



Lung-MAP Update Forum

SWOG FALL MEETING
OCTOBER 9, 2026



Agenda

- Welcome & Introductions– *Karen Reckamp, MD & Saiama Waqar, MD*
- Lung-MAP Accomplishments – *Karen Reckamp, MD*
- Lung-MAP Retreat Summary– *Saiama Waqar, MD*
- *S1800E Update– Saiama Waqar, MD*
- Manuscript and Accrual Updates– *Mary W. Redman, PhD*
- Presentation: Association Between Grade of irAEs and Outcomes – *Christina Baik, MD*
- *S1900G Update– Sarah Goldberg, MD*
- *S1900J Update– Christian Rolfo, MD*
- *S1900K Update– Paul K. Paik, MD*
- *S1900P Update– Paul K. Paik, MD*
- *S1900N Update– John Wrangle, MD*
- Q&A– *Karen Reckamp, MD*
- *S1900Q Update– Konstantin Dragnev, MD*
- Q&A– *Karen Reckamp, MD & Mary W. Redman, PhD*

There will be
two Q & A
sessions during the
Update Forum.

Welcome

KAREN RECKAMP, MD, MS

CHAIR, LUNG-MAP (SWOG)

CEDARS-SINAI MEDICAL CENTER
DEPT OF MEDICINE

SAIAMA WAQAR, MD, MSCI

VICE CHAIR, LUNG-MAP (NRG)

WASHINGTON UNIVERSITY SCHOOL OF
MEDICINE IN ST. LOUIS

SWOG Fall Meeting—Lung-MAP Update October 9, 2026



- Lung Master Protocol
- (LUNGMAP)

 LUNG-MAP Accomplishments

Disclosures

- **Consultant with honoraria to self:** Amgen, AstraZeneca, Daiichi Sankyo, Genentech, GlaxoSmithKline, Johnson & Johnson, Lilly, Novocure, Novartis, Pfizer, TORL.
- **Research funding to institution:** Avenzo; Genentech; BNT; Daiichi Sankyo; Johnson & Johnson.



Current Scientific Leadership

October 2024-2027



Lung-MAP Chairs:

Karen Reckamp (SWOG) CHAIR
Saiana Waqar (NRG) VICE CHAIR
Mary Redman (SWOG) STATISTICS CHAIR

Scientific Committees:



Drug Selection

Konstantin Dragnev (Alliance)



Scientific and Sub-study Leadership

Corey Langer (NRG)

Lung-MAP Statistics and Data Management

Mary Redman (SWOG)



Translational Medicine/Scientific

Joel Neal (ECOG-ACRIN)



Lung-MAP Champions:



Alliance

Konstantin Dragnev
Helen Ross



ECOG-ACRIN

Joel Neal
Ticiana Leal

NRG

Martin Edelman
Anjali Rohatgi



SWOG

David Gandara
John Wrangle



Past Chair: Hossein Borghaei (ECOG-ACRIN) 2022-2024

Past Vice Chair: Jyoti Patel (Alliance) 2020-2022, Karen Reckamp (SWOG) 2022-2024

Chair Emeritus/Special Advisor: Roy Herbst (SWOG), Vice Chair 2013-2019, Chair: 2019-2022

Founding Chair: Vassilki Papadimitrakopoulou (SWOG), Chair: 2013-2019



NCTN Lung/Thoracic Chairs

Alliance:

Thomas Stinchcombe

ECOG-ACRIN:

Julie Brahmer

NRG:

Kristin Higgins

SWOG:

Jhanelle Gray



Mission and Vision Statements



Mission

Lung-MAP aims to transform metastatic NSCLC treatment through precision medicine, tailoring therapies to each tumor's genetic makeup. Our mission is to enhance patient outcomes by partnering with key stakeholders to expedite innovative research and clinical application, while leveraging patient data to inform future advancements.



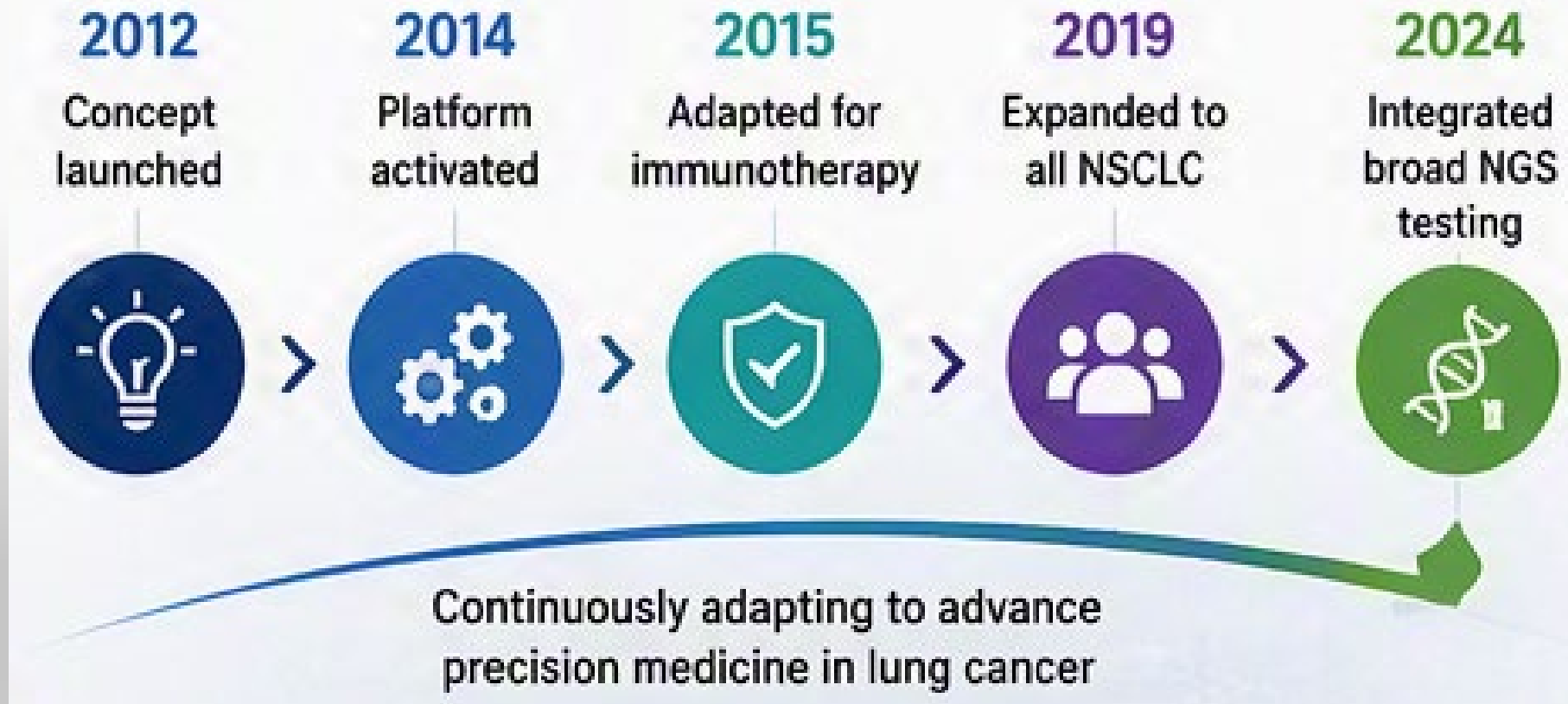
Vision

We envision a future where personalized care for metastatic NSCLC, rooted in precision medicine and the latest research, is accessible to all. Our goal is to continually foster a collaborative environment that fosters breakthroughs, making lung cancer a manageable condition while eliminating disparities in care and treatment outcomes.



LUNG-MAP

Lung-MAP Milestones



LUNG-MAP

Lung-MAP Strategic Priorities

1

INCREASE ACCRUAL



- Remove barriers
- Improve site support
- Broaden access

2

ADDRESS SCIENTIFIC GAPS



- New biomarker opportunities
- Resistance mechanisms
- Novel trial concepts

3

BUILD THE NEXT GENERATION



- Junior investigator development
- Translational expansion
- Cross-group engagement

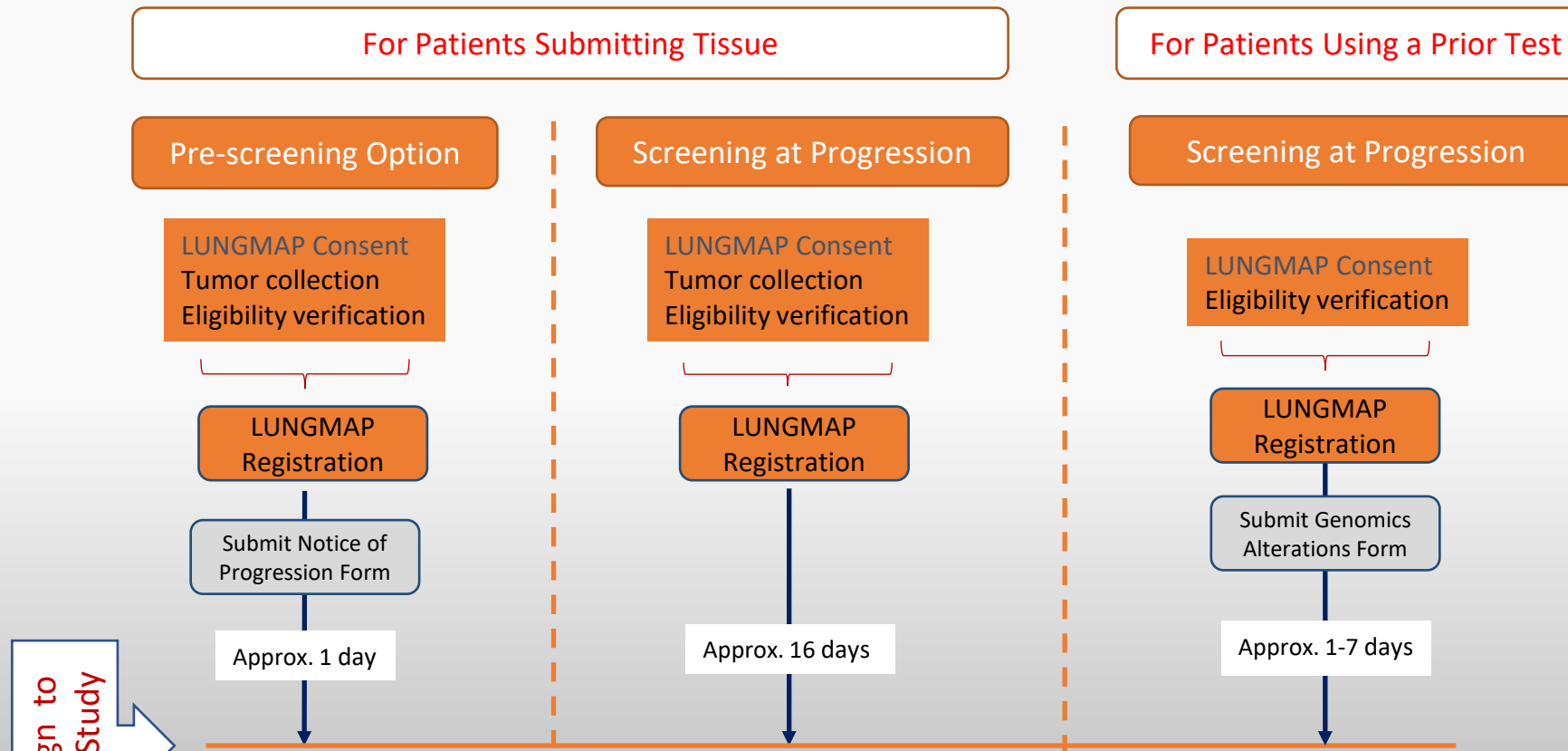


LUNG-MAP

LUNGMAP Objectives

- **Title:** A Master Protocol to Evaluate Biomarker-Driven Therapies and Immunotherapies in Previously-Treated Non-Small Cell Lung Cancer (Lung-MAP Screening Study)
- **Primary Objectives**
 - Determine eligibility for participation in the biomarker-driven and non-match sub-studies included within the Lung-MAP umbrella protocol, by testing participant specimens or collecting results of prior testing by protocol-approved biomarker assays.
- **Secondary Objectives**
 - Screening Success Rate Objective
 - Evaluate the percentage of participants assigned to a sub-study that register to a sub-study.
 - Translational Medicine Objective
 - Summarize the prevalence of biomarkers either reported through previously completed tests or determined sub-study biomarker testing.

LUNGMAP Screening and Sub-study Assignment

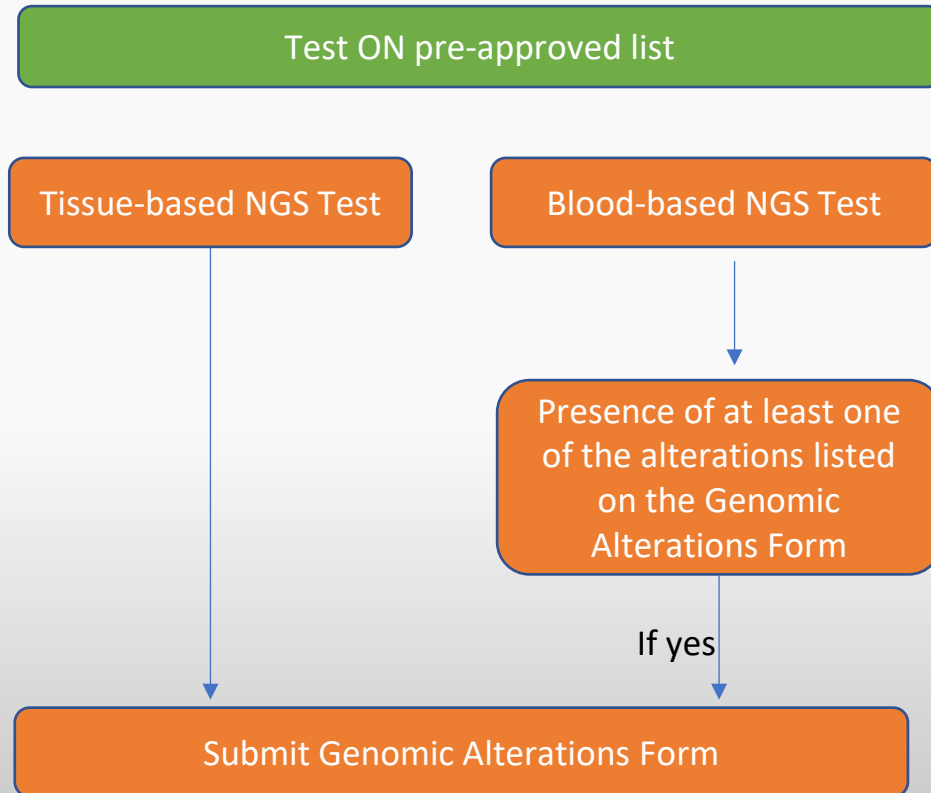


Notes:

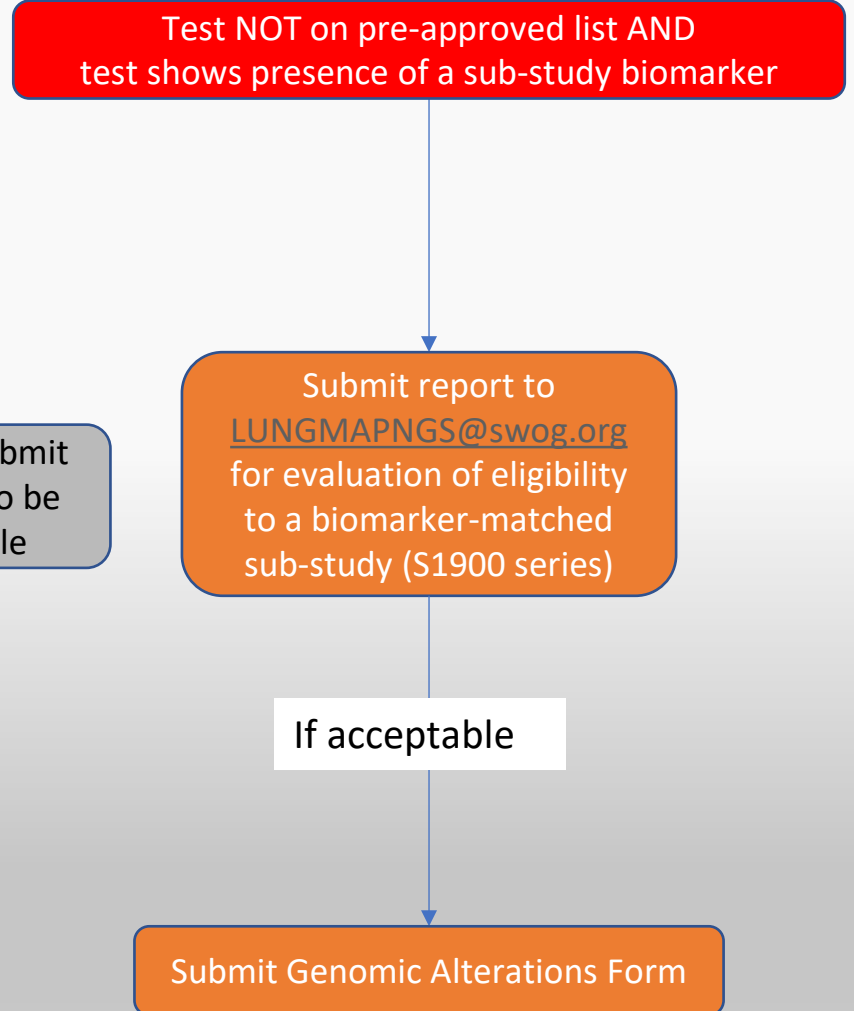
- Use of existing lab tests/facilities will increase patient identification as well as save time.
- There is a list of prequalified tests.
- Processes include real-time qualification of new CLIA tests not on pre-approved list.
- If a patient is not eligible for their assigned sub-study, they can submit a form to request a new sub-study assignment.
- Patients may participate in additional sub-studies if/when they have progressive disease on a sub-study.

