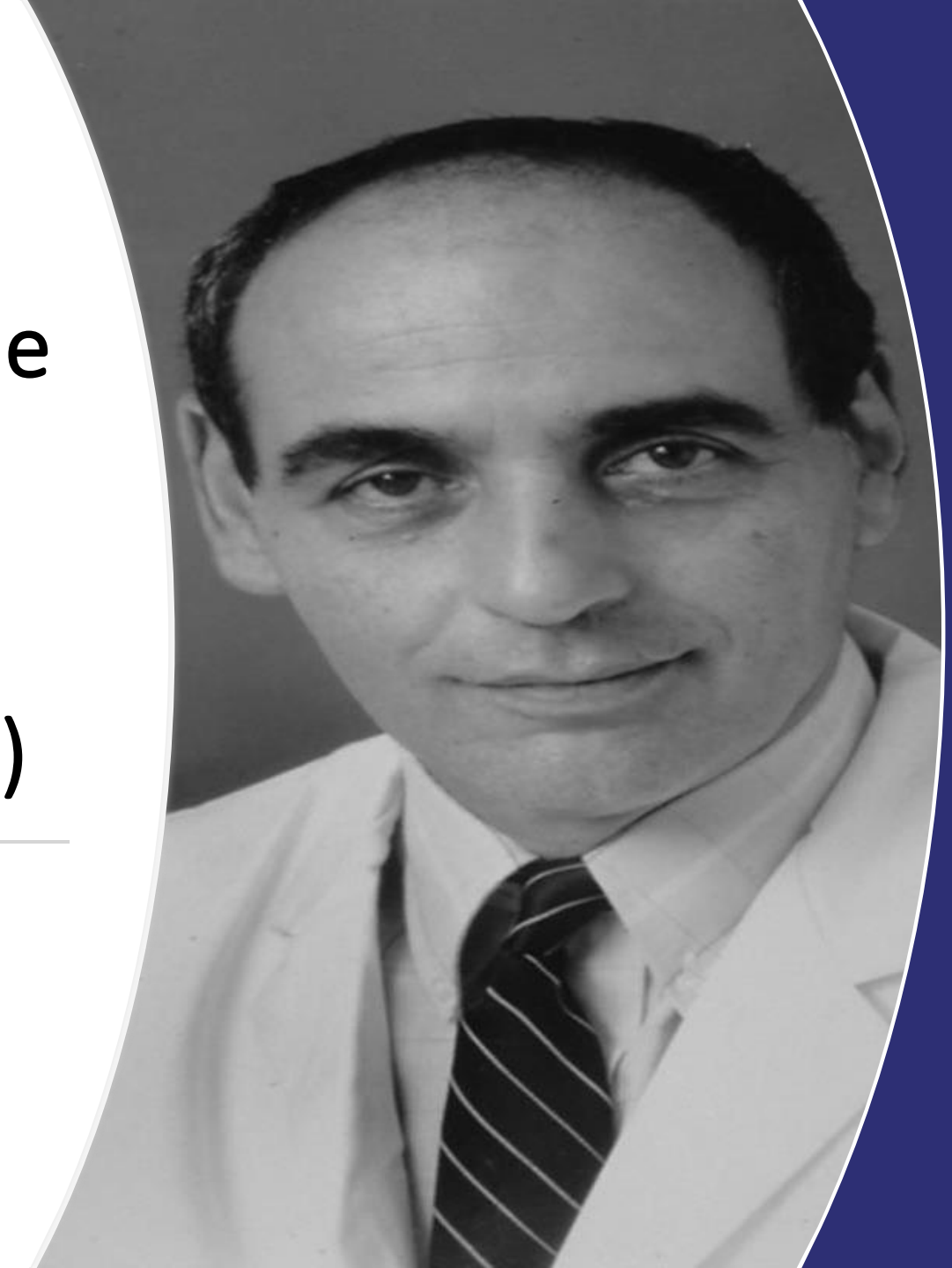
Welcome to the Robert J. Ginsberg Clinical Trials (Ginsberg Day)

We will begin at

1:30 pm EST



Disclosures

Commercial Interest	**Relationship(s)**
Astra Zeneca	Advisory Board for Adaura Trial dissemination
On Target Laboratories	Steering Committee for ELUCIDATE trial
Genentech	Speakers Bureau
Ethicon	Speakers Bureau

Agenda for today

- Dr. Altorki – Keynote speaker
- NCI trials
- What's new for Ginsberg Day:
  - TSOG – Thoracic Surgery Outcomes Group
  - TSTN – Thoracic Surgery Trials Network
  - THORN – Thoracic Surgery Outcomes Research Network
  - COC – Commission on Cancer

Alphabet soup you will want to know

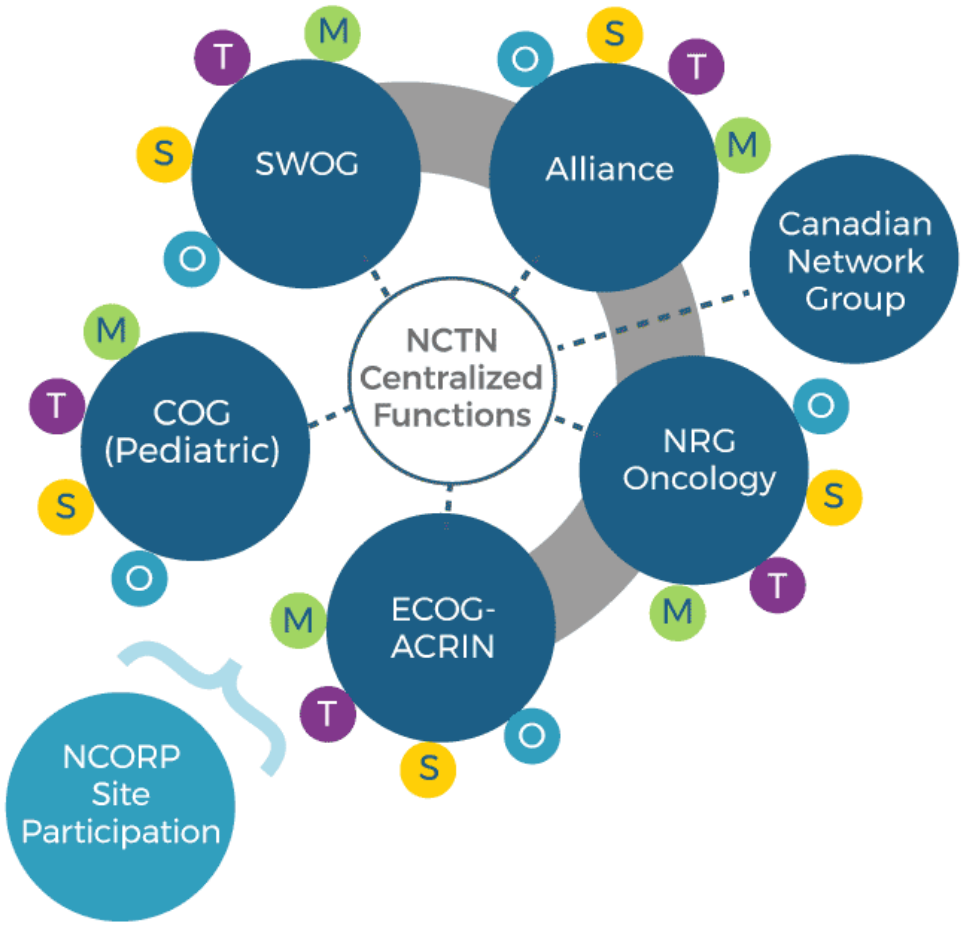
Alphabet Soup

- **OS: Overall Survival** – duration from date of diagnosis (or intervention) to death ***Traditionally used to assess adjuvant therapy***
- **DFS: Disease Free Survival** - the length of time after primary treatment for a cancer ends that the patient survives **without any signs or symptoms of that cancer** ***used for recent adjuvant trials (ADAURA, IMPOWER 010)***
- **EFS: Event Free Survival** **–**time from randomization to any progression of disease precluding surgery, progression or recurrence of disease after surgery, progression of disease in the absence of surgery, or death from any cause. ***used for CM816***
- **PFS: Progression Free Survival** - The length of time during and after the treatment of a disease, such as cancer, that a patient **lives with the disease** but it does not get worse.
- **HR: Hazard Ratio** - hazard ratios are often used in clinical trials to measure survival at any point in time in a group of patients who have been given a specific treatment compared to a control group given another treatment or a placebo. ***<1 IS GOOD***

Alphabet Soup

- pCR: Pathologic Complete Response – ypT0N0
- NCI: National Cancer Institute
- SWOG: Southwest Oncology Group
- ECOG: Eastern Cooperative Oncology Group
- NRG: **N**sabp, **R**tog, **G**og (mostly radiation oncology group)
- CTSU – Cancer Trials Support Unit – supports enrollment/access to cooperative groups across sites
- CTEP – Cancer Therapy Evaluation Program – Plans, reviews, coordinates clinical trials
- NCTN – National Clinical Trials Network

NCI National Clinical Trials Network Structure



LEGEND

- Centralized Functions:
  - Centralized Institutional Review Board
  - Cancer Trials Support Unit
  - Imaging and Radiation Oncology Core (IROC) Group
  - Common Data Management System Central Hosting
- 32 Lead Academic Participating Sites (LAPS)
- O — Operations
- S — Statistics & Data Management
- T — Tissue Banks
- M — Member Sites

cancer.gov

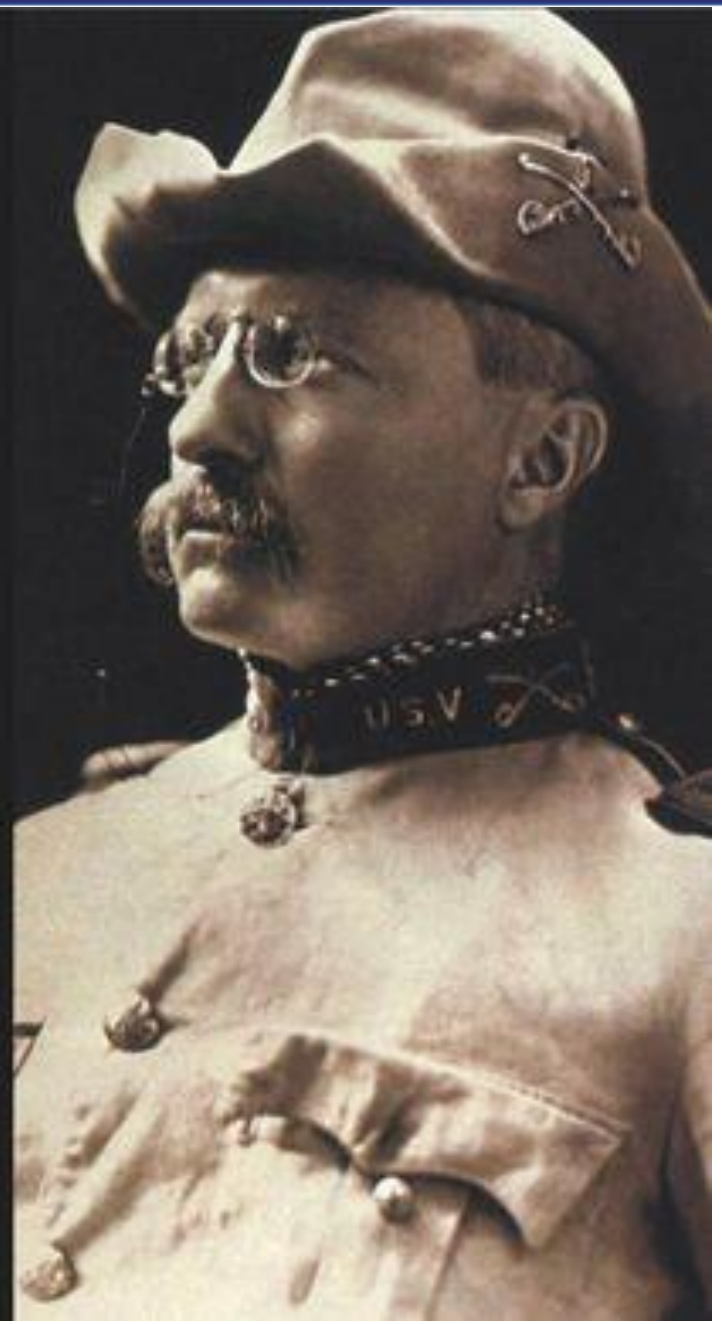
The answer is 17 years, what is the question: understanding time lags in translational research

J R Soc Med 2011: ***104:*** *510–520. DOI 10.1258/jrsm.2011.110180*

THE MAN IN THE ARENA

"IT IS NOT THE CRITIC WHO COUNTS; NOT THE MAN WHO POINTS OUT HOW THE STRONG MAN STUMBLES, OR WHERE THE DOER OF DEEDS COULD HAVE DONE THEM BETTER. THE CREDIT BELONGS TO THE MAN WHO IS ACTUALLY IN THE ARENA, WHOSE FACE IS MARRED BY DUST AND SWEAT AND BLOOD; WHO STRIVES VALIANTLY; WHO ERRS, WHO COMES SHORT AGAIN AND AGAIN, BECAUSE THERE IS NO EFFORT WITHOUT ERROR AND SHORTCOMING; BUT WHO DOES ACTUALLY STRIVE TO DO THE DEEDS; WHO KNOWS GREAT ENTHUSIASMS, THE GREAT DEVOTIONS; WHO SPENDS HIMSELF IN A WORTHY CAUSE; WHO AT THE BEST KNOWS IN THE END THE TRIUMPH OF HIGH ACHIEVEMENT, AND WHO AT THE WORST, IF HE FAILS, AT LEAST FAILS WHILE DARING GREATLY, SO THAT HIS PLACE SHALL NEVER BE WITH THOSE COLD AND TIMID SOULS WHO NEITHER KNOW VICTORY NOR DEFEAT."

Theodore Roosevelt



Contacts

- Alliance – Thoracic Surgery group:
  - Linda Martin, MD, MPH, U of Virginia – chair
  - Jeff Yang, MD, MGH – vice chair
- SWOG – Thoracic Surgery group:
  - Wayne Hofstetter, MD – MDACC
- ECOG-ACRIN – Thoracic Surgery group:
  - Onkar Khullar, MD, Emory
  - Erin Gillaspie, MD, Vanderbilt
- NRG – Thoracic Surgery group:
  - Jessica Donington, MD, University of Chicago
- NCIC – Thoracic Surgery group:
  - Gail Darling, MD, University of Toronto
- TSOG – Thoracic Surgery Oncology Group
  - Maria Singh singhm1@mskcc.org
  - David Jones
- Thoracic Trials Network
  - Link available on GTSC website

Trials available by Disease, Stage:

NSCLC:

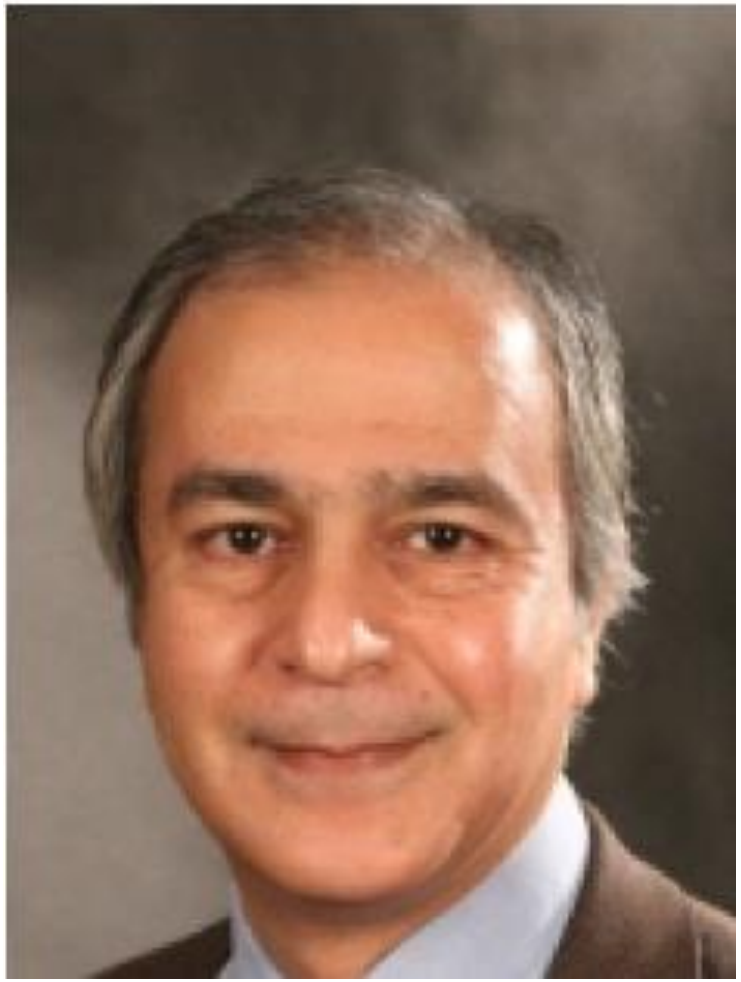
- Stage IA
- Stage IA, IB INOPERABLE or MARGINAL:
- Stage IB-IIIA (occult N2):
- Stage IIIA/B (cN2):
- Stage IV –

Small Cell:

Esophageal cancer:

Mesothelioma:

Nasser Altorki, MD



@AltorkiNasser

- David Skinner, MD Professor of Cardiothoracic Surgery
- Director of the Division of Thoracic Surgery at New York Presbyterian-Weill Cornell Medical Center.
- Gerald J. Ford-Wayne Isom Research Professor in Cardiothoracic Surgery

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 9, 2023 VOL. 388 NO. 6

Lobar or Sublobar Resection for Peripheral Stage IA Non–Small-Cell Lung Cancer

Nasser Altorki, M.D., Xiaofei Wang, Ph.D, David Kozono, M.D., Ph.D., Colleen Watt, B.S., Rodney Landrenau, M.D., Dennis Wigle, M.D., Ph.D., Jeffrey Port, M.D., David R. Jones, M.D., Massimo Conti, M.D., Ahmad S. Ashrafi, M.D., Moishe Liberman, M.D., Ph.D., Kazuhiro Yasufuku, M.D., Ph.D., Stephen Yang, M.D., John D. Mitchell, M.D., Harvey Pass, M.D., Robert Keenan, M.D., Thomas Bauer, M.D., Daniel Miller, M.D., Leslie J. Kohman, M.D., Thomas E. Stinchcombe, M.D., and Everett Vokes, M.D.

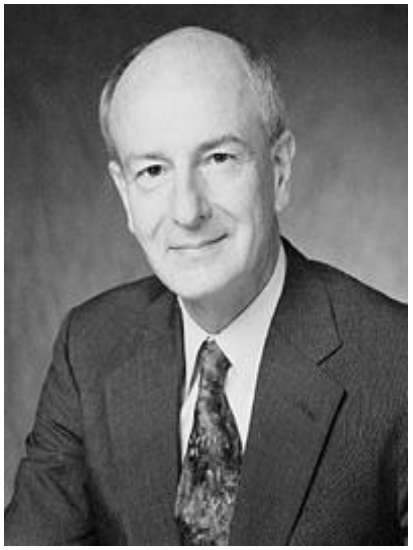
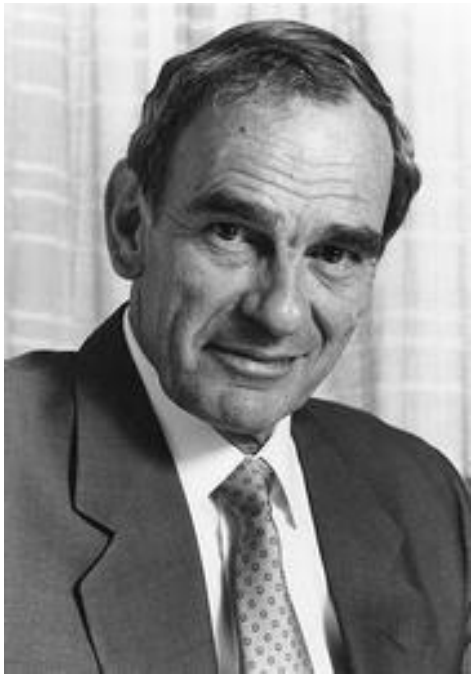
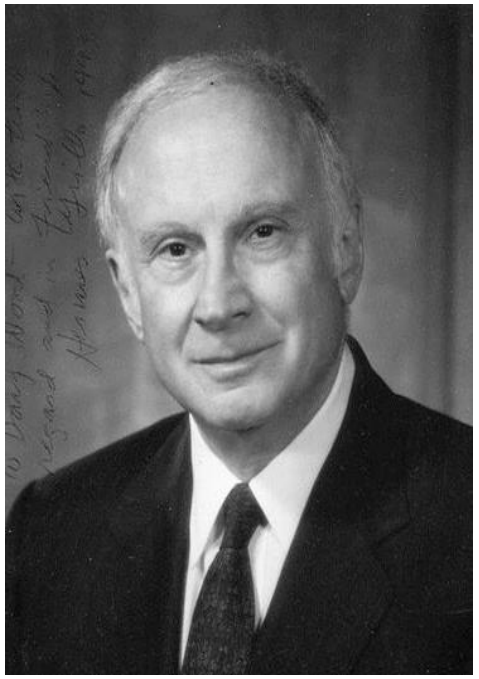
- 352 pubmed articles

Weill Cornell Medicine

My "*trials*" with clinical trials

Nasser Altorki M.D.
Vice Chairman Department Cardiothoracic Surgery
Chief,Thoracic Surgery
David B. Skinner Chair in Thoracic Surgery
Leader of Experimental Therapeutics Program MCC



Basic science research

"A systematic study directed toward fuller scientific knowledge or understanding of fundamental aspects of phenomena ***without scientific application in mind***. Basic research is performed without thought to practical ends."

National Science Foundation

Translational research

"The transfer of new understandings of mechanisms of disease discovered in the laboratory into the development of new methods for diagnosis, therapy and prevention of disease."

Must be informed by clinically relevant questions

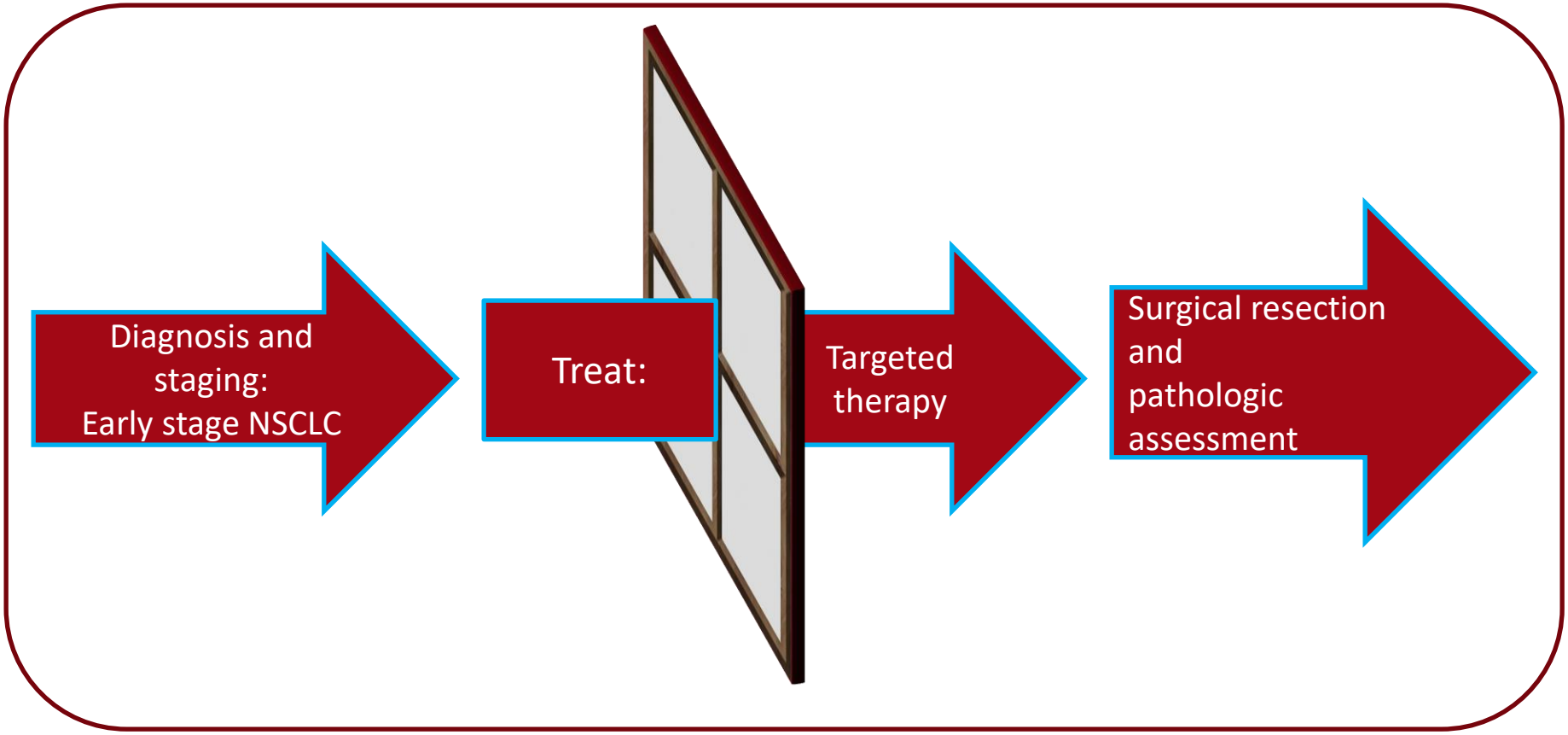
Institute of Medicine, Clinical research Roundtable

Team science:
Translational Trial in early stage disease

- Surgeons
- Medical oncology
- Radiology
- Imaging technology
- Basic scientists
- NCI/ Industry

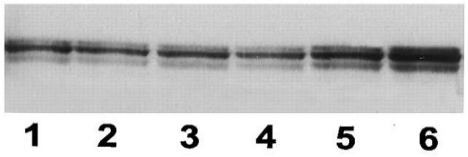
- Research co-ordinator
- Biobank
- Clinical-data base
- Data-base manager

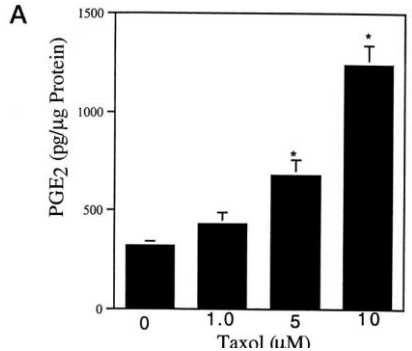
"Window of Opportunity" trials: Targeted therapy in patients with surgically resectable non-small cell lung cancer

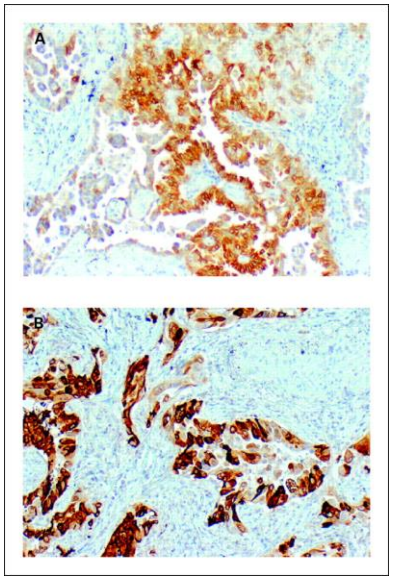


Microtubule-interfering Agents Stimulate the Transcription of Cyclooxygenase-2

Cox-2 protein







K. Subbaramiah;Journal of Biological Chemistry , 2000

- Patients with c-stages IB-IIIA NSCLC
- ECOG PS score 0 or 1

↓

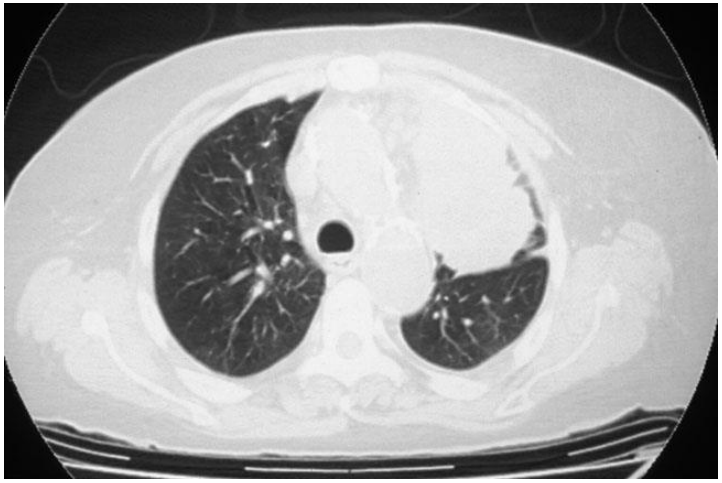
Two cycles of paclitaxel+ platinum + celecoxib

