process, fostering proliferation, survival, and migration”.

## Wound Healing

## Invasive Tumor Growth

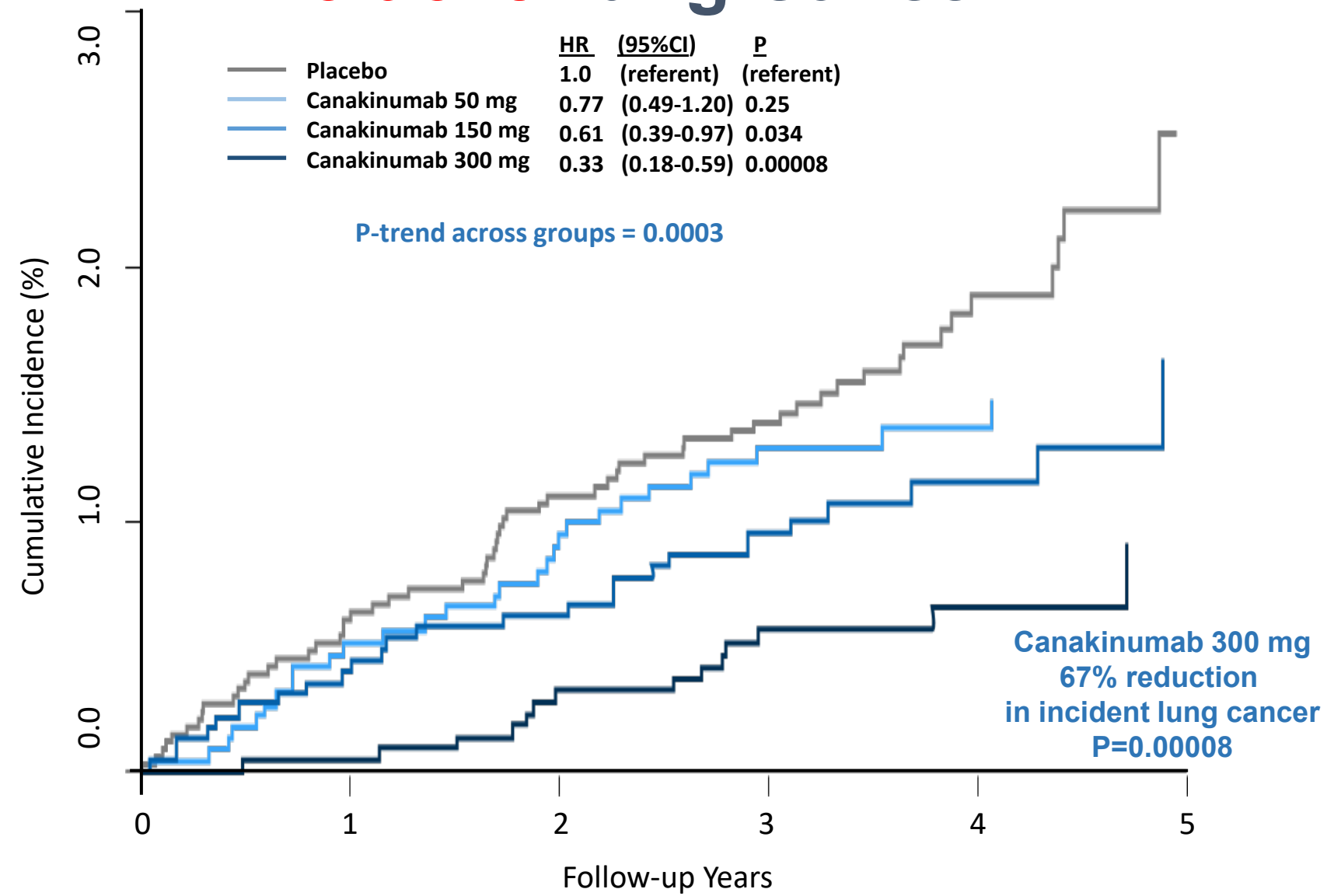


# Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS)