- Patients submitting tissue can be pre-screened while on treatment or screened upon progression.
- Patients using previously completed tests may only enroll for screening upon progression.

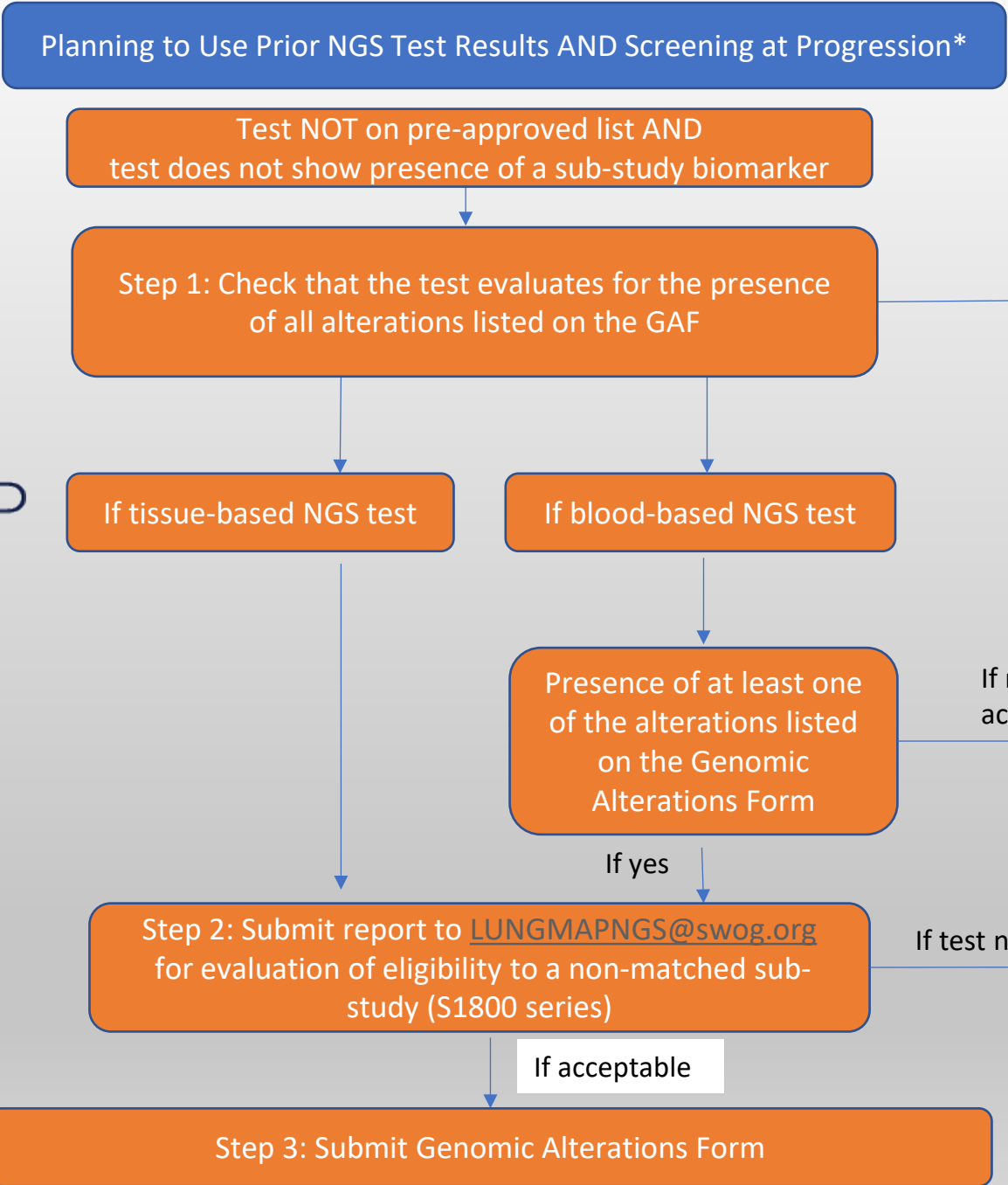
Planning to Use Prior NGS Test Results AND Screening at Progression*



Planning to Use Prior NGS Test Results AND Screening at Progression*



*Pre-screening is not an option if using a prior test



*Pre-screening is not an option if using a prior test

Current Lung-MAP Schema

- All NSCLC (Actively Accruing)
- All NSCLC (In Development)
- Squamous-Cell only (Actively Accruing)
- Squamous-Cell only (In Development)
- Non-Squamous only (Actively Accruing)
- Non-Squamous only (In Development)

**Previously-Treated
Stage IV/Recurrent NSCLC**

**Biomarker-Driven
Sub-Studies**

**Non-match
Sub-Studies**

Targeted therapy-Naive

TKI-Treated/Resistant

**ICI Acquired
Resistance¹**

Closed/
Completed
10 studies

Open 9/27/24

Open 12/18/23

Estimated: Q3 2027⁴

Closed/
Completed
1 study

Open 4/3/23

Open 8/3/26

Estimated: Q3/Q4 2027⁴

ICI Naive:
2 Closed

ICI Exposed:
2 Closed

Open 4/28/25

**S1900J
Phase II
MET
amplification**

**S1900K
Phase II
MET Exon
14 skipping**

**S1900P
Phase II
NFE2L2, KEAP1 or
PI3K pathway**

**S1900G
Phase II
EGFR mutation
w/ acquired MET
amplification at
resistance**

**S1900N
Phase II
Actionable genomic
alterations and TKI
Relapsed/refractory**

**S1900Q
Phase II
HER2 Dysregulated
Relapsed/Refractory**

**S1800E
Phase II/III**

Amivantamab
Hyaluronidase

Tepotinib
+/-
Ramucirumab

mTOR inhibitor +
taxane +/-
PI3K Inhibitor

INC280 (Capmatinib)
+ Osimertinib
+/-
Ramucirumab

Sacituzumab
Govitecan vs.
Ivonescimab vs.
both drugs combined

HER-2 TKI +
HER2-directed
antibody-drug
conjugate

Docetaxel +
Ramucirumab
+/-
Cemiplimab

¹ Acquired Resistance is defined as progression at least ($\geq$) 84 days from initiation of the most recent line of anti-PD-1/PD-L1 and best response of stable disease, partial response, or complete response.

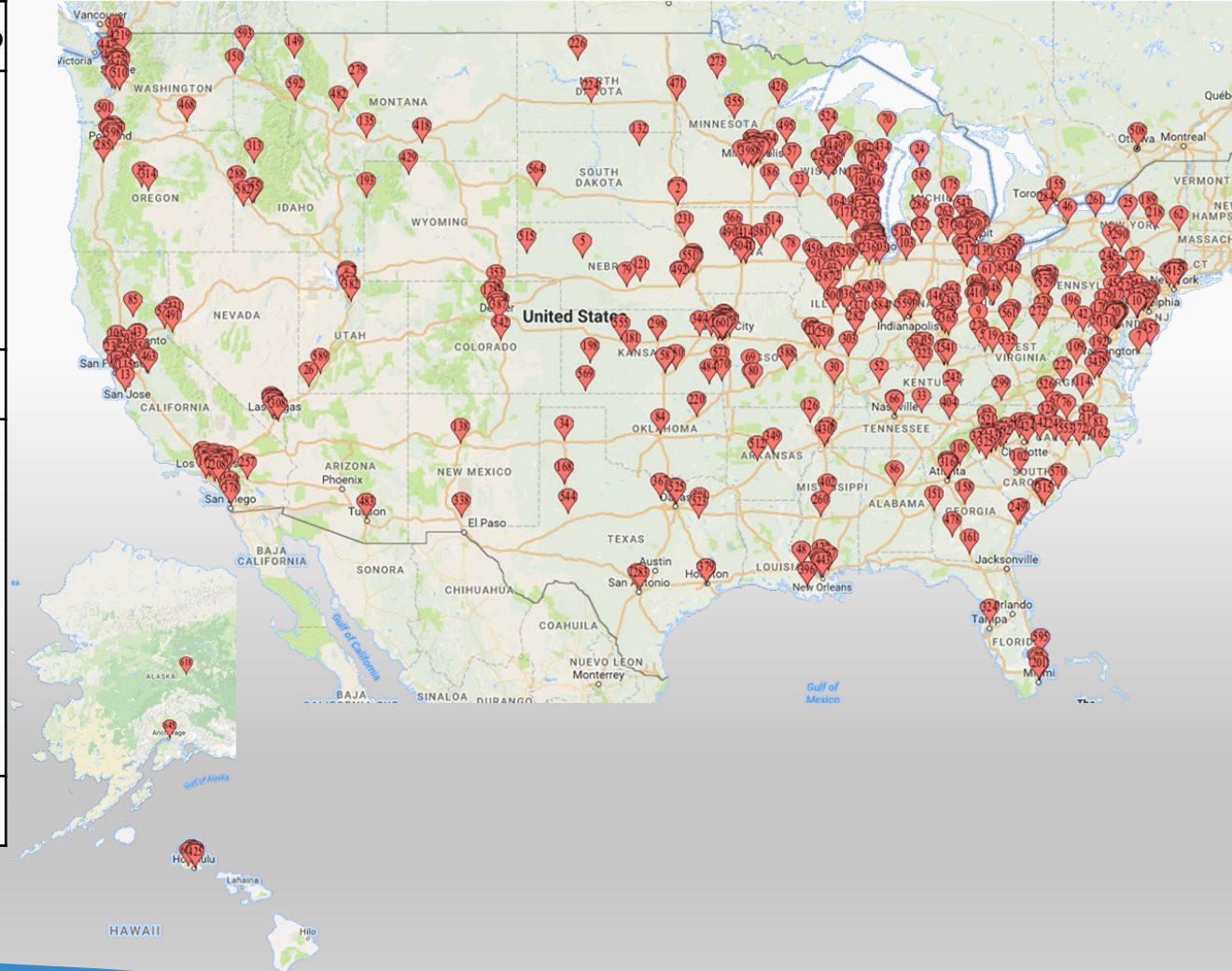
² Approved by the Lung-MAP Drug Selection Committee

³ Includes both Acquired and Primary Resistant Groups

⁴ Estimated activation

Where are we now?

As of 9/14/26	Total	S1400	LUNGMAP
Screening Registrations	5968	1864	4104
Screened at PD	2685	1127	1558
Pre-screened	3257	737	2520
Treatment-naïve	26	na	26
ctDNA submissions	315	na	315
Sub-study Assignments	3749	1484	2265
Among Screened at PD	2323	996	1327
Among Pre-screened	1268	414	854
Additional Assignments after PD on a Sub-study	132	74	58
Sub-study Registrations	1361	690	671



Benefits of Lung-MAP

Some of
Lung-MAP's
industry partners
have included ...

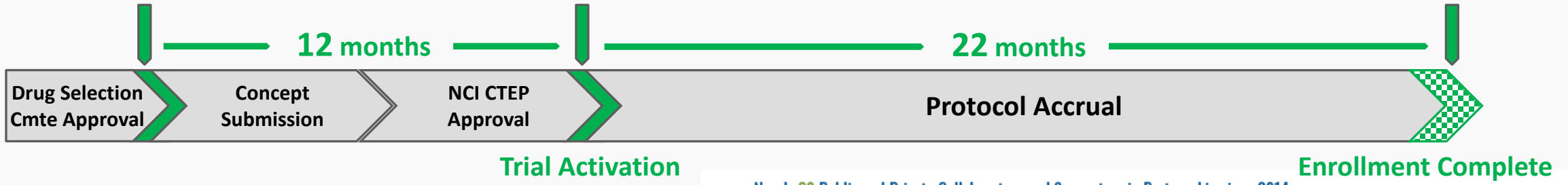


- Facilitates testing novel agents or combinations in non-matched and matched biomarker study designs within NSCLC.
- Offers a range of study platform options.
- Collects biospecimen resources and screening data that can be used in exploratory studies.
- Offers access to leading lung cancer researchers.
- Facilitates interactions with the FDA.
- Provides drug distribution to participating sites that is managed through the NCI.
- Provides a well-organized trial development and project management system, utilizing SWOG Operations, SWOG Statistics and Data Management Center, and FNIH, to create a streamlined process for study activation.
- Provides partnership with Friends of Cancer Research who engages with advocacy organizations, offers critical patient insight on major trial decisions, and manages communications to patient advocate partners and the lung cancer community.



Lung-MAP Impact

Accelerated Timelines → Example: Lung-MAP S1800A



Nearly 30 Public and Private Collaborators and Supporters in Partnership since 2014

13

PARTNERING PRECISION MEDICINE DIAGNOSTIC COMPANIES AND LEADING PHARMACEUTICAL COMPANIES

15

INVESTIGATIONAL DRUGS OR DRUG COMBINATIONS TESTED

16 Initiated | 14 Completed

SUB-STUDIES CONDUCTED

10

AGENTS AGAINST SPECIFIC TUMOR MUTATIONS/GENETIC SIGNATURES TESTED IN NSCLC

12

MONTH AVERAGE SUB-STUDY STAND UP TIME FROM APPROVAL BY THE LUNG-MAP DRUG SELECTION COMMITTEE TO ACTIVATION

22

MONTH AVERAGE TIME TO TARGET ACCRUAL COMPLETION FOR ~80 PERSON STUDY, DRIVEN BY BIOMARKER PREVALENCE

7

SUPPORTING PATIENT ADVOCACY GROUPS

~4,250 | ~650 Per Year

PATIENTS SCREENED

~2,750

PATIENTS ELIGIBLE FOR A TREATMENT IN A WELL-DESIGNED TRIAL

~1,000 | 150+ Per Year

PATIENTS TREATED WITH CUTTING-EDGE THERAPIES

300+

ALTERED GENES INTERROGATED IN EACH PATIENT'S TUMOR

24%

UNDERSERVED MINORITY PARTICIPANTS ENROLLED

8

ORGANIZATIONS, INCLUDING NCI AND FDA, WORKING TOGETHER TO CONDUCT AND OVERSEE THE STUDY

10,000+

ANNOTATED SPECIMENS IN A TISSUE BANK TO ALLOW DEEPER SCIENTIFIC STUDIES TO INFLUENCE FUTURE TRIALS

35+

PUBLICATIONS AND ABSTRACTS

Additional Benefits of Lung-MAP

SHARED COSTS AND RISKS OF TESTING THERAPEUTICS FOR COMPANIES
FOSTERING DRUG COMBINATION COLLABORATIONS BETWEEN COMPANIES
ACCELERATED TIMEFRAMES FOR EVALUATION OF TREATMENT EFFICACY DUE TO THE LARGE NETWORK
STRONG SUPPORT FROM THE FDA WITH ABILITY FOR STUDIES TO HAVE REGULATORY INTENT



LUNG-MAP

Lung-MAP Patient Testimonial

I said ‘absolutely!’ If I can go on the trial and help someone else, I would gladly do it ... because they are fighting – excuse my language – a hell of a battle.

~ Austin A., on his response when asked to join Lung-MAP



The Future of Lung-MAP



The future of Lung-MAP depends on expanding therapeutic opportunities, addressing underrepresented populations, and cultivating the next generation of investigators.