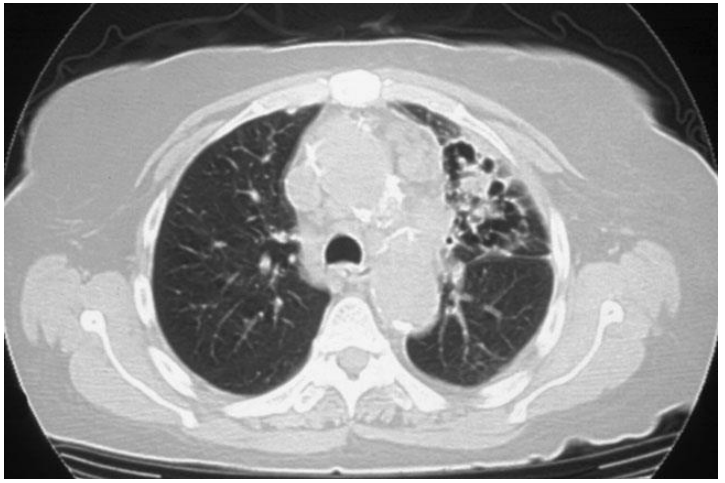
↓

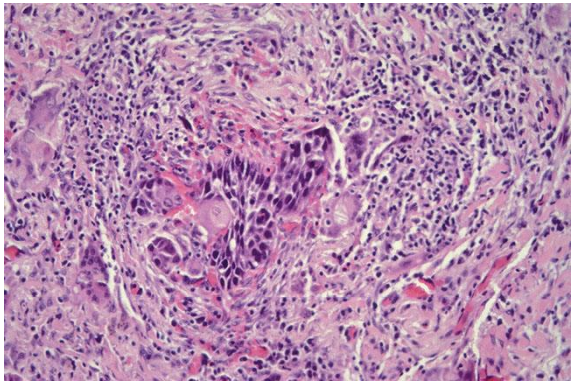
Surgical resection

Altorki et al; JCO 2003

Celecoxib enhances response to preoperative chemotherapy



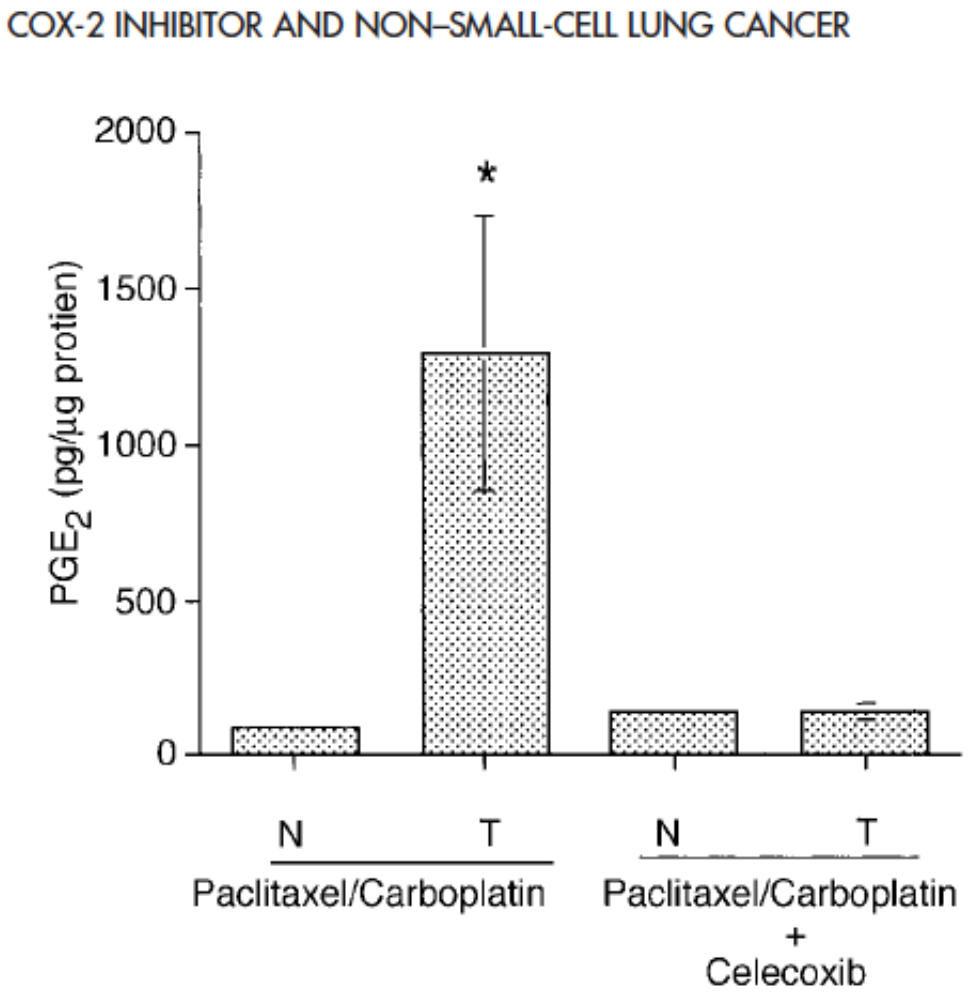




Complete clinical response	17%
Major path. response	24%

Altorki et al, JCO 2003

Celecoxib completely abrogated taxane mediated increase in intra-tumoral PGE2



Altorki et al, JCO 2003

Celecoxib, a Selective Cyclo-Oxygenase-2 Inhibitor, Enhances the Response to Preoperative Paclitaxel and Carboplatin in Early-Stage Non–Small-Cell Lung Cancer

By N.K. Altorki, R.S. Keresztes, J.L. Port, D.M. Libby, R.J. Korst, D.B. Flieder, C.A. Ferrara, D.F. Yankelevitz, K. Subbaramaiah, M.W. Pasmantier, and A.J. Dannenberg

Purpose: **Preclinical studies suggest that treatment with a selective cyclo-oxygenase-2 (COX-2) inhibitor may augment the antitumor effects of chemotherapy. In this study, patients with non–small-cell lung cancer (NSCLC) were preoperatively treated with celecoxib in combination with chemotherapy. End points were toxicity, response rates, and measurement of intratumoral levels of prostaglandin E_2 (PGE_2).**

Methods: **In this phase II trial, 29 patients with stages IB to IIIA NSCLC were treated with two preoperative cycles of paclitaxel and carboplatin, as well as daily celecoxib, followed by surgical resection. Levels of PGE_2 in the primary tumors and adjacent normal lung tissue were compared in 17 study patients versus 13 controls, who received preoperative paclitaxel/carboplatin without celecoxib.**

Results: **All patients completed preoperative chemotherapy, and 26 completed preoperative celecoxib. The overall clinical response rate was 65% (48% with partial response; 17% with complete response). Grade 3 or 4 neutropenia was observed in 18 patients (62%). Twenty-eight patients were explored and underwent complete resection of their tumors. There were no complete pathologic responses, but seven patients (24%) had minimal residual microscopic disease. The addition of celecoxib to a regimen of paclitaxel and carboplatin abrogated the marked increase in levels of PGE_2 detected in primary tumors after treatment with paclitaxel and carboplatin alone.**

Conclusion: **In comparison with historically reported response rates, these data suggest that the addition of a selective COX-2 inhibitor may enhance the response to preoperative paclitaxel and carboplatin in patients with NSCLC. Moreover, treatment with celecoxib 400 mg twice daily was sufficient to normalize the increase in PGE_2 levels found in NSCLC patients after treatment with paclitaxel and carboplatin. Confirmatory trials are planned.**

J Clin Oncol 21:2645-2650.

Altorki et al, JCO 2003

EDITORIAL

Combining Cytotoxic Chemotherapy With Cyclooxygenase-2 Inhibition

of tumor angiogenesis, promotion of apoptosis, or other possible mechanisms. A paclitaxel-containing regimen was selected for study because prior work of this team found that this chemotherapeutic agent induced COX-2 and prostaglandin biosynthesis.[2] A selective COX-2 inhibitor would be expected to prevent the possible negative action of this chemotherapeutic agent.

Preclinical and clinical evidence have established COX-2 as an attractive therapeutic or chemopreventive target in the lung. Inducible COX-2 affects synthesis of prostaglandins from arachidonic acid and is frequently activated during inflammation and carcinogenesis.[3] COX-2 inhibition can induce apoptosis and chemotherapy cytotoxicity as well as antagonize angiogenesis.[4,5] A rationale for selectively targeting COX-2 rather than constitutive COX-1 in lung carcinogenesis comes from the finding that differential overexpression of COX-2 (in neoplastic as compared with normal lung) has a negative prognostic influence in stage 1 non–small-cell lung cancer (NSCLC).[6] COX-2 is also overexpressed in preneoplastic lung lesions[7] and inducible prostaglandin synthase is overexpressed in NSCLC.[8] It is also notable that epidemiologic data demonstrated a role for aspirin in suppressing lung carcinogenesis.[9] Celecoxib, a selective COX-2 inhibitor, also inhibits polyp formation in familial adenomatous polyposis coli,[10] thus indicating a potential role for selective COX-2 inhibition in treating early steps of carcinogenesis in other malignancies. Preclinical evidence for targeting COX-2 in lung carcinogenesis was established by COX-2 inhibition, which reduced lung adenomas in the A/J murine model.[11] Taken together, these and other findings provided a strong rationale for the trial reported here.[1]

These investigators should be commended for designing and conducting this trial, which is an excellent example of translational research, by addressing whether celecoxib can be admin-

This clinical trial provides a strong rationale for confirmatory randomized clinical trials that would assess the benefit of adding celecoxib to cytotoxic chemotherapy for lung cancer treatment. In advance of such trials, it is important to determine the optimal celecoxib dosage to administer as part of this regimen. In the meantime, more could be learned from this trial, especially if pretreatment biopsies were available to assess changes in COX-2 expression, proliferation, apoptosis, and neoangiogenesis in neoplastic, preneoplastic, or normal lung tissues. If pretreatment frozen tissues were accrued, then examination of changes in PGE_2 levels would become possible. This underscores the value of proof of principle trials,[3] in which an initial preoperative biopsy, followed by a short course of therapy before a second biopsy at surgical resection, would permit assessment of the pharmacologic effects on the desired target as well as on tissue and plasma pharmacokinetics. Short-term clinical responses could also be assessed in these trials.

This is an exciting time in clinical oncology because the molecular genetic alterations that form the basis of carcinogenesis are becoming better understood. Many of these genetic alterations are also pharmacologic targets. The current trial advances prior preclinical work that implicated synergistic effects of combining COX inhibitors with cytotoxic chemotherapy[12] by assessing whether favorable interactions occur in the clinic. The results of this phase II trial are encouraging given the high proportion of clinical responses that was associated with suppression of intratumoral PGE_2 levels. A relationship between inflammation and carcinogenesis has long been recognized. We do not know which pharmacologic agent or target would optimally disrupt inflammation. In addition to COX-2, other targets should be evaluated in the treatment of lung carcinogen-

ORIGINAL ARTICLE

Cardiovascular Events Associated with Rofecoxib in a Colorectal Adenoma Chemoprevention Trial

Robert S. Bresalier, M.D., Robert S. Sandler, M.D., Hui Quan, Ph.D., James A. Bolognese, M.Stat., Bettina Oxenius, M.D., Kevin Horgan, M.D.,

From the Department of Gastroi
Medicine and Nutrition, University
M.D. Anderson Cancer Center, H
(R.S.B.); the Department of Medic
versity of North Carolina at Cha
Chapel Hill (R.S.S.); Merck Resea
oratories, West Point, Pa. (H.Q.,
lognese, B.O., K.H., C.L.); the Dep
of Pathology, Mount Sinai Hospita
to (R.R.); the Department of Surg
versity of Birmingham, Birmingha
ed Kingdom (D.M.); the Depart
Medicine, Clinic University Hospit
goza, Spain (A.L.); the Department
icine, Tufts–New England Medica
Boston (M.A.K.); and the Departr
Medicine and Community and
Medicine, Dartmouth Medical Sch
nover, N.H. (J.A. Baron). Address
requests to Dr. Bresalier at the
ment of Gastrointestinal Medic
Nutrition, University of Texas M.D
son Cancer Center, 1515 Holcomb
Houston, TX 77030-4009, or at rb
mdanderson.org.

*The members of the APPROVe
listed in the Appendix.

This article was published at ww
org on February 15, 2005.

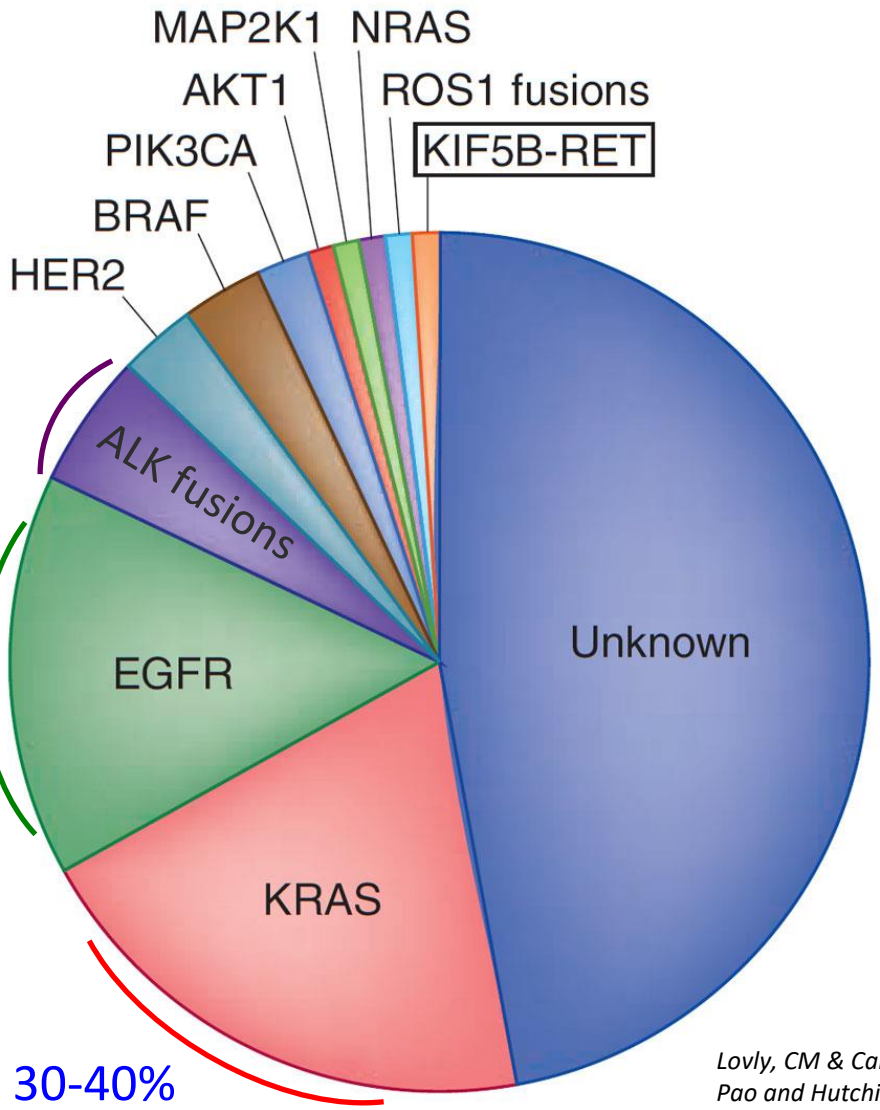
N Engl J Med 2005;352:1092-102.

the two groups.

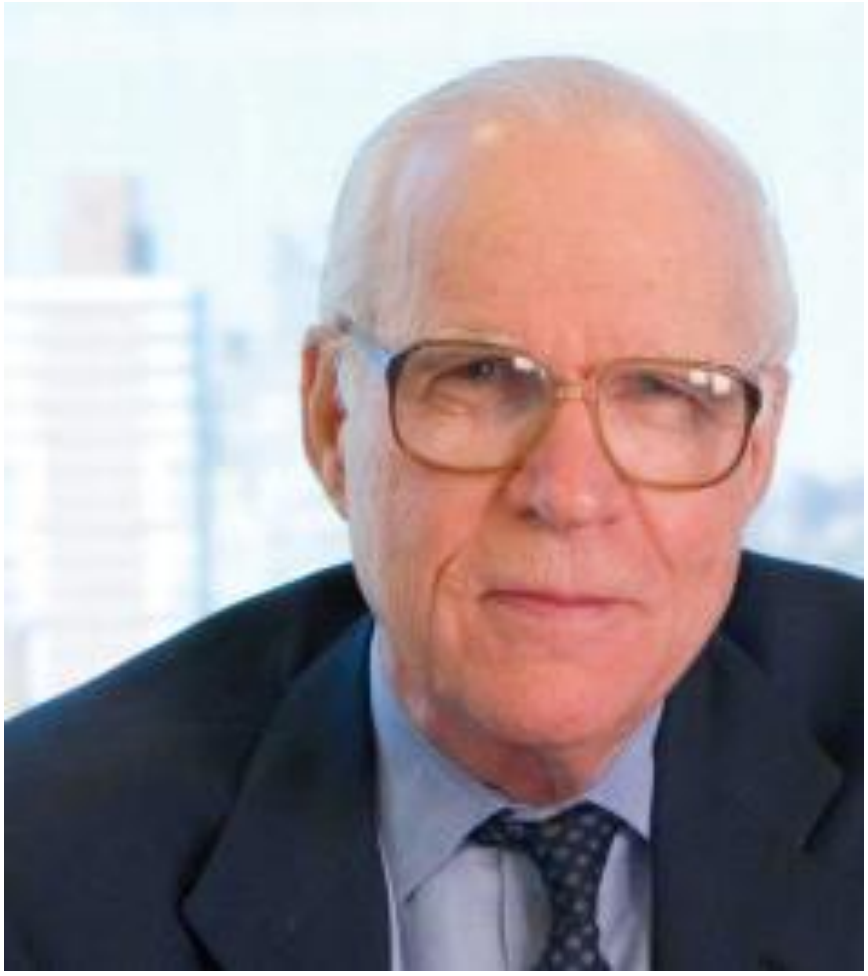
CONCLUSIONS

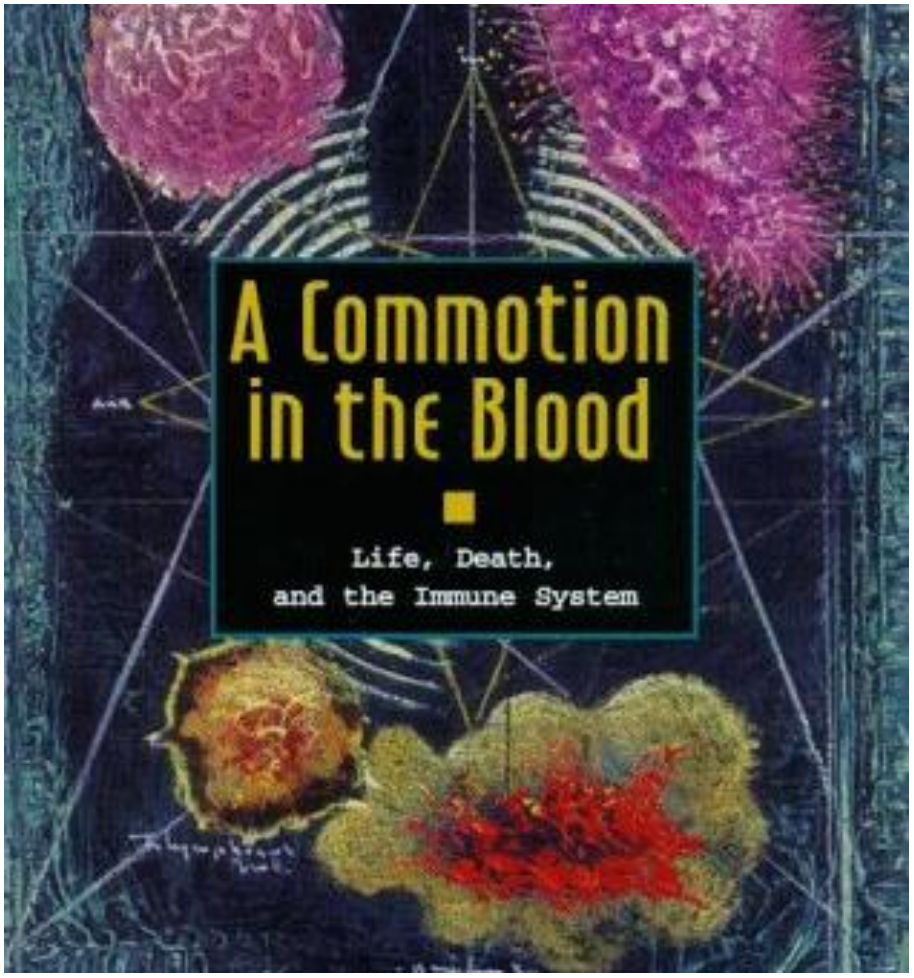
Among patients with a history of colorectal adenomas, the use of rofecoxib was associated with an increased cardiovascular risk.

The genomic revolution



Lovly, CM & Carbone, DP. Nat.Rev.Clin.Oncol 2011
Pao and Hutchinson, Nature Medicine 2012




A Commotion in the Blood
Life, Death,
and the Immune System

Volume 82, Number 5 November 1981

The Journal of THORACIC AN
CARDIOVASCULAR SURGER

J THORAC CARDIOVASC SURG 82:649-657, 1981

Original Communicati

Surgical adjuvant intrapleural BCG treatment for Stage I non–small cell lung cancer

*Preliminary report of the National Cancer Institute Lung Cancer Study Group**

The Lung Cancer Study Group (LCSG) has tested the efficacy of intrapleural bacillus Calmette-Guérin (BCG) as surgical adjuvant treatment in a double-blind, randomized comparison against intrapleural saline. This clinical trial included specific anatomic and pathological staging requirements and careful follow-up monitoring. At this time, with a median follow-up of 516 days in 216 treated and 209 control patients, no evidence has yet been found that postoperative instillation of intrapleural BCG improves survival or extends the disease-free interval in patients with completely resected Stage I squamous cell carcinoma, adenocarcinoma, or large cell carcinoma of the lung. There have been 93 recurrences and 77 deaths, which are remarkably evenly distributed in both arms of the study. An unexpectedly superior survival rate for the Stage I group has been observed, and the prognostic importance of cell type, TN† status, and elevations in initial white cell count and alkaline phosphatase measurement has been confirmed.

Clifton F. Mountain, M.D.,** *Houston, Texas,* and
Mitchell H. Gail, M.D., Ph.D.*** (by invitation), *Bethesda, Md.*

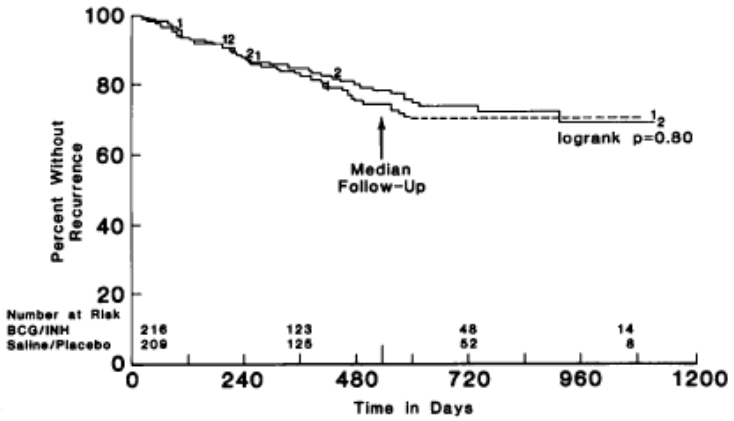
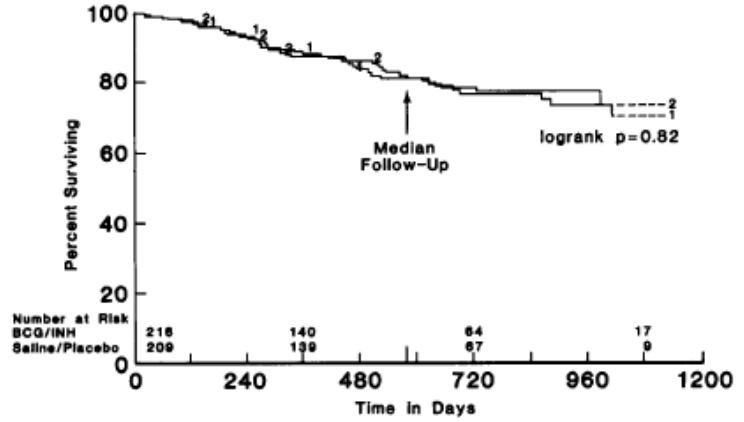
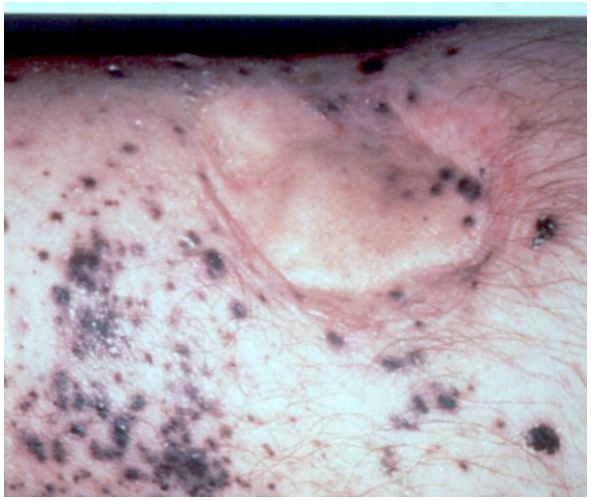


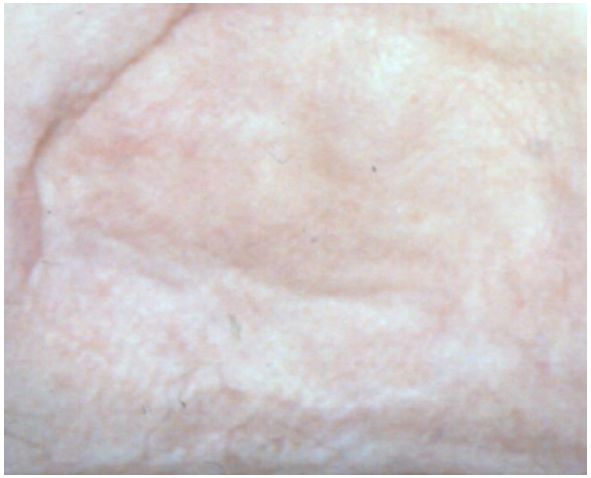
Fig. 2. Stage I non–small cell lung cancer. Time to recurrence following apparent complete resection and adjuvant immunotherapy with intrapleural BCG/INH (isoniazid) or saline/placebo.



Proof of Concept

- BCG for Superficial Bladder Carcinoma
- Herceptin for Breast Cancer
- Vaccines for cervical cancer
- Vaccines for melanoma

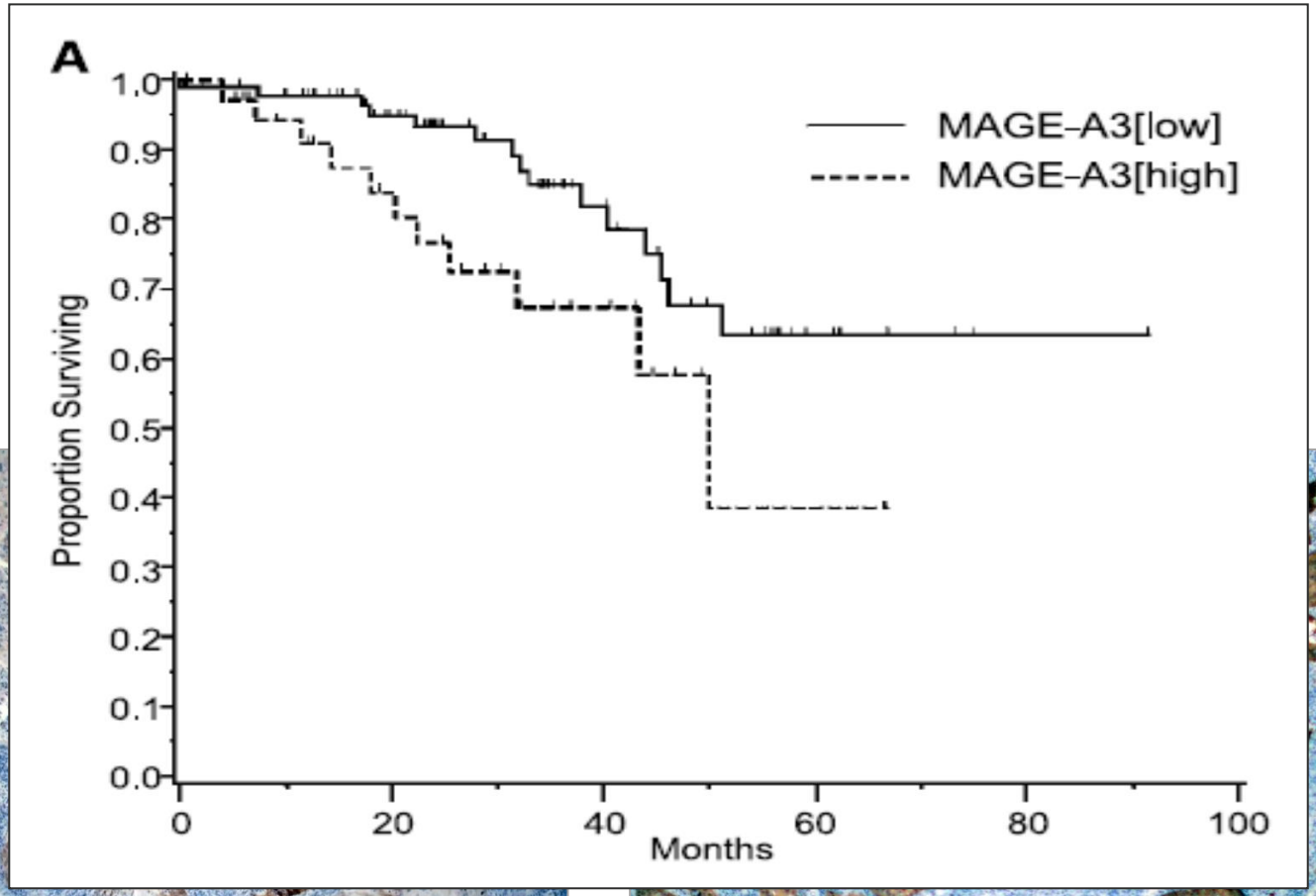




Cancer-Testis Antigens

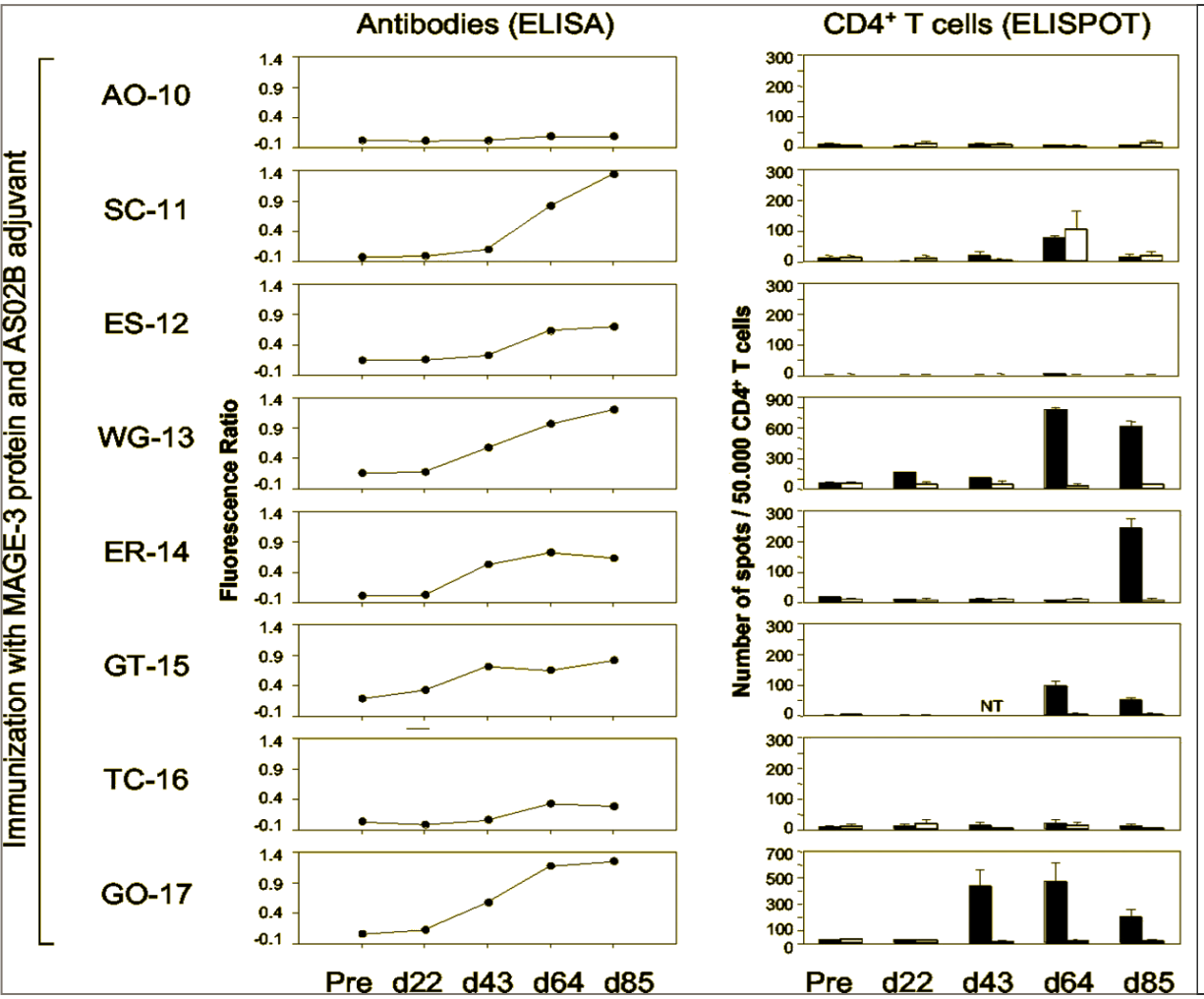
- Large family of antigens (>280) encoded by genes on the X chromosome.
- Absent or minimal expression in normal tissues.
- Stably expressed in a broad range of tumors inluding lung cancer.
- Highly immunogenic.

