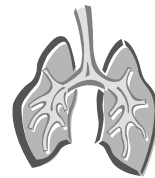




## CALGB 30506:

**A Randomized Phase III Trial to Evaluate the Potential Utility of a Genomic Prognostic Model to Identify Stage I NSCLC Patients as Candidates for Adjuvant Chemotherapy**

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Duke University Medical Center  
Clinical Research Coordinator  
Thoracic Oncology-Surgery



November 13th, 2008

## Study Personnel

- Study Chair:
  - David Harpole, MD – Duke
- Co-Chairs
  - Anil Potti, MD – Duke
  - Robert Kratzke, MD – UMN
  - Jack Burhalter, PhD – MSKCC
- Data Coordinator
  - Susan Sutherland – Duke
- Protocol Coordinator
  - Colleen RB Watt – U. of Chicago

Slide 2

## Background

- Pathological Stage 1 NSCLC represent the fastest growing segment of NSCLC
- Current standard of care = observation
- Prior studies
  - Protein expression
  - Identify relative risk for IA and IB NSCLC
- Need a model with greater predictive power
  - Individualized assessment

Slide 3

## Lung Metagene Score

A molecular based tumor model, which relies on the genetic elements of that tumor, to determine risk of tumor recurrence

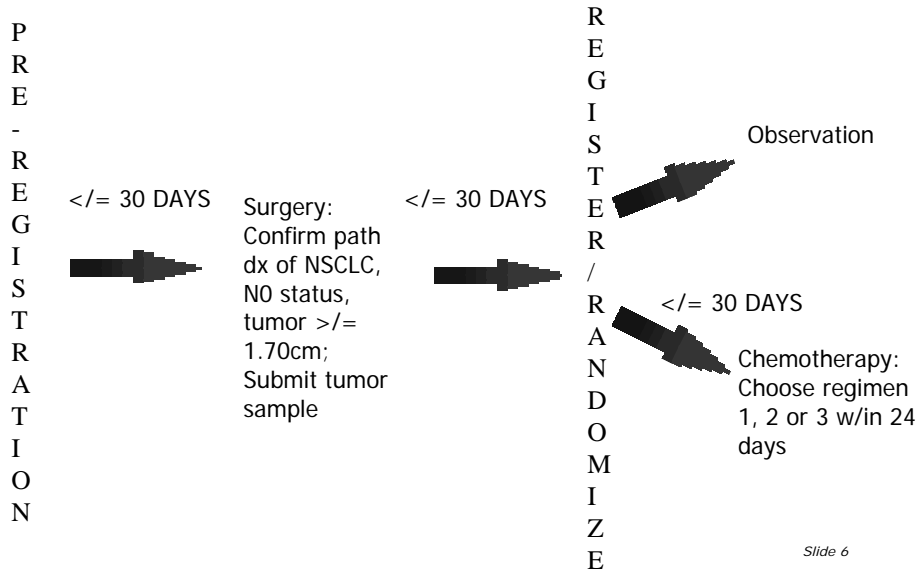
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# Study Objectives

1. Evaluate the use of LMS for selecting (resected) early stage NSCLC patients as candidates for adjuvant chemotherapy (AC) and its effect on survival

Slide 5

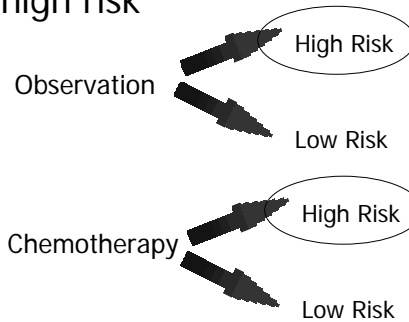
# Study Summary



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## Study Objectives

2. Determine survival benefit of AC compared to observation in pts. predicted (by the LMS) as "high risk"



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## Pre-Registration Eligibility

- Known or suspected Stage I NSCLC
  - Tumor > 2cm and <6cm on CT scan
- Node negative
- No hx of prior/concurrent malignancy
  - No tx within 5 yrs of randomization
- $\geq 18$  y/o
- ECOG = 0-1
- Non-pregnant/nursing

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## Randomization Eligibility

- Confirmed diagnosis of NSCLC
- Primary tumor > 1.7cm and <3.01cm
- T1N0 status
- Initial lab values:

Granulocytes	≥1,500/μL
Platelets	≥ 100,000/μL
Bilirubin	≤ 1.5 mg/dL
SGOT (AST)	< 1.5 x ULN
Serum Creatinine	≤ 1.5 x ULN

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## Protocol Treatment

- 21 days for a total of 4 cycles
- 3 options
  1. Cisplatin/Vinorelbine
  2. Cisplatin/Docetaxel
  3. Cisplatin/Gemcitabine

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## Required Data

- Within 30 Days before *pre-registration*
  - Hx and physical
  - All baseline exams for screening
  - Imaging studies
- Within 16 Days before *registration*
  - Initial labs
  - Hx and physical