SWOG Fall Meeting—Lung-MAP Update October 9, 2026



- Lung Master Protocol
- (LUNGMAP)

**Lung-MAP Strategic Initiative
Retreat at ASCO 2026**



LUNG-MAP

Disclosures for Dr. Waqar

- **Advisory Board**: Astra Zeneca, Pfizer, Amgen, Daiichi Sankyo, Boehringer Ingelheim, Gilead, Janssen, Adcendo, Merck, Nuvalent, EMD Serono
- **Consulting**: Boehringer Ingelheim, Astra Zeneca, Gilead, CurioScience
- **Research Grant Support**: SWOG Clinical trial partnership, Astra Zeneca, Genentech, Gilead, Abbvie, Advenchen, Daiichi Sankyo, Nuvalent, Elevation Oncology, Ribon, Janssen, Turning Point, Immunomedics, Angiex, ADC Therapeutics, Astellas, Verastem, Abbvie

Lung-MAP Strategic Initiative Retreat (5/29/26) at ASCO 2026

8:00 AM	Welcome and Introductions	Karen Reckamp, MD
8:05 AM	Lung-MAP Update and Overview	Mary Redman, PhD
8:15 AM	Updates Since Last Retreat	Saiama Waqar, MD
8:25 AM	Lessons Learned from Engaging with Sites on Accrual & Q/A	Lucy Gansauer, MSN
8:40 AM	CTEP Priorities and Interactions with Lung-MAP & Q/A	Shakun Malik, MD



NCI Strategic Vision for Clinical Trials: 2030 and Beyond

Develop flexible, faster, simpler, less expensive, high-impact clinical trials that seamlessly integrate with clinical practice

Streamline processes for trial design and execution

Focus on essential endpoints

Decrease regulatory hurdles and broaden trial access

Increase efficiency of data collection

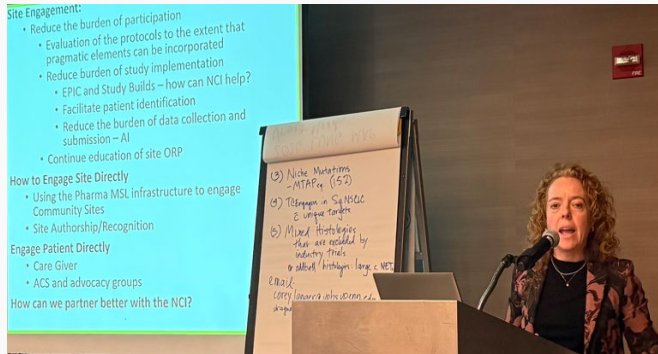
NCI/CTEP extra efforts to help Lung-MAP

- Pre-concept Review
- Special agreement for Drug distribution
- Lung-MAP Policy Committee involvement
- Drug Selection Committee involvement



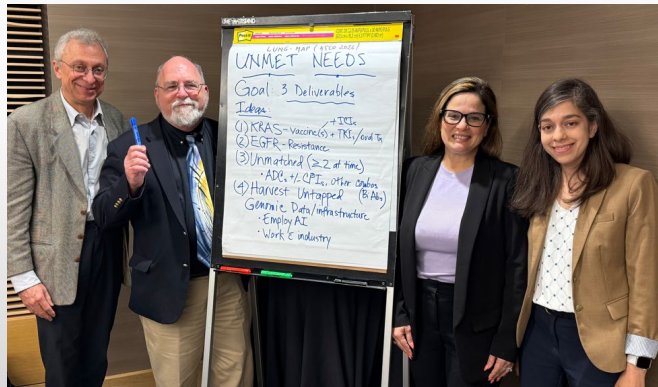
LUNG-MAP

Breakout sessions



Boosting Accrual – Mary Redman, PhD, Martin Edelman, MD, Lucy Gansauer, MSN, Crystal Miwa

Deliverables: Three strategies to increase enrollment in Lung-MAP



Unmet Needs – Konstantin Dragnev, MD, Corey Langer, MD, Ticiana Leal, MD, Anjali Rohatgi, MD, PhD

Deliverables: Three novel trials to pursue for Lung-MAP



Increasing Engagement – Joel Neal, MD, PhD, David Gandara, MD, Helen Ross, MD, Roy Herbst, MD, PhD

Deliverables: Three areas to improve junior faculty engagement and expand TM and ancillary projects in Lung-MAP

Boosting Accrual Through Partnership



NCI/NCTN

- Reduce the burden of participation
 - Include pragmatic elements when possible
- Reduce burden of study implementation
 - EPIC and Study Builds
 - Reduce the burden of data collection and submission – use of AI
 - Continue education of site ORP

Sites

- Increase site authorship
- Promote site/PI/staff recognition
- Facilitate patient identification
- Engage Pharma MSL infrastructure to engage community sites

Patients

- Caregivers
- ACS
- Advocacy groups

Make trials easier to run, find, and for patients to access.

Addressing Unmet Needs



Expand unmatched trial opportunities

- ADC + Biomarker + ICI combinations
- Bispecific antibodies + ADCs
- Open multiple unmatched sub-studies simultaneously

Study clinical niche cohorts

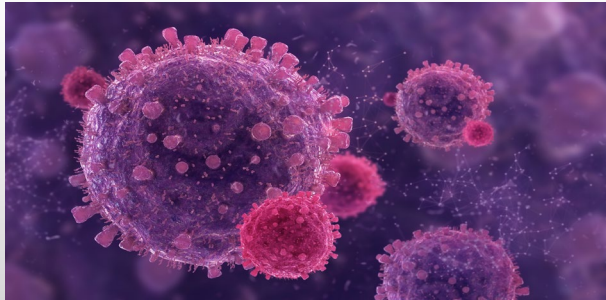
- Rare disease cohorts
- CNS metastases
- Leptomeningeal disease
- CSI proton approaches
- Integration of radiation and local therapies

Advance precision oncology

- MTAP-mutant NSCLC
- T-cell engagers for squamous disease
- *EGFR* resistance
- KRAS vaccine combinations
- Pan-KRAS strategies
- KRAS *G12C* programs

Address populations and scientific questions that remain understudied by conventional trials.

Building the Next Generation of Leaders



Develop investigators— create a sustainable leadership pipeline

- Pair junior investigators with experienced mentors
- Include junior faculty in Drug Selection Committee discussions
- Promote meaningful authorship opportunities
- Increase visibility through collaborative publications

Expand translational medicine engagement— increase participation and scientific productivity

- Open invitations to translational medicine meetings
- Improve visibility of available projects and datasets
- Connect junior investigators with active projects
- Promote grant opportunities and funding mechanisms

Grow the network of collaborators— expand geographic and institutional participation

- Increase engagement in less represented regions
- Consider Canadian collaborations when possible
- Build broader community participation

Grow Lung-MAP by investing in people, enabling science, and expanding partnerships.

S1800E

A Randomized Phase II/III Study of Docetaxel and Ramucirumab with or without Cemiplimab for Participants Previously Treated with Platinum-based Chemotherapy and Immunotherapy for Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Non-Matched Sub-Study)

SAIAMA N. WAQAR, MD

Study Chair (NRG)

Tina Li, MD

Study Co-Chair (SWOG)

Mary W. Redman, PhD

Statistics Chair (SWOG)

David Gandara, MD

Study Champion (SWOG)

Disclosures for Dr. Waqar

- **Advisory Board**: Astra Zeneca, Pfizer, Amgen, Daiichi Sankyo, Boehringer Ingelheim, Gilead, Janssen, Adcendo, Merck, Nuvalent, EMD Serono
- **Consulting**: Boehringer Ingelheim, Astra Zeneca, Gilead, CurioScience
- **Research Grant Support**: SWOG Clinical trial partnership, Astra Zeneca, Genentech, Gilead, Abbvie, Advenchen, Daiichi Sankyo, Nuvalent, Elevation Oncology, Ribon, Janssen, Turning Point, Immunomedics, Angiex, ADC Therapeutics, Astellas, Verastem, Abbvie



S1800E Background/Overview

- **PD-1/PD-L1 inhibitors, either alone or in combination with platinum-based chemotherapy doublets, have become the standard of care (SOC) for patients with newly diagnosed, unresectable NSCLC.**
- However, the majority of patients experience disease progression.
- Docetaxel, alone or with anti-angiogenesis inhibitor ramucirumab, remains the current SOC 2nd line therapy.
- **Both the chemotherapy docetaxel and the VEGFR2 inhibitor ramucirumab may play important roles in overcoming acquired resistance to PD(L)1 inhibitor-containing first-line systemic therapy in mNSCLC.**
 - Ivonescimab data strengthens the idea that combining PD-1 inhibition with VEGF pathway blockade can provide benefit over PD-1 inhibition alone in patients with first-line mNSCLC.
- **We hypothesize that the addition of cemiplimab to docetaxel and ramucirumab will improve OS compared to docetaxel and ramucirumab alone in the patient population studied in the Pragmatica-Lung trial.**
 - S1800E is a non-match study for patients with stage IV or recurrent NSCLC, previously treated with platinum doublet and anti-PD(L)-1 therapy with disease progression $\geq$ 84 days after start of anti-PD(L)1 therapy
 - No clinical data available on the triplet combination of cemiplimab, ramucirumab and docetaxel. So, 10 patient safety lead-in.

S1800E: A Randomized Phase II/III Study of Docetaxel and Ramucirumab with or Without Cemiplimab (REGN2810) for Participants Previously Treated with Platinum-Based Chemotherapy and Immunotherapy for Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Non-Matched Sub-Study)

Status:

Study activation: 4/28/2025

First participant registered: 5/22/2025

Sites with S1800E open as of 10/2/2026: 361

Accrual as of 10/2/2026: 142 patients

(72 to Arm A and 70 to Arm B)

Study Chairs: Waqar , Li

Statisticians: Redman, Minichiello

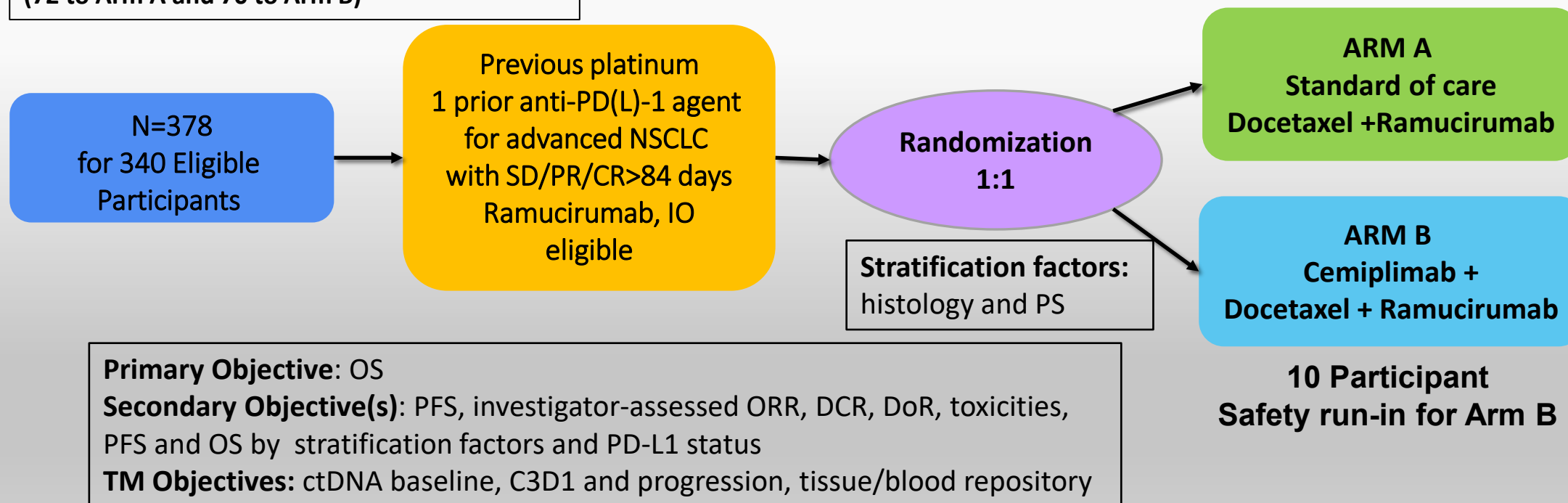
Data Coordinators: Highleyman, Ahmadzai

Protocol Project Manager: Beeler

Study Champion: Gandara

Lung-MAP Chairs: Borghaei, Reckamp (2022-2024)

Reckamp, Waqar (2024-Present)



Status Update

- CTEP Full Approval: 4/24/2025
- Activation Date: 4/28/2025
- First Patient Registered: 5/22/2025
- Sites with S1800E open as of 10/2/2026: 361
- Registrations as of 10/2/2026: 142 participants
- Accrual Goal: 378 participants (for 340 eligible)

S1800E Contacts

Study Chairs:

- Saiama Waqar, M.D.
 - Siteman Cancer Center/Washington University School of Medicine
- Tianhong (Tina) Li, M.D., Ph.D.
 - University of California Davis Comprehensive Cancer Center

Questions:

Medical Questions for Study Chairs:

S1800EMedicalQuery@swog.org

Eligibility/Specimen/Data Submissions:

LUNGMAPquestion@crab.org

General Protocol/Regulatory:

jbeeler@swog.org

Manuscript & Accrual Updates

MARY W. REDMAN, PHD
STATISTICS CHAIR, LUNG-MAP
FRED HUTCHINSON CANCER CENTER



Immune-related adverse event severity and clinical outcomes with immune checkpoint inhibitor immunotherapy in participants with non–small cell lung cancer: Analysis of the Lung-MAP sub-studies S1400A, S1400I, S1400F, and S1800A.

DIANE TSENG, JAMES MOON, YUZHENG ZHANG, LYUDMILA BAZHENOVA, NATASHA B. LEIGHL, HOSSEIN BORGHAEI, KONSTANTIN H. DRAGNEV, COREY J. LANGER, JOEL NEAL, DAVID GANDARA, KAREN KELLY, JHANELLE E. GRAY, ROY S. HERBST, SAIAMA N. WAQAR, KAREN L. RECKAMP, CHRISTINA S. BAIK, MARY W. REDMAN

Presented by:

Christina Baik MD MPH

Associate Professor

Clinical Research Director, Thoracic/Head and Neck

Oncology

Fred Hutchinson Cancer Center

University of Washington



LUNG-MAP

Background

- **Question: How does the severity of immune related adverse events (irAE) impact the clinical outcome of patients (pts) with non-small cell lung cancer (NSCLC) treated with immune checkpoint inhibitors (ICIs)?**
- Previously, a pooled analysis of Impower 130, 132 and 150 examined the relationship between irAE severity and clinical outcomes for atezolizumab + chemotherapy for pts with non-squamous NSCLC treated in the first line (1L) setting. Pts with mild irAE (grade 1 – 2) had better overall survival compared to pts with severe irAE (Socinski et al, JAMA Oncol 2023).
- It is not known how irAE severity impacts clinical outcomes for (1) pts with squamous cell NSCLC (sqNSCLC) (2) pts receiving ICI (without chemotherapy) and (3) according to prior ICI exposure .
- We **hypothesized** that NSCLC pts treated with ICIs in the 2L + setting with lower grade irAEs would have better outcomes than those with higher grade irAEs and those without irAEs .



All NSCLC



Squamous-Cell Only

**Non-match Sub-Studies
Previously-Treated
Stage IV/Recurrent NSCLC**



ICI Naive

**S1400A
Phase II**

**Durvalumab
Vs.
Docetaxel**

**S1400I
Phase III**

**Nivolumab
+/-
Ipilimumab**

Previous ICI Treatment

**S1400F
Phase II**

**Durvalumab
+
Tremelimumab**

**S1800A
Phase II**

**Pembrolizumab
+ Ramucirumab
Vs.
SoC**



LUNG-MAP

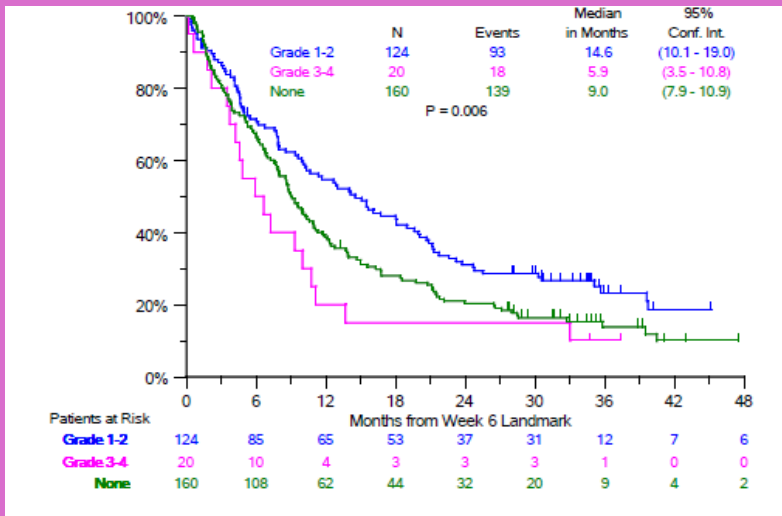
Methods

- Analyzed the relationship between maximum irAE severity grouped as: no irAE, Grade 1 or 2, or Grade 3-4, by 6-, 12-, and 24 weeks from randomization with overall survival (OS) measured from the landmark timepoint.
- Modeling used a Cox model using Grade 1-2 as reference category compared with no irAEs and Grade 3-4, respectively.