MAGE A-3 Expression in NSCLC (n = 523)



Ali O. Gure,CCR 2005

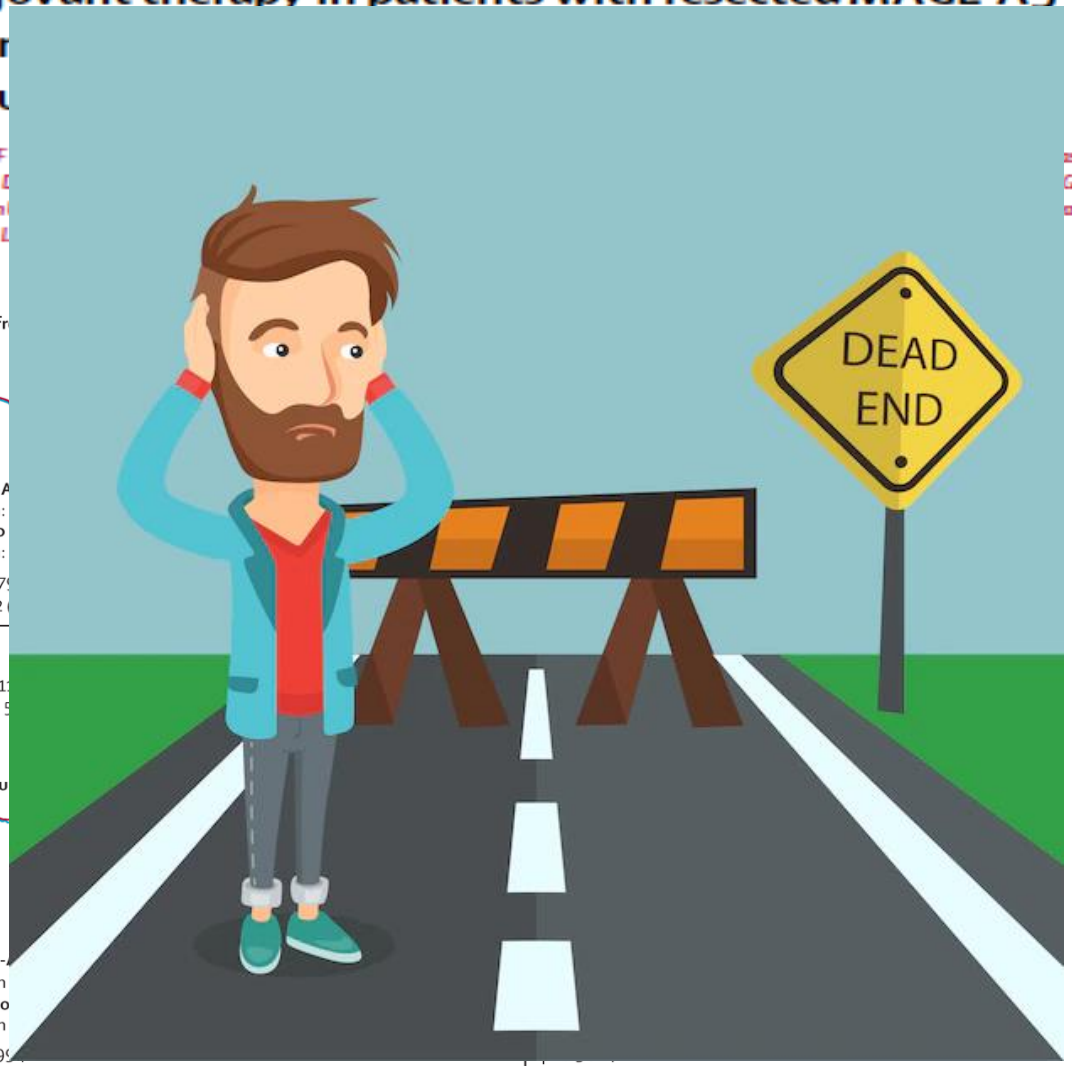
MAGE 3 Antibody and CD4+ T Cell Responses to MAGE-3 Protein + Adjuvant



Djordje Atanackovic , *The Journal of Immunology*, 2004, 172: 3289-3296

Efficacy of the MAGE-A3 cancer immunotherapeutic as adjuvant therapy in patients with resected MAGE-A3-positive nor
dou

Johan F
Jubrail
Katalin
Jamila
sahiro Yoshimura,
Gladkov,
an-Louis Pujol,



A Disease-fr

Disease-free survival (%)

MAGE-A
Median:
Placebo
Median:
p=0·737
HR 1·02

Number at risk
MAGE-A3 1515 1257 1
Placebo 757 639 5

C Overall su

Overall survival (%)

MAGE-
Median
Placebo
Median
p=0·69
HR 1·04 (95% CI 0·86–1·24)

HR 1·00 (95% CI 0·78–1·29)

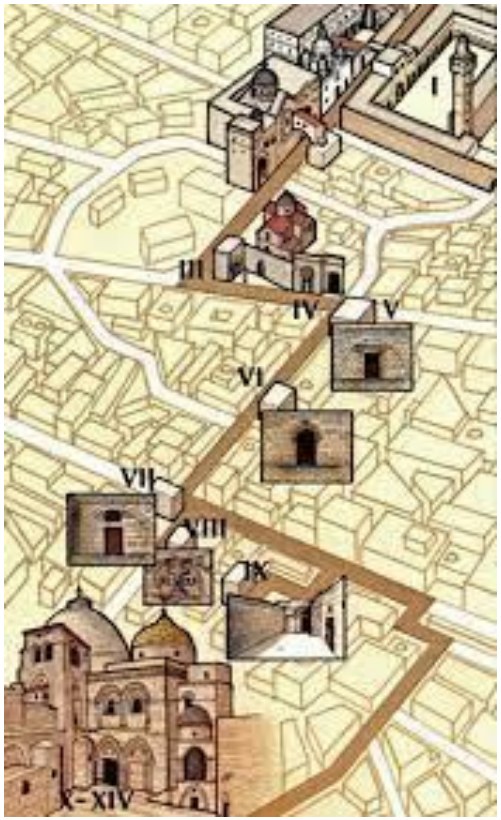
Time since randomisation (months)

Number at risk

MAGE-A3	1515	1459	1370	1273	1101	827	607	421	275	159	31	6
Placebo	757	731	693	654	570	427	330	235	145	78	14	5

	731	694	655	611	544	413	310	216	142	77	17	1
	365	353	335	315	283	210	169	122	74	39	6	3

CALGB140503 or La Via Dolorosa



- 9/9/2005: Concept submission to CALGB EC
- 9/13/2005: Concept approved by EC
- 7/ 2007: Concept submitted to CTEP
- 6/2007 : Concept approval by CTEP
- 6/15/2007: Activation by CALGB
- **First pt. on trial: 10/2007**
- Threat of sudden death: Target accrual 22/month vs actual accrual 15 in 8th quarter
- 2/15/2010 : target accrual reduced from 908 to 692, 8 pts/months
- **Accrual completed 3/2017**

ALLIANCE
FOR CLINICAL TRIALS IN ONCOLOGY

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Monica M. Bertagnolli, MD
Group Chair

May 23, 2022

Nasser Altorki, MD
NYP/Weill Cornell Medical Center
Department of Cardiothoracic Surgery
525 East 68th Street
Box 110 M404
New York, NY 10065

RE: C140503, A Phase III Randomized Trial of Lobectomy versus Sublobar Resection for Small (<2 CM) Peripheral Non-Small Cell Lung Cancer

Dear Dr. Altorki:

The Alliance Data and Safety Monitoring Board (DSMB) reviewed C140503, A phase III randomized trial of lobectomy versus sublobar resection for small (</=2 CM) peripheral non-small cell lung cancer, on Friday, May 13, 2022.

Recommendation:The DSMB reviewed the current adverse events, and no issues requiring intervention were identified. The DSMB noted the decrease in the data delinquency and applauded the study team efforts to improve the delinquency rates since the last report. The DSMB reviewed the updated analyses of the protocol planned seventh interim analysis, noting that the pre-specified stopping boundaries for futility and non-inferiority are not crossed. Based on the current data and the different analyses presented, the DSMB noted that there was minimal chance that the trial may yield a different conclusion at the final analysis (estimated to occur in 2030). The DSMB accepted the study team's conclusion that limited resection is not inferior to lobectomy, and recommended unanimously to release the data to the study team, and terminate further DSMB monitoring of the trial. The DSMB recommended that the study team include in the trial publication that the trial results were released from the DSMB based on an unscheduled analysis, to ensure that all remaining data delinquency issues are addressed prior to a publication and to continue follow-up of patients who are still eligible for primary endpoint follow-up.

Action: Recommendation accepted.

Best regards,

Monica M. Bertagnolli, MD
Associate Surgeon, Brigham and Women's Hospital
Professor of Medicine, Harvard Medical School
Chair, Alliance for Clinical Trials in Oncology

The NEW ENGLAND JOURNAL of MEDICINE

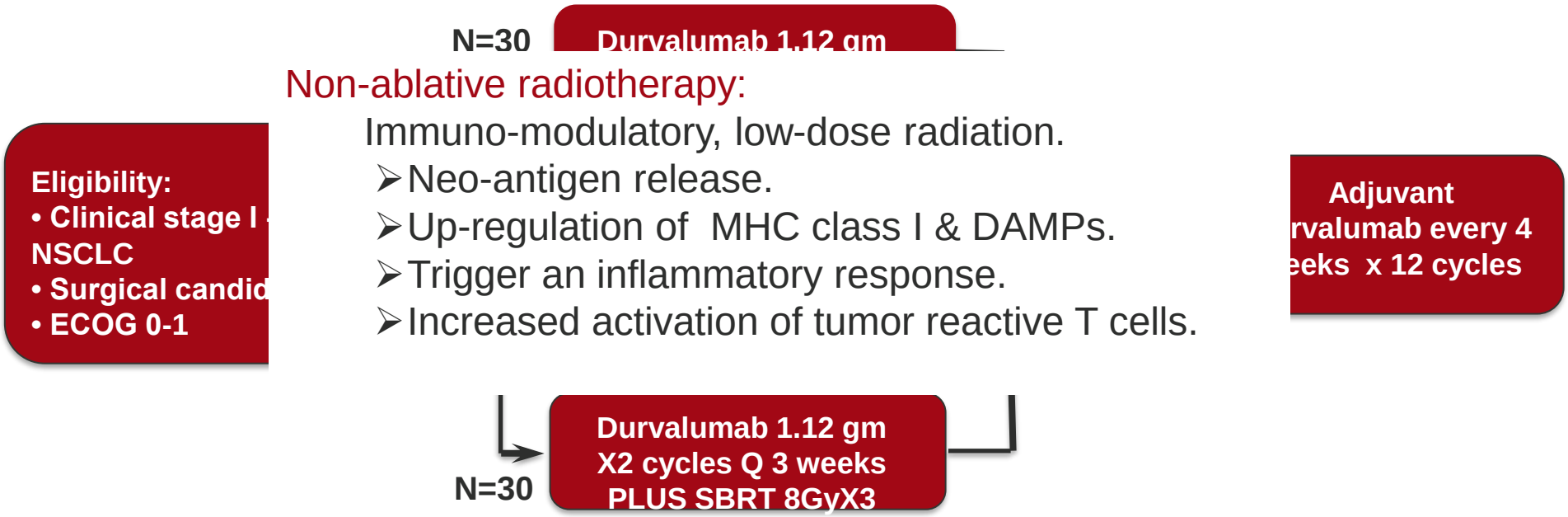
ESTABLISHED IN 1812 FEBRUARY 9, 2023 VOL. 388 NO. 6

Lobar or Sublobar Resection for Peripheral Stage IA Non–Small-Cell Lung Cancer

Nasser Altorki, M.D., Xiaofei Wang, Ph.D, David Kozono, M.D., Ph.D., Colleen Watt, B.S., Rodney Landrenau, M.D., Dennis Wigle, M.D., Ph.D., Jeffrey Port, M.D., David R. Jones, M.D., Massimo Conti, M.D., Ahmad S. Ashrafi, M.D., Moishe Liberman, M.D., Ph.D., Kazuhiro Yasufuku, M.D., Ph.D., Stephen Yang, M.D., John D. Mitchell, M.D., Harvey Pass, M.D., Robert Keenan, M.D., Thomas Bauer, M.D., Daniel Miller, M.D., Leslie J. Kohman, M.D., Thomas E. Stinchcombe, M.D., and Everett Vokes, M.D.

ABSTRACT

A randomized phase 2 trial of Durvalumab with or without SBRT in clinical stage I-IIIA non-small cell lung cancer



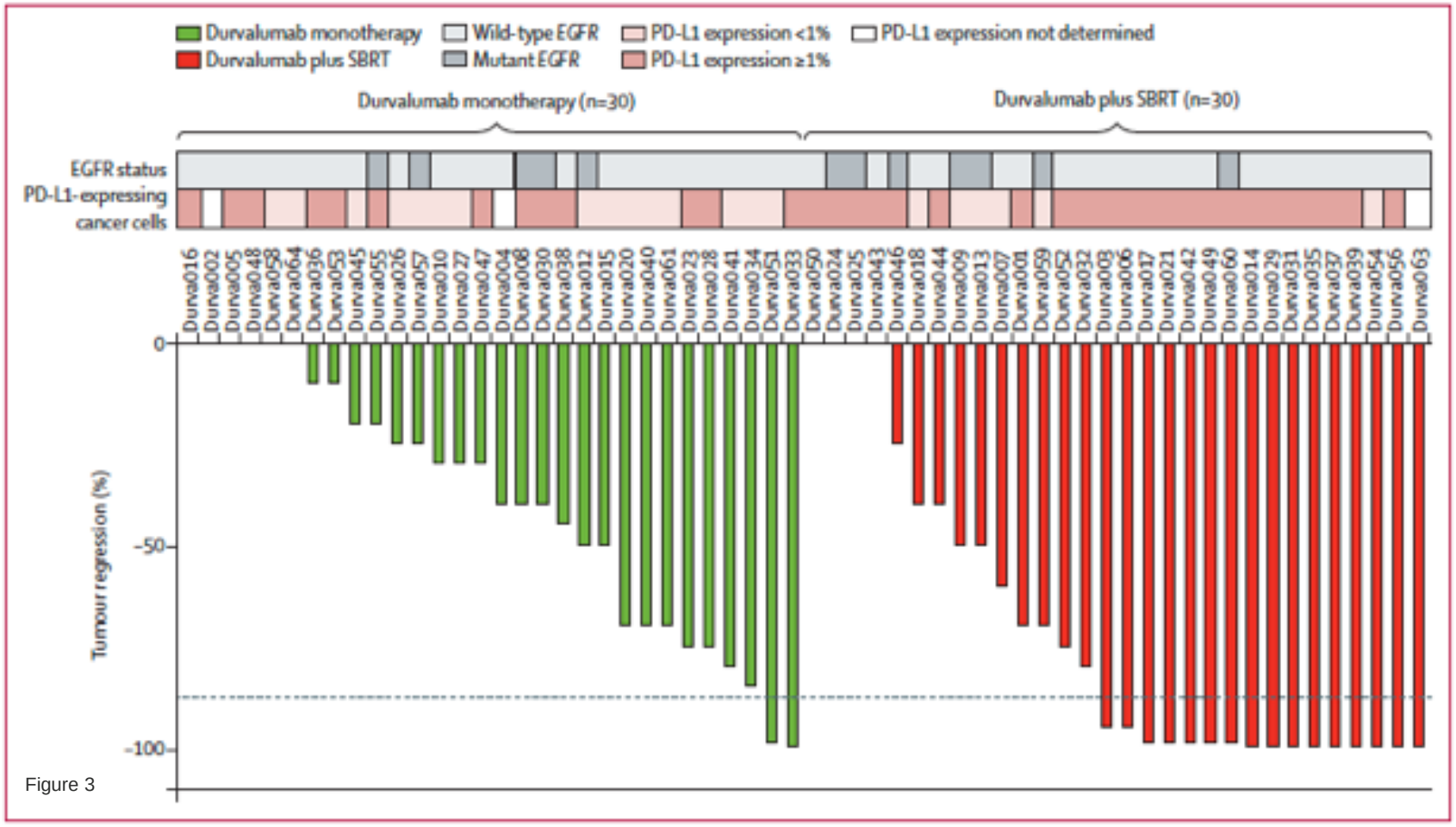


Figure 3

CPR in SBRT/IO arm : 8/21 (38%)

Neoadjuvant durvalumab with or without stereotactic body radiotherapy in patients with early-stage non-small-cell lung cancer: a single-centre, randomised phase 2 trial

Nasser K Altorki, Timothy E McGraw, Alain C Borczuk, Ashish Saxena, Jeffrey L Port, Brendon M Stiles, Benjamin E Lee, Nicholas J Sanfilippo, Ronald J Scheff, Bradley B Pua, James F Gruden, Paul J Christos, Cathy Spinelli, Joyce Gakuria, Manik Uppal, Bhavneet Binder, Olivier Elemento, Karla V Ballman, Silvia C Formenti

Summary

Background Previous phase 2 trials of neoadjuvant anti-PD-1 or anti-PD-L1 monotherapy in patients with early-stage non-small-cell lung cancer have reported major pathological response rates in the range of 15–45%. Evidence suggests that stereotactic body radiotherapy might be a potent immunomodulator in advanced non-small-cell lung cancer (NSCLC). In this trial, we aimed to evaluate the use of stereotactic body radiotherapy in patients with early-stage NSCLC as an immunomodulator to enhance the anti-tumour immune response associated with the anti-PD-L1 antibody durvalumab.

Methods We did a single-centre, open-label, randomised, controlled, phase 2 trial, comparing neoadjuvant durvalumab alone with neoadjuvant durvalumab plus stereotactic radiotherapy in patients with early-stage NSCLC, at NewYork-Presbyterian and Weill Cornell Medical Center (New York, NY, USA). We enrolled patients with potentially resectable early-stage NSCLC (clinical stages I–IIIA as per the 7th edition of the American Joint Committee on Cancer) who were aged 18 years or older with an Eastern Cooperative Oncology Group performance status of 0 or 1. Eligible patients were randomly assigned (1:1) to either neoadjuvant durvalumab monotherapy or neoadjuvant durvalumab plus stereotactic body radiotherapy (8 Gy × 3 fractions), using permuted blocks with varied sizes and no stratification for clinical or molecular variables. Patients, treating physicians, and all study personnel were unmasked to treatment assignment after all patients were randomly assigned. All patients received two cycles of durvalumab 3 weeks apart at a dose of 1·12 g by intravenous infusion over 60 min. Those in the

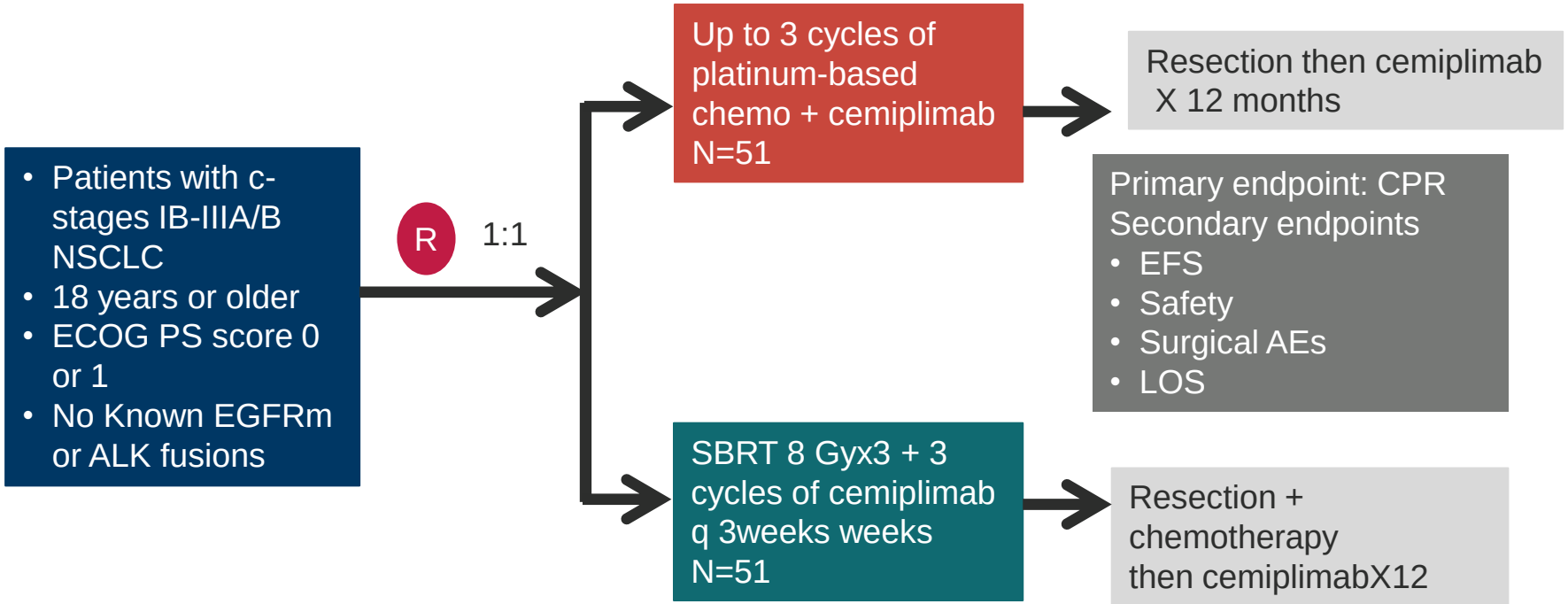
Lancet Oncol 2021

Published Online
May 17, 2021
https://doi.org/10.1016/S1470-2045(21)00149-2

See Online/Comment
https://doi.org/10.1016/S1470-2045(21)00261-8

Department of Cardiothoracic Surgery (Prof N K Altorki MD, Prof J L Port MD, B M Stiles MD, B E Lee MD, C Spinelli BS, J Gakuria MPH), **Department of Biochemistry** (Prof T E McGraw PhD), **Department of Pathology and Laboratory Medicine** (Prof A C Borczuk MD, Prof O Elemento PhD), **Division of Hematology Oncology**

Randomized multicenter phase II trial of neoadjuvant chemotherapy + cemiplimab vs SBRT 8Gyx3 plus cemiplimab for c-stage IB-III NSCLC



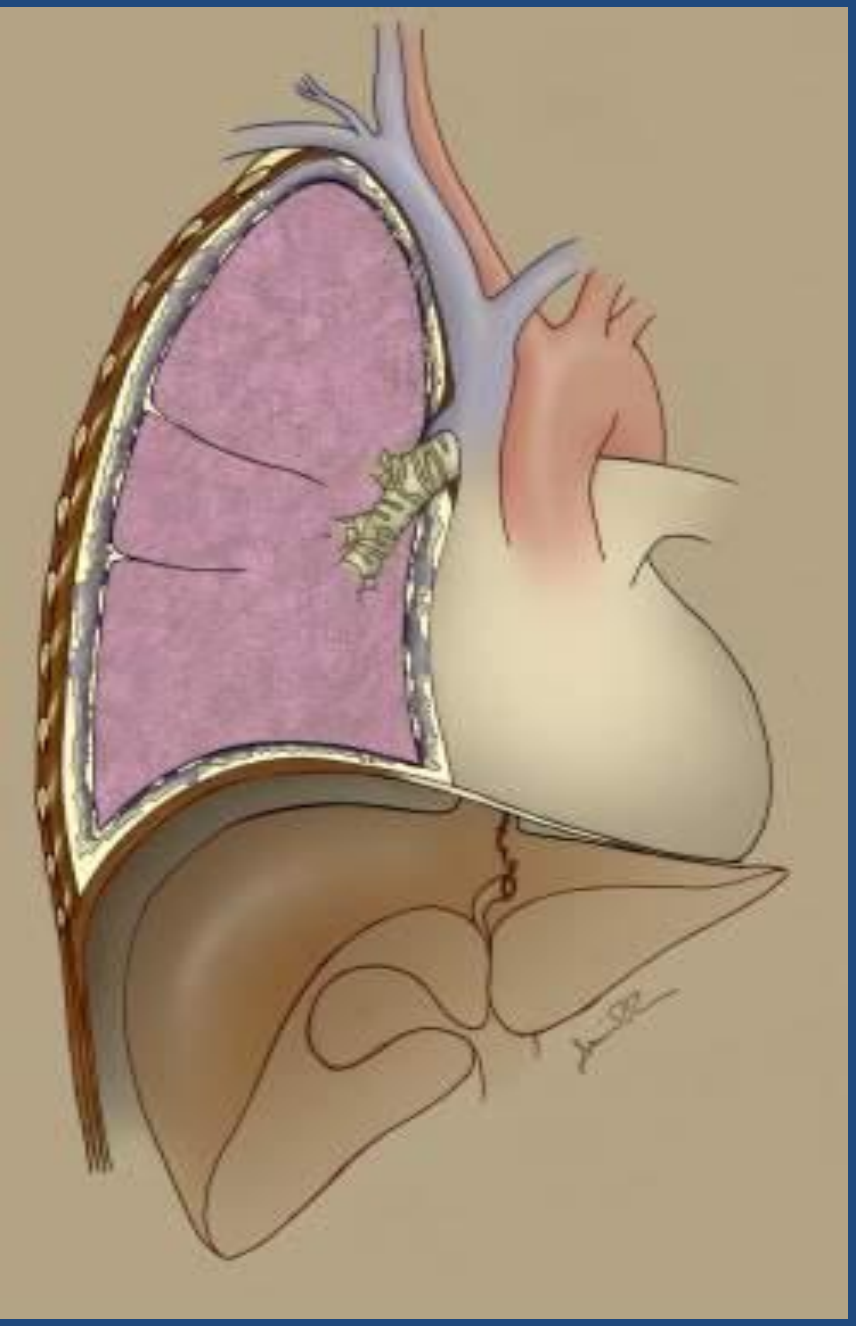
Stratification:
-PD-L1 expression <1% vs ≥1%
-Stage IB/II vs III A

Final thoughts

- Whatever floats your boat.
- Remember the secret sauce.

Success is going from failure to failure without losing enthusiasm

- Nothing worth doing is ever done alone.
- Get in the weeds (but not too much).
- Be generous and share the credit.



SWOG Clinical Trials Lung Committee

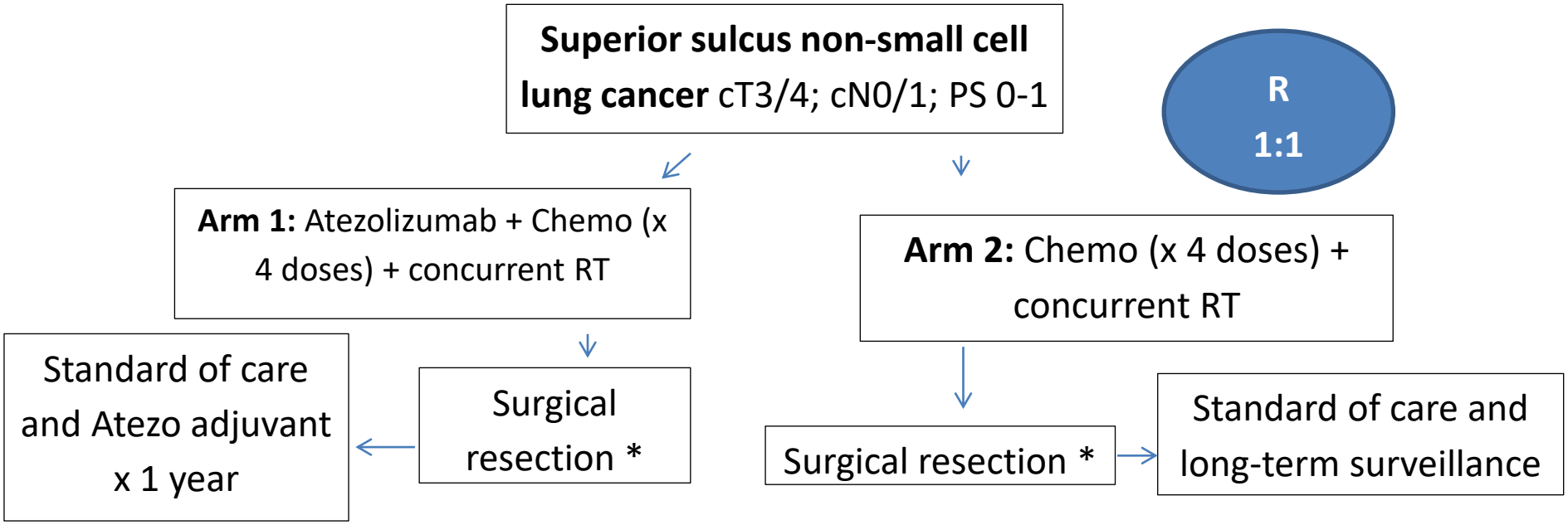
GTSC
2023

S1934: NASSIST

Neoadjuvant Chemoradiation +/- Immunotherapy before Surgery for Superior Sulcus Tumors

A Randomized Phase II Trial of Trimodality +/- Atezolizumab in Resectable Superior Sulcus Non-Small Cell Lung Cancer

S1934



Arm 1: Preoperative investigators' choice platinum doublet chemotherapy (platinum with etoposide/ paclitaxel/ pemetrexed) + atezolizumab iv q3 weeks x4, + 61.2 Gy concurrent radiation; surgical resection.
Arm 2: same, minus atezolizumab.

*For patients who do not undergo surgical resection, one year of consolidation durvalumab will be strongly recommended as standard of care. Data from these patients, typically approximately 20% of superior sulcus trial patients, will be collected and evaluated in exploratory comparative analyses of definitive non-surgical treatment in the setting of immunotherapy.