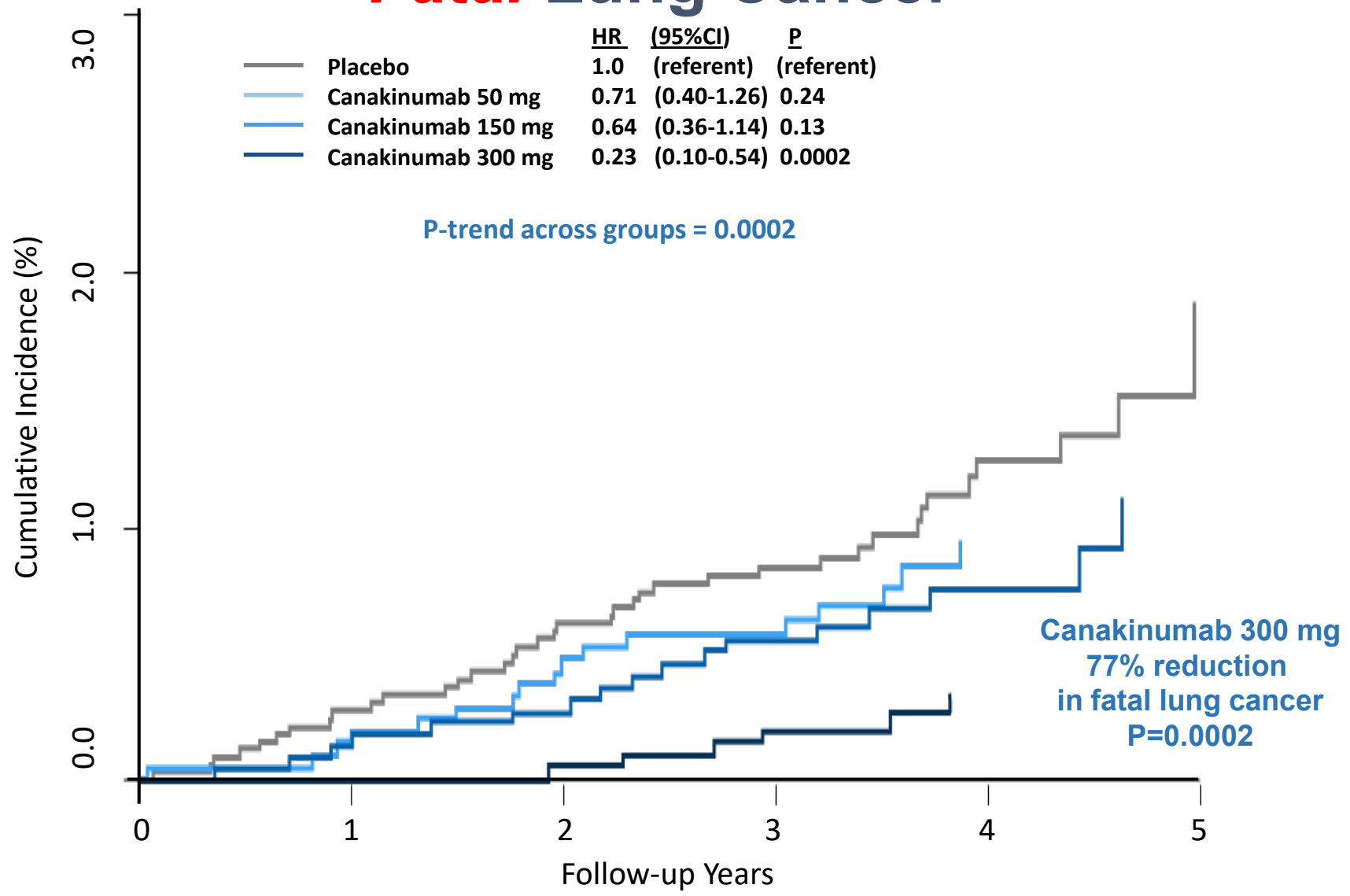
# CANTOS: Additional Non-Cardiovascular Clinical Benefits

## *Incident* Lung Cancer



# CANTOS: Additional Non-Cardiovascular Clinical Benefits

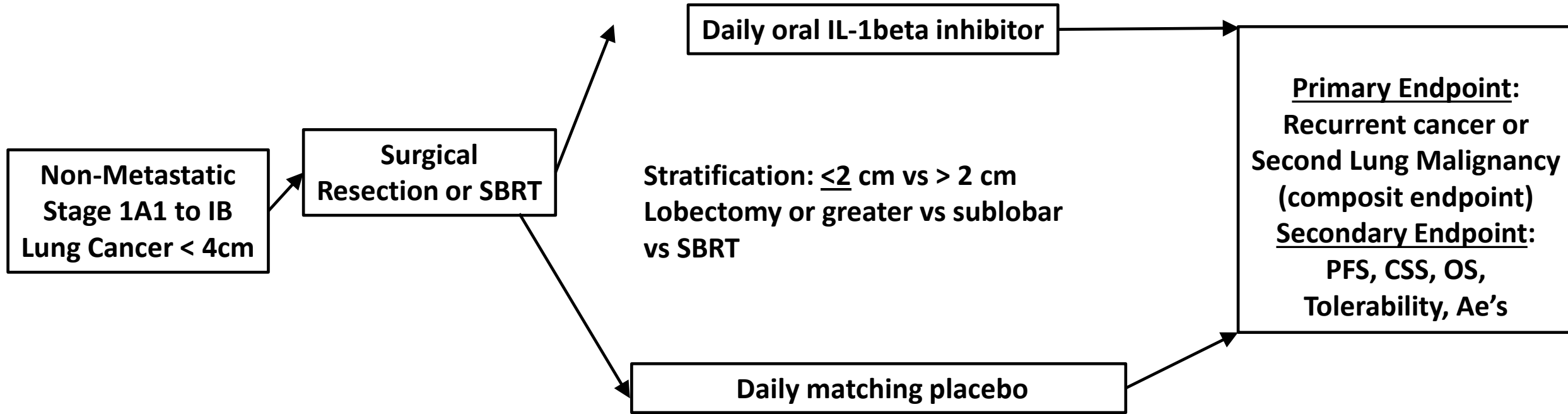
## *Fatal* Lung Cancer



Can blockade of IL-1 $\beta$  prevent lung cancer recurrence? Or prevent second primary lung cancers?

# C-PROTECT: Colchicine to Prevent Recurrences Of Treated Early Cancers of the Thorax

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Central Biobank

Tumor markers and genetics  
ctDNA

Q 6 thoracic surgery visits - CT surveillance  
- safety blood work  
- ascertain for endpoints  
- ascertain for adverse events

# Decisions to make

- This would be a SURGEON, RAD-ONC run protocol
- Could enroll every stage 1 resection
- Need about 1000 patients
- Duration of drug therapy – 5 years?