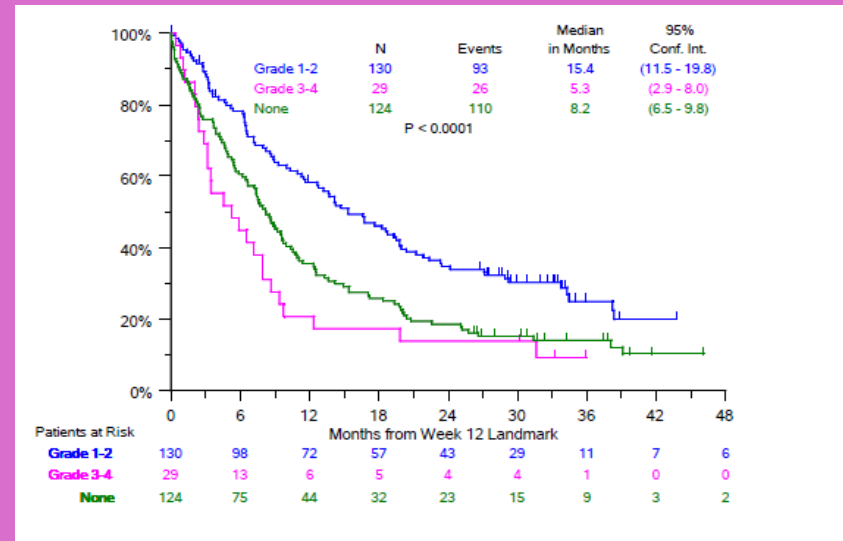
Overall Survival: ICI Naïve (S1400A, S1400I)

6-week Landmark



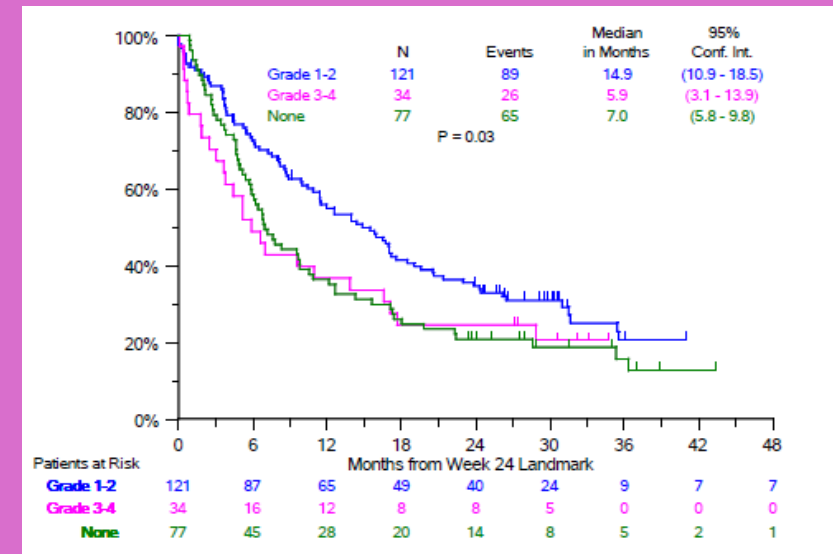
Landmark Time	irAE Group	HR (95% C)*)	p-value
6 weeks	No irAE	1.42 (1.09 – 1.85)	<0.01
	Grade 3-4	1.94 (1.16 – 3.22)	0.011

12-week Landmark



Landmark Time	irAE Group	HR (95% C)*)	p-value
12 weeks	No irAE	1.68 (1.28 – 2.22)	<0.01
	Grade 3-4	2.28 (1.47 – 3.53)	<0.01

24-week Landmark



Landmark Time	irAE Group	HR (95% C)*)	p-value
24 weeks	No irAE	1.48 (1.07 – 2.04)	0.02
	Grade 3-4	1.52 (0.98 – 2.36)	0.06

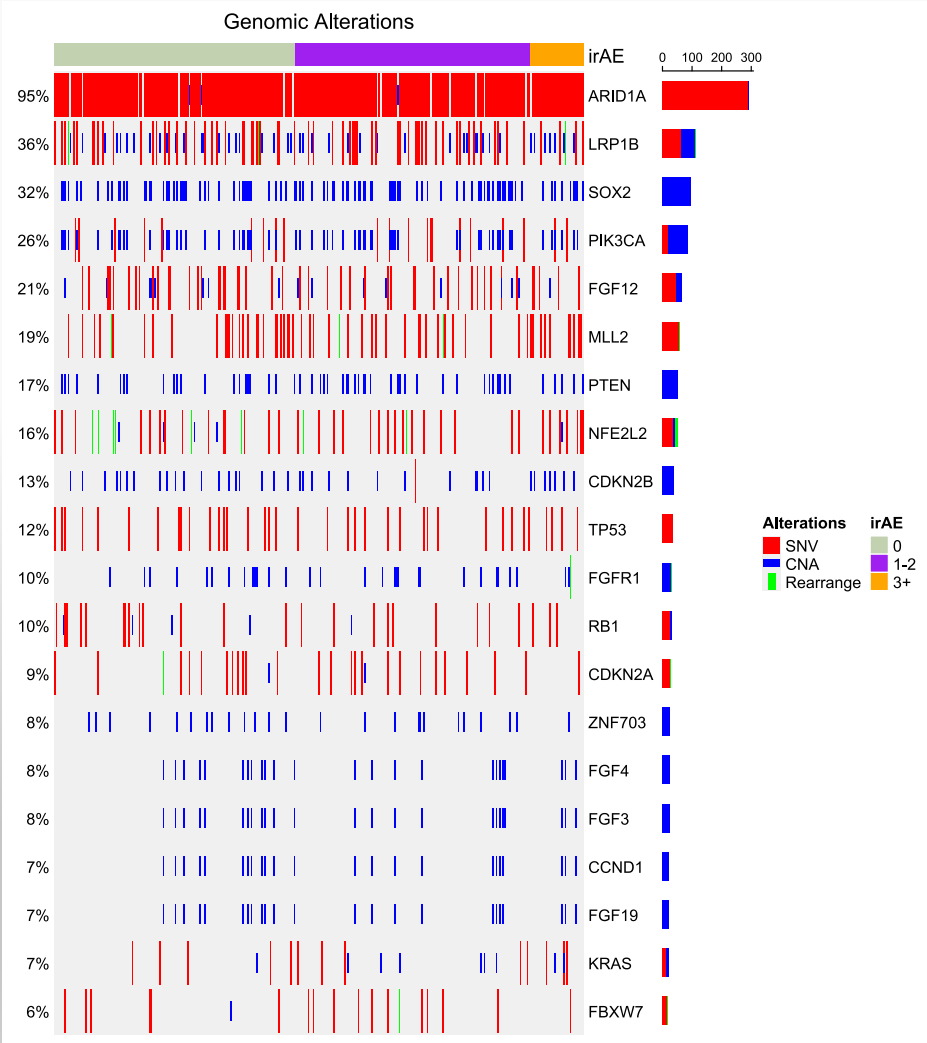
No association between clinical / lab / tumor genetic mutations and irAE severity: ICI Naïve (S1400A, S1400I)

Clinical Factors	P-value
Age	0.36
Sex	0.58
BMI	0.77
Smoking status	0.12
Performance status	0.41

Lab values	P-value
ANC	0.94
Platelets	0.57
Creatinine Clearance	0.54
PD-L1	0.78
Tumor mutation burden	0.54

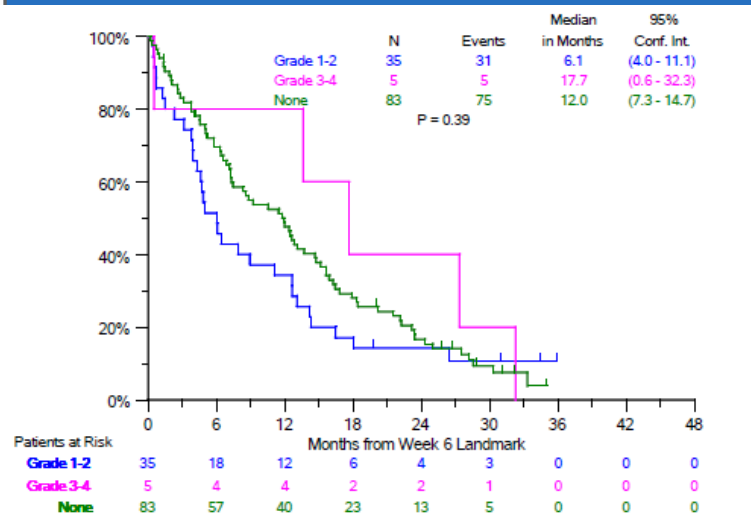
irAE grade 3 – 5 (n = 33) vs. 1 – 2 (n = 140) Likelihood Ratio Test

OncoPrint – top 20 genes for worst irAE grade within 12 wks:



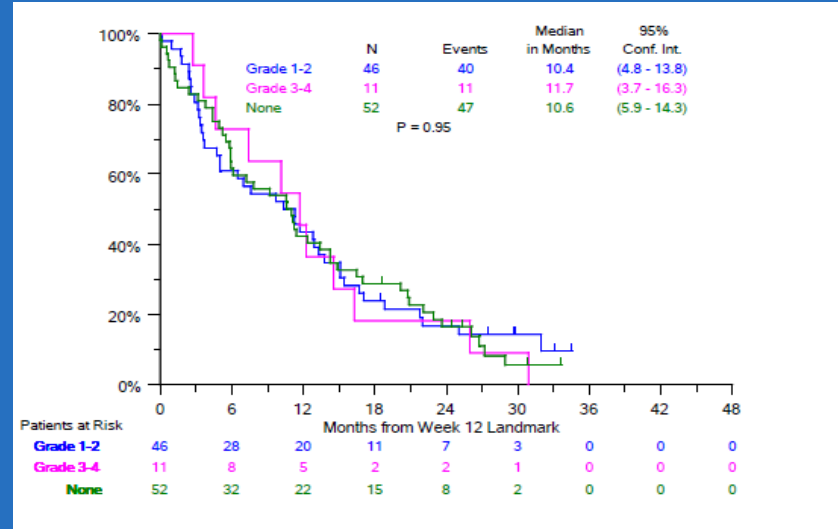
Overall Survival: ICI Refractory (S1400F, S1800A)

6-week Landmark



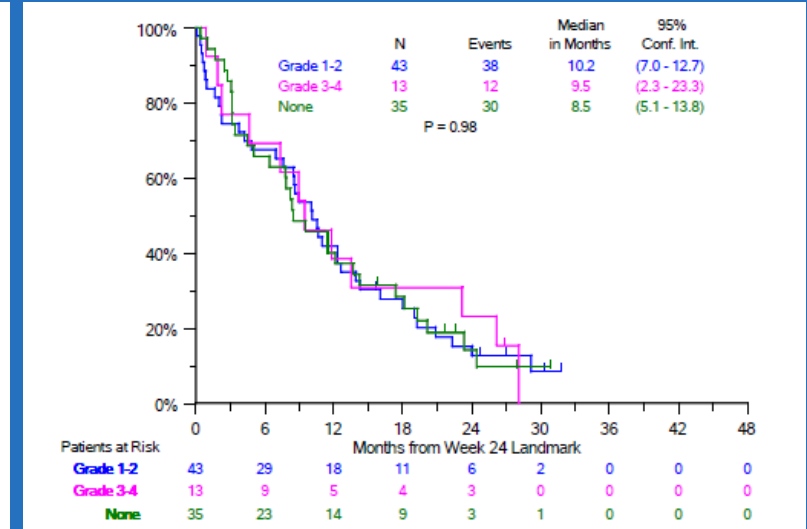
Landmark Time	irAE Group	HR (95% CI)*	p-value
6 weeks	No irAE	0.78 (0.51 – 1.20)	0.26
	Grade 3-4	0.59 (0.23 – 1.53)	0.28

12-week Landmark



Landmark Time	irAE Group	HR (95% CI)*	p-value
12 weeks	No irAE	1.04 (0.68 – 1.59)	0.85
	Grade 3-4	1.11 (0.57 – 2.16)	0.77

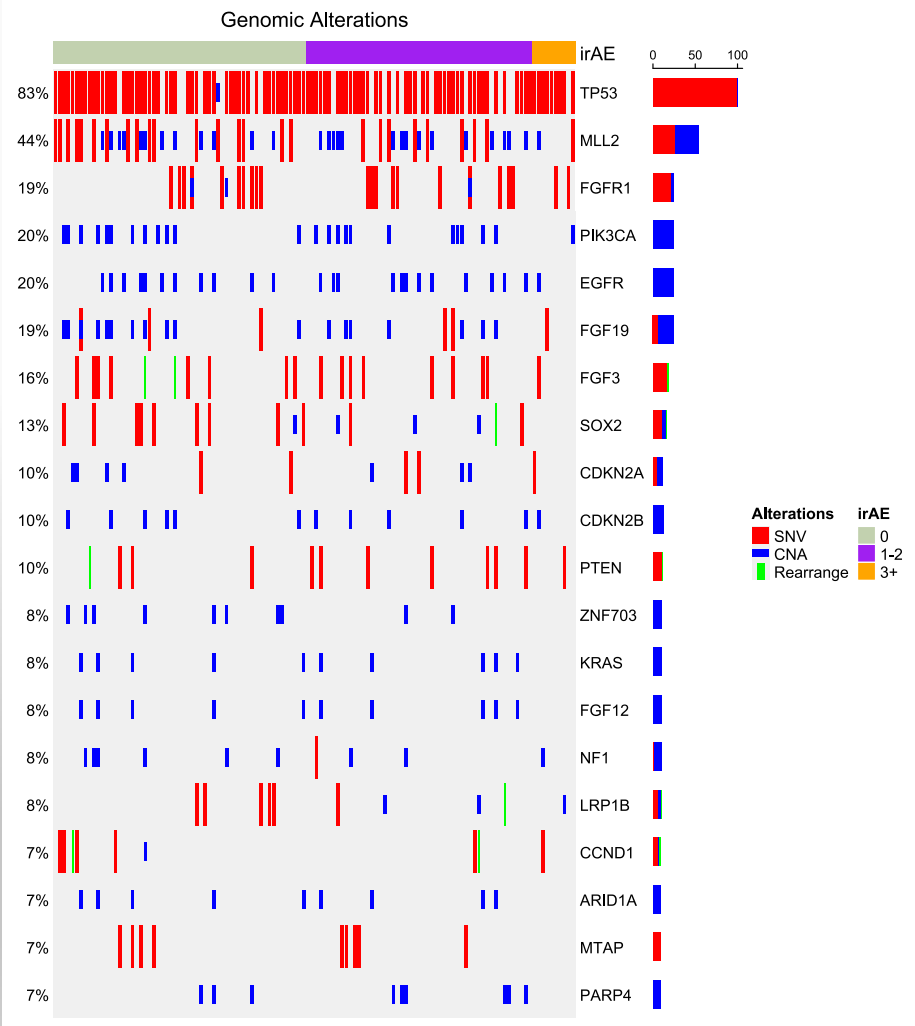
24-week Landmark



Landmark Time	irAE Group	HR (95% CI)*	p-value
24 weeks	No irAE	1.00 (0.62 – 1.62)	0.99
	Grade 3-4	0.94 (0.49 – 1.81)	0.85

No association between clinical / lab / tumor genetic mutations and irAE severity: ICI Refractory (S1400F, S1800A)

OncoPrint – top 20 genes for worst irAE grade within 12 wks:



Clinical Factors	P-value
Age	0.27
Sex	0.26
BMI	0.13
Smoking status	Not evaluable
Performance status	Not evaluable

Lab values	P-value
ANC	0.36
Platelets	0.57
Creatinine Clearance	0.48
PD-L1	0.5
Tumor mutation burden	0.77

irAE grade 3 – 5 (n = 11) vs. 1 – 2 (n = 55) Likelihood Ratio Test

Conclusions

- In ICI-naïve sqNSCLC patients treated with ICI in the 2L+ setting (Lung-MAP S1400A and S1400I), mild (Grade 1 – 2) immune related adverse events (irAEs) were associated with better overall survival compared to no irAEs and severe irAEs (Grade 3 – 4).
- This observation was consistent across multiple landmark time points: 6, 12, and 24 weeks
- This association was not observed in the checkpoint immunotherapy-refractory NSCLC cohort (S1400F and S1800A).



Thank you

- We thank the patients and families for participating.
- We thank Alliance, ECOG-ACRIN, NRG Oncology, SWOG, NCI CTEP, FoCR, FNIH
- Funding: NIH/NCI grants U10CA18088, U10CA180819



LUNG-MAP





All NSCLC



Squamous-Cell Only

**Non-match Sub-Studies
Previously-Treated
Stage IV/Recurrent NSCLC**

ICI Naive

S1400A
Phase II/III

Nivolumab
vs.
Docetaxel

S1400I
Phase III

Nivolumab
+/-
Ipilimumab

Previous ICI Treatment

S1400F
Phase II

Durvalumab
+
Tremelimumab

S1800A
Phase II

Pembrolizumab
+ Ramucirumab
Vs.
SoC



LUNG-MAP

S1900G

A Randomized Phase II Study of Capmatinib plus Osimertinib with or without Ramucirumab in Participants with EGFR-Mutant, MET-Amplified Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Sub-Study)

Sarah Goldberg, MD, MPH
Study Chair (SWOG)

Ross Camidge, MD, PhD
Study Co-Chair (SWOG)

Mary W. Redman, PhD
Statistics Chair (SWOG)

Helen Ross, MD
Study Champion (Alliance)

Disclosures

Consulting

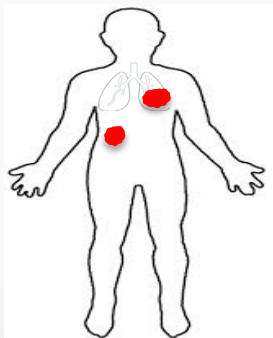
AstraZeneca, Eli Lilly, Daiichi-Sankyo, Johnson & Johnson, Summit Therapeutics, Merck, Regeneron, Bayer, SyntheKine, Tubulis, Blossom Hill, Pfizer

Research Support

AstraZeneca, Boehringer Ingelheim, Mirati, Adela

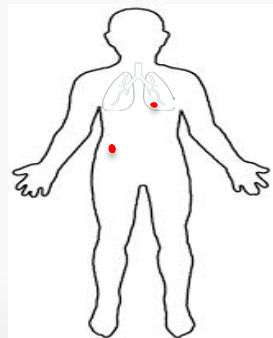
Treatment paradigm for EGFR-mutant lung cancer

**Treatment-naïve
EGFR-mutant NSCLC**



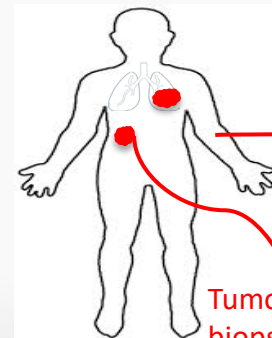
→
**EGFR inhibitor (such
as osimertinib), alone
or in combination**