Children's Oncology Group AOST2031: A Phase 3 Randomized Controlled Trial Comparing Open vs Thoracoscopic Management of Pulmonary Metastases in Patients with Osteosarcoma

John J. Doski MD

COG Surgery, UT Health San Antonio

Fall 2021 SWOG Virtual, again

CHILDREN'S ONCOLOGY GROUP

COG Study AOST2031

- A COG Study randomizing surgical management of oligometastatic (≤ 4 lesions) pulmonary metastatic osteosarcoma to open or thoracoscopic surgery

AOST2031 Overview

- Eligibility: <50 years of age; control of primary disease, pulmonary only metastatic osteosarcoma with ≤4 lesions per hemithorax. (=oligometastatic)
- At least one ≥3 mm lesion: peripheral, appearance consistent with metastases, no central lesions. Amenable to wedge resection or segmentectomy
- Real time Preop Central Radiologic Review to confirm eligibility
- Randomized to open or VATS, surgery within 28 days of imaging.
- QOL studies preop, post op @ 48hrs, 7-14 days, and 4-6wks

Primary and Secondary Objectives AOST2031

- **Primary**
  - To determine if open surgical resection is superior to thoracoscopic resection for thoracic event free survival (tEFS) in patients with resectable oligometastatic pulmonary osteosarcoma
- **Secondary**
  - To determine if open surgical resection is superior to thoracoscopy for event free survival (EFS)
  - To determine if open surgical resection is superior to thoracoscopy for overall survival (OS)
  - To determine if thoracoscopy is superior to open surgical resection for post-operative pain interference

SWOG/NRG S1914

A Randomized Phase III Trial of Induction/Consolidation Atezolizumab + SBRT versus SBRT Alone in High risk, Early Stage NSCLC

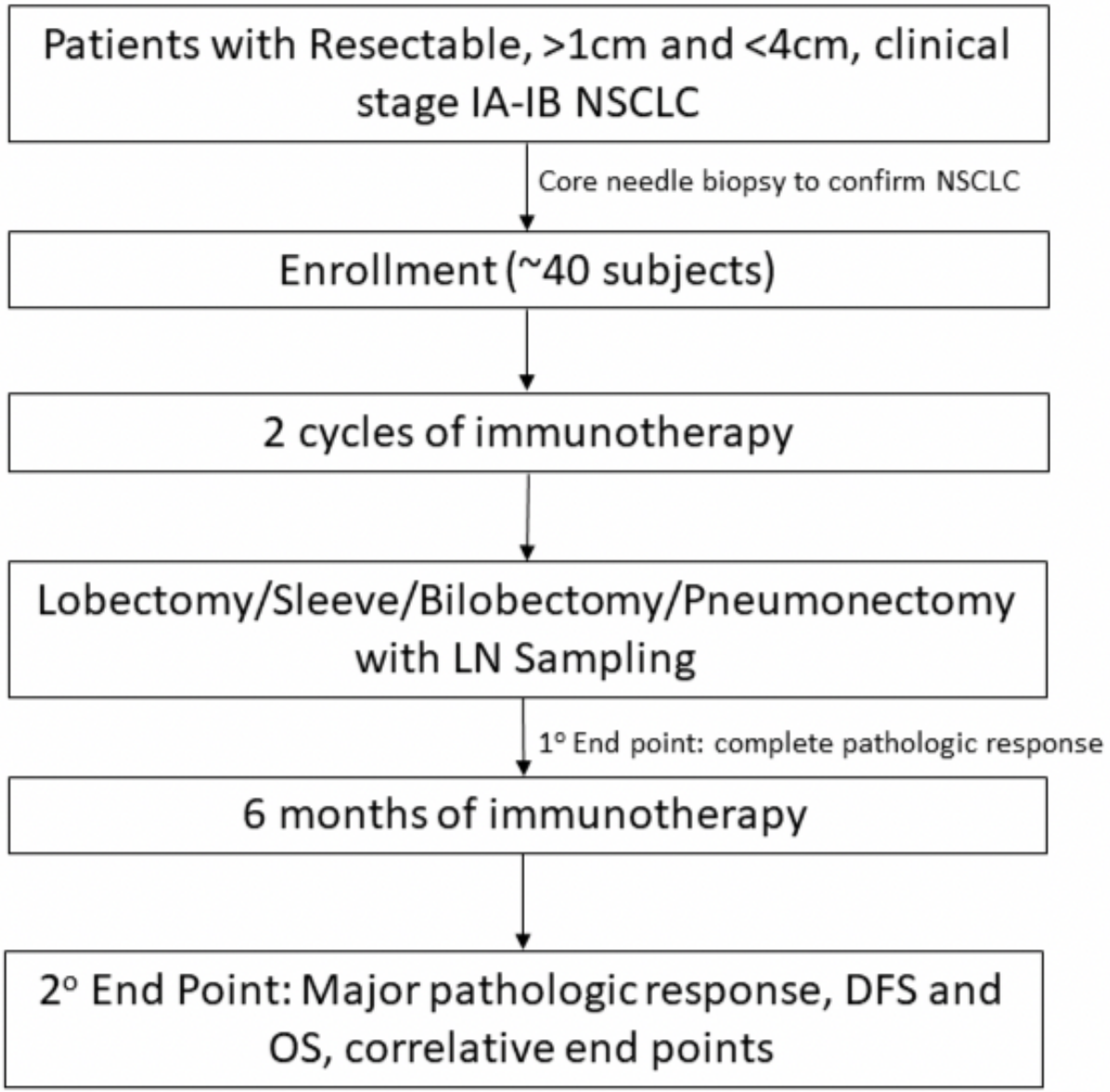
- **Hypothesis:** the addition of atezolizumab to standard SBRT for early stage, medically inoperable NSCLC will improve overall survival and progression free survival as compared to SBRT alone
- **Primary objective:** compare overall survival in medically inoperable, early stage NSCLC patients randomized to SBRT with or without atezolizumab
- **Key Inclusion criteria:**
  - Histologically proven stage I-IIA or limited T3N0M0 (stage IIB) NSCLC ≤7 cm diameter without nodal or distant involvement
  - Medically or surgically inoperable OR unwilling to undergo surgical resection
  - One or more high-risk features identified:
    - Tumor diameter ≥ 2 cm
    - Tumor SUV max ≥ 6.2
    - Moderately or poorly differentiated or undifferentiated histology

In Development

- **Study Title: *Neoadjuvant and Adjuvant immunotherapy for clinical stage IA Non-small Cell Lung Cancer: a phase II trial***

- **Principal Investigators**: Barry C. Gibney, DO Medical University of South Carolina (thoracic surgeon, junior investigator) and John Wrangle, MD, MPH Medical University of South Carolina (medical oncologist, senior investigator);

Fig 2. Study Schema



2023 NRG Lung Trial Portfolio

Submitted by Jessica Donington, MD

Presented by Linda Martin, MD, MPH

NRG Lung Group

SWEET SPOT

RELABLLY STRONG TRIAL ACCRUAL AND COMPLETION

SCLC

- **LU005**: Phase III, Chemoradiation vs. Chemoradiation + Atezolizumab in Limited Stage SCLC US accrual complete
- **LU007**: Randomized Phase II/III, Consolidation Thoracic Radiation + Immunotherapy in Ext Stage SCLC: RAPTOR Trial

Mesothelioma

- **LU006**: Phase III, Pleurectomy/Decortication + Chemotherapy With or Without Adjuvant Hemithoracic Intensity-Modulated Pleural Radiation Therapy (IMPRINT)

  Accrual: 12/150 pts

ONLY TRIAL INCLUDES SURGERY

Inoperable Early-stage NSCLC

- **S1914**-SWOG/NRG Joint Study: Phase III, Induction/ Consolidation Atezolizumab + SBRT vs. SBRT Alone in high risk tumors

  Accrual: 162/480 pts
- **Pacific 4**: Phase III, SBRT alone vs. SBRT + Durvalumab

  Accrual: 472/630 pts

Unresectable Stage II-III NSCLC

- **RTOG-1308**: Phase III Randomized Trial Comparing Overall Survival After Photon vs. Proton Chemoradiotherapy

  Accrual: 300/330 pts
- **LUOO4:** Randomized Phase II Durvalumab + concurrent 60 gy XRT in 15 vs. 30 fx

  Accrual complete 24/24
- **LU008:** Phase III, Pacific vs. SBRT to primary + chemo/XRT to nodes + Durvaulmab

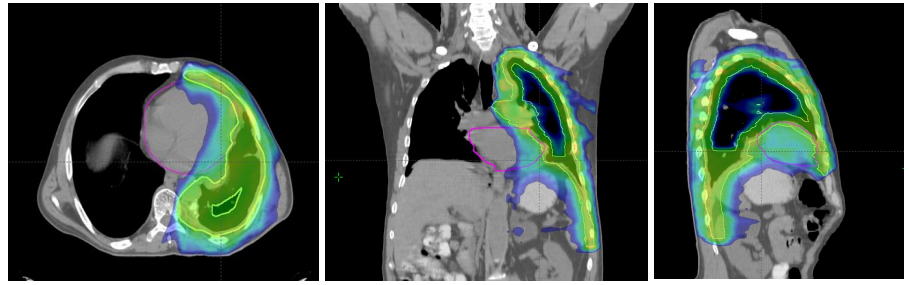
  Activated Feb 2023

Metastatic NSCLC

- LU002: Maintenance Systemic Therapy Versus Local Consolidative Therapy + Maintenance Therapy For Limited Metastatic NSCLC: A Randomized Phase II/III Trial

  Accrual:

NRG-LU006



Phase III Randomized Trial of Pleurectomy/Decortication + Chemotherapy +/- Adjuvant Hemithoracic Intensity-Modulated Pleural Radiation Therapy (IMPRINT) for Malignant Pleural Mesothelioma

Eligibility:
- Stage I-III MPM
- Resectable by lung-sparing P/D
- Epithelioid or biphasic subtype
- Age ≥18 and ≤80 years
- KPS ≥80%
- FEV1 ≥40%, DLCO ≥40% predicted

P/D (MCR)

Pemetrexed (500mg/m2) + Cisplatin (or carboplatin) (75mg/m2)

q21 days x4 cycles

R

1:1
n=150

IMPRINT (50.4/60 Gy in 28 fractions)

No adjuvant IMPRINT

Permissible alternatives:
- Neoadjuvant chemo → P/D
- Intensity-Modulated Proton Therapy

NRG-LU006: Phase III Randomized Trial on IMPRINT for MPM

Primary Objective:

- Improvement in median OS from 12 months to 20 months (calculated from the time of randomization)

Secondary Objectives:

- Local Failure-Free Survival
- Distant Metastases-Free Survival
- Progression-Free Survival
- Toxicities per CTCAE v5.0
- QOL (QLQ-Q30 and LC13) (10-point change at 9 months)

Exploratory Objectives:

- To build a multiparametric prognostic imaging model to improve clinical staging and target delineation
- To identify genomic and immunologic predictive biomarkers of radiation sensitivity and potential future therapeutic targets

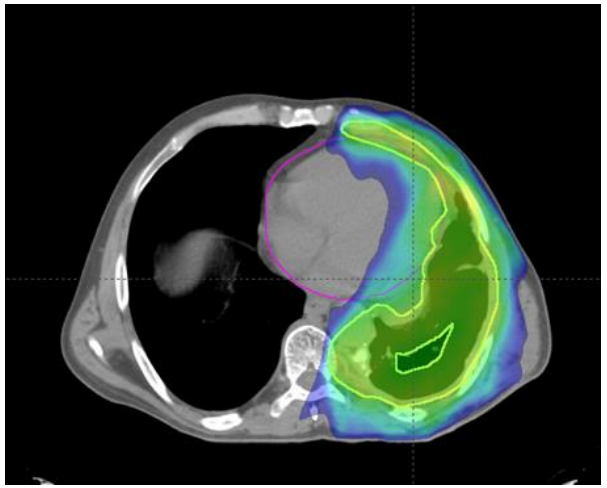
NRG-LU006: Phase III Randomized Trial on IMPRINT for MPM

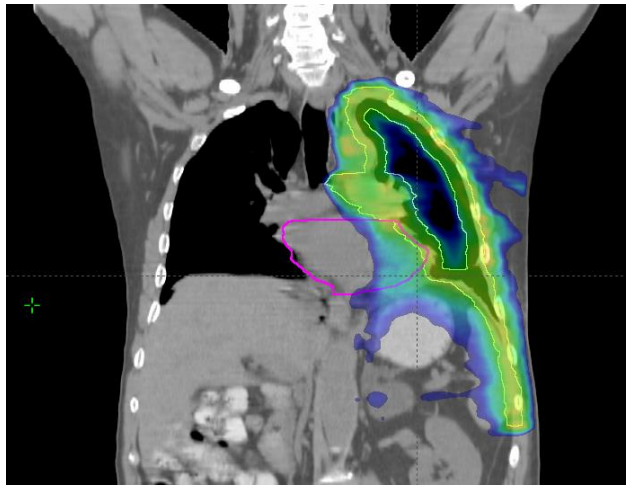
Surgical Requirements

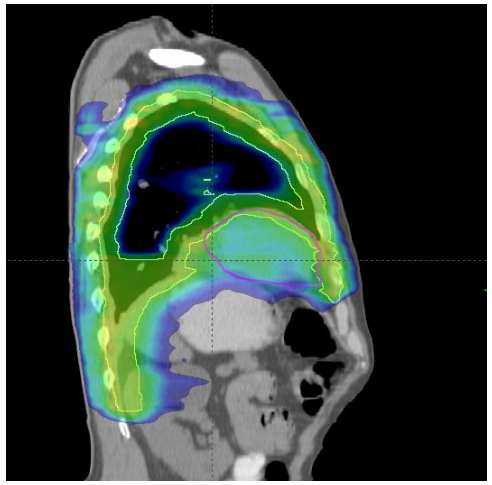
- Credentialling: >5 MPM surgeries Numw/ limited grade 4-5 toxicities in the past 2 years
- MCR = goal of surgical resection in every patient per IASLC/IMIG guidelines
- Documentation of diaphragmatic, pericardial and chest wall invasion for accurate T-staging
- Documentation of unresectable areas + clip placement
- No intraoperative adjunctive therapies
- Systematic nodal sampling

Radiation Oncology Requirements

- Site credentialing
- Central review of each patient assigned to IMPRINT arm
  1) Review of target and OAR delineation
  2) Review of radiation treatment plan
- 48-hour turnaround







NRG-LU006: Phase III Randomized Trial on IMPRINT for MPM

Recent Changes

- Amendment #1
  - Allow for neoadjuvant systemic therapy prior to enrollment
  - Allow for chemo/anti-PD-1/L1 therapy or ipilimumab/nivolumab
  - Adjust window for randomization to 0-8 weeks prior to RT

NRG-LU006: Phase III Randomized Trial on IMPRINT for MPM

Current Status

- Accrual: 12 patients (1 Alliance, 5 NRG credits)
- Applications for Site Registration: 75
- Sites approved: 20
- Monthly conference calls with participating sites (3rd Friday of the month, 11:00 a.m. EST)

- Main challenge: Surgical volumes for MPM are markedly down nationwide, reasons somewhat unclear (apart from the Covid pandemic)

Conclusion

- A paucity of trials which include thoracic surgery
- Always looking for new trial ideas
- Innovative ways to choose appropriate therapy for early-stage disease or integrate surgery and radiation in locally advanced

Alliance Thoracic Group:

Linda Martin and Jeff Yang

Disclosures – L Martin

Commercial Interest	**Relationship(s)**
Astra Zeneca	Advisory Board
On Target Laboratories	Steering Committee for ELUCIDATE trial
Genentech	Speakers Bureau
Ethicon	Speakers Bureau

Alliance Trials

- Champions for Esophageal trial (EA2174 – Dr Khullar to present today)
- Small Cell Concept – Jeff Yang
- ALCHEMIST – ACCIO
- CHIO3 (AFT 46)
- Mesothelioma trial
- New ideas

ALCHEMIST Study updates

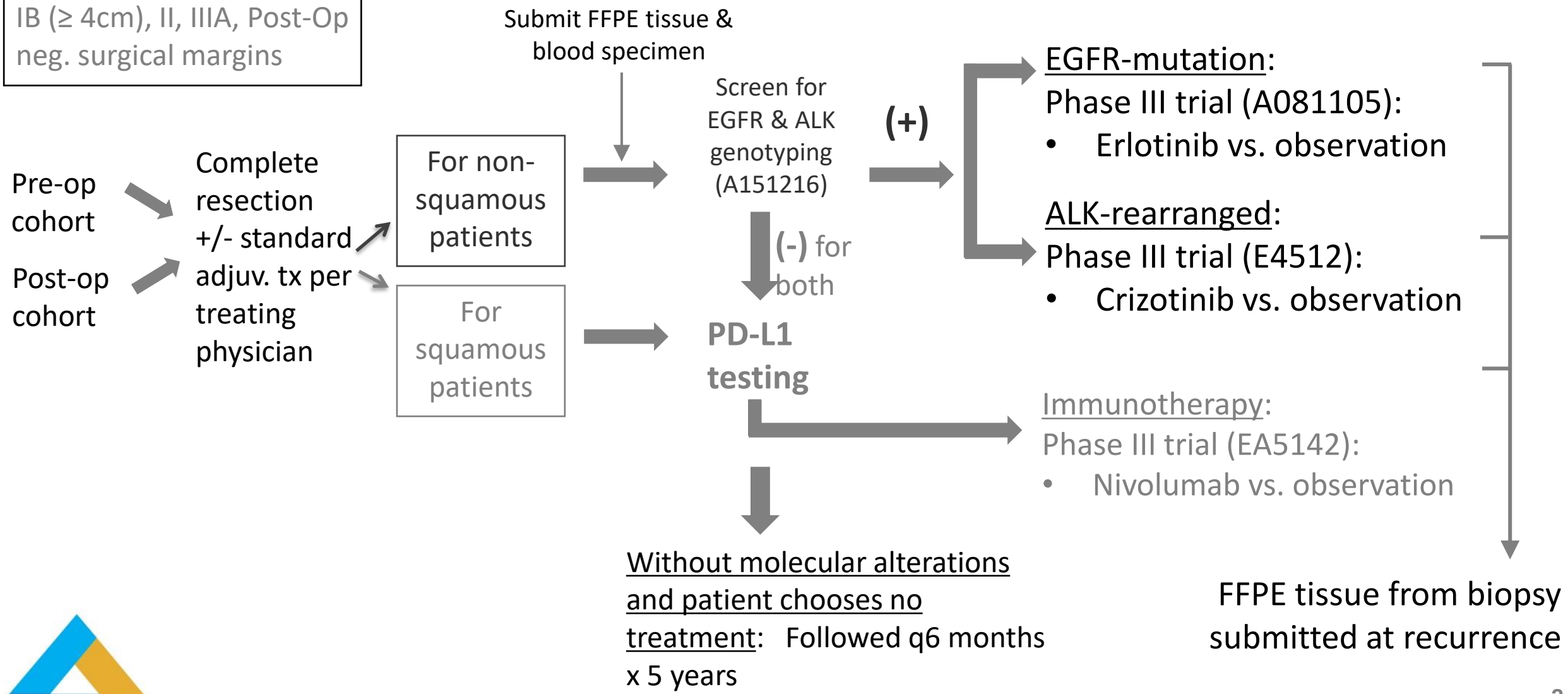
Dennis Wigle

GTSC Trials Day, Duck Key FLA

Thursday March 9, 2023

ALCHEMIST Schema & Update

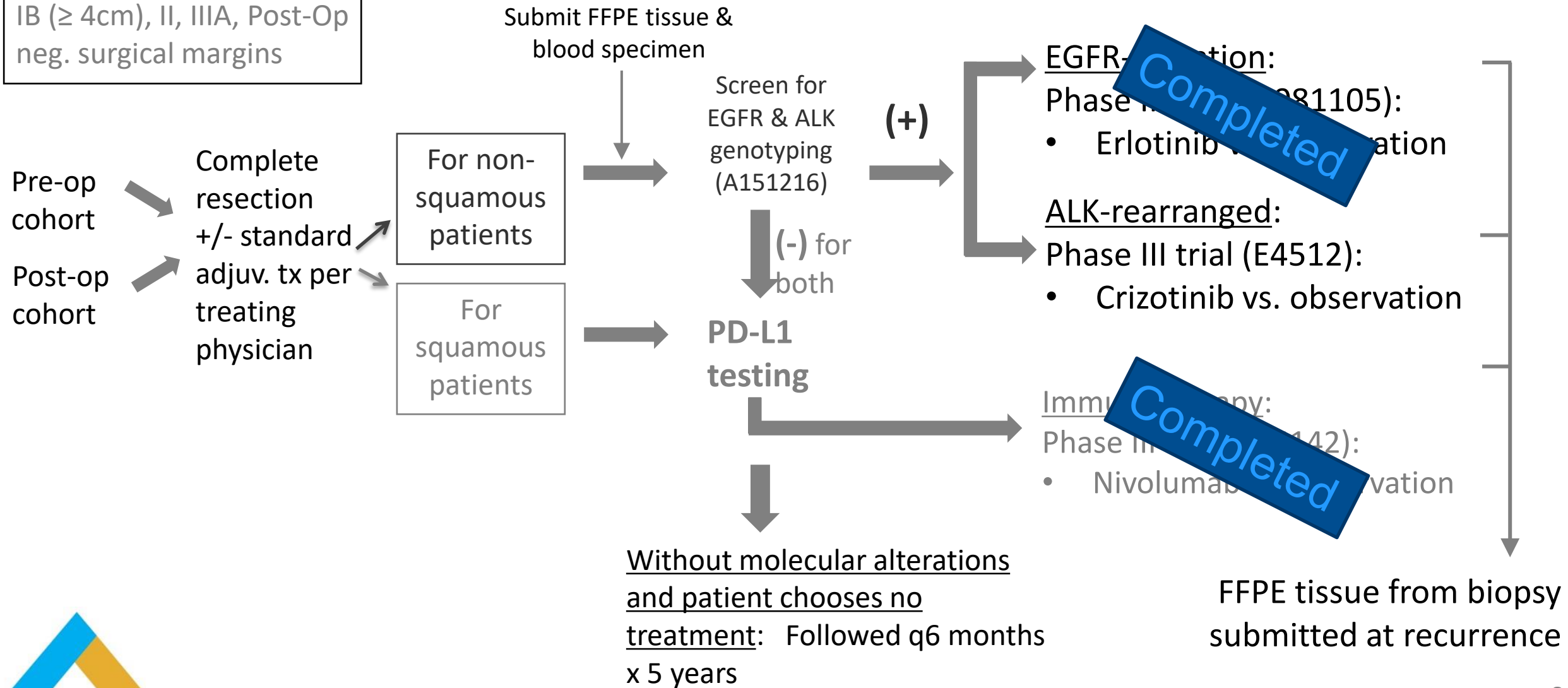
Non-squamous & Squamous NSCLC
Clinical/Pathologic Stage IB (≥ 4cm), II, IIIA, Post-Op neg. surgical margins



ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

ALCHEMIST Schema & Update

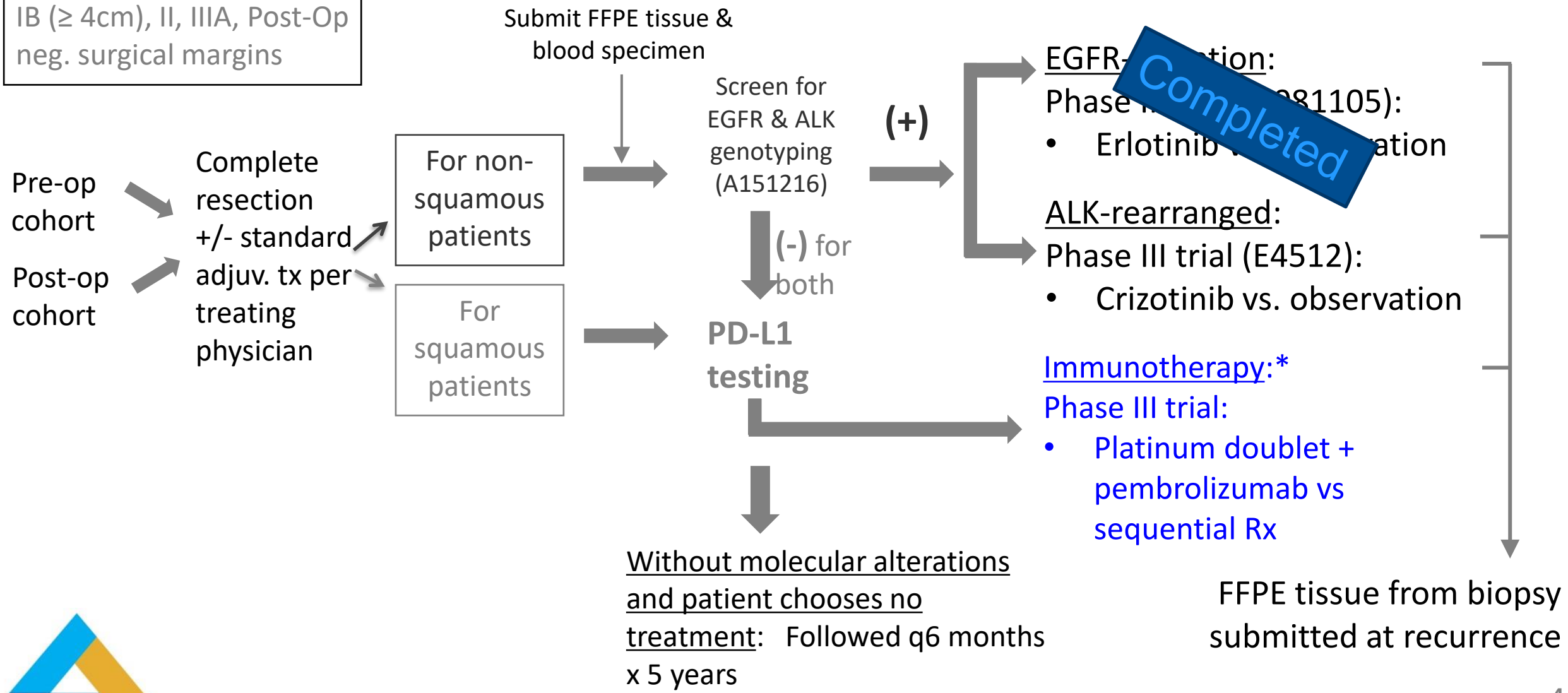
Non-squamous & Squamous NSCLC
Clinical/Pathologic Stage IB (≥ 4cm), II, IIIA, Post-Op neg. surgical margins



ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

ALCHEMIST Schema & Update

Non-squamous & Squamous NSCLC
Clinical/Pathologic Stage IB (≥ 4cm), II, IIIA, Post-Op neg. surgical margins



ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

ALCHEMIST Accrual Update
(as of Feb 2023)

Status	N
Total sites open for A151216 (screening trial)	1234
Total pts registered to A151216 (screening trial)	6796
Total pts registered to A081105 (adjuvant erlotinib)	390 closed
Total pts registered to E4512 (adjuvant crizotinib)	146
Total pts registered to EA5142 (adjuvant nivolumab)	935 closed
Total pts registered to A081801 (adjuvant chemo-pembro)	361

ALCHEMIST trial

Dennis Wigle, Mayo Clinic

Biospecimen Core Resource (update Feb 2023)

- 6,790 patients with various samples at the BCR (tumor, blood, or slide)
- 3,440 cases have shipped to Genomic Characterizations Centers
- 9,745 kits have shipped to sites (2 Streck tubes per kit)
- 14,752 Streck tubes received (for 4883 patients) at the BCR

ALCHEMIST trial

Dennis Wigle, Mayo Clinic

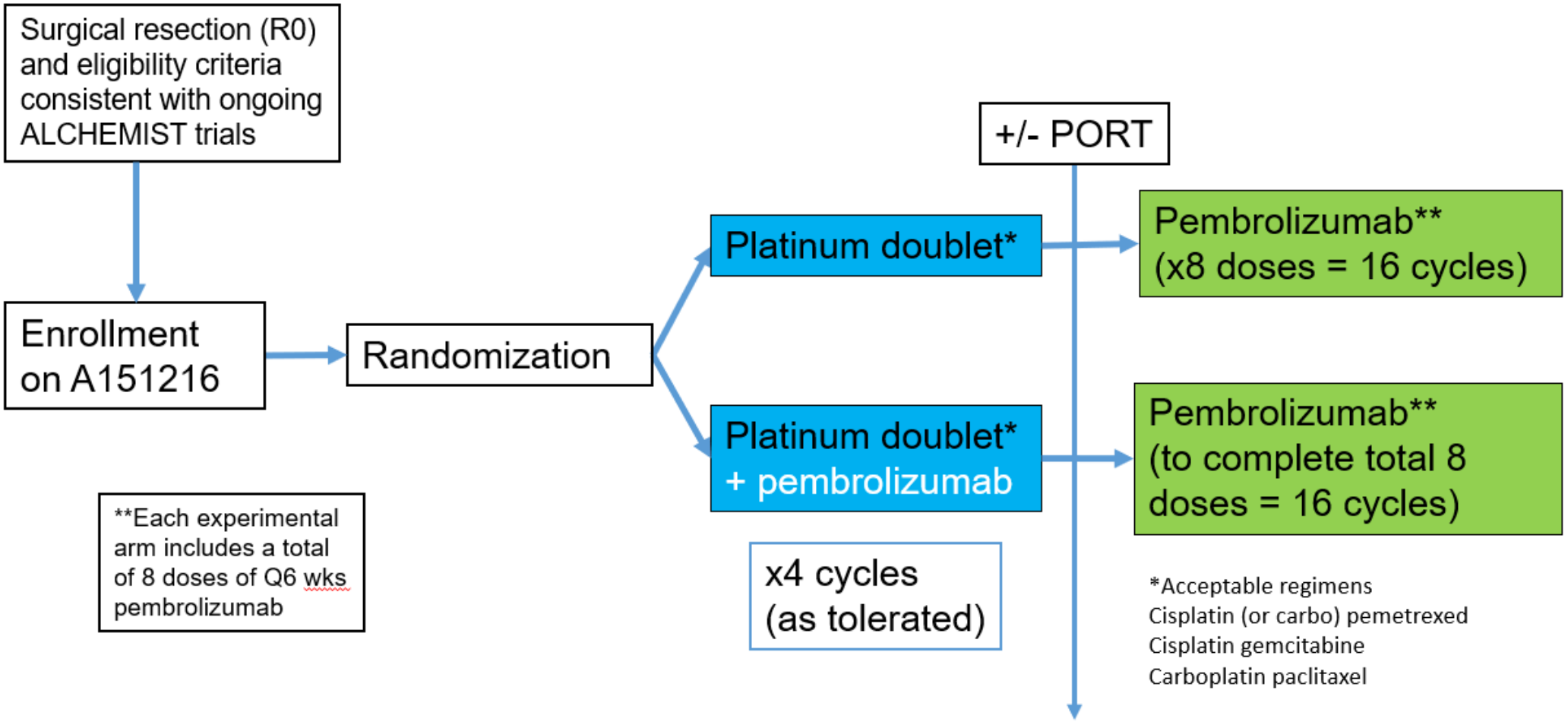
Thanks & enjoy the meeting!