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## Sample Procurement

- Cut 1.0x1.0x0.5cm block from fresh lung tumor
- 3 dermal punch core biopsies (0.5cm)
- Place in cryovials and freeze in liquid nitrogen for 1min.
- Store in shipping container in -80°C until shipped

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## Sample Submission

Genome Trial Support Facility  
C/O Michael Datto, MD, PhD  
326M Davison Bldg, Green Zone  
Duke South Hospital  
Duke University Medical Center  
Durham, NC 27710

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## QOL Companion Study

- Objective is to compare:
  - Intensity of treatment-related physical symptoms
  - Fear of cancer recurrence
  - Emotional function
- Pts may opt to not participate
- Must complete QOL questionnaire

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	Prior to Pre-registration	Prior to Registration (post-surgery) <sup>*</sup>	Chemo pts: Day 1 of Each Cycle	Chemo and obs pts: Post Treatment Follow up <sup>**</sup>
<b>Tests &amp; Observations</b>				
Physical Examination (physician visit)	X		X	X
Pulse, Blood Pressure	X	X	X	X
Height	X			
Weight/Body Surface Area <sup>Δ</sup>	X	X	X	X
Performance Status	X	X	X	X
Tumor Measurements	X	X		X
Toxicity Assessment			X	X (for chemo pts only)
<b>Laboratory Studies</b>				
CBC, Differential, Platelets	PRN	X	A	
Electrolytes	PRN	X	X	
Serum creatinine, BUN	PRN	X	X	
LDH	PRN	X		
AST, Alk Phos, Bili, Albumin, Ca	PRN	X	X	
Tissue Submission		C		
<b>Staging</b>				
Chest CT scan (including adrenals) <sup>***</sup>	X	X		X
Bone or PET or Brain Scan	PRN	PRN		PRN
<b>Companion Study</b>				
Quality of Life	B			

**\* Prior to registration labs may be used for day 1 of cycle 1 tests if obtained within 14 days prior to day 1 of Cycle 1. For subsequent cycles labs may be obtained within 48 hours prior to day of treatment.**

**\*\* Following surgery at least every 4 months for 2 years, then every 6 months for 3 years, for a total of 5 years.**

**\*\*\* See Section 13.5.3 for further details regarding the chest CT requirements.**

**Δ It is not necessary to change the dose of chemotherapy unless the calculated dose changes by > 10% (from the previous cycle).**

**A. Obtain on days 1 and 8 during chemotherapy for regimens that include vinorelbine and/or gemcitabine.**

Form*	Submission Schedule
<b>Submit for all <u>pre-registered</u> patients:</b>	
C-1803 30506 Sample Submission Form	Submit original form with RNA tumor sample to Genome Trials Support Facility; submit copy of form to Data Operations
C-1799 30506 Pre-surgical Eligibility Checklist Report 30506 Pre-study/Surgical Resection Form Baseline Chest CT report	Within one month of registration or decision to not register patient
<b>Submit for all <u>registered</u> patients:</b>	
C-1804 30506 Post-surgical Eligibility Checklist Report 30506 Baseline Abnormalities Form Operative and Pathology reports	For chemo and obs pts: Within one month of registration.
C-1800 30506 Treatment Form C-1801 30506 Adverse Event Form <sup>**</sup>	For chemo pts only: Each cycle during protocol therapy.
C-1802 30506 Follow-up and Response Form Report Chest CT/X-ray reports	For chemo and obs pts: Every 4 months for first 2 years after surgery, then every 6 months for 10 years.
C-1803 30506 Sample Submission Form	For chemo and obs pts: Submit original form with paraffin block to PCO; submit copy of form to Stat Ctr
C-1742 Confirmation of Lost to Follow-up Form	Follow form instructions.
Quality Of Life Forms	For chemo and obs pts: For patients who consented to 708XX QOL companion, see section 10.3

## Protocol Deviations

- Major
  - Intra-operative exam NOT performed on nodes seen on CT > 1cm
  - Inclusion of pts. with positive nodes at surgery
  - Resection less than lobectomy
- Minor
  - Inadequate documentation of nodal sampling

*\*\*Have surgeons review requirements for mediastinal lymph node systematic sampling*

## VATS Credentialing

- 10 VATS lobectomies
- Submit letter detailing VATS experience over the last 1 year:
  - 3 operative reports + path reports
  - # of cases
  - # of mortalities
  - # of major complications/prolong hospitalizations
- Send to

Linda Veit  
Surgery Committee Administration  
Surgery Dept., Room 8140  
Upstate Medical University  
750 E. Adams St.  
Syracuse, NY 13210

## **AER**

- AdEERS expedited reporting required for adverse events that occur within 30 days of last day of treatment

*Slide 19*

## **As a result....**

- Validate genomic-based prognostic methods
- Understand the role of adjuvant chemotherapy in high risk stage 1A patients
- Create a tissue repository/gene expression databank for future investigations

*Slide 20*

## Contact Information

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