Treated



→ → →
**Ongoing EGFR
inhibitor treatment**

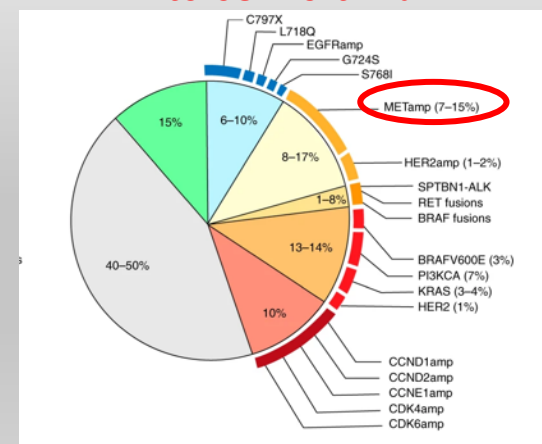
**EGFR inhibitor-
resistant disease**



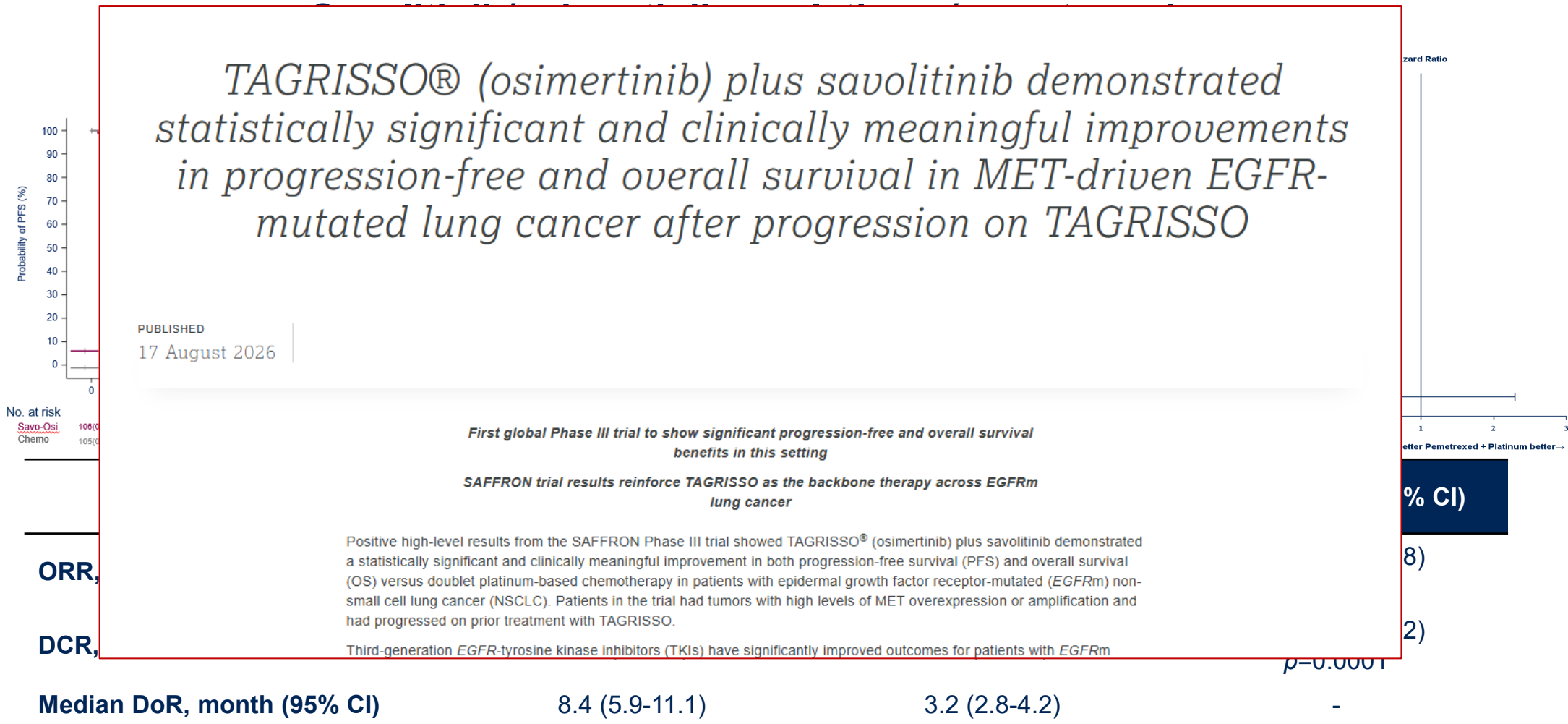
Tumor
biopsy

Blood
(ctDNA)

**Mechanisms of resistance
to osimertinib**



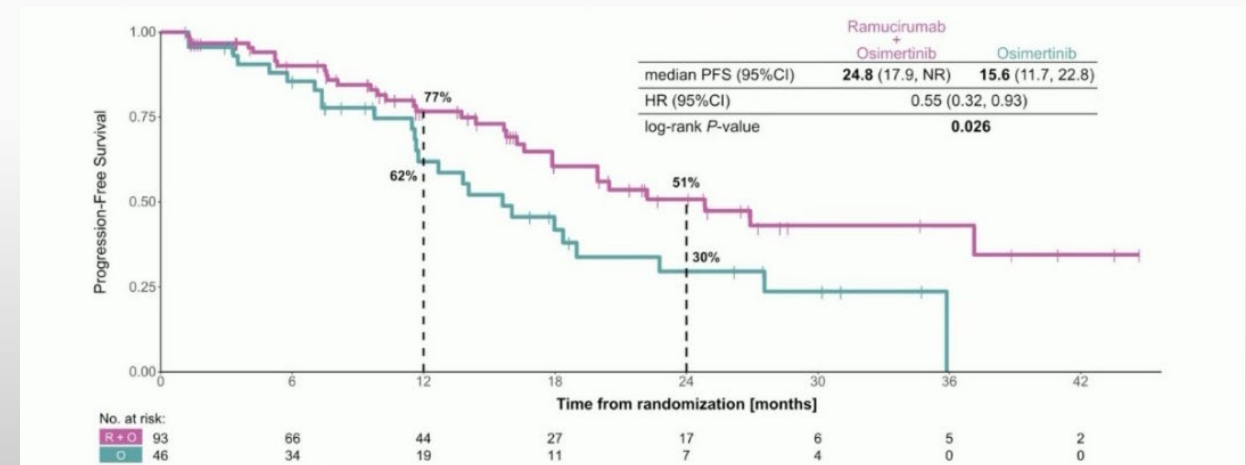
MET inhibitors in EGFR-mutant, MET-amplified NSCLC



VEGF inhibition might improve both efficacy AND toxicity

- The addition of a VEGF or VEGFR2 inhibitor can increase the progression-free survival when added to an EGFR TKI in EGFR-mutant lung cancer
- Preclinical data demonstrates the crosstalk between VEGF and MET signaling
- Dual inhibition of VEGFR and MET may be able to delay or overcome resistance to EGFR TKIs
- The addition of a VEGF pathway inhibitor may improve toxicity associated with MET inhibition by decreasing peripheral edema

Osimertinib with or without ramucirumab (RAMOSE)



Le X, ESMO 2023

S1900G Schema

Study Chairs: Goldberg, Camidge
Statisticians: Redman, Minichiello
Data Coordinator: Highleyman
Protocol Project Manager: Chadwell
Study Champion: Ross
Lung-MAP Chairs: Herbst, Patel (2019-2022)
Borghaei, Reckamp (2022-2024)
Reckamp, Waqar (2024-Present)

KEY ELIGIBILITY

- Advanced *EGFR*-mutant NSCLC
- At least 1 prior *EGFR* TKI, including osimertinib as the most recent prior treatment
- Osimertinib may be given alone or in combination with other agents
- *MET* amplification*
- Chemotherapy +/- immunotherapy is allowed but not required
- No prior *MET* tyrosine kinase inhibitor (prior amivantamab allowed)
- Prior VEGF pathway inhibitors allowed
- Untreated, asymptomatic brain metastases allowed

Randomize

Capmatinib at 400 mg BID**
plus osimertinib 80mg QD plus
ramucirumab 10mg/kg Q2w

Capmatinib at 400 mg BID**
plus osimertinib 80mg QD

Primary Endpoints:

- Progression-free survival

Secondary Endpoints:

- Toxicity by CTCAE
- Response
- Duration of response
- Overall survival
- Edema
- Changes in weight

N = 40 eligible (44 total)

Stratification factors: Brain metastases and 2L vs 3+L prior lines of therapy

* *MET* amplification as determined by tissue-based or blood-based (ctDNA) NGS assay obtained after progression on osimertinib. Testing for *MET* amplification can be done locally using a tissue or blood-based NGS test; testing through the LUNGMAP screening protocol is also available.

** The study will include a safety run-in on the 1st 10 participants in each arm; if too toxic, regimen will include capmatinib at 200mg BID

Biomarker identification on S1900G

- EGFR mutation must have been detected at baseline
- MET amplification must be detected after radiographic or clinical progression on osimertinib
- Any level of MET amplification is allowed
- There are several possible ways to demonstrate MET amplification:
 - In ctDNA from blood OR in a tumor tissue biopsy
 - Testing can be done centrally OR locally (using acceptable assays including Foundation, Guardant, Caris, and Tempus)

S1900G Accrual and Updates

Accrual goal: 44 (40 eligible)

Monthly accrual goal: **2** patients

- Opened 4/3/23
- 28 patients registered
- This trial is still actively enrolling patients but will likely close to accrual in the next few months

S1900G Contacts

Study Chairs:

- Sarah Goldberg, M.D.
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Submissions:

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General Protocol/Regulatory:
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\$1900J

A Phase II Study of Amivantamab Hyaluronidase in Participants with MET Amplification-Positive Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Sub-Study)

Christian Rolfo, MD

Study Chair (SWOG)

Shirish Gadgeel, MD

Study Co-Chair (SWOG)

Mary W. Redman, PhD

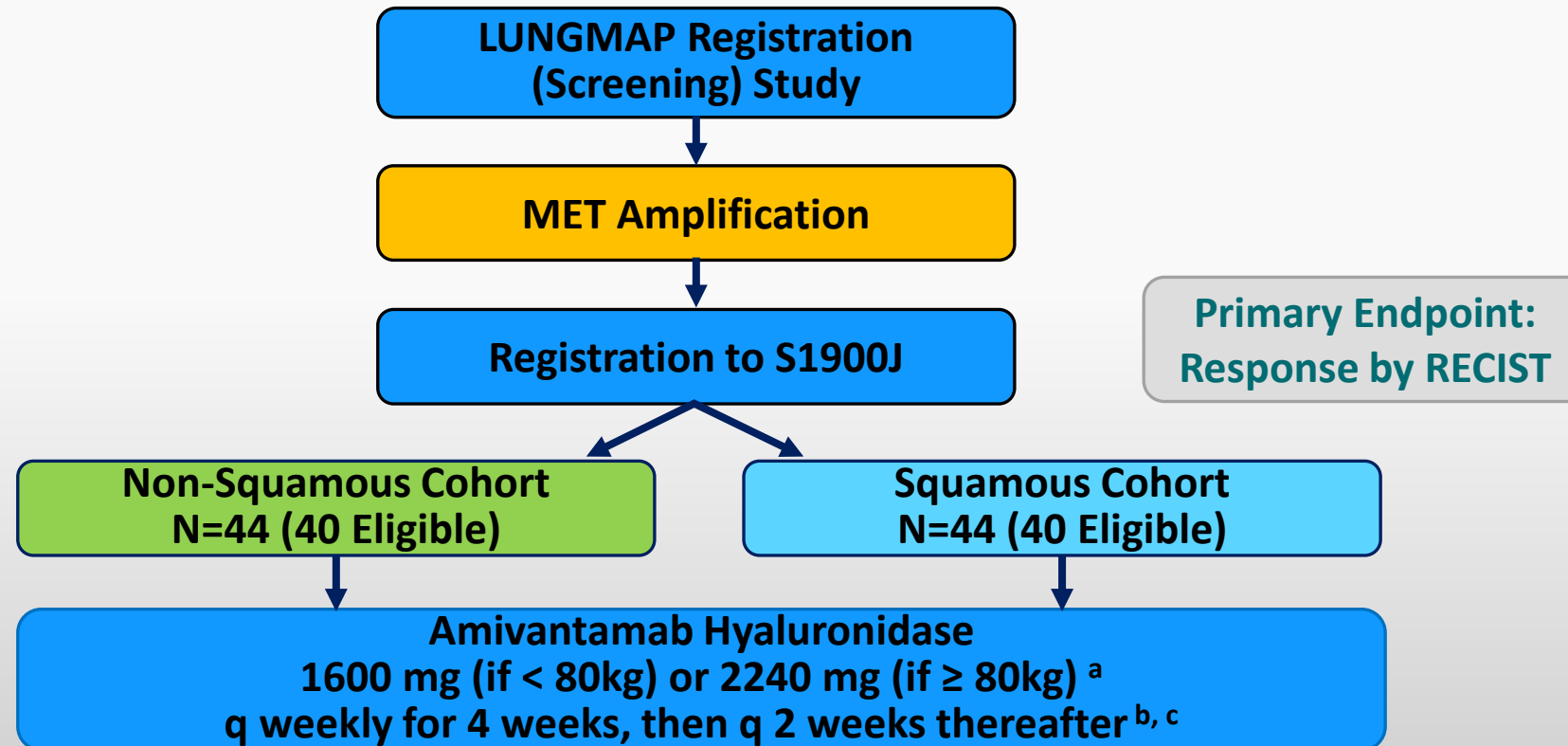
Statistics Chair (SWOG)

David Gandara, MD

Study Champion (SWOG)

S1900J Schema

Study Chairs: Rolfo, Gadgeel
Statisticians: Redman, Minichiello
Data Coordinator: Ahmadzai
Protocol Project Manager: Beeler
Study Champion: Gandara
Lung-MAP Chairs: Borghaei, Reckamp (2022-2024)
Reckamp, Waqar (2024-Present)



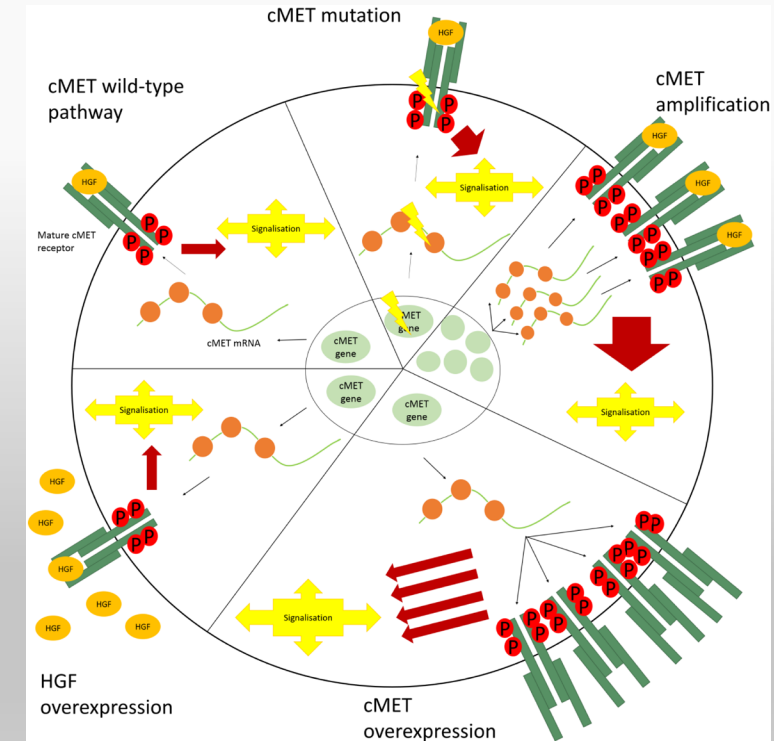
^a The dosage will be based on the participant's body weight at screening.

^b Cycle 1: Days 1, 8, 15 and 22. Cycles 2+: Days 1 and 15. See protocol Section 7.2

^c Continue treatment until one of the criteria in Protocol Section 7.5 is met.

Background/Overview

- The MET gene represents one of the drivers of tumorigenesis due to genetic aberrations, including germline or somatic point mutations, splice-site mutations leading to the skipping of exon 14 (MET exon 14 skipping) or gene amplification
- Amplification of the cMET gene is a rare potentially actionable, primary oncogenic driver in patients with NSCLC. For primary amplification, the median percentages in literature vary around 2.9% in the large series.
- The majority of the data are collected in non-squamous, but recently, new data on squamous cell carcinoma are available
- It is also necessary to make a distinction between its role as an acquired resistance pathway to tyrosine kinase inhibitors (TKIs) in NSCLC or as a concurrent alteration within patients with MET exon 14 with NSCLC.
- The amplification itself can be targeted with multikinase or MET-specific inhibitors to improve the outcome (Table 1) with a median ORR of 30%, PFS 4 months and OS of approximately 9 months.



Van der Steen N et al, (Rollo) *Cancers* 2015, 7(2), 556-573

Key Eligibility Criteria

- NSCLC with MET amplification determined by FMI tissue-based NGS assay.
- Measurable disease documented by CT or MRI.
 - Pleural effusions, ascites and laboratory parameters are not acceptable as the only evidence of disease.
- CT or MRI scan of the brain to evaluate for CNS disease within 42 days prior to S1900J registration.
- Participants with asymptomatic CNS metastasis (brain metastases or leptomeningeal disease) must be clinically stable and asymptomatic for at least 14 days prior to sub-study registration.
 - Participants can be on a low-dose corticosteroid treatment (≤ 10 mg prednisone or equivalent) for at least 14 days prior to study treatment.
- No other known actionable oncogenic alterations, such as (but not limited to) EGFR sensitizing mutations, EGFR T790M mutation, MET Exon-14 skipping mutant NSCLC, ALK gene fusion, ROS1 gene rearrangement, RET gene rearrangement, NTRK rearrangement, HER2 mutation, KRAS activating mutations, and BRAF V600E mutation.
- Must have received at least one line of systemic treatment for Stage IV or recurrent NSCLC and participants must have progressed (in the opinion of the treating physician) following the most recent line of therapy.
- No prior treatment with MET TKIs, such as: tepotinib, capmatinib, and crizotinib.
- No prior systemic therapy (systemic chemotherapy, immunotherapy or investigational drug) within 21 days prior to S1900J registration.
- Zubrod PS 0-2 within 28 days prior to registration.