wigle.dennis@mayo.edu

ALCHEMIST - ACCIO

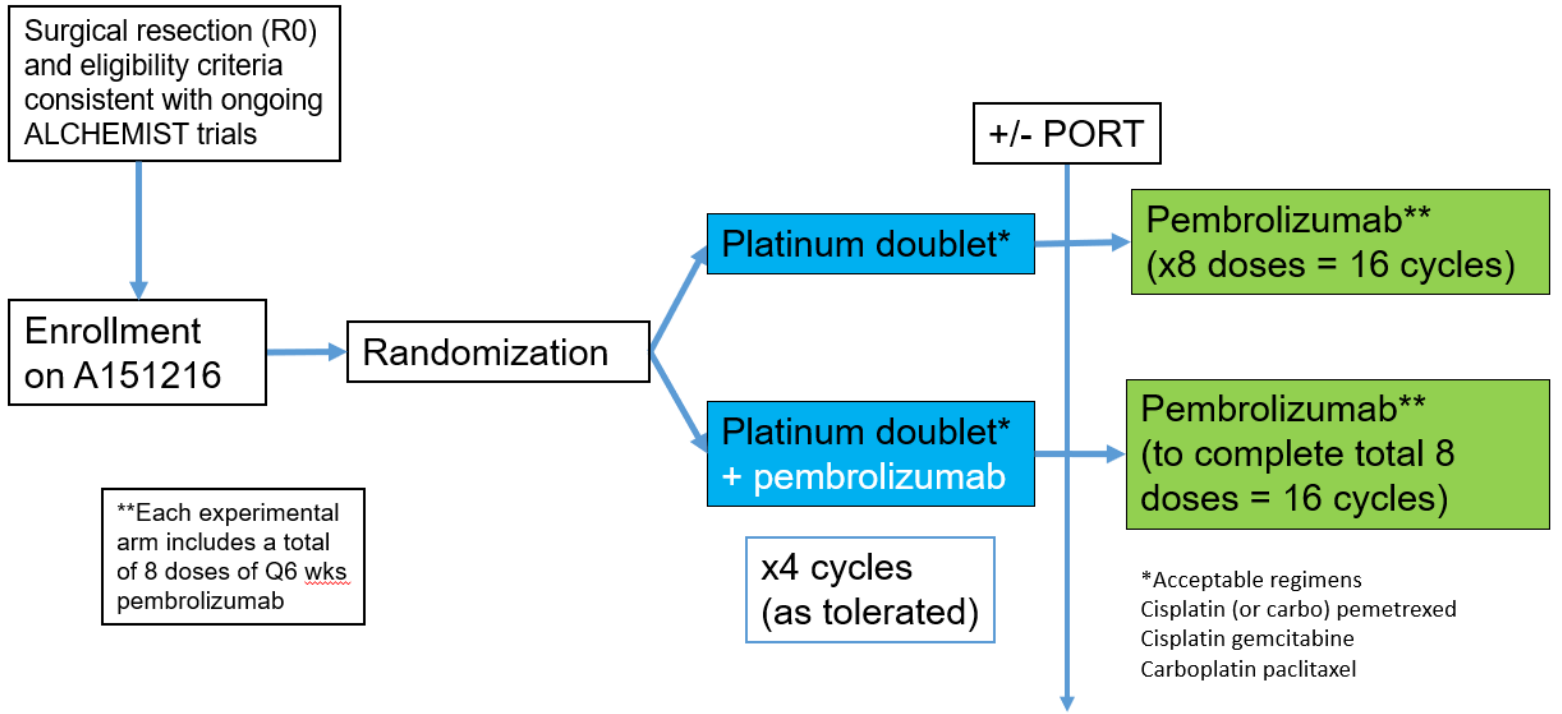
Study Design

Alliance ACCIO: A081801
Clinicaltrials.gov: NCT04071223

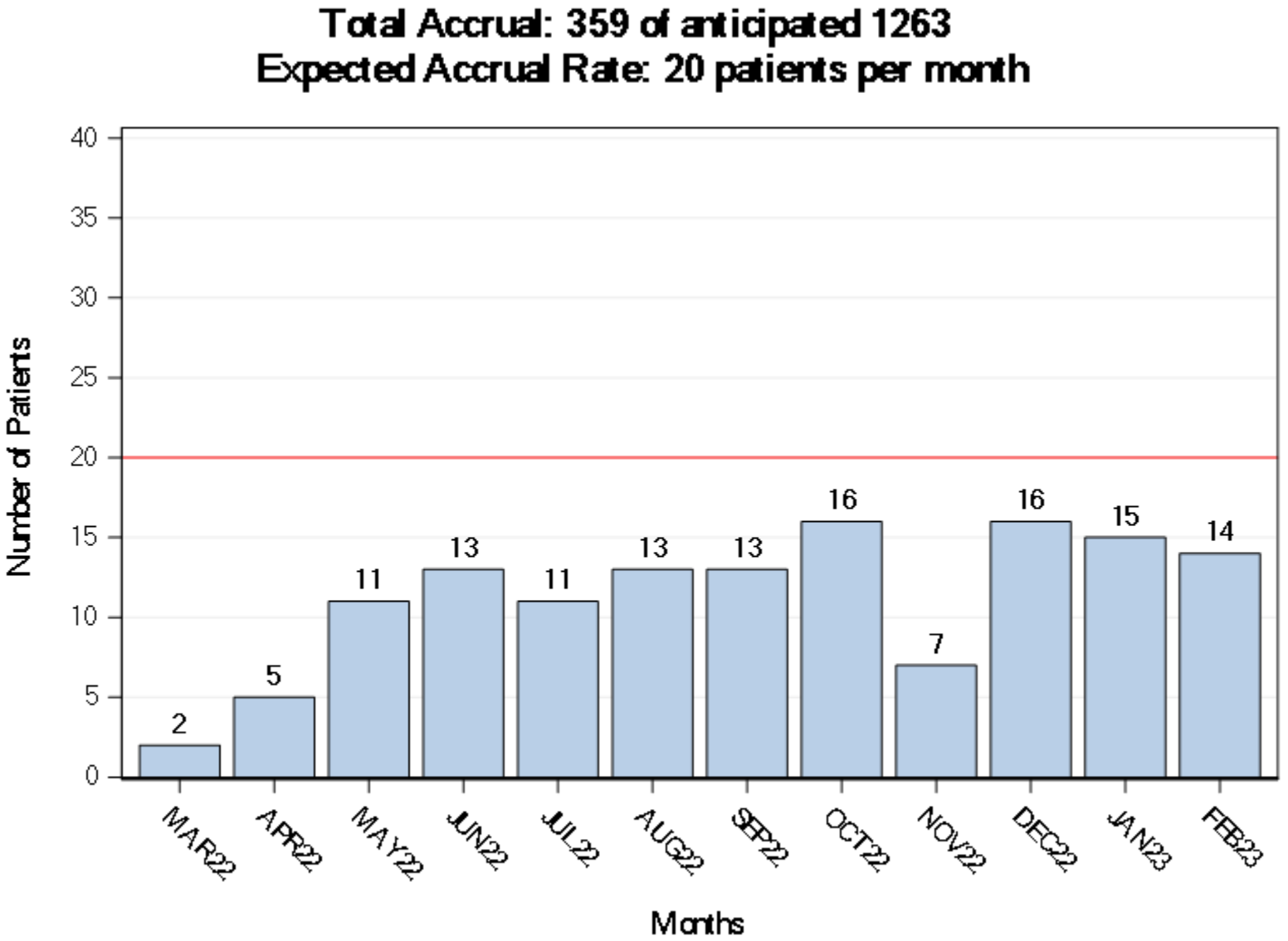


ALCHEMIST Chemo-IO (ACCIO)

- 2 arm trial (sequential vs concurrent)
- Eligibility: R0 resection and enrolled to ALCHEMIST
  - All PD-L1 expression
  - IB (>4cm)-IIIA
- Potentially greater benefit with concurrent in low PD-L1 expression vs sequential?



ALCHEMIST Chemo-IO (ACCIO)



Top 10 Accruing Sites (All Time)	
Site	**Accrual**
Moffitt Cancer Center	12
Baptist TN029	11
Springfield Clinic	8
Veterans Affairs Connecticut Healthcare System-Wes	7
Duke	7
State University of New York Upstate Medical	7
Memorial FL023	6
Washington U MO	6
U of Pitt	6
Med U SC	6

Alliance Foundation Trial-46

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

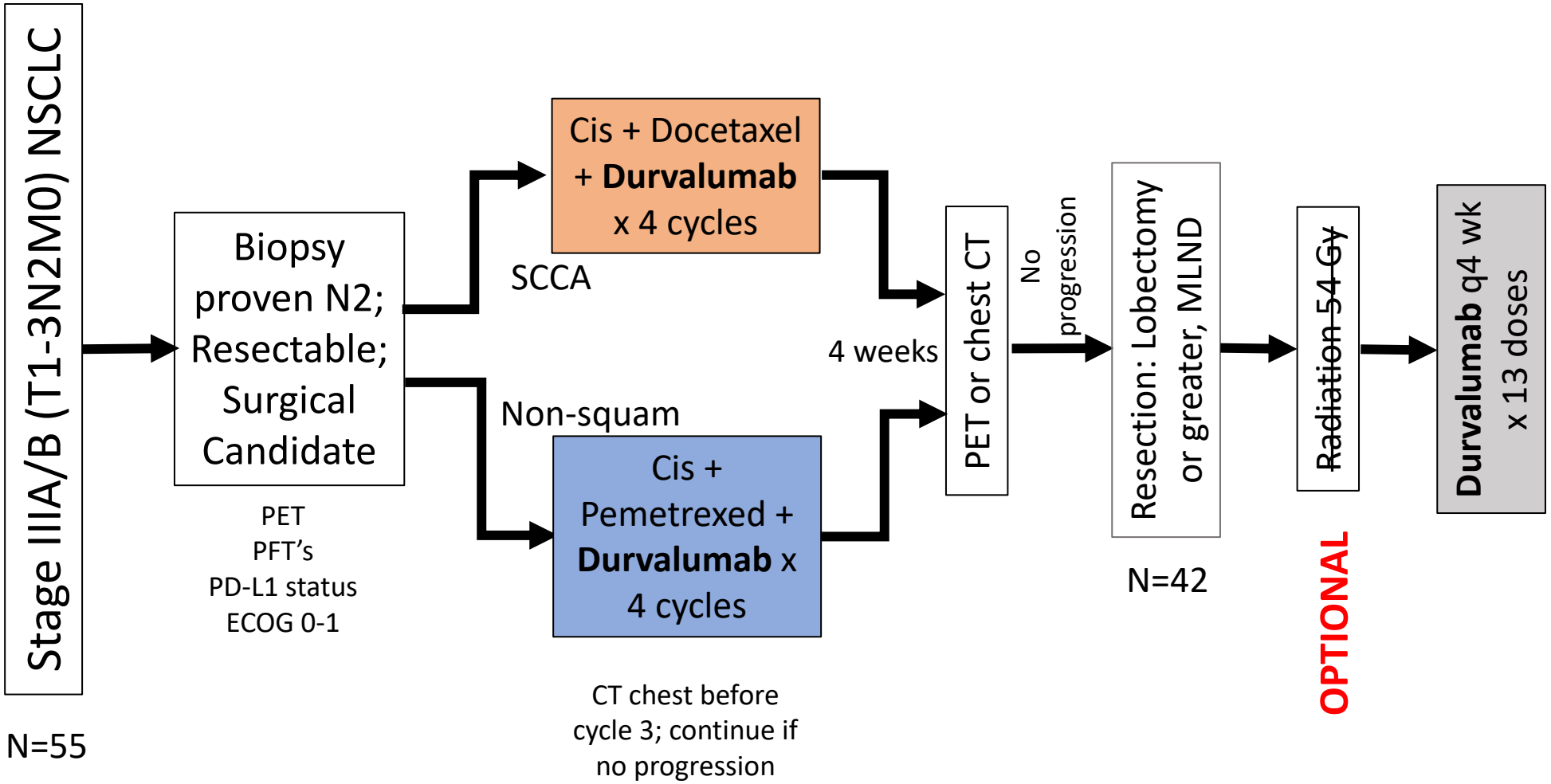
Linda W Martin, MD, MPH - Thoracic Surgery, University of Virginia

Jyoti Patel, MD - Medical Oncology, University of Chicago

James Urbanic, MD - Radiation Oncology, UC San Diego

AFT 46 Phase II Single Arm Trial

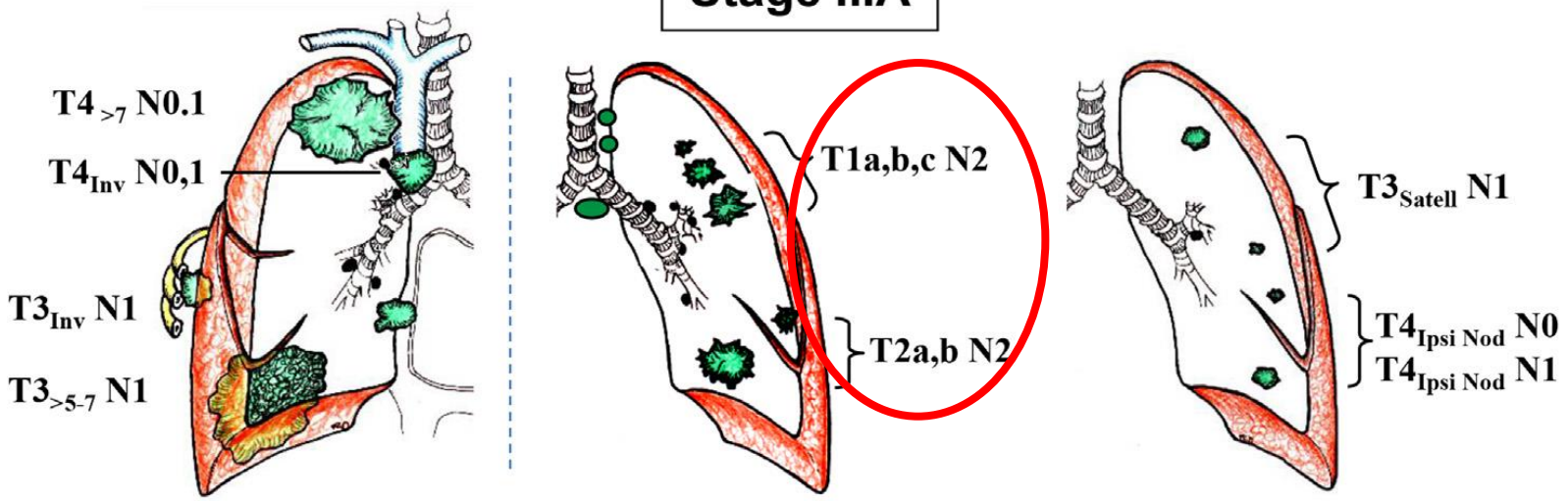
CHIO 3: Chemotherapy Combined with Immune Checkpoint Inhibitor for Operable Stage III NSCLC



Primary Endpoint: N2 nodal clearance (Estimated 50%, historical control 30%)

L Martin, J Patel, J Urbanic

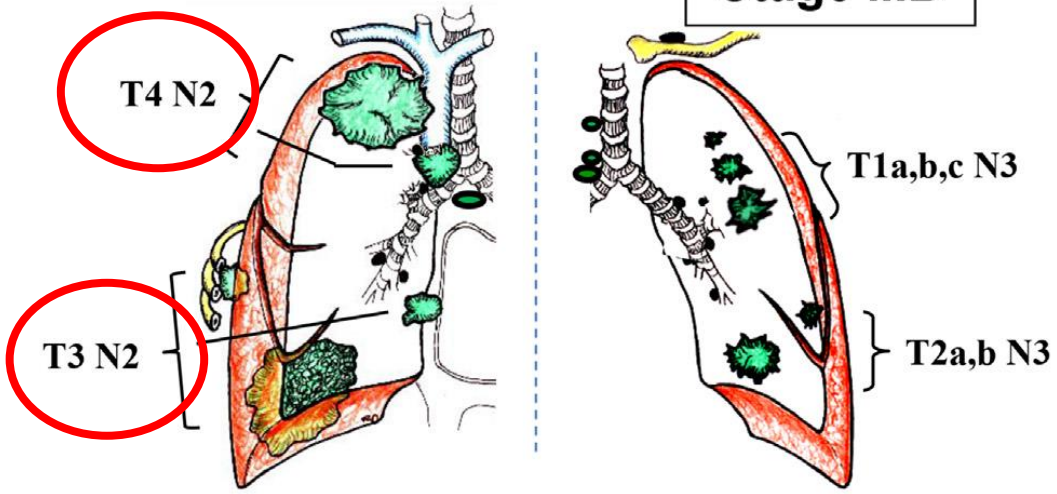
Stage IIIA



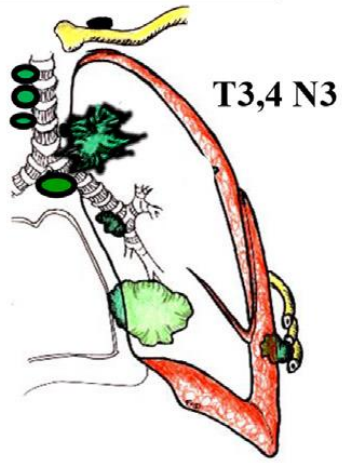
Specific Notes:

- 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



AJCC 8th edition: CHEST 2017; 151(1):193-203

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

- 32 patients enrolled

AFT-46 Study Status – Enrolling Sites

Partner Oncology Group	Enrolling Sites
Baptist Memorial Hospital and Cancer Center-Memphis	5
Brigham & Women's Hospital	4
Dartmouth Hitchcock Medical Center	0
Lowell General Hospital Cancer Center	0
Massachusetts General Hospital	1
Northwestern University	8
Roswell Park Cancer Institute	0
SUNY Upstate Medical University	6
Trinity Health Saint Joseph Mercy Hospital Ann Arbor	0
UCSD Moores Cancer Center	0
University of Chicago Medical Center	2
University of Texas MD Anderson Cancer Center	5
University of Virginia Cancer Center	1
Total:	**32**

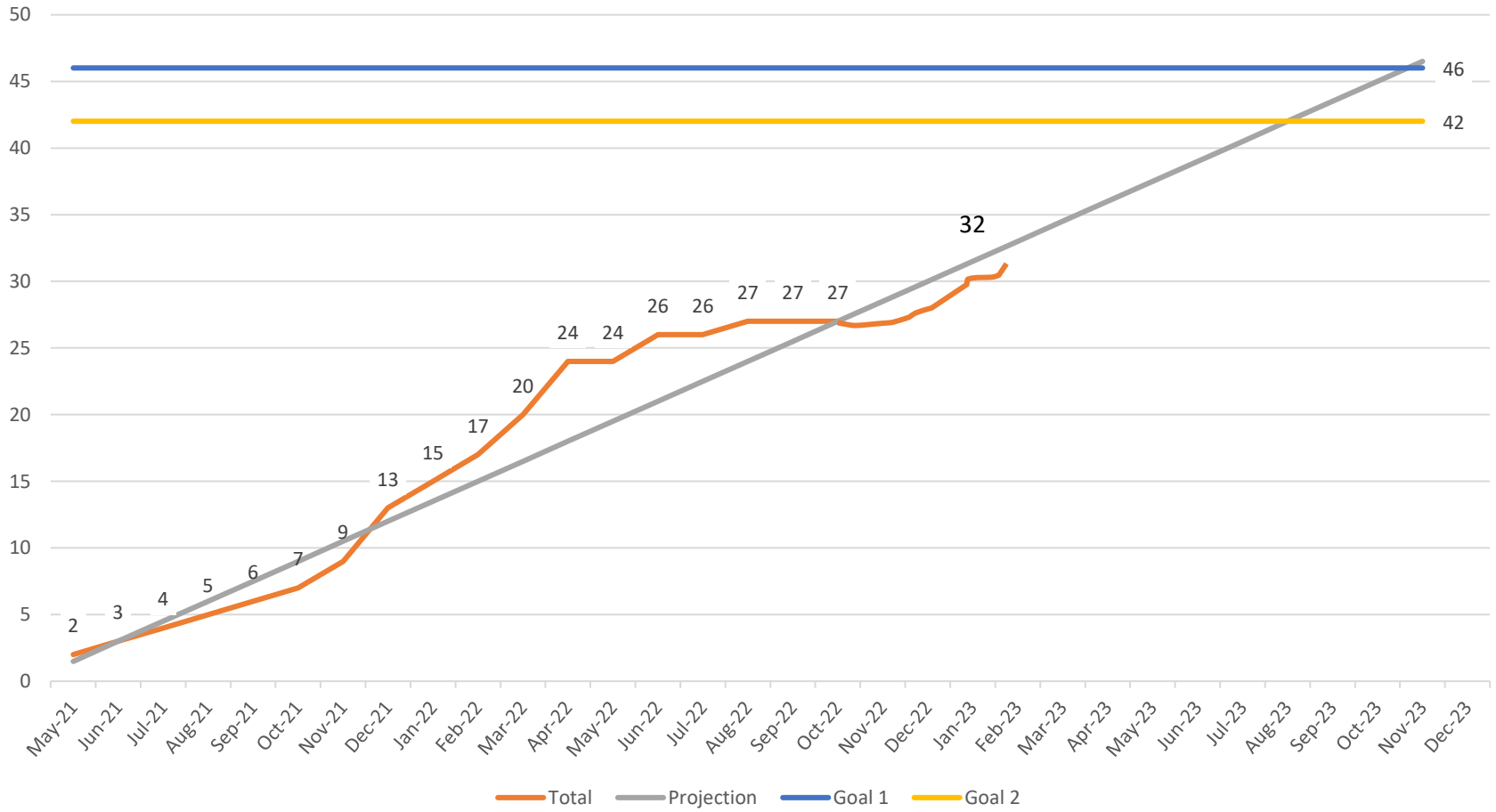
Need 42 surgical patients, have had very few not go to surgery

Anticipate completion by November 2023

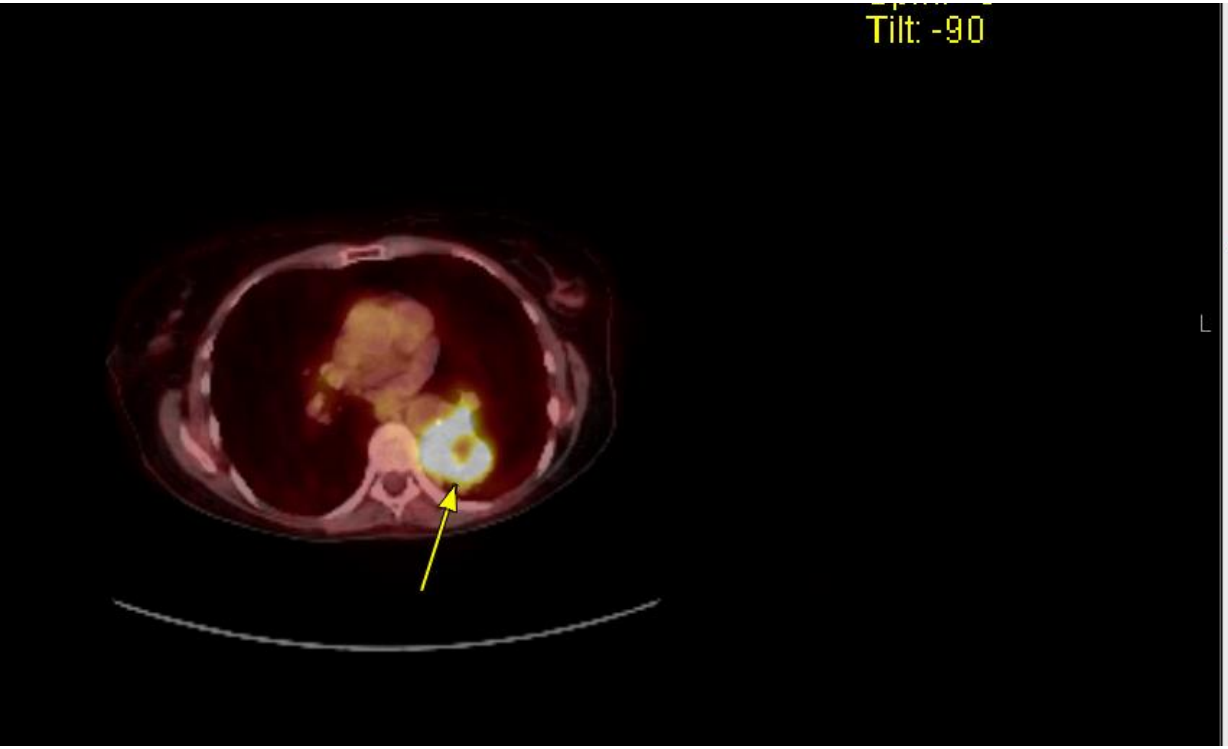
Pending Activation:

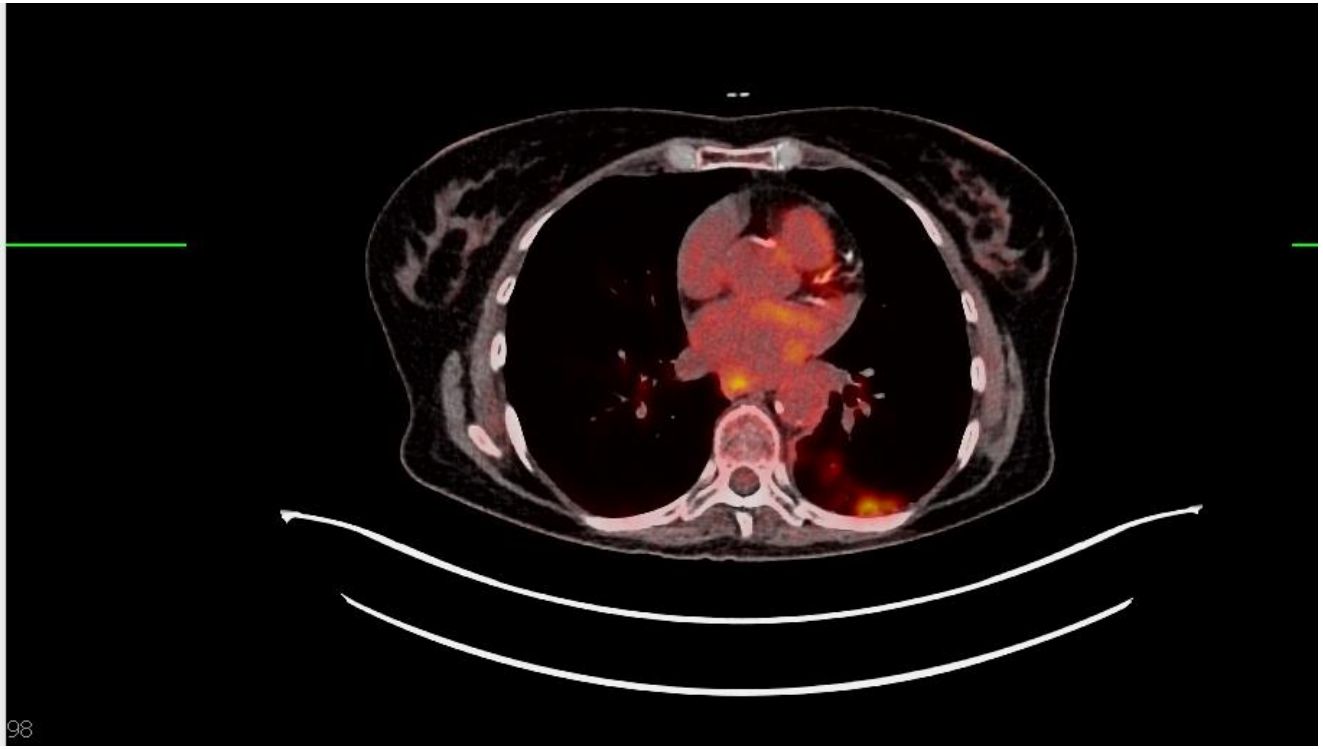
- Mayo Clinic
- University of Oklahoma

AFT-46 Enrollment Projections



Patient numero uno





Neoadjuvant nivolumab, ipilimumab for non-epithelioid mesothelioma

Aaron Mansfield, Xiaofei Wang and Dennis Wigle

Alliance Respiratory Committee
November 2022

Rationale

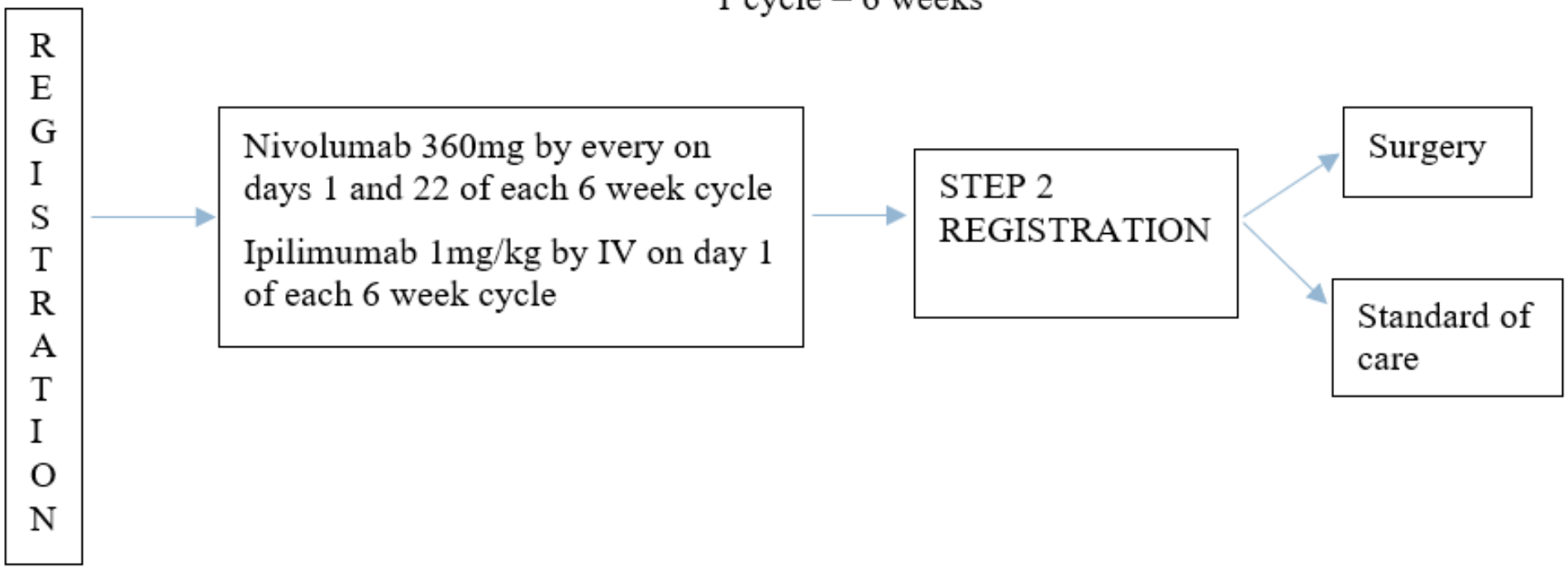
- Immunotherapy is now an FDA approved frontline option
- Survival for patients with non-epithelioid disease now approaches that of patients with epithelioid histology
- Should we reconsider whether surgery should be offered to patients with non-epithelioid histologies?