Revision 1 Updates

Expansion of NGS Testing Platforms

- S1900J will allow NGS testing platform beyond FMI (approved NGS) tissue and liquid biopsy
- Participants who provided documentation of MET amplification in LUNGMAP from a previously completed non-FMI test must agree to submit archival tissue (if available) for retrospective FMI testing (results will not be required for registration to S1900J).

Eligibility Expansion

- No other known actionable oncogenic alterations, such as (but not limited to) EGFR sensitizing mutations, EGFR T790M mutation, MET Exon-14 skipping mutant NSCLC, ALK gene fusion, ROS1 gene rearrangement, RET gene rearrangement, NTRK rearrangement, HER2 mutation, **KRAS G12C**, and BRAF V600E mutation.
 - Revision specifies that participants with KRAS G12C mutation are not allowed.
 - Participants with other KRAS activating mutations will be allowed.

S1900J Amivantamab Hyaluronidase Administration

- Amivantamab hyaluronidase will be delivered by means of a manual injection at alternating locations on the abdomen in the periumbilical area. Dosage will be based on the participant's body weight at screening.
- Cycle 1: Administer amivantamab hyaluronidase weekly for 4 weeks.
- Cycle 2+: Administer amivantamab hyaluronidase every 2 weeks until any criteria in S1900J Protocol Section 7.5 is met.

Amivantamab Hyaluronidase Administration Schedule

Cycle (one cycle = 28 days)	Schedule
Cycle 1	Days 1, 8, 15, and 22
Cycle 2 and onwards	Days 1 and 15

Table for Dosing

Body Weight at Baseline ^a	Total Amivantamab/Hyaluronidase Planned Dose (mg/units)	Volume of Amivantamab Hyaluronidase (mL)
<80 kg	1,600 mg amivantamab/ 20,000 units hyaluronidase	10
>= 80 kg	2,240 mg amivantamab/ 28,000 units hyaluronidase	14

^a Dose adjustment not required for subsequent body weight changes.

S1900J Study Updates

Study Updates

- S1900J opened 9/27/24
- S1900J Revision 1 to allow for additional NGS testing was released to sites 9/15/25
- Most recent patient enrolled: March 6, 2026
- Most recent patient assigned: April 2, 2026
- Patients assigned: 3 in 2026; 5 in the past 12 months
- Patients enrolled: 1 in 2026; 2 in the past 12 months

S1900J Contacts

Study Chairs:

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The James CCC

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\$1900K

A Randomized Phase II Study of Tepotinib With Or Without Ramucirumab In Participants With MET Exon 14 Skipping Positive Stage IV Or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Sub-Study)

PAUL K. PAIK, MD

Study Chair (ECOG-ACRIN)

XIUNING LE, MD

Study Co-Chair (SWOG)

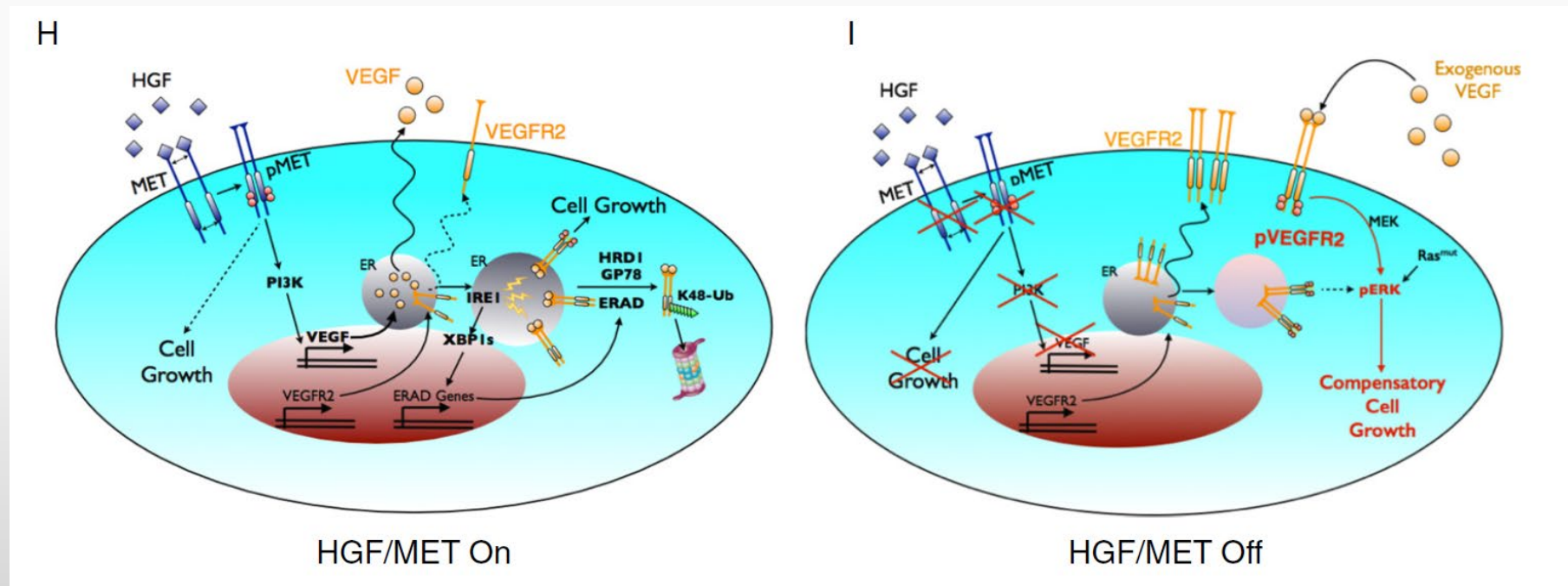
Mary W. Redman, PhD

Statistics Chair (SWOG)

Hossein Borghaei, DO

Study Champion (ECOG-ACRIN)

MET inhibition relieves VEGFR2 degradation, engenders compensatory switch to VEGFR2 signaling

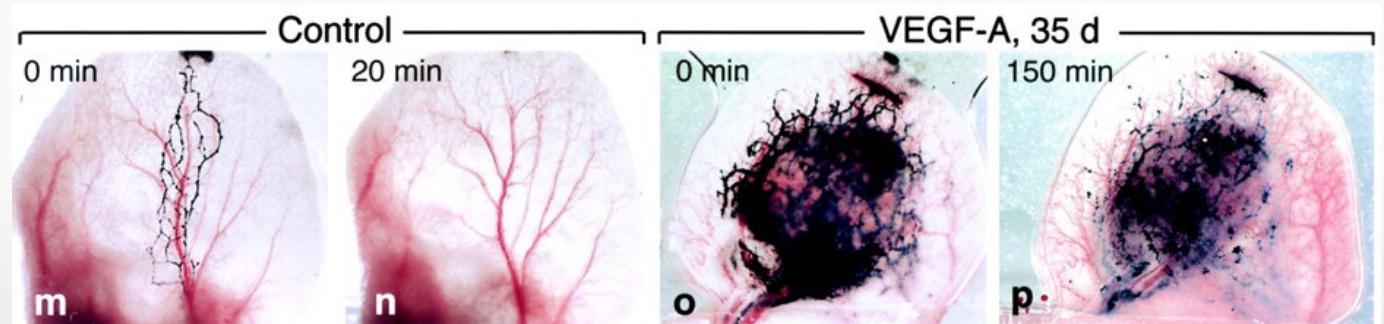


MET induced VEGF via PI3K, folded in ER with VEGFR2 -> ubiquitination and degradation

MET inhibition shuts off VEGF induction, prevents VEGFR2 degradation, potentiates VEGFR2 signaling

VEGF-A implicated in lymphangiogenesis

- VEGF-A induces a strong lymphangiogenesis response
- New lymphatics are abnormal
 - Very large
 - Incompetent valves
 - Sluggish flow
 - Delayed lymph clearance



Murine ear lymphatics after intravital infusion of colloidal carbon, injected w/ Ad-VEGF-A.

Kinetics of lymphatics clearance in Control (m,n) and Ad-VEGF-A (o,p) mice. Clearance occurs within 20 minutes in control mice but persists for at least 150 min. in Ad-VEGF-A mice.

Hypothesis: dual VEGFR2 and MET inhibition will increase efficacy while decreasing toxicity

- MET inhibition leads to an inducible increase in VEGF/VEGFR2 dependence as bypass pathway, also causing changes in the microvasculature that instigate many of the MET inh class-associated side effects
- Administration of ramucirumab with tepotinib will effectively abrogate the inducible intratumoral switch to VEGFR2 signaling as a bypass pathway while also blunting the effect of VEGF/VEGFR2 interaction in the periphery, decreasing the frequency and magnitude of peripheral edema, effusions, and hypoalbuminemia caused by tepotinib



S1900K Schema

Key Eligibility

- Stage IV or recurrent NSCLC with a MET exon 14 skipping mutation
- **Participants may have received any number of prior lines of therapy for Stage IV or recurrent NSCLC (including zero)**
- No other known actionable alterations
- If CNS metastases, eligibility is still a possibility in some circumstances
- No prior MET inhibitor or angiogenesis inhibitor therapies.

Treatment

Tepotinib 450mg po qd
+
Ramucirumab 10mg/kg q3wk
(21-day cycles)

Tepotinib 450mg po qd
(21-day cycles)

Endpoints

Primary:

- ORR

Secondary:

- PFS
- Frequency of all grade edema
- **Lymphoscintigraphy scan changes (now optional)**

Based on the VISION trial (Thomas et al., WCLC 2022), the estimated response rate with tepotinib alone is 45% (n=149).

With 50 eligible participants, this study has 90% power to rule out a difference in response rates of 34% at the 1-sided 10% level. The estimated minimal detectable difference in response rates is 18%. The power of this comparison using a continuity correction is 83%.

The projected accrual duration to this study is 38 months based on an accrual rate of 1-2 patients per month.

Study Chairs: Paik, Le
Statisticians: Redman, Minichiello
Data Coordinator: Moralda
Protocol Project Manager: Beeler
Study Champion: Borghaei
Lung-MAP Chairs: Herbst, Patel (2019-2022)
Borghaei, Reckamp (2022-2024)
Reckamp, Waqar (2024-Present)

Accrual status (October 2, 2026)

Arm	N	Target N
Tepotinib	9	25
Tepotinib + ramucirumab	21	25

S1900K Contacts

Study Chairs:

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- Xiuning Le, M.D., Ph.D.
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Eligibility/Specimen/Data
Submissions:

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General Protocol/Regulatory:

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S1900P

A Randomized Phase II Study of Paclitaxel plus TORC1/2 inhibitor vs. Paclitaxel plus TORC1/2 inhibitor plus PI3K inhibitor in Participants with NFE2L2, KEAP1 or PI3K Pathway-Positive Stage IV Squamous Cell Lung Cancers (ECOG-ACRIN Lung-MAP Sub-Study)

PAUL K. PAIK, MD

Study Chair (ECOG-ACRIN)

IVY L. RIANO MONSALVE, M.D.

Study Co-Chair (Alliance)

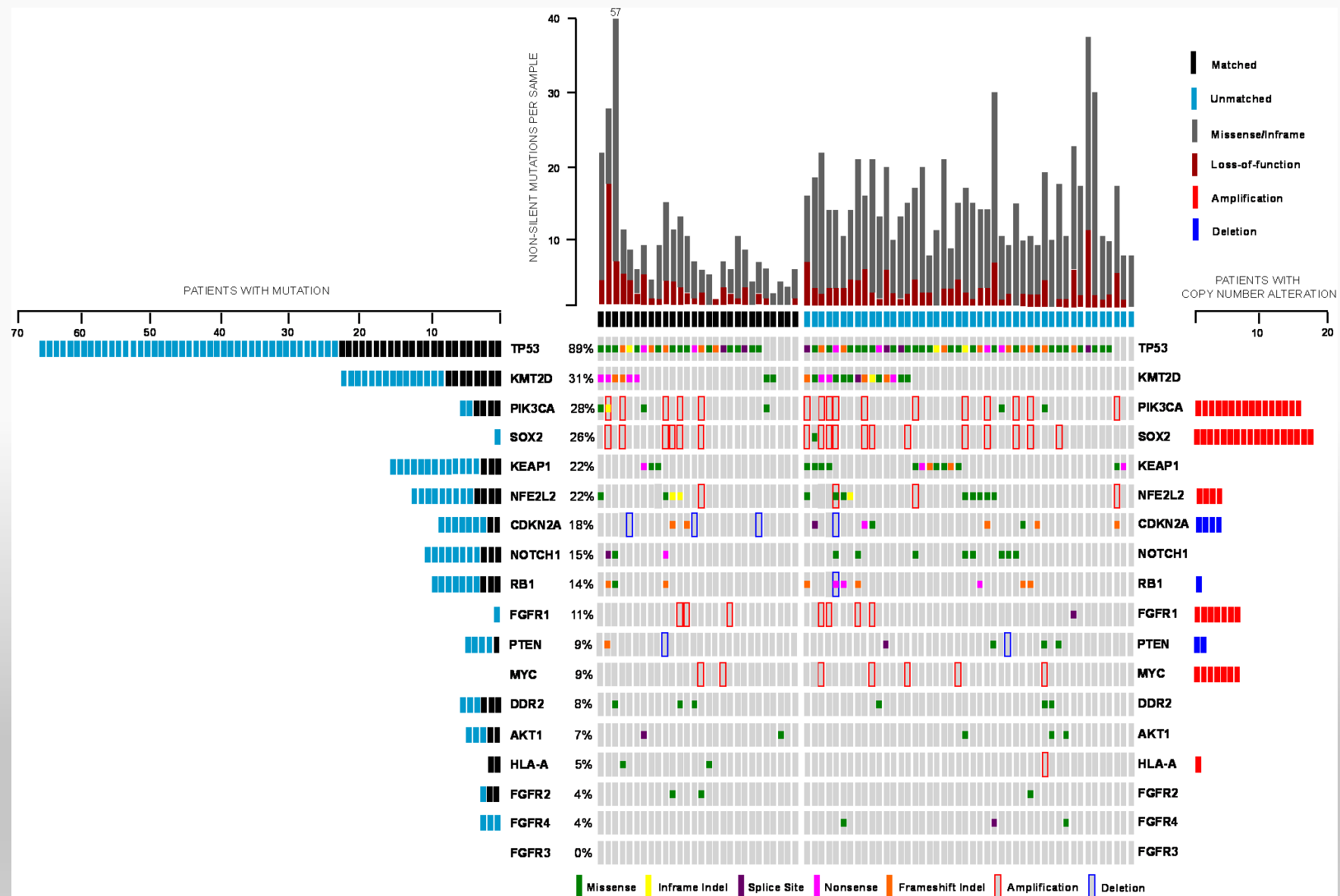
Mary W. Redman, PhD

Statistics Chair (SWOG)

Ticiana Leal, MD

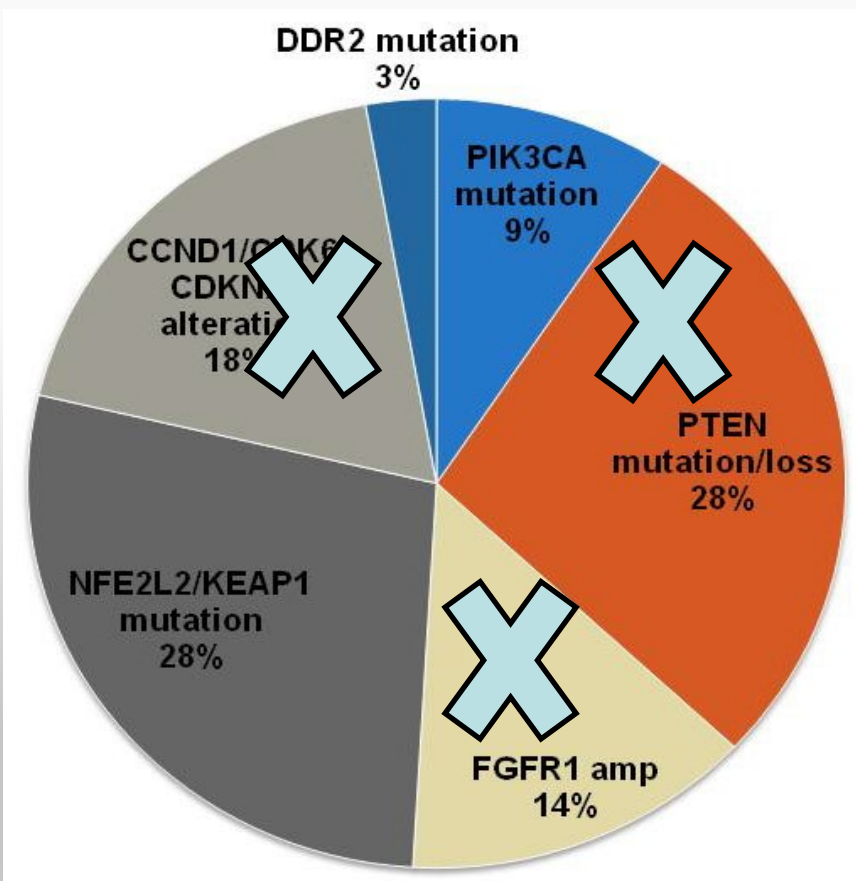
Study Champion (ECOG-ACRIN)

Squamous cell lung cancer genomics



Paik et al, Cancer Discovery 2015
TCGA Nature 2012

Targeted therapy efforts to date



Target	Drug	Result	ORR
FGFR1	AZD4547	Negative	8%
	BGI398	Negative	15%
	Dovitinib	Negative	11.5%
PTEN/PIK3CA	Buparlisib	Negative	4.5%
	Taselisib	Negative	5%
G1/S checkpoint	Abemaciclib	Negative	17%
NFE2L2/KEAP1	TAK228	ongoing	NA

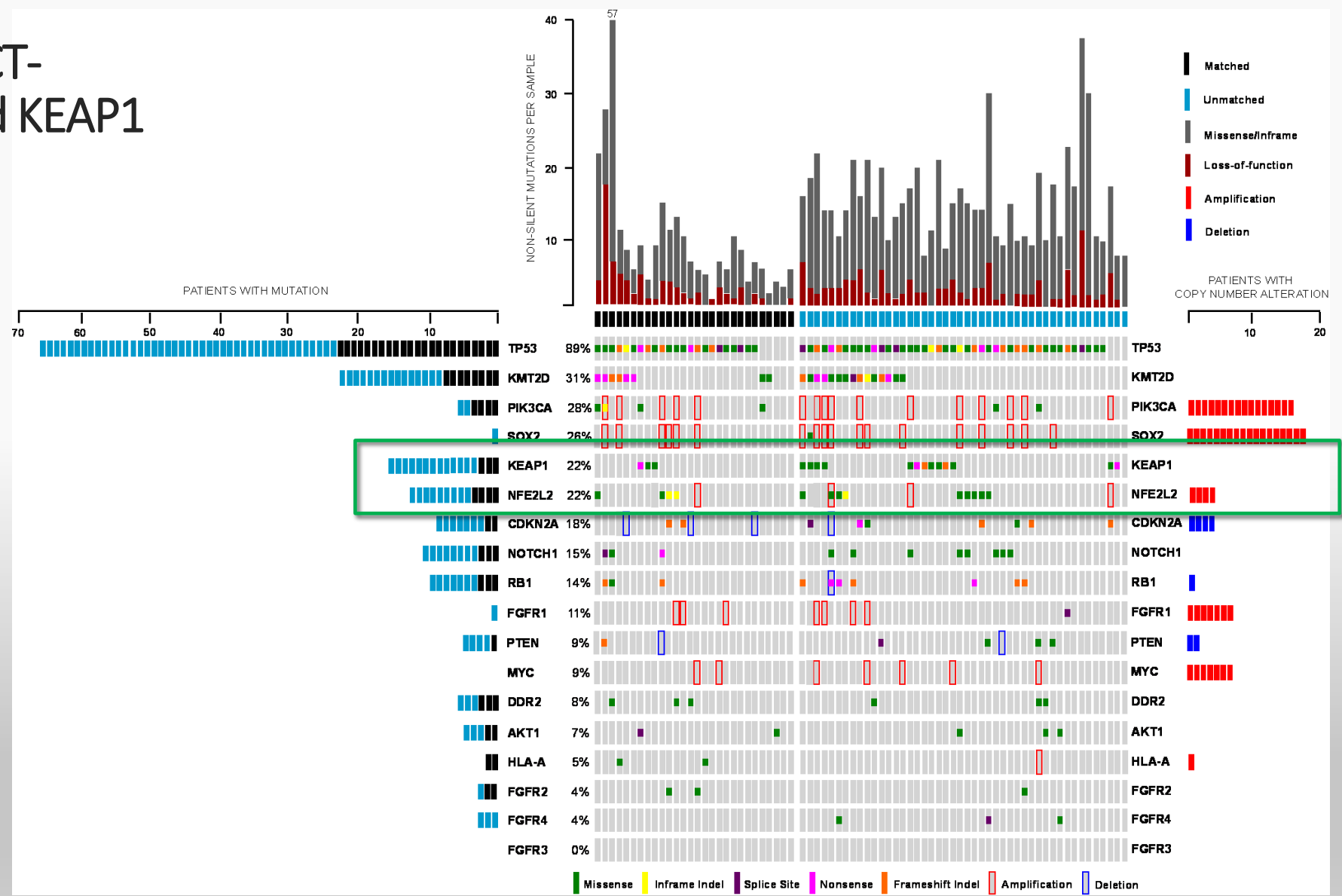
Wade, et al. ASCO 2017 Abstract 9054

Paik et al. Clin Cancer Res 2017

Patnaik et al. Cancer Disc 2017

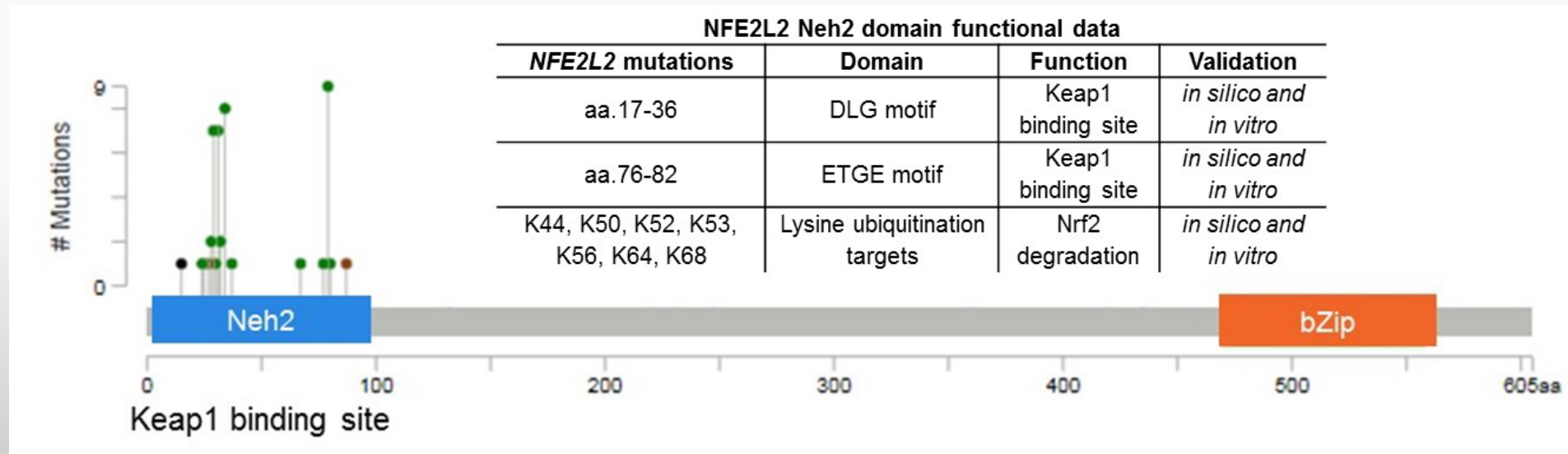
Vansteenkiste et al. J Thorac Oncol 2015

MSK IMPACT- NFE2L2 and KEAP1 mutations

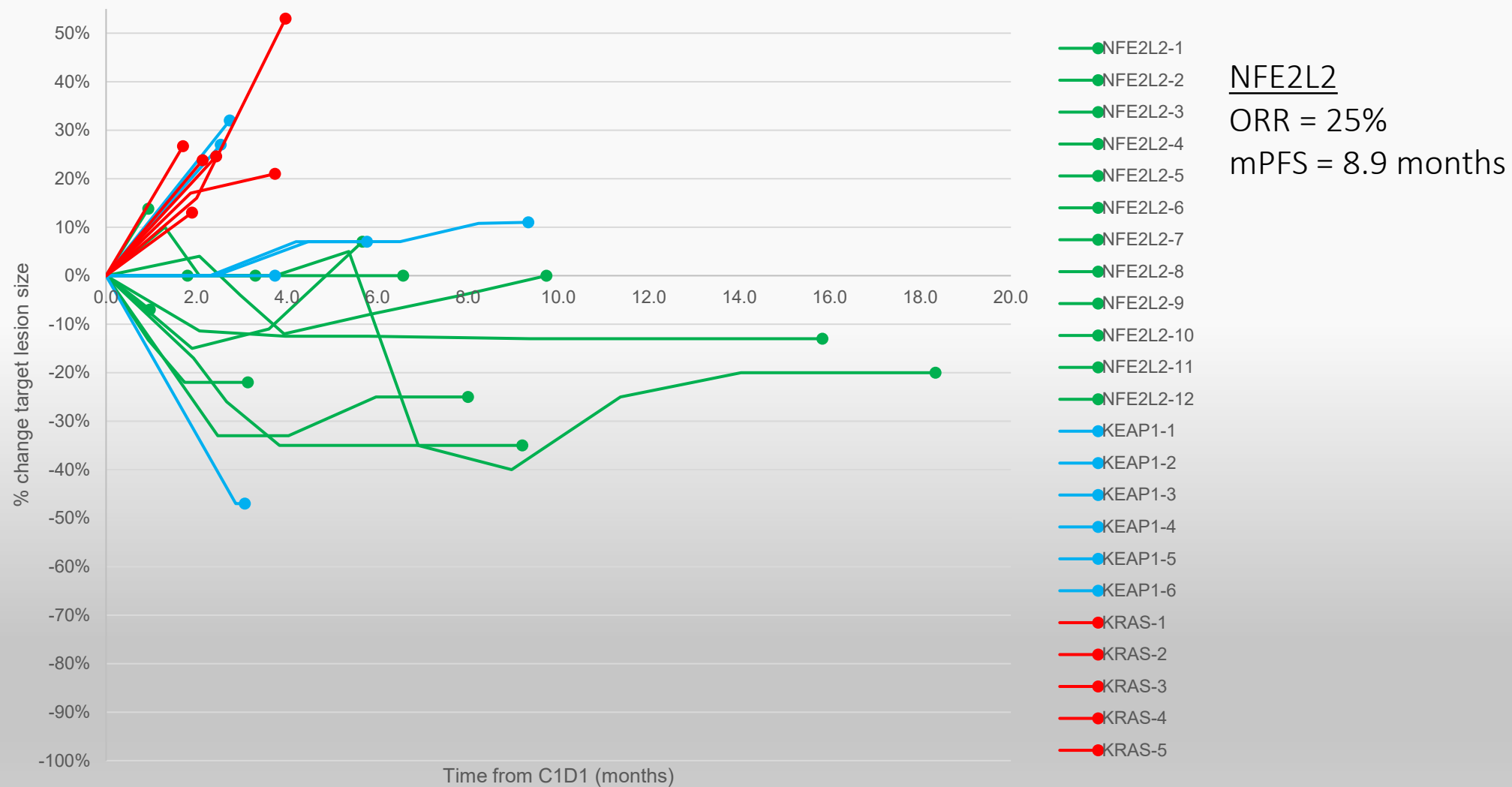


Paik et al, Cancer Discovery 2015

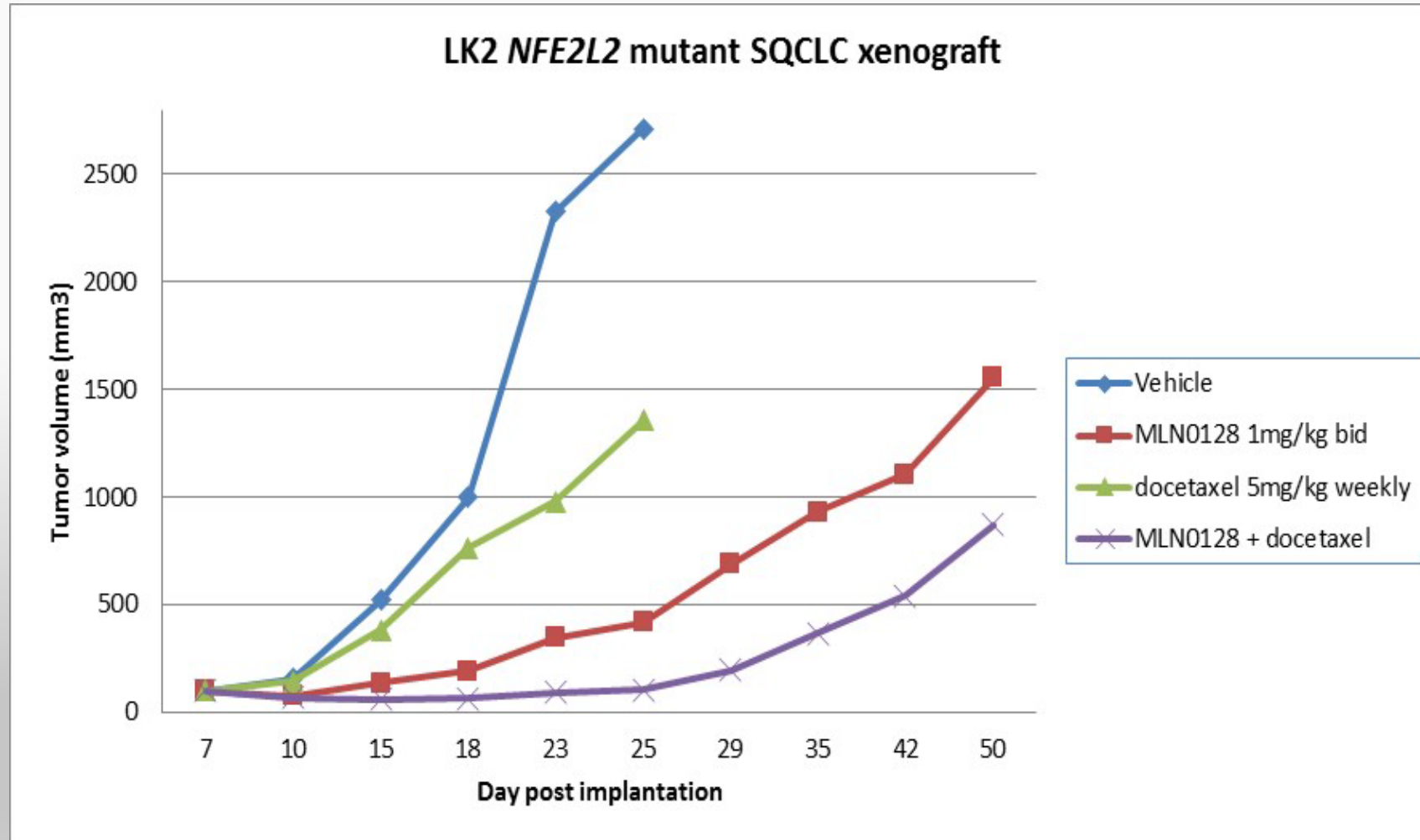
NFE2L2 mutations in SQCLC



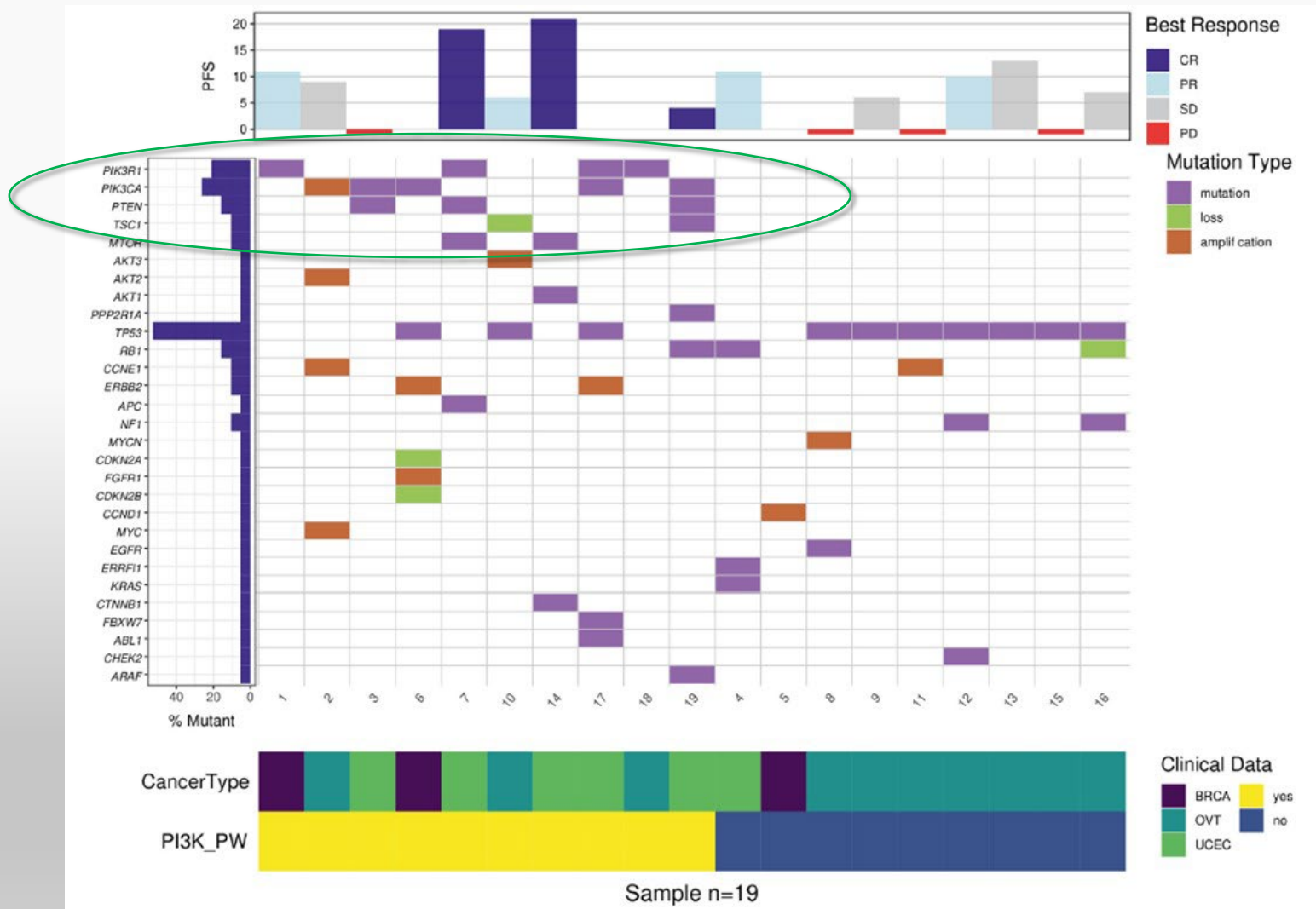
Spider plot of responses to TORC1/2 inh: differential activity by mutation