Design

- We propose a single arm pilot study to determine the safety and feasibility of neoadjuvant immunotherapy for non-epithelioid mesothelioma

Schema

1 cycle = 6 weeks



objectives

- Primary:
  - (1) determine the percentage of patients with potentially resectable non-epithelioid mesothelioma are able to proceed with surgery after neoadjuvant ipilimumab and nivolumab
  - (2) determine the progression-free survival rate at 12 months after the initiation of neoadjuvant therapy
- Secondary:
  - (1) determine the rate of intra-operative or post-operative complications following neoadjuvant immunotherapy
  - (2) determine the response rate per modified pleural RECIST, the major pathologic response rate, and the time to recurrence after surgery

Correlative:

peripheral T cell clonality, PD-L1 and tumor junction burden

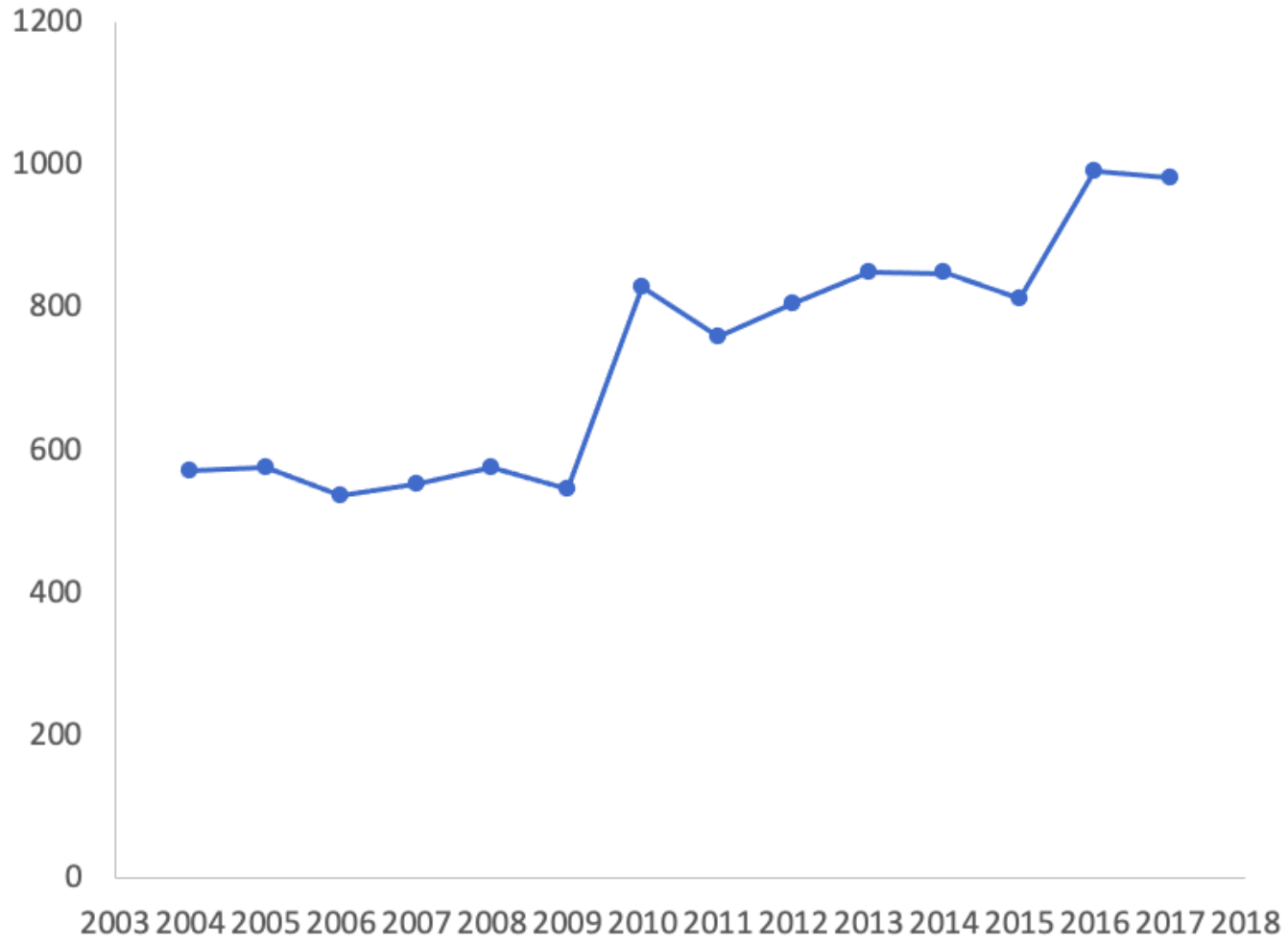
Updates

- NCI CTEP Approval on hold granted October 28, 2022
- Forms developed; testing expected to be complete early December
- OEWG date December 12, 2022

AFT 61: Adjuvant Chemotherapy and Immunotherapy for Completely Resected Small Cell Lung Cancer

Alliance for Clinical Trials in Oncology

Number of SCLC Resections from 2003-2018



Current studies on immunotherapy for SCLC

Study	Stage	Centers
CASPIAN[1] : Durvalumab +/- tremelimumab, + platinum–etoposide vs platinum–etoposide	Extensive-Stage	805
IMpower133[2] : Atezolizumab plus Chemotherapy	Extensive-Stage	403
ADRIATIC[3]**:** Durvalumab +/- Tremelimumab After Concurrent Chemoradiotherapy	Limited Stage	600 (approx.)
NRG LU005[4]**:** Atezolizumab plus Chemotherapy	Limited Stage	444

1. Paz Ares et al. *Lancet.* 2019; 394:1929-19392.
2. Horn et al. *NEJM* 2018; 379:2220-2229
3. Senan et al. *Clin Lung Cancer* 2020; 21(2): e84-e88
4. Ross et al. ASCO 2020.

AFT 61: Adjuvant Chemotherapy and Immunotherapy for Completely Resected Small Cell Lung Cancer

Study Design

Surgery
Patients with
Path T1–T2 N0-1 M0 SCLC

ECOG PS 0-1,
Age > 18 & < 80 years

ENROLL

Adj. chemotherapy * with immunotherapy

ECOG PS: Eastern Cooperative Oncology Group Performance Status;
DFS: disease-free survival

Primary endpoint
- 2 year DFS

Secondary endpoints
- 3-year DFS rate, 5-year DFS rate, 5-year OS rate

* Durvalumab

Updates

- **Approved by the Alliance Respiratory Committee**
- **Approved by the Alliance Foundation**
- **Approved from Astrazeneca**
- **Protocol draft done**
- **Awaiting final contract details (negotiation between AFT and Az)**
- **Protocol under review at AFT**

SCLC Registry/Multi-institutional database

- **Evaluating outcomes of operable SCLC from 2010-2023**
  - specific focus on disease-free survival

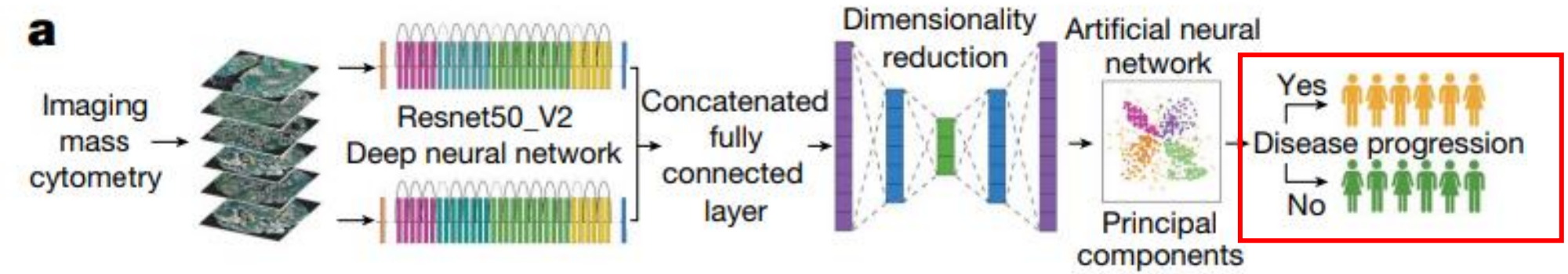
- **Welcome all centers to participate!**
  - Shouldn't be too time consuming

Predicting Recurrence Among Stage IA NSCLC Patients

nature

Article

Single-cell spatial landscapes of the lung tumour immune microenvironment



*Deep learning analysis, integrating spatial information of the tumor immune microenvironment, could predict recurrence after surgery for stage I adenocarcinoma with 95.9% accuracy.

Sorin et. al, *Nature,* 2023

How does this compare to other strategies to predict recurrence?

- AstraZeneca's methylation-based approach can only detect ctDNA in ~15% of stage I patients
- Natera's ctDNA test can detect ctDNA in ~60% of patients diagnosed with stage I NSCLC
  - Many patients who do not develop recurrence may be ctDNA positive
  - Requires both blood and tissue
  - Requires whole exome sequencing to design custom probes for each patient
  - More of a surveillance tool rather than a tool to predict recurrence at the time of surgery
- Parse-seq (developed by Max Diehn and Ash Alizadeh)
  - Requires whole genome sequencing, costs $5000 / person
  - More of a surveillance tool rather than a tool to predict recurrence at the time of surgery

How does this compare to other strategies to predict recurrence?

The Method by Sorin, Walsh & Jon Spicer:

- Deep learning analysis of integrating spatial information of the tumor immune microenvironment
  - Only requires one micron tumor cores (or a 5 micron slide)
  - Very cheap ($3 dollars per slide)
  - Technology to stain slides is not complicated and can be done by most pathology labs
  - *Predicted recurrence after surgery for stage I NSCLC with 95.9% accuracy*

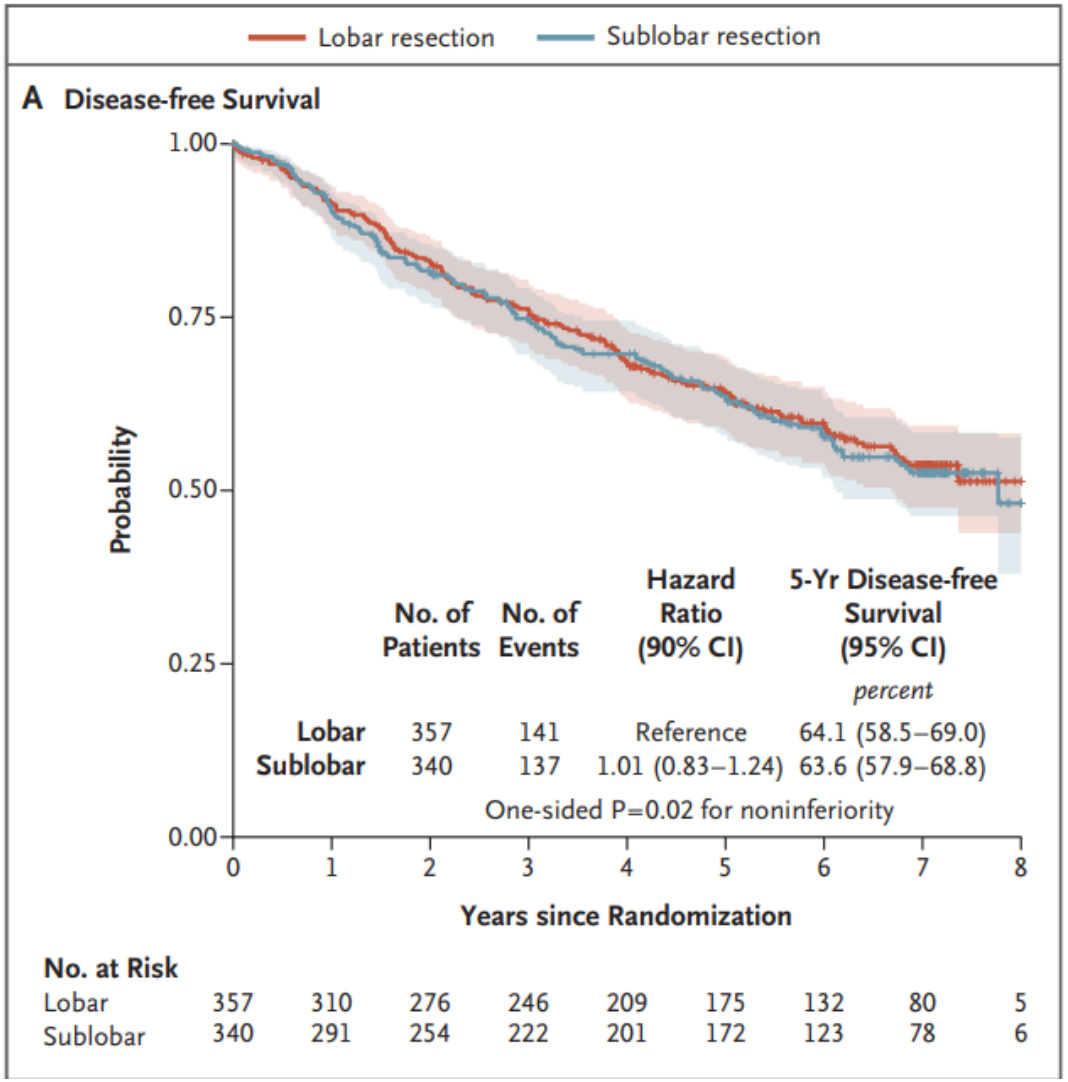
Further Refining the Deep Learning Model Using Additional Lung Tumor Samples

- Retrospectively obtaining lung tumor samples (ideally from >5 years ago)
  - 5-micron slide, unstained, for each sample
  - Tumor Microarray Builder (if available) would be ideal
- Their study team would ship each institution a kit to stain the 5-micron slide
- Images and outcomes (i.e., whether patients had a recurrence) would be deidentified and uploaded to the cloud
- Aim to get 1000+ lung tumor samples in total (~50-200 from each institution)

Would any institutions be interested in participating?

Can we use this technology to help us design a really good clinical trial evaluating Adjuvant Therapy for Stage IA Lung Cancer Patients?

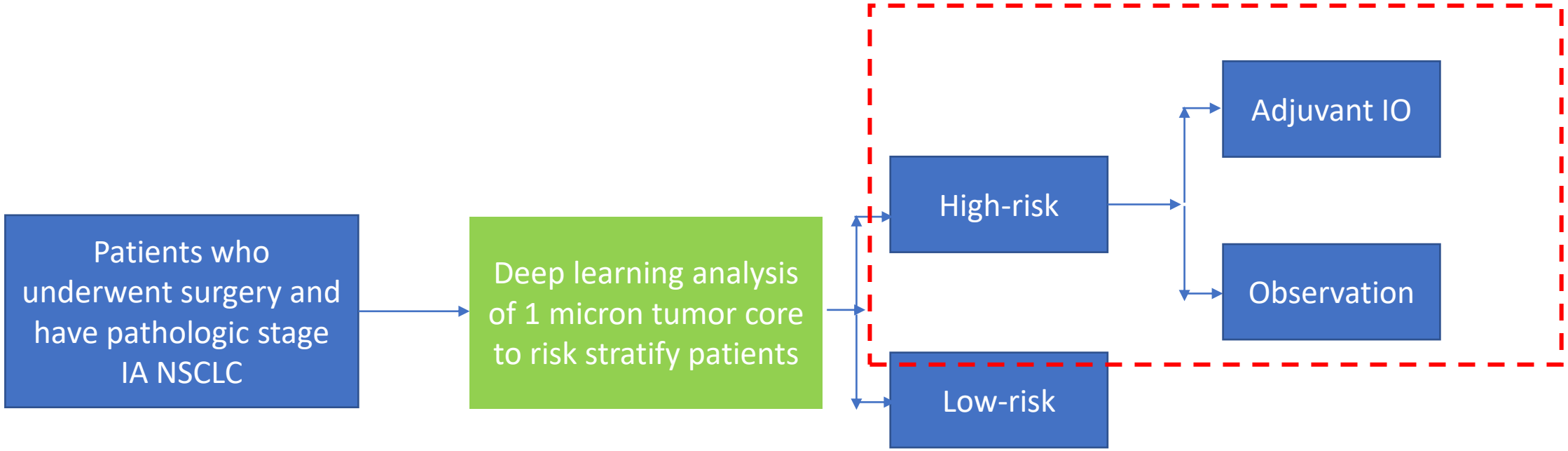
Predicting Recurrence Among Stage IA NSCLC Patients



- In CALGB 140503, 5-year DFS among patients with stage IA (<2 cm) NSCLC was 64.1% for those receiving lobectomy and 63.6% for those receiving sublobar resection.
- During a median follow-up of 7 years, 30% of patients developed a recurrence, with over 50% at distant sites.

Altorki et. al, *NEJM,* 2023

Next Steps: Applying This Technology to Risk Stratify Stage IA Patients



Among patients with pathologic stage IA NSCLC who are determined to be at high-risk for recurrence, does adjuvant immunotherapy improve recurrence free survival and overall survival?

Questions/recommendations

Email: cjyang@mgh.harvard.edu

Cell: 814 574 8695

ECOG-ACRIN
cancer research group
Reshaping the future of patient care

EMORY
UNIVERSITY
SCHOOL OF
MEDICINE

Review of Active ECOG Clinical Trials

Onkar Khullar MD, MSc
Assistant Professor of Thoracic Surgery
Emory University School of Medicine

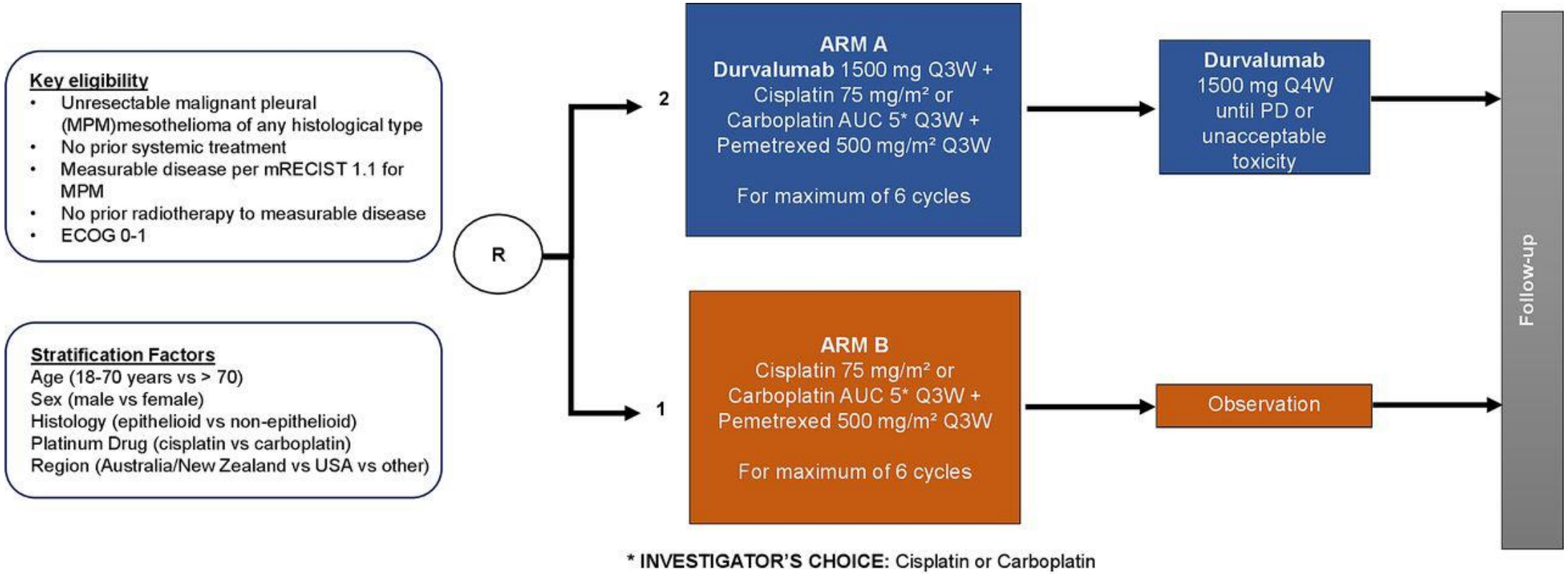
Erin Gillaspie, MD, MPH
Assistant Professor of Thoracic Surgery
Vanderbilt University Medical Center

Robert J. Ginsberg Clinical Trials Day
General Thoracic Surgery Club
March 9th, 2023

LUNG STUDIES

EA5162	NSCLC Stage IIIB to IV	Phase II: Osimertinib EGFR Exon 20 Insertion Mutations	Objective RR
EA5163 / S1709 / INSIGNA	NSCLC Stage IIIB- IV (IIIB and C if not candidate for Pacific)	Phase III: pembrolizumab alone as a first-line treatment, followed by pemetrexed and carboplatin with or without pembrolizumab	OS
EA5181	NSCLC Stage III (unresectable)	Phase III: concurrent durva + chemo + rads with durva 12 months vs. sequential chemo + rads then durva	OS
EA5182	NSCLC Stage IIIB - IV	Phase III: bevacizumab + osimertinib vs. osimertinib alone for EGFR (EGFR exon 20 insertions)	PFS
EA5191	NSCLC (non-squam) Stage IV	Phase II: cabozantinib vs. cabo + nivo vs. standard chemo	PFS
E4512, an ALCHEMIST Trial	NSCLC Stage IB-IIIA	Phase III: crizotinib post complete resection in ALK positive NSCLC	DFS

PrE0506: Durvalumab with Chemotherapy as first line treatment in advanced pleural mesothelioma: A phase 3 randomized trial (DREAM3R)

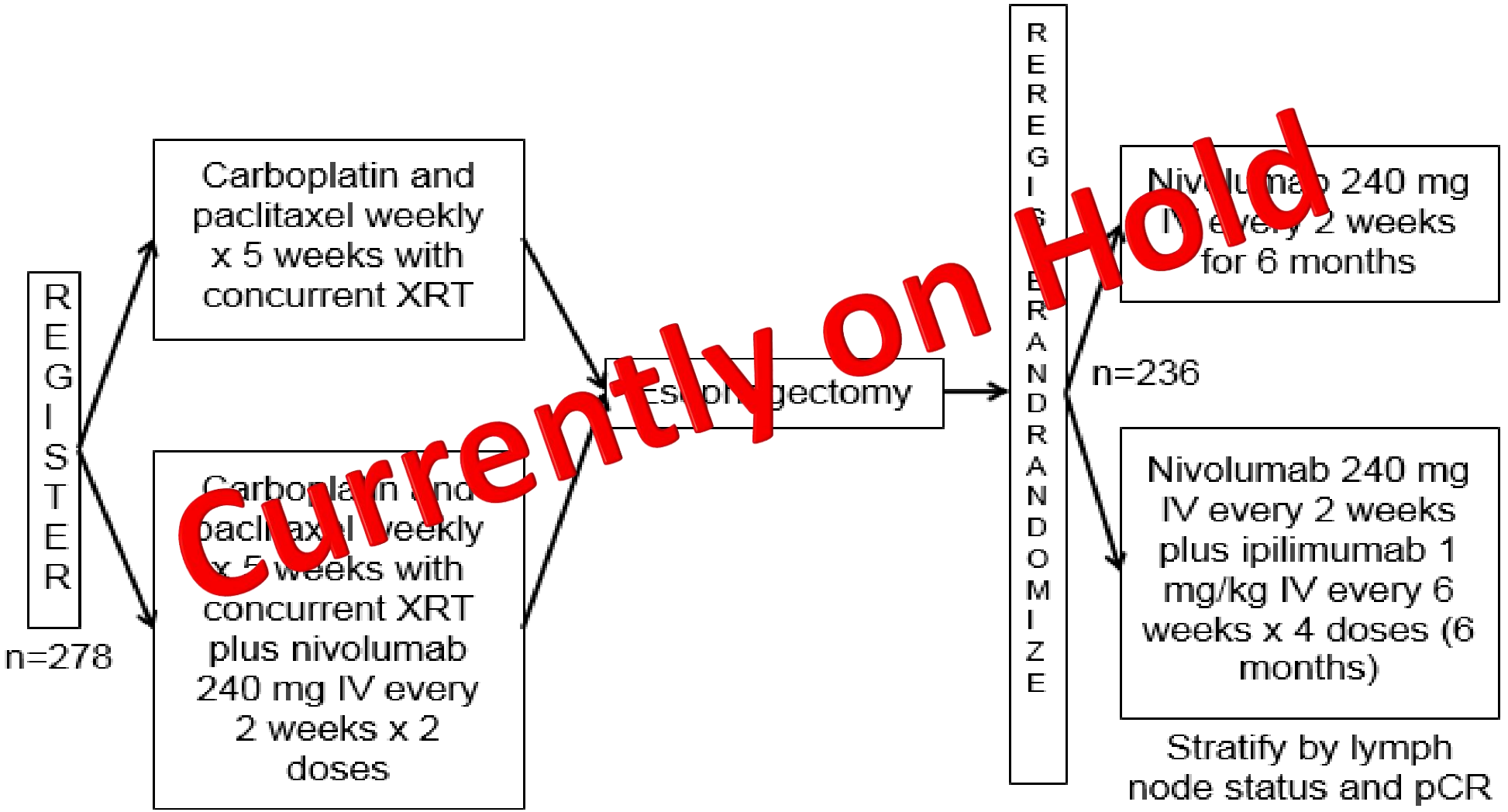


Primary endpoint: OS
Secondary endpoints: PFS, OTRR, AEs, HRQoL, healthcare resources
Tertiary endpoints: Possible prognostic/predictive biomarkers in tissue and serial blood samples: PD-L1, HLA subtypes, tumour mutation burden, genomic characteristics; validation of radiological measures of response and radiomic biomarkers

ESOPHAGEAL STUDIES

EA2174	Esophageal/GEJ Adenocarcinoma Resectable	Phase II/III: nivo + ipi with standard of care chemo + radiation in patients with planned resection	Path CR DFS
EA2183	Oligometastatic esophageal or GEJ adenocarcinoma	Phase III: HER2 (-), PDL1 (+). Standard chemotherapy + local radiation to oligometastatic disease.	OS

EA2174: A Phase II/III Study of Peri-operative Nivolumab and Ipilimumab in Patients with Locoregional Esophageal and Gastroesophageal Junction Adenocarcinoma



Eligibility and End Points

- Tumor factors:
  - Histologically confirmed
  - Esophageal or GEJ (Siewert I or II) adenocarcinoma
  - Resectable
  - Stage: T1N1-3M0 or T2-3N0-2M0 cancer
- Patient factors:
  - ECOG 0-1 (able to tolerate multi-D therapy)
  - 18+
  - No active infections, uncontrolled illness, chronic immunosuppression or autoimmune disease
  - No prior therapy
- Endpoints
  - Neoadjuvant: pathCR
  - Adjuvant: DFS

Toxicity	Arm A (n=16)		Arm B (n=15)	
	Grade 3	Grade 4	Grade 3	Grade 4
Anemia			2 (13.3%)	
Pericardial Effusion				1 (6.7%)
Pericardial Tamponade				1 (6.7%)
Lymphocytes decreased	5 (31.3%)	1 (6.3%)	2 (13.3%)	3 (20%)
WBC decreased			4 (26.7%)	
Hypotension			2 (13.3%)	

Surgical Complication	Arm A (N=12)	Arm B (N=13)
Anastomotic leak	1 (6.3%)	2 (13.3%)
Chyle leak	1 (6.3%)	1 (6.7%)
Pleural effusion needing intervention	0 (0%)	2 (13.3%)
Pneumonia	0 (0%)	1 (6.7%)
Pneumothorax	1 (6.3%)	1 (6.7%)
Pulmonary embolism	1 (6.3%)	0 (0%)
Atrial fibrillation/flutter	1 (6.3%)	1 (6.7%)
Deep vein thrombosis	1 (6.3%)	0 (0%)
Wound complication	0 (0%)	1 (6.7%)

EA5142: Adjuvant Nivolumab in Resected Lung Cancers (ANVIL) – A Randomized Phase III Study of Nivolumab After Surgical Resection and Adjuvant Chemotherapy in Non-Small Cell Lung Cancers

Schema

Eligibility
- Patient registered to ALCHEMIST screening trial (A151216)
- If non-squamous, no ALK rearrangement or EGFR Exon 19 deletion/Exon 21 L858R mutation
- No contraindication to nivolumab

Stratification
- Stage AJCC 7th edition: IB/IIA vs IIB/IIIA[1]
- Histology: squamous vs. non-squamous[2]
- Prior adjuvant treatment for lung cancer (none vs. chemotherapy vs. chemotherapy + radiation)
- PD-L1 status: positive (≥ 1%) vs. negative (< 1%)/non-evaluable) membranous expression determined centrally[3]

RANDOMIZE

ARM A
Nivolumab 480 IV q4 weeks for up to 1 year

ARM B
Observation per standard of care for up to 1 year

LONG-TERM FOLLOW-UP[4]

Cycle = 4 weeks (28 days)
Accrual Goal = 903 patients

1. If Stage 1B, then tumor must be ≥ 4cm
2. Adenosquamous should be grouped as non-squamous
3. PD-L1+ is defined as ≥ 1% by IHC
4. Patients will be followed for recurrence and survival for 10 years

Thanks!!

General Thoracic Surgery Club Meeting

March 9, 2023 2:00pm-3:00pm EST

AATS Thoracic Surgery Oncology Group

A joint venture between AATS and Memorial Sloan Kettering Cancer Center

David R. Jones MD
Chair, TSOG

Executive Committee
Ara Vaporciyan MD
Raphael Bueno MD
David Harpole MD

Project Manager: Maria Singh

AATS Thoracic Surgery Oncology Group

A joint venture between AATS and Memorial Sloan Kettering Cancer Center

Thoracic Surgery Oncology Group (TSOG)
March 2017

The Thoracic Surgery Oncology Group (TSOG) supports a network of North American thoracic surgery clinical trials to improve the understanding of thoracic oncologic diseases and enhance patient care.

Formed in 2017 by the American Association for Thoracic Surgery Fiona and the Stanley Druckenmiller Center for Lung Cancer Research at Memorial Sloan Kettering Cancer Center, the Group administers multisite trials focused on recent advances in precision medicine, immunotherapy, intraoperative imaging, and related surgical questions. By actively accruing patient to relevant investigator-initiated clinical trials, as well as select industry-sponsored clinical trials, TSOG aims to improve outcomes for patients with thoracic malignancies.

Learn more about the initiative and how to join the network by visiting aats.org.

Thoracic Surgery Oncology Group

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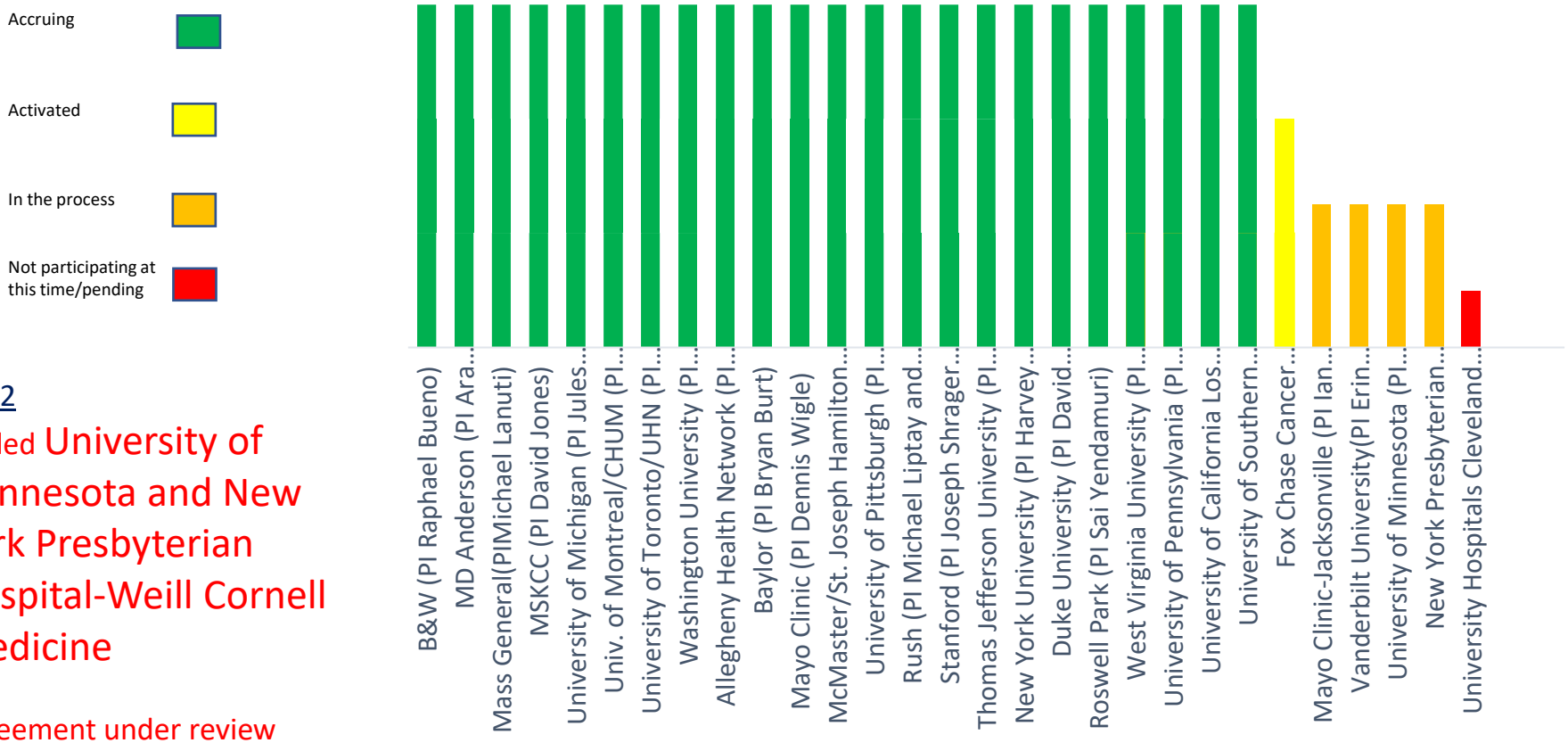
TSOG Sites Activation Status

Now at 29 TSOG Sites-all contracts signed!



2022

Added University of Minnesota and New York Presbyterian Hospital-Weill Cornell Medicine

Agreement under review

University of California San Diego

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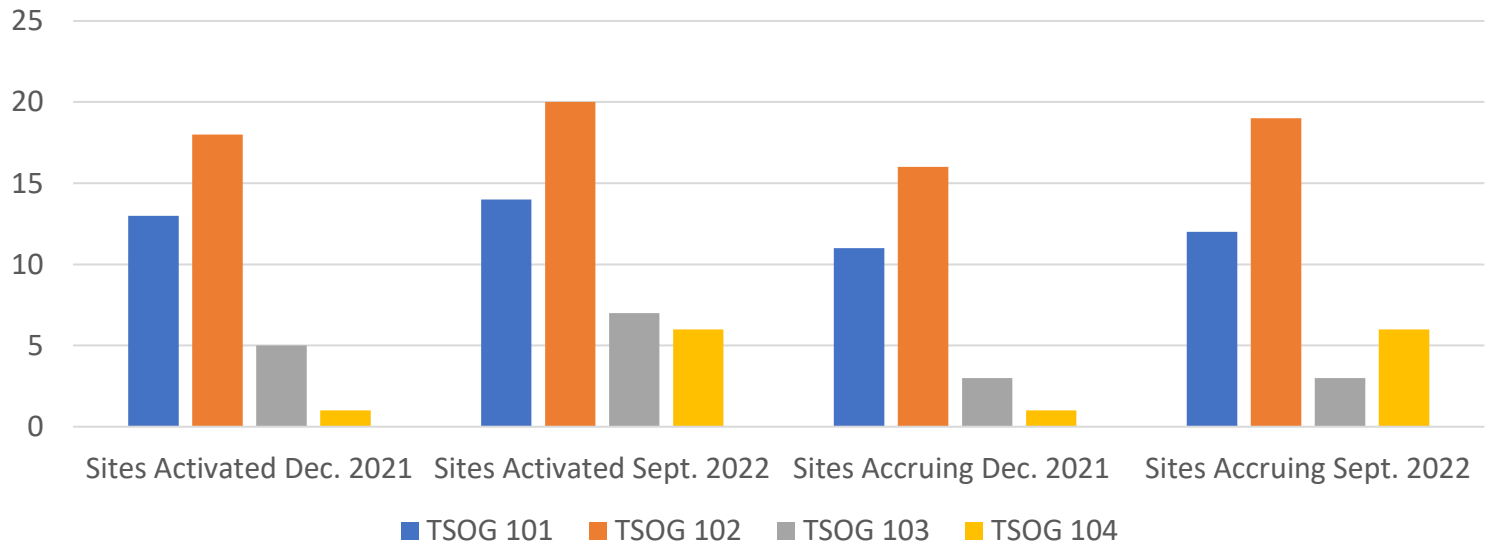
TSOG Sites Activated and Accruing Status Dec.2021 vs. Sept.2022



2022 Site Activation and Accrual Changes

- Sites activating trials: 36 to 47 (31% increase)
- Sites accruing to trials: 30 to 40 (33% increase)

TSOG 101 Update

Perioperative Circulating Tumor DNA as a Predictive and Prognostic Biomarker in Patients Undergoing Neoadjuvant Therapy for Resectable NSCLC

Study PI: James Isbell, MD, MSCI

isbellj@mskcc.org

Sponsor: Memorial Sloan Kettering Cancer Center

TSOG 101

AATS Thoracic Surgery Oncology Group

Concept:

A valid biomarker is needed to assess for treatment response and the presence of minimal residual disease (MRD) in patients undergoing curative-intent treatment for NSCLC

Hypotheses:

- The percentage change in ctDNA variant allele fractions (VAF) before and after neoadjuvant therapy will correlate with pathological response (percent viable tumor in resection specimen).
- The VAF after complete surgical resection will be predictive of recurrence, disease-free survival and overall survival at 3 and 5 years.
- The change in VAF will correlate with PET SUV

Eligibility Criteria:

- ≥ 18 years of age
- Resectable and medically operable stage IIA-IIIB NSCLC
- Undergoing neoadjuvant cytotoxic, targeted or checkpoint inhibitor therapy with or without radiotherapy

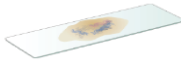
Target Enrollment:

- 100 evaluable subjects

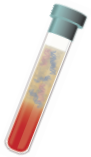
TSOG 101

AATS | Thoracic Surgery Oncology Group

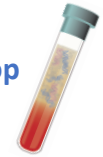
Resectable stage IIA-IIIB NSCLC
- Neoadjuvant therapy
  - Cytotoxic/Immune/Targeted
  - +/- Radiation
- Pre-treatment tissue for WGS (if available)



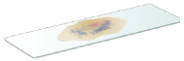
Pre-neoadjuvant cfDNA blood draw



Post-neoadjuvant/Preop cfDNA blood draw

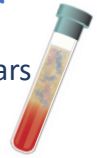


Surgical Resection
- Assess pathologic response
- Tumor tissue for WGS (if pre-treatment tissue insufficient)



Postop cfDNA blood draw
- 3-6 weeks postop

Surveillance chest CTs & cfDNA blood draws
- Every 6 months x 2 years



TSOG 101

Sites open to accrual: 14

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Accrual as of March 2023: 90 of 100

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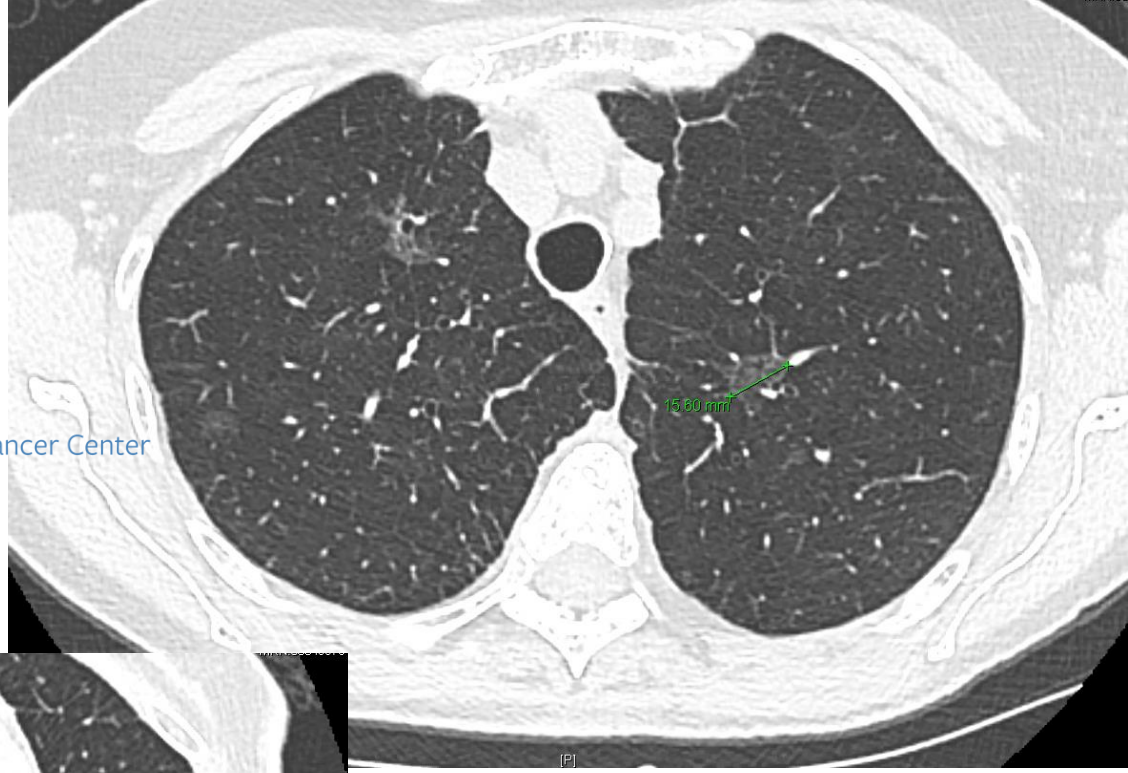

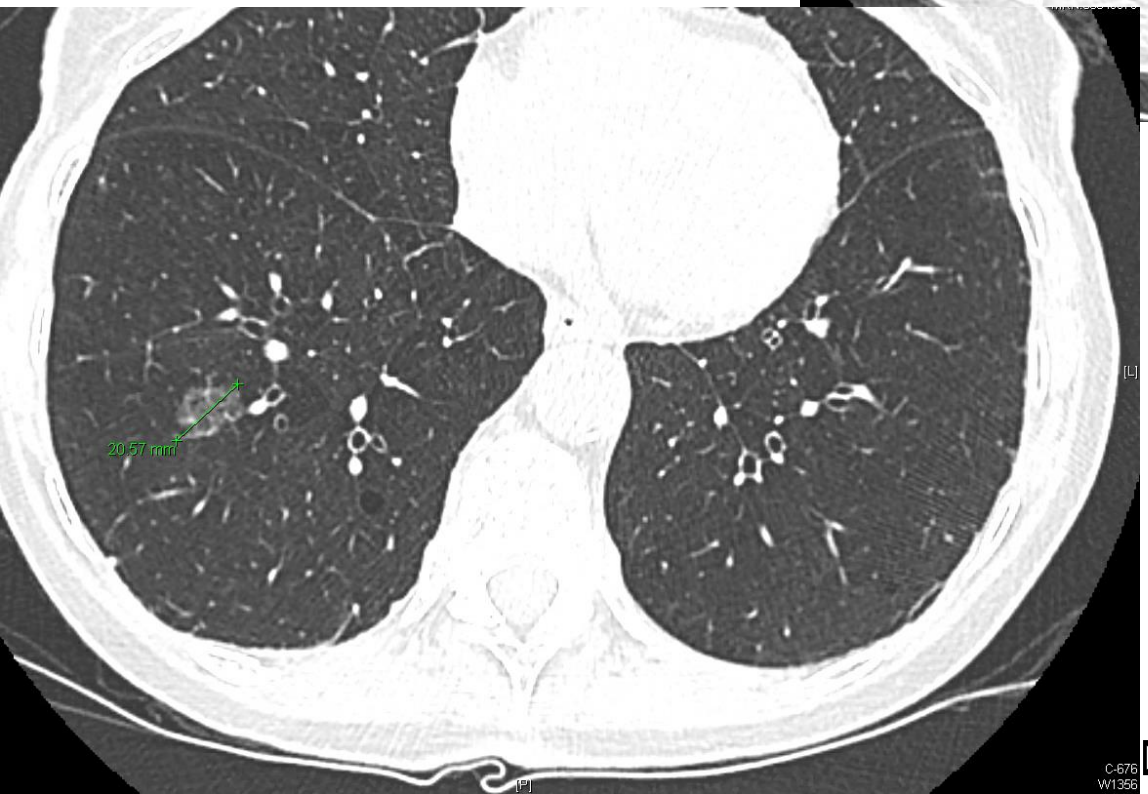

TSOG-102 Protocol:

Registry Trial of Active Surveillance for Multifocal Ground Glass Opacities (GGO)

PI: James Huang, MD

✉ huangj@mskcc.org

Thoracic Surgery Oncology Group
AATS
A joint venture between AATS and Memorial Sloan Kettering Cancer Center

TSOG 102 Update

Concept and Hypothesis

- Registry of GGO coupled with active surveillance
  - Mirrors common practice
  - Prospective data about the natural history of these lesions
  - Standardized guidelines for surveillance and intervention
- Hypothesis:
  - Active surveillance for GGO is feasible and safe

Study Design:

- Patients with 2 or more GGO
- Each lesion tracked in registry
  - CT scan every 6-12 mo
  - Progression defined as:
    - Growth ≥ 50% or more over baseline
    - Increase in solid component > 50% solid
- At progression (growth ≥ 50% or more over baseline; or increase in solid component > 50% solid)
  - Intervention (biopsy or resection) recommended, but remains discretion of treating clinician
- Surveillance on protocol for 5 years

Thoracic Surgery Oncology Group

AATS

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TSOG 102

Eligibility:

- Inclusion Criteria
  - 2 or more GGO (each ≥ 0.6cm and ≤ 3cm)
- Exclusion Criteria
  - GGO > 3cm
  - GGO > 50% solid
    - (Consolidation/Tumor Ratio > 0.5)
  - Prior history of lung cancer > stage IA
  - Active cancer treatment

Objectives

- Primary
  - Lung cancer-specific survival at 5 years
- Secondary
  - Cumulative incidence of intervention
  - Cumulative incidence of new GGO
  - Cumulative incidence of lung cancer diagnosis
  - Freedom from any/nodal/distant progression
  - Overall survival

AATS Thoracic Surgery Oncology Group

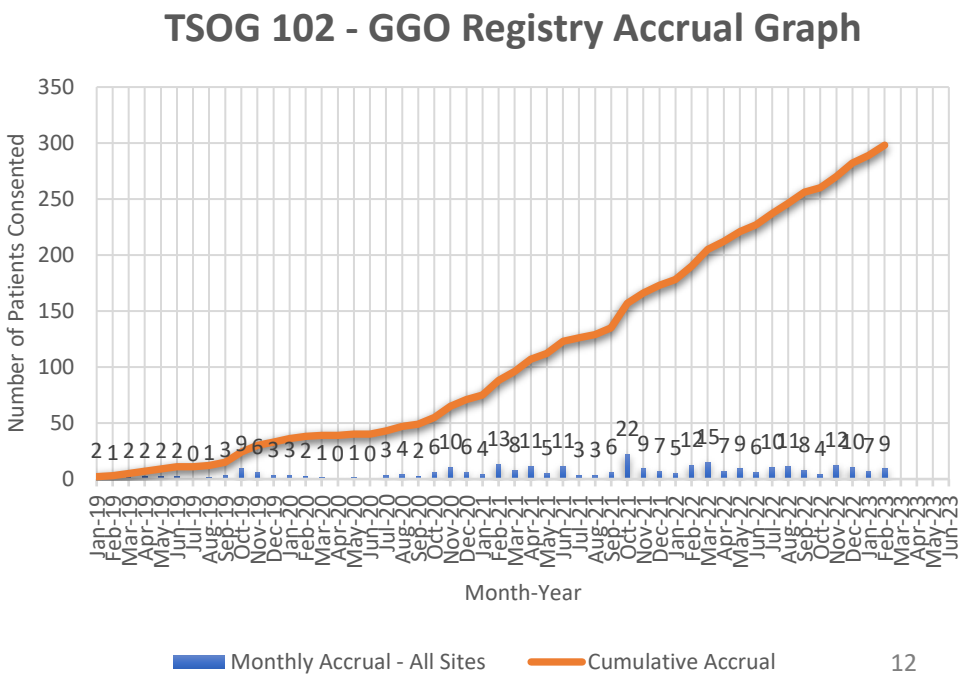
A joint venture between AATS and Memorial Sloan Kettering Cancer Center

TSOG 102

TSOG 102 Sites
Memorial Sloan Kettering Cancer Center
Massachusetts General Hospital
Washington University in St. Louis
University of Pennsylvania
Baylor College of Medicine
Centre Hospitalier Universitaire de Montreal
Brigham and Women's Hospital
University of Michigan
Rush University Medical Center
MD Anderson Cancer Center
MSK Alliance - Lehigh Valley Health Network
University of Toronto/ University Health Network
University of Pittsburgh
Roswell Park Cancer Institute
Duke University
Stanford University
Mayo Clinic
Thomas Jefferson University Hospital
Allegheny Health Network
McMaster University
MSK Alliance - Hartford Healthcare Alliance
Fox Chase

Sites open to accrual: 22

Accrual as of March 2023: 304 of 330



Thoracic Surgery Oncology Group

AATS

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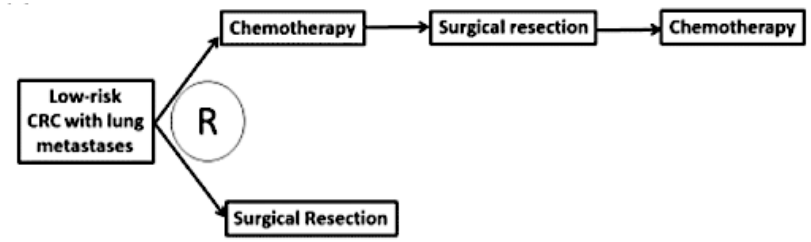
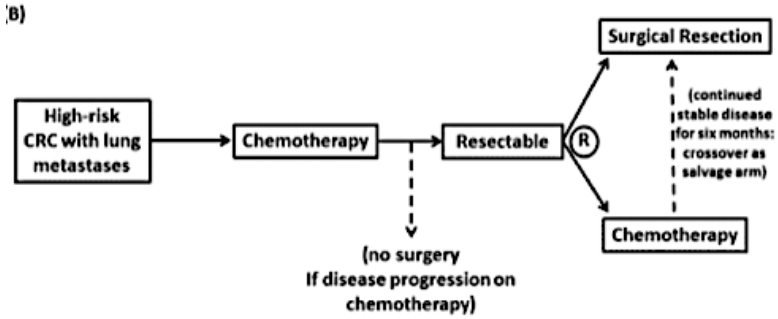
TSOG 103 Update





Stratification of lung-limited mCRC by risk group

Risk group	DFI (months)		Number of metastases
LOW	≥ 12	AND	≤ 3
*INTERMEDIATE**	*6-12*	*OR*	*4-6*
HIGH	< 6	OR	>6

The role of multimodality management in risk-stratified patients with lung limited metastatic colorectal cancer PI Dr. Mara Antonoff

MBAntonoff@mdanderson.org

- Primary objectives:
  1. To compare progression-free survival in patients with "low-risk" lung-limited mCRC undergoing pulmonary metastasectomy with or without perioperative chemotherapy.
  2. To compare overall survival in patients with "high-risk" lung-limited mCRC receiving systemic chemotherapy with or without surgical resection.
- Exploratory objective *(optional for TSOG sites)*:
  - To evaluate for changes in circulating tumor DNA following surgical resection and/or systemic chemotherapy in patients with lung-limited mCRC.

*Intermediate group is not eligible for enrollment at this time

Thoracic Surgery Oncology Group

AATS

A joint venture between AATS and Memorial Sloan Kettering Cancer Center

TSOG 103

The role of multimodality management in risk-stratified patients with lung limited metastatic colorectal cancer

Update:

- Trial up and running
- Accrual status as of March 2023
  - Screened – 208 at MDACC
  - Total consented - 43
    - LOW RISK – 20 consented, 15 on active study (1- University of Toronto, 1- Thomas Jefferson University Hospital)
    - HIGH RISK – 23 consented, 19 on active study (1- University of Toronto, 1- Thomas Jefferson University Hospital)
  - ctDNA blood samples - 85 (9 samples for recurrence)
  - 34 active patients (MDACC, UHN, TJU)
- Study is open to accrual at MDACC, CHUM, UHN, & TJU

AATS Thoracic Surgery Oncology Group

A joint venture between AATS and Memorial Sloan Kettering Cancer Center

TSOG 104 Update
Blinded Prospective Validation Trial of Pleural Effusion FBLN3 As a Specific Biomarker of Malignant Pleural Mesothelioma

Harvey I. Pass, MD- NYU

Prasad Adusumilli, MD-MSKCC

R. Taylor Ripley, MD-Baylor College of Medicine

Raphael Bueno, MD-BWH

Marc De Perrot, MD-University of Toronto

David Harpole, MD-Duke University

Site Initiation Visit TSOG Mesothelioma Centers

Harvey.Pass@nyulangone.org

TSOG 104
Hypothesis and Specific Aims

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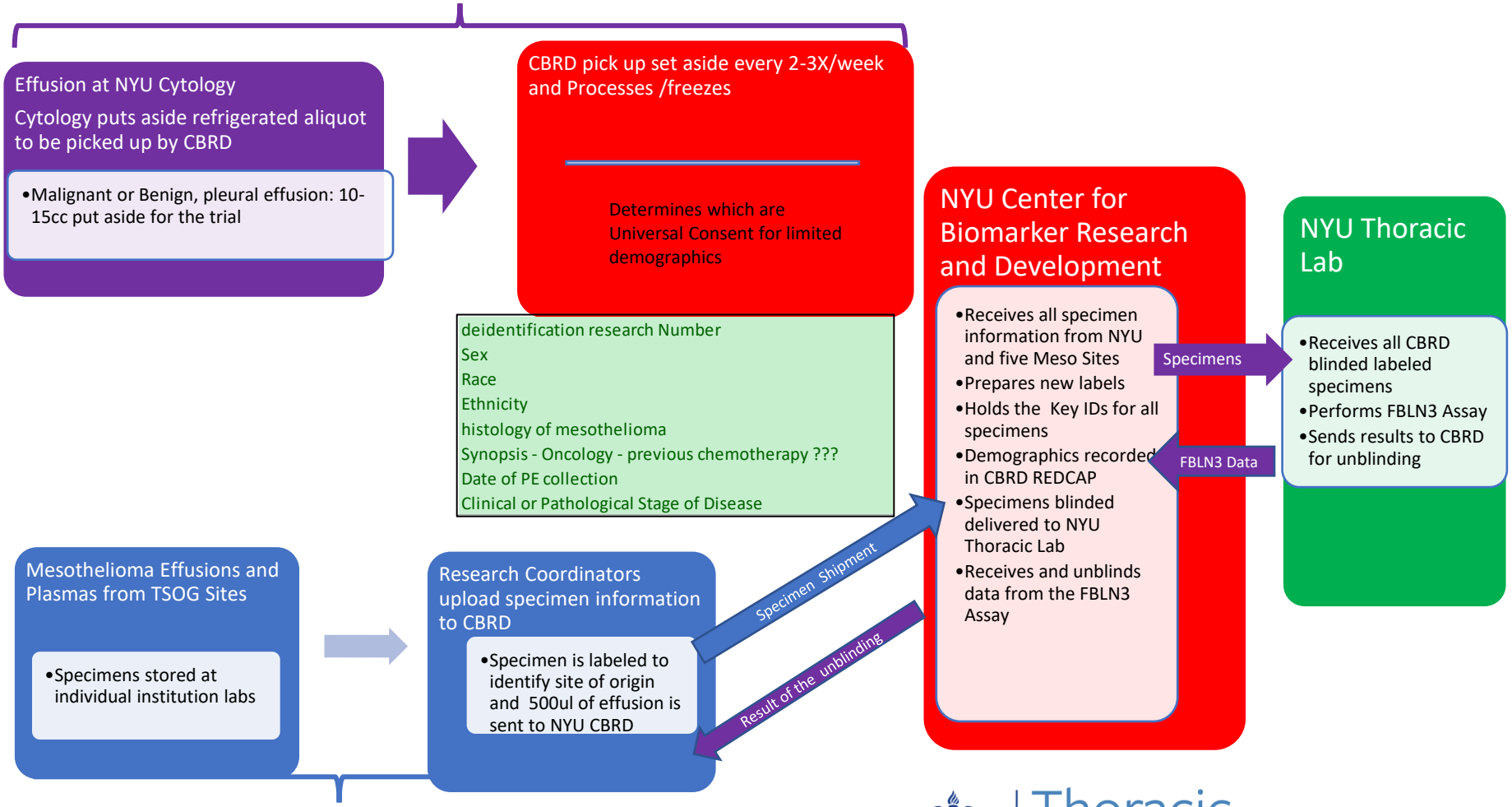
- **Hypothesis:** FBLN3 is differentially overexpressed in MPM compared to other malignancies that present as pleural effusions
- **Specific Aim 1:** Prospectively collect pleural effusion from newly diagnosed or treated patients with pleural effusions
  - **1.1** This will also establish a national reference collection of pleural effusion collected under standard SOPs known as the TSOG Effusion Archive
- **Specific Aim 2:** Measure FBLN3 levels in de-identified, blinded prospectively collected specimens using the mab428.2 ELISA in the NYU Thoracic Surgery Laboratory
- **Specific Aim 3:** Unblind levels of FBLN3, construct ROC curves for pleural effusion for MPM vs other
  - **3.1** Establish cut-offs if possible for FBLN3 level separation

CONTROL PLEURAL EFFUSION COLLECTION AT NYU



MESOTHELIOMA PLEURAL EFFUSION COLLECTIONS AT TSOG SITES

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Thoracic Surgery Oncology Group
AATS
A joint venture between AATS and Memorial Sloan Kettering Cancer Center

TSOG 104

Sites open to accrual: 6

Accrual as of February 2023: 451

Mesothelioma Samples:38

Control Samples: 413

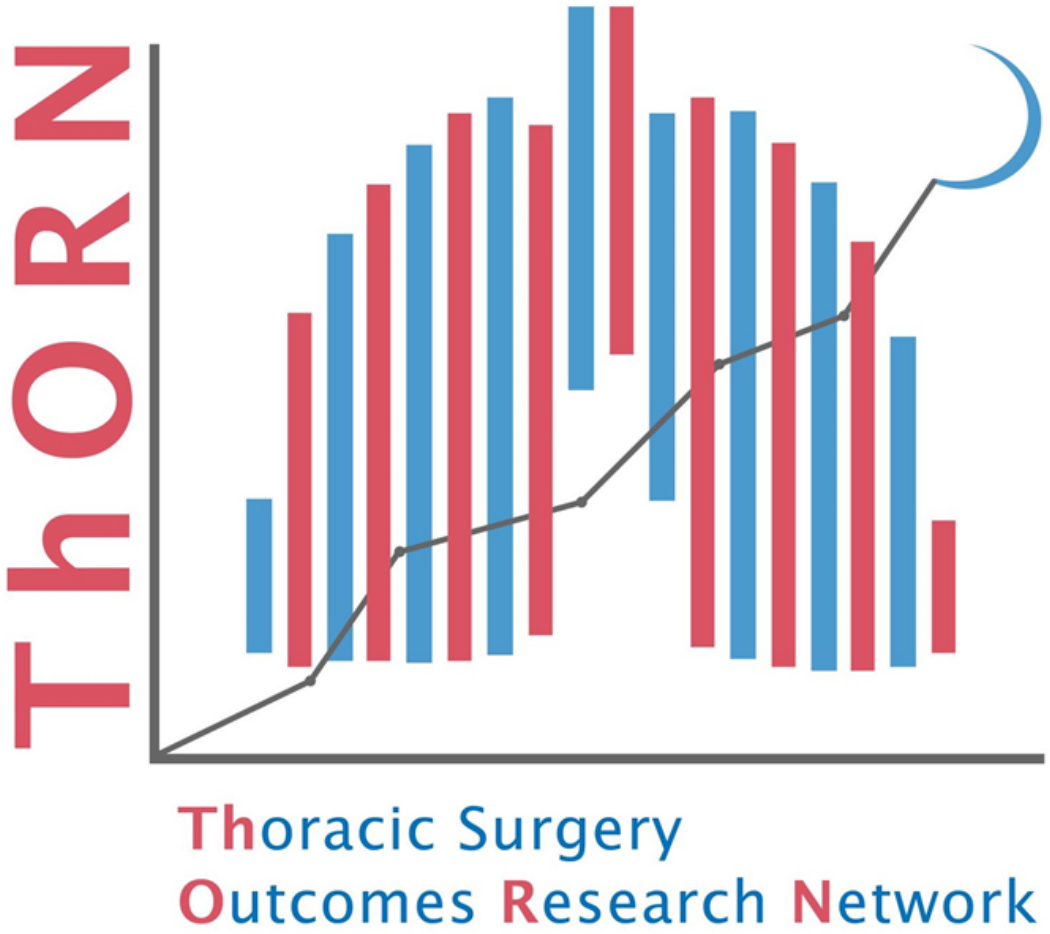
- Would like to accrue 50-60 mesotheliomas from TSOG centers.
- Once NYU has all of the mesothelioma pleural effusions from all the centers, and they are reblinded; NYU will run the specimens (all the controls and all the mesothelioma pleural effusions) for FBLN3 and have NYU CBRD interpret the final results.

AATS Thoracic Surgery Oncology Group

A joint venture between AATS and Memorial Sloan Kettering Cancer Center

Conclusions

- RFA for 3 new trials completed and trials now moving forward to open at PI sites, then across the TSOG network.
- TSOG 101 and 102 will reach accrual in 2023!!
- TSOG 103 trial to close – important lessons learned
- Concept sheets being prepared for 2 new registry studies
- TSOG collaboration with pharma a reality ... More to come
- Plans to engage NCI still immature and not ready for prime time
- Need champions at each site
- Much work to be done as we move into year 7 of TSOG



The Thoracic Surgery Outcomes Research Network (ThORN)

David Odell, MD MS

ThORN President

Associate Professor of Surgery and Director of Quality

Northwestern Canning Thoracic Institute

Disclosures

- 501c3 organization
- Pending collaboration with Genentech

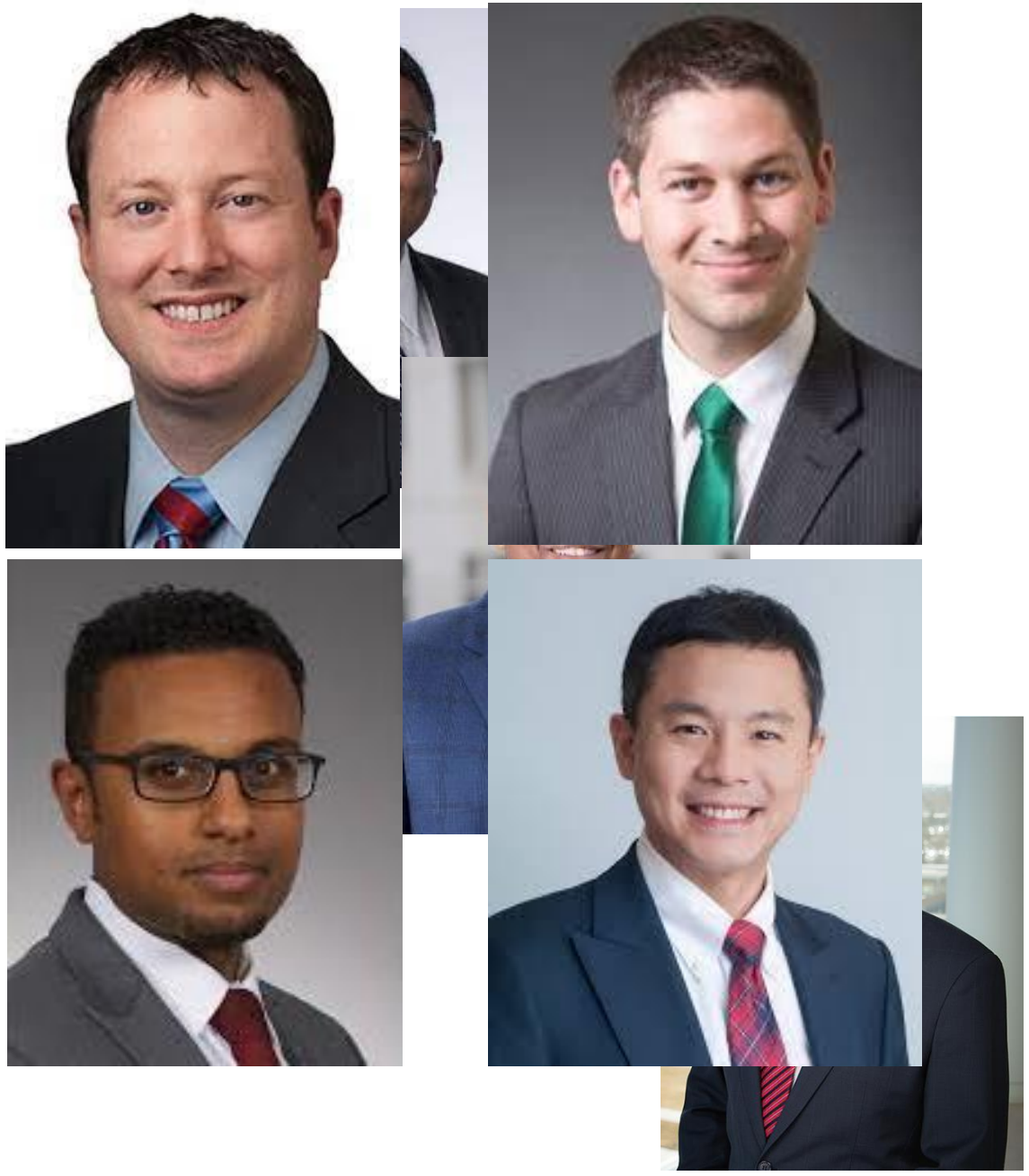
Who in ThORN anyway?

- Initially conceived at the Surgical Outcomes Club meeting in 2015
  - Need for HSR ‘home’
  - Opportunities to share data
  - Collaborative trials
- Started with a group of ~10 surgeons
- Now includes over 40 institutions in the US and Canada

SURGICAL OUTCOMES CLUB

Initial Years

- Very informal structure
- Monthly calls
  - Open forum
  - Study ideas
  - Collaborative HSR trials
- Ad hoc meetings at conferences



Current Structure

Monthly Meetings

- Tuesday evenings at 7 central
- Present project ideas
  - Feedback
  - Development
  - Recruitment

Annual Events

- ACS Clinical Congress
  - Social meeting
- STS
  - Business meeting
- AATS
  - Scientific meeting

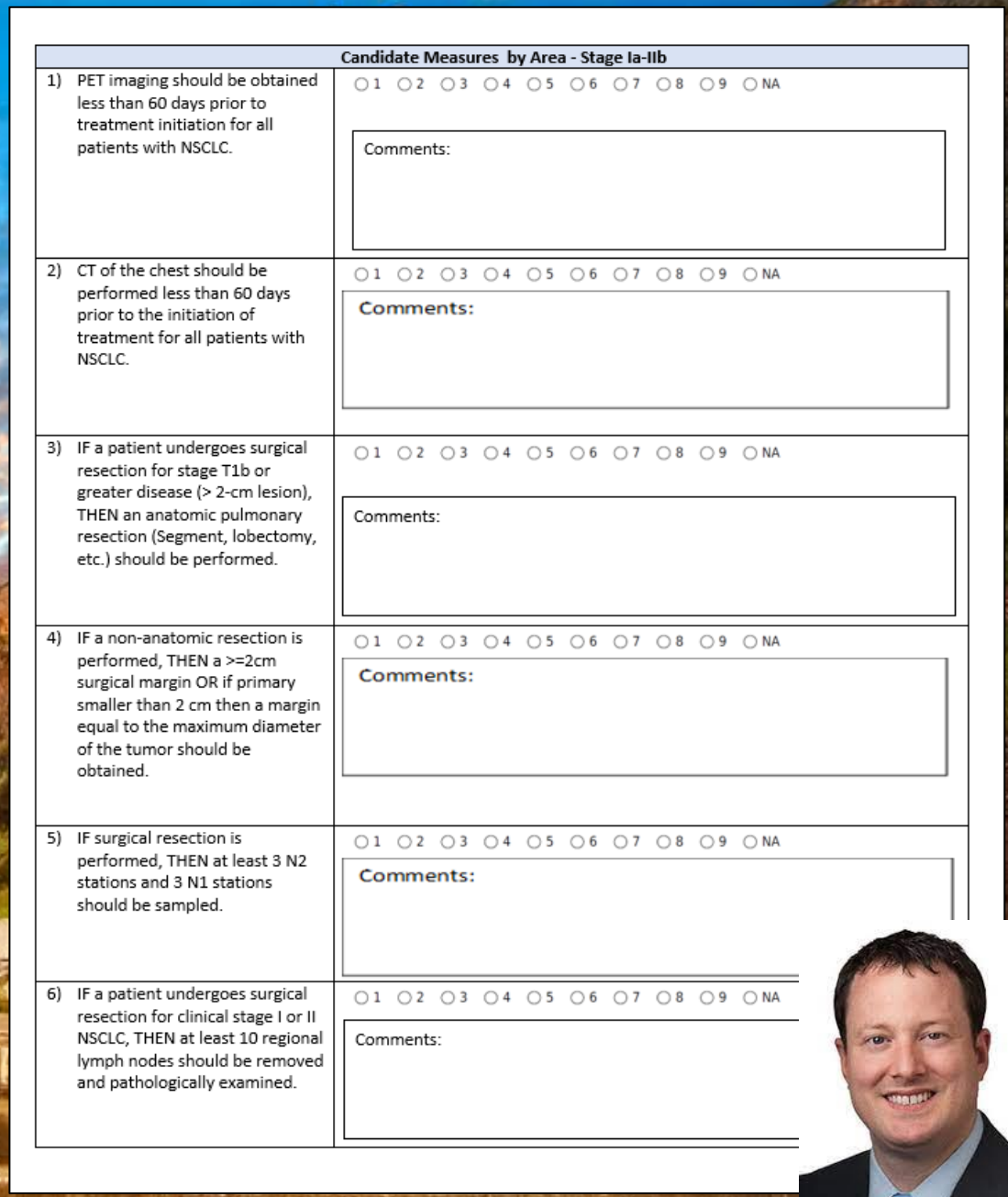
Not for Profit Status

- 2019 formally incorporated 501c3
- Allows ThORN to act as a central agency for funding
  - Supported NIH/VA MERIT grant submissions
  - Foundation sponsorship opportunities

Thorn Projects

Developing Measures

- Utilized a Modified Delphi process to define measures
  - 67 participants, 12 institutions
- 33 endorsed measures
  - 7 measures addressing patient evaluation
  - 11 measures for early stage disease
  - 5 for advanced disease
  - 3 for cancer surveillance
  - 2 for smoking cessation
  - 5 outcome measures
- Measure type
  - Structure - 2
  - Process - 26
  - Outcome - 5

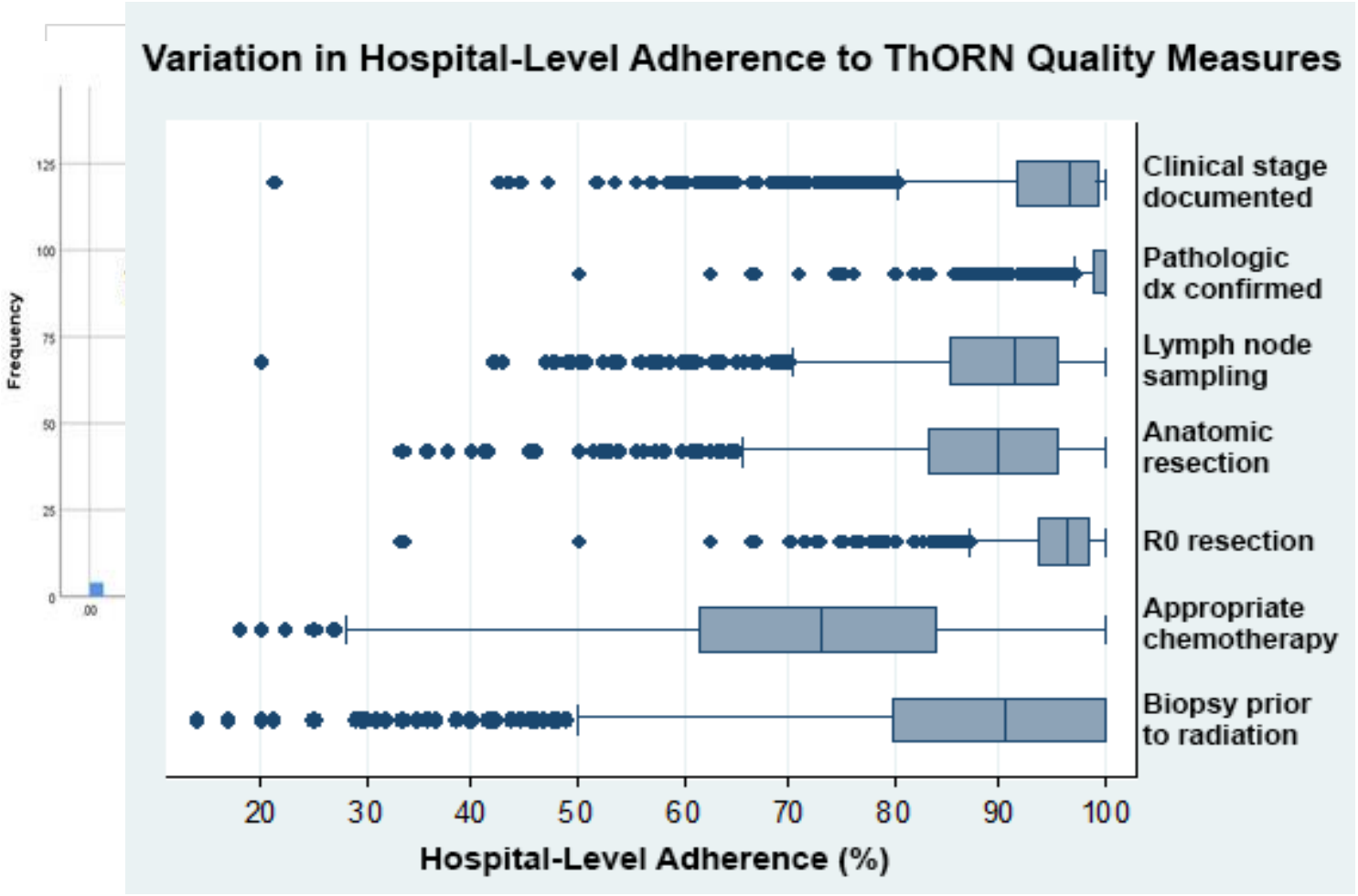


Candidate Measures by Area - Stage Ia-IIb	
1) PET imaging should be obtained less than 60 days prior to treatment initiation for all patients with NSCLC.	○1 ○2 ○3 ○4 ○5 ○6 ○7 ○8 ○9 ○NA Comments:
2) CT of the chest should be performed less than 60 days prior to the initiation of treatment for all patients with NSCLC.	○1 ○2 ○3 ○4 ○5 ○6 ○7 ○8 ○9 ○NA Comments:
3) IF a patient undergoes surgical resection for stage T1b or greater disease (> 2-cm lesion), THEN an anatomic pulmonary resection (Segment, lobectomy, etc.) should be performed.	○1 ○2 ○3 ○4 ○5 ○6 ○7 ○8 ○9 ○NA Comments:
4) IF a non-anatomic resection is performed, THEN a >=2cm surgical margin OR if primary smaller than 2 cm then a margin equal to the maximum diameter of the tumor should be obtained.	○1 ○2 ○3 ○4 ○5 ○6 ○7 ○8 ○9 ○NA Comments:
5) IF surgical resection is performed, THEN at least 3 N2 stations and 3 N1 stations should be sampled.	○1 ○2 ○3 ○4 ○5 ○6 ○7 ○8 ○9 ○NA Comments:
6) IF a patient undergoes surgical resection for clinical stage I or II NSCLC, THEN at least 10 regional lymph nodes should be removed and pathologically examined.	○1 ○2 ○3 ○4 ○5 ○6 ○7 ○8 ○9 ○NA Comments:

ThORN
Thoracic Surgery Outcomes Research Network

Odell, et al. Ann. Thor Surg 2019

Measuring Quality of Care



1) Odell, et al. JTCVS 2019,; 2) Khorfan *et al.* JTCVS 2019; 3) Odell *et al.* Ann Thor Surg 2020

Improving Hospital Ratings

U.S.News & WORLD REPORT HEALTH » Hospitals Doctors Senior Living Wellness Diets Medicare Drugs & Treatments

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Best Hospi … rt Surgery

Compare hospital ratings for car… op 50 that care for patients with challengin… devices such as pacemakers and defibril… other complex conditions such as end… ttack, Congestive Heart Failure (CHF), Heart Bypass, Aortic Valve Repla… gist, heart surgeon or vascular surgeon near you.

HOW WE RANK AND RATE HOSPITALS »

Following

Dr. David Tom Cooke
@DavidCookeMD Follows you

Husband, Dad, expert lung/esophagus cancer surgery, #MedEd. Chief, Division of General Thoracic Surgery @UCDavisSurgery. Co-founder #LCSM & @TOutcomes

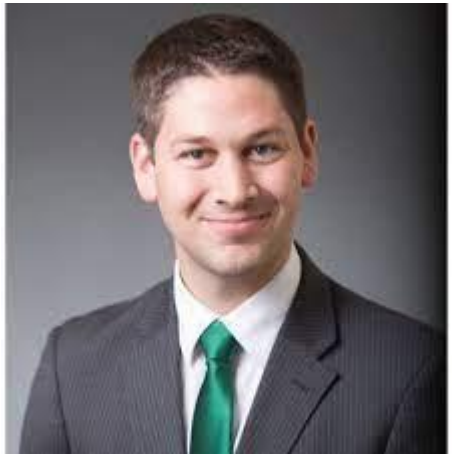
BEST HOSPITALS U.S.News & WORLD REPORT RANKINGS

ThORN Construct

- Cohort 1 – General Thoracic Surgeon
  - >1 Primary claim for pulmonary surgery
  - < 50% of total case load in Medicare part A claims consisting of cardiac surgery
- Cohort 2 – Cardiothoracic Surgeon
  - >1 Primary claim for pulmonary surgery
  - ≥ 50% of their case load in Medicare part A claims consisting of cardiac surgery
- Cohort 3 – Cardiac Surgeons
  - 0 Primary claims for pulmonary surgery
  - ≥ 50% of their case load in Medicare part A claims consisting of cardiac surgery

Agreement (Ag) Expected Agreement (Exp) Kappa P-value	**COHORT1**	**COHORT2**	**DISCLUS3_M**	**DISCLUS3_O**	**DISCLUS4_M**	**DISCLUS4_O**	**DISCLUS5**
COHORT1		Ag=44.84% Exp=59.39% Kappa= -0.36 P=1.000	Ag=90.81% Exp=67.65% Kappa=0.72 P<0.0001	Ag=93.85% Exp=69.36% Kappa=0.80 P<0.0001	Ag=99.41% Exp=65.56% Kappa=0.98 P<0.0001	Ag=99.41% Exp=65.56% Kappa=0.98 P<0.0001	Ag=99.37% Exp=65.58% Kappa=0.98 P<0.0001
COHORT2			Ag=47.96% Exp=60.43% Kappa=-0.32 P=1.000	Ag=51.00% Exp=61.44% Kappa=-0.27 P=1.000	Ag=44.25% Exp=59.19% Kappa=-0.37 P=1.000	Ag=44.25% Exp=59.19% Kappa=-0.37 P=1.000	Ag=44.29% Exp=59.20% Kappa=-0.37 P=1.000
DISCLUS3_M				Ag=96.96% Exp=71.50% Kappa=0.89 P<0.0001	Ag=91.40% Exp=67.27% Kappa=0.74 P<0.0001	Ag=91.40% Exp=67.27% Kappa=0.74 P<0.0001	Ag=91.44% Exp=67.30% Kappa=0.74 P<0.0001
DISCLUS3_O					Ag=93.25% Exp=68.95% Kappa=0.78 P<0.001	Ag=93.25% Exp=68.95% Kappa=0.78 P<0.0001	Ag=93.29% Exp=68.98% Kappa=0.78 P<0.0001
DISCLUS4_M						Ag=100.00% Exp=65.23% Kappa=1.000 P<0.0001	Ag=99.97% Exp=65.25% Kappa=1.00 P<0.001
DISCLUS4_O							Ag=99.97% Exp=65.25% Kappa=1.00 P<0.0001
DISCLUS5							

Social Determinants of Health



- Impact of food deserts on patient outcomes following esophagectomy
  - Collaboration of ThORN hospitals
- Featured paper at the STS this January
- Data only possible through this network

The Society of Thoracic Surgeons

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STS » Publications » STS News

- The Annals of Thoracic Surgery
- STS News
- STS National Database News
- STS Advocacy Monthly
- STS International Connection
- STS Trainee Connection
- Aspiring CT Surgeons Blog
- Career Development Blog
- In the News - A Surgeon's View
- Videos
- Podcast Episodes

Esophageal Surgeons Urge Added Intervention for Patients with Cancer Who Live in Food Deserts

Investigators will discuss the real—yet easily identified—risk that living in a food desert may have on patients recovering from esophagectomy on Day 1 of STS 2023.

Mortality risks for patients with colon and breast cancers who live in food deserts have been reported in recent years as part of a large administrative database review. On Saturday, January 21 at 1:25 p.m. PT, surgeons from six high-volume medical centers will present the first multi-institutional research that identifies patients who undergo tri-modality therapy for esophageal cancer have increased risk of readmission following surgery.

Joseph Phillips, MD, from Dartmouth Hitchcock Medical Center in Lebanon, New Hampshire, will present the study exploring the association between food deserts and patient re-hospitalizations after esophagectomy.

In this retrospective research, surgeons reviewed records from a diverse US patient population that underwent neoadjuvant chemoradiation followed by esophagectomy. Of 425 patients included, 73 lived in a food desert, which are areas where access to nutritious foods is

Methodological Expertise

- Group has a broad experience in HSR methods
  - Database expertise
  - Analytic methods
  - Qualitative research
  - Implementation science
  - Healthcare ecponomics
- Share expertise internally
- Publish for the community

ADULT

Administrative and clinical databases: General thoracic surgery perspective on approaches and pitfalls

Check for updates

Biniam Kidane, MD, MSc,[a,b,c] Elliot Wakeam, MD, MPH,[d] Robert A. Meguid, MD, MPH,[e,f] and David D. Odell, MD, MMSc,[g] for Thoracic Surgery Outcomes Research Network (ThORN) Inc

Database research has become so common that it has essentially become the lingua franca of clinical research. Since the vast majority of studies using databases are observational in nature, various statistical methods are employed to control for the inherent biases in such nonrandomized data. However, even the most sophisticated causal inference technique cannot overcome limitations that are inherent to the nature of the data and how they are collected. Most databases are created with a particular purpose, which leads to limitations in the ways they can be used for research. Organizations and professional societies have created databases for national and international benchmarking and research, the archetypical example being the Society of Thoracic Surgeons (STS) cardiac surgery database, which was subsequently expanded to include general thoracic surgery and pediatric cardiac surgery. These databases all have some element of "pay to play"; they depend on subscription fees paid by the institutions that comprise the membership and contribute data. As such, they cannot be considered population-based, as they only represent the cases contributed to them. However, in general, they are clinical, outcomes-focused, high-quality, and reliable and in certain instances can be used for high-quality policy, clinical epidemiology, and quality improvement work.

Thus, we posit that databases are often created to serve 1 of 2 fundamental functions: (1) research to answer questions and (2) benchmarking/quality. In this paper, we discuss various examples of different types of big clinical and administrative databases; more importantly, we discuss how the construction and nature of said databases affects the extent to which they can accomplish these fundamental functions. This paper is meant as a companion piece to that of Subramanian and colleagues, which focused on introducing the concept of clinical versus administrative data and described some of the commonly used databases. Thus, readers should refer to that paper for descriptions of commonly used databases such as National Inpatient Sample, Surveillance, Epidemiology, and End Results, and the National Cancer Database.[1]

Left: Biniam Kidane, MD, MSc *(top)*, Robert A. Meguid, MD, MPH; *right:* Elliot Wakeam, MD, MPH *(top)*, David D. Odell, MD, MMSc

CENTRAL MESSAGE

Databases are created to serve 1 of 2 fundamental functions: (1) research and (2) benchmarking/quality. Their construction and nature affects the extent to which they can accomplish these functions.

This Invited Expert Opinion provides a perspective on the following paper: *J Am Coll Surg.* 2009 Nov;209(5):551-6. https://doi.org/10.1016/j.jamcollsurg.2009.08.008; *J Am Coll Surg.* 2016 Oct;223(4):551-557.e4. https://doi.org/10.1016/j.jamcollsurg.2016.06.393.

See Commentaries on pages 1154 and 1155.

From the [a]Section of Thoracic Surgery, Department of Surgery, Rady Faculty of Health Sciences, and [b]Department of Community Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada; [c]Research Institute in Oncology and Hematology, Cancer Care Manitoba, Winnipeg, Manitoba, Canada; [d]Section of Thoracic Surgery, Department of Surgery, University of Michigan, Ann Arbor, Mich; [e]Surgical Outcomes and Applied Research Program, Department of Surgery, and [f]Adult and Child Center for Health Outcomes Research and Delivery Science, University of Colorado School of Medicine, Aurora, Colo; and [g]Surgical Outcomes and Quality Improvement Center, Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, Ill.

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0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2021.03.057

ThORN-Sponsored STS Session

‘Reaching for the Stars’

- Focus on quality measurement and ratings systems
  - How ratings are constructed
  - What stakeholders value
  - How to use data to influence change
  - How to positively interact with ratings agencies

Looking to the Stars: Making Sense of Hospital Ratings

Saturday, January 21, 2023 11:00 AM – 12:00 PM PT

Location: San Diego Convention Center, Room 32AB

Moderator(s)

Joseph Phillips, MD

Assistant Professor of Surgery
Dartmouth-Hitchcock Medical Center
Lebanon, New Hampshire, United States

Disclosure(s): No financial relationships to disclose

David Cooke, MD

Professor & Chief, Division of General Thoracic Surgery
University of California, Davis Medical Center
Sacramento, California, United States

Disclosure(s): DaVinci Intuitive Surgical: Food and travel costs (Ongoing)

David Odell, MD, MMSc

Canning Thoracic Institute, Department of Surgery, Northwestern University, Feinberg School of Medicine
Chicago, Illinois, United States

Disclosure(s): Astra Zeneca: Consultant (Ongoing), Research Grant (includes principal investigator, collaborator or consultant and pending grants as well as grants already received) (Ongoing)

Disclosure(s):

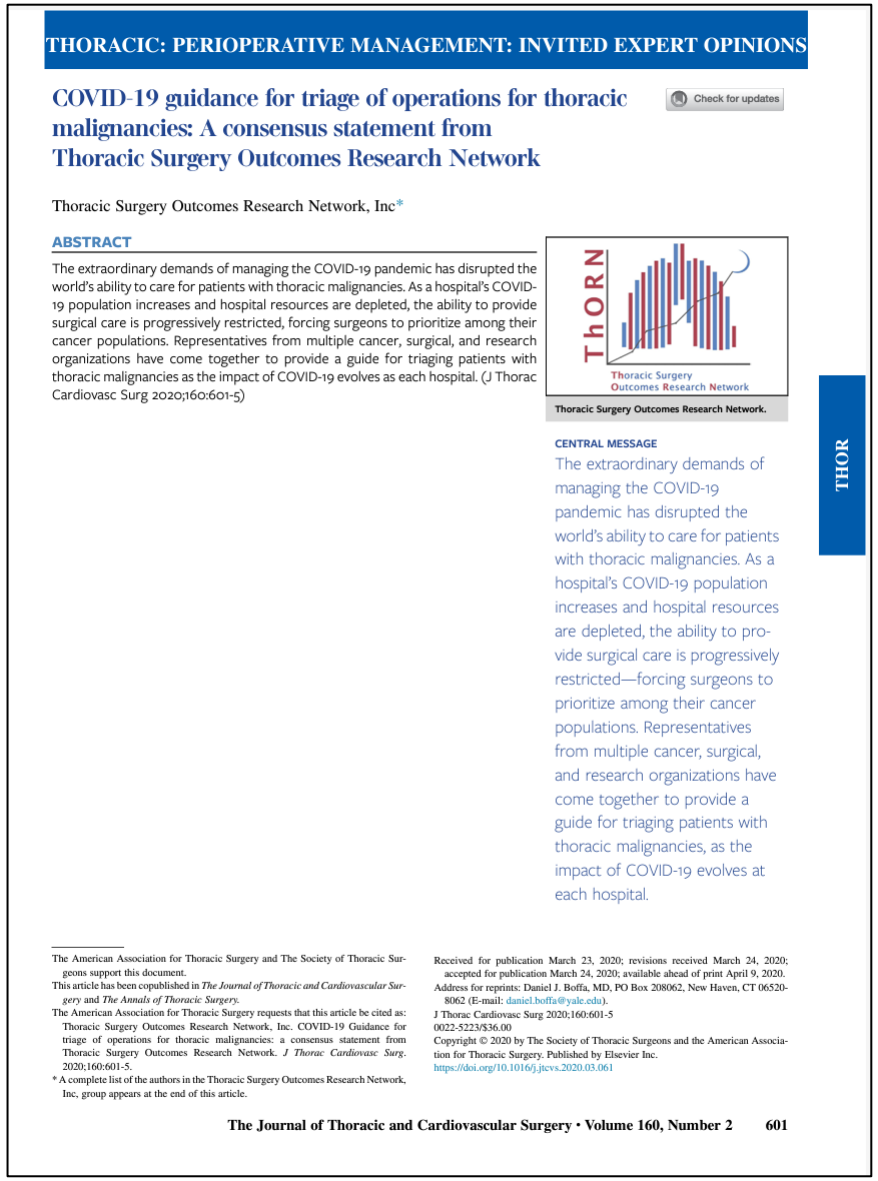
Joseph D. Phillips, MD: No financial relationships to disclose

David Tom Cooke, MD: DaVinci Intuitive Surgical: Food and travel costs (Ongoing)

David D. Odell, MD, MMSc: Astra Zeneca: Consultant (Ongoing), Research Grant (includes principal investigator, collaborator or consultant and pending grants as well as grants already received) (Ongoing)

Rapid Consensus

- Group of people who can rapidly adapt and collaborate
  - Meet new challenges for the specialty collaboratively
- Developed initial COVID triage guidelines for thoracic operations
  - ACS
  - STS
  - AATS



THORACIC: PERIOPERATIVE MANAGEMENT: INVITED EXPERT OPINIONS

COVID-19 guidance for triage of operations for thoracic malignancies: A consensus statement from Thoracic Surgery Outcomes Research Network

Check for updates

Thoracic Surgery Outcomes Research Network, Inc*

ABSTRACT

The extraordinary demands of managing the COVID-19 pandemic has disrupted the world's ability to care for patients with thoracic malignancies. As a hospital's COVID-19 population increases and hospital resources are depleted, the ability to provide surgical care is progressively restricted, forcing surgeons to prioritize among their cancer populations. Representatives from multiple cancer, surgical, and research organizations have come together to provide a guide for triaging patients with thoracic malignancies as the impact of COVID-19 evolves as each hospital. (J Thorac Cardiovasc Surg 2020;160:601-5)

ThORN
Thoracic Surgery Outcomes Research Network

Thoracic Surgery Outcomes Research Network.

CENTRAL MESSAGE

The extraordinary demands of managing the COVID-19 pandemic has disrupted the world's ability to care for patients with thoracic malignancies. As a hospital's COVID-19 population increases and hospital resources are depleted, the ability to provide surgical care is progressively restricted—forcing surgeons to prioritize among their cancer populations. Representatives from multiple cancer, surgical, and research organizations have come together to provide a guide for triaging patients with thoracic malignancies, as the impact of COVID-19 evolves at each hospital.

THOR

The American Association for Thoracic Surgery and The Society of Thoracic Surgeons support this document.
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The American Association for Thoracic Surgery requests that this article be cited as: Thoracic Surgery Outcomes Research Network, Inc. COVID-19 Guidance for triage of operations for thoracic malignancies: a consensus statement from Thoracic Surgery Outcomes Research Network. *J Thorac Cardiovasc Surg*. 2020;160:601-5.
* A complete list of the authors in the Thoracic Surgery Outcomes Research Network, Inc, group appears at the end of this article.

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Address for reprints: Daniel J. Boffa, MD, PO Box 208062, New Haven, CT 06520-8062 (E-mail: daniel.boffa@yale.edu).
J Thorac Cardiovasc Surg 2020;160:601-5
0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2020.03.061

Soon to Open: Multisite Funded Trial

- National Study
- Assess real-world use of adjuvant immunotherapy following resection
  - Chart review
  - Pathologic testing
  - Patient follow-up
  - Regimen completion
- Funding from Genentech to support

Please get involved!

- Meetings open to anyone interested
  - Next meeting Tuesday 3/14 - 7 central
- Membership required to participate in ThORN sponsored projects
  - $150 membership ‘donation’ for surgeons
    - $25 per person for trainees
  - $500 Institutional Membership
- dodell@northwestern.edu