TORC1/2 inh + taxane has increased efficacy in LK2 NFE2L2 mutant xenograft



TORC1/2 inh + PI3K inh + paclitaxel phase 1 trial results suggest synergistic clinical activity



ORR = 47%
mPFS = 11 months

Stark et al. Gynecol Oncol 2022

Trial Design

S1900P A Randomized Phase II Study of Paclitaxel plus TORC1/2 inhibitor vs. Paclitaxel plus TORC1/2 inhibitor plus PI3K inhibitor in Participants with NFE2L2, KEAP1 or PI3K Pathway-Positive Stage IV Squamous Cell Lung Cancers (ECOG-ACRIN Lung-MAP Sub-Study)

Study Chairs: Paik (ECOG-ACRIN), Riano (Alliance)

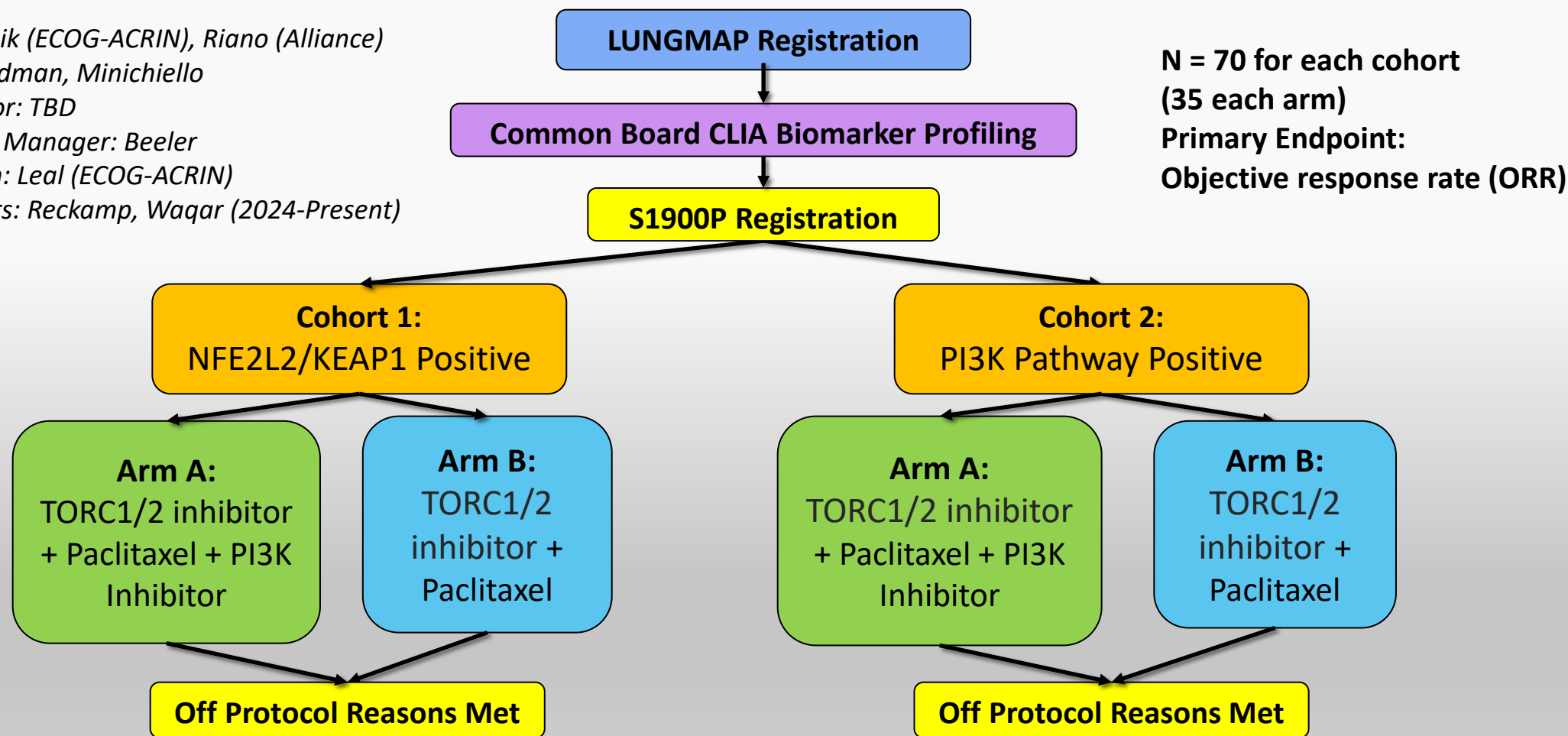
Statisticians: Redman, Minichiello

Data Coordinator: TBD

Protocol Project Manager: Beeler

Study Champion: Leal (ECOG-ACRIN)

Lung-MAP Chairs: Reckamp, Waqar (2024-Present)



Biostatistics PFS

- Within a cohort, if both treatment arms meet the criteria to suggest a signal of activity (≥ 8 responses/35), then progression-free survival will be compared between the arms
- Log-rank test at the 1-sided 15% level once at least 57 PFS events have been reported.
- 90% power to rule out no difference, if the true hazard ratio were 0.54.
- The observed hazard ratio associated with this level of testing (under exponential survival) is 0.76, which if the median PFS in the doublet arm were 4.5 months, would represent around a 1.5-month difference in median PFS between the doublet and triplet arms/cohort.

S1900N

A Randomized Phase II Study of Sacituzumab Govitecan alone, Ivonescimab alone, or combination Sacituzumab Govitecan and Ivonescimab in Participants with Previously-Treated Actionable Genomic Alteration Positive Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Sub-Study)

SUSAN SCOTT, MD

Study Chair (ECOG-ACRIN)

JONATHAN RIESS, MD

Study Co-Chair (SWOG)

Mary W. Redman, PhD

Statistics Chair (SWOG)

John Wrangle, MD

Study Champion (SWOG)

Disclosures

Research Funding (to institution):

Pfizer, Boehringer Ingelheim, Revolution Medicines, ArriVent, Nuvalent, Kinnate, IO Biotech, AstraZeneca, Summit, Merck, Novartis.

Consulting/Advisory Board:

BMS, Janssen, Roche/Genentech, Regeneron, Oncohost, Merck, Pfizer, GSK, Bicycle Therapeutics, Daiichi Sankyo, Replimmune, AstraZeneca



LUNG-MAP

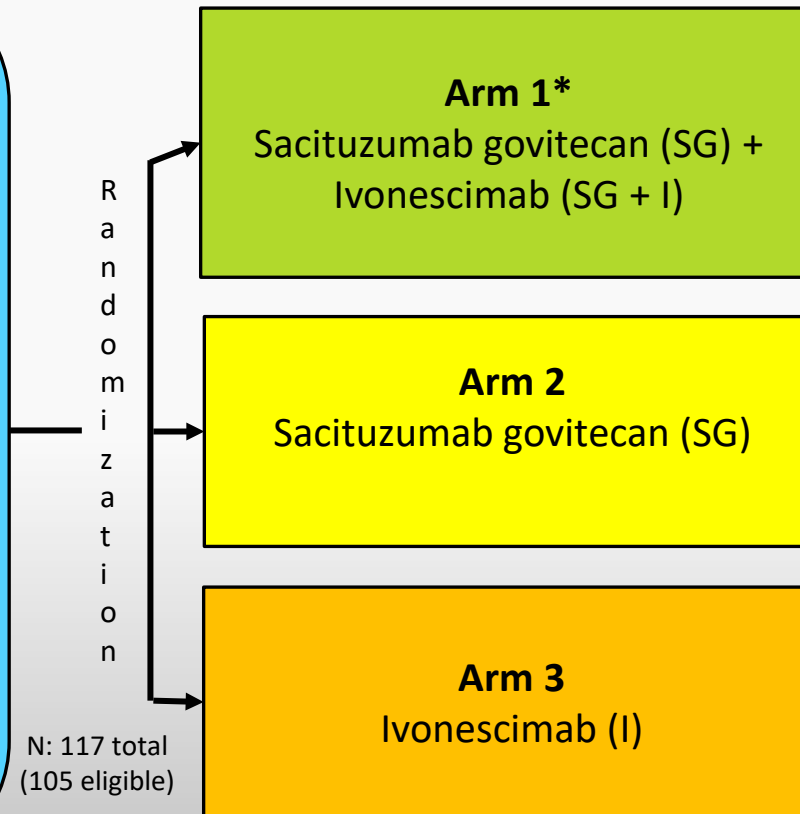


Study Chairs: Scott, Riess
Statisticians: Redman, Minichiello
Data Coordinator: Moralda
Protocol Project Manager: Chadwell
Study Champion: Wrangle
Lung-MAP Chairs: Borghaei, Reckamp (2022-2024)
Reckamp, Waqar (2024-Present)

- Metastatic NSCLC
- Tumor must harbor an actionable genomic alteration (EGFR, ALK, ROS1, MET, RET, HER2, NTRK)
- Progression on or after platinum-based chemo and approved targeted therapy
- No prior anti-PD-(L)1 therapy
- No prior TROP2 ADC
- No limit on prior lines of treatment (no more than 3 lines of prior cytotoxic chemotherapy)
- Stable, treated or untreated brain metastases are allowed

Stratification factors:

Any EGFR mutation (yes/no)
Brain metastasis (yes/no)



***Safety run-in** on 1st 10 patients in arm 1.
Primary endpoint: DLT = grade 3+ non-heme/grade 4 heme. Neutropenia only DLT if G4 febrile neutropenia. Acceptable DLT rate 30%.

- Primary Endpoint(s):
PFS and Response
- Secondary Endpoints:
DOR, toxicity, OS, CNS PFS
- Exploratory objectives:
PFS by PD-L1 status, ctDNA clearance, PFS by PROphet blood-based assay, TROP2 IHC

Activated: August 2026

Anticipated study duration: ~30 months (4-5 pts per month)

Virtual attendees–

Place your questions in the chat box and a team member will read it out loud for the Lung-MAP team to answer.

Q & A Session

KAREN RECKAMP, MD,MS, CHAIR, LUNG-MAP (SWOG)

ALL ATTENDEES

S1900Q

A Phase II Study of TKI + ADC in HER2 Mutant Relapsed/Refractory Advanced Non-Small Cell Lung Cancer (Alliance Lung-MAP Sub-Study)

KAUSHAL PARIKH, MD

Study Chair (Alliance)

DEBORAH DOROSHOW, MD

Study Co-Chair (SWOG)

Mary W. Redman, PhD

Statistics Chair (SWOG)

Konstantin Dragnev, MD

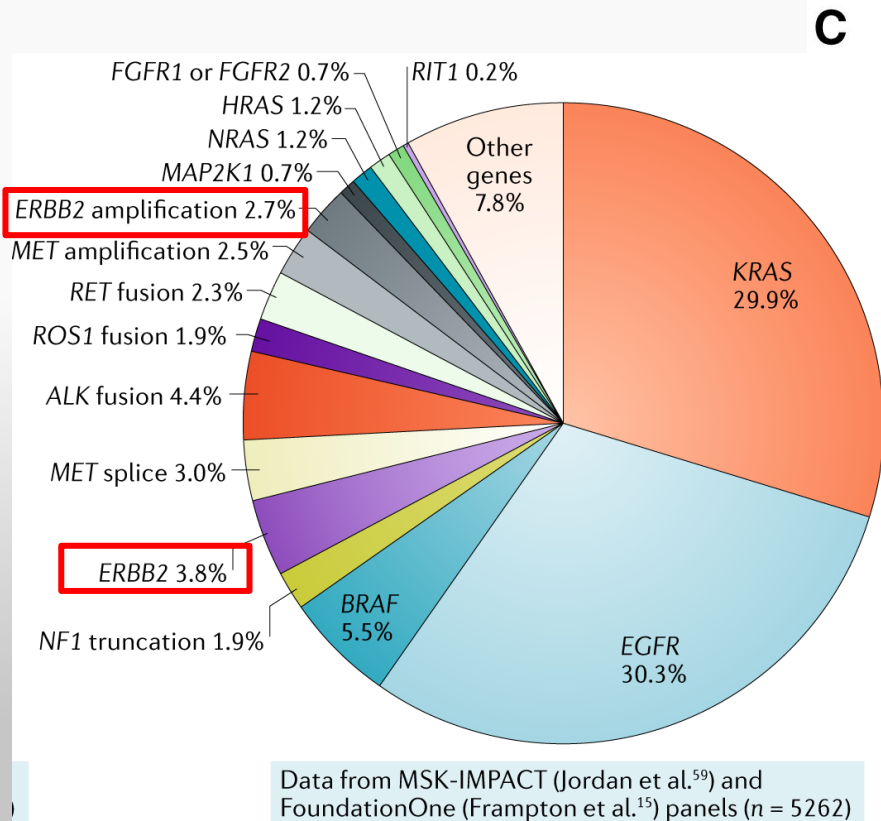
Study Champion (Alliance)

Outline

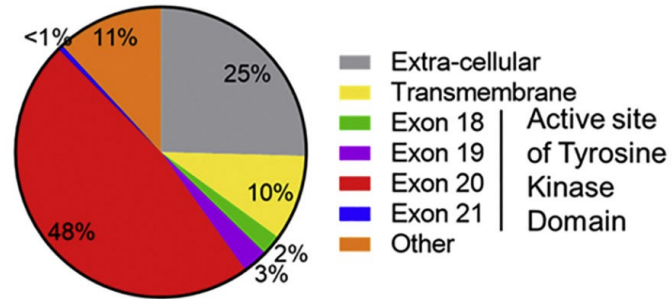
- HER2 Alterations in NSCLC
- Current Strategies for HER2 altered NSCLC
- Preclinical data for combining HER2 TKI plus HER2 ADC
- Clinical Trial Concept

HER2 Alterations in NSCLC

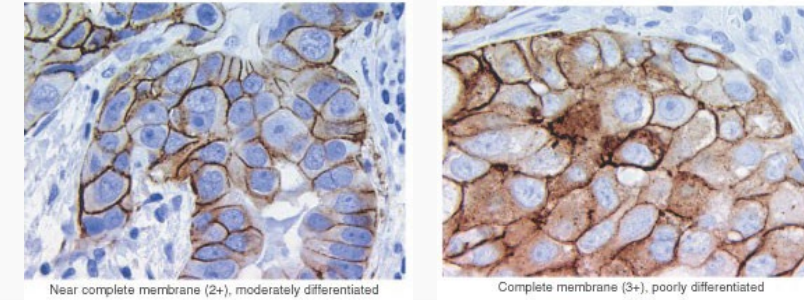
NSCLC molecular landscape



TKD vs non-TKD mutations



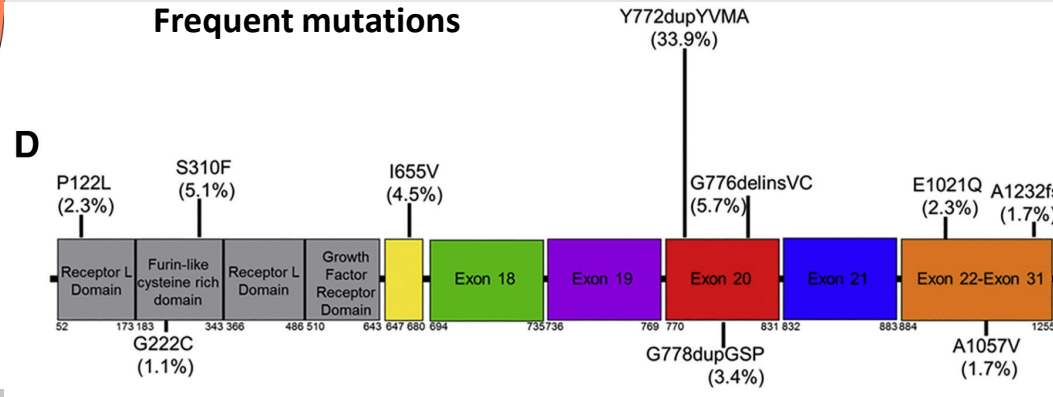
HER2 overexpression



2+/3+ seen in 20-35% of LuAds

Hirsch et al. BJC 2003

Frequent mutations



Robichaux et al. Cancer Cell 2019

Skoulidis and Heymach. Nature Reviews Cancer 2019

Current Approved Therapies for HER2 Dysregulated NSCLC

TRASTUZUMAB DERUXTECAN (T-DXD)

- Antibody drug conjugate targeting HER2 receptor
- Topoisomerase-1 inhibitor payload (exatecan)
- DAR 8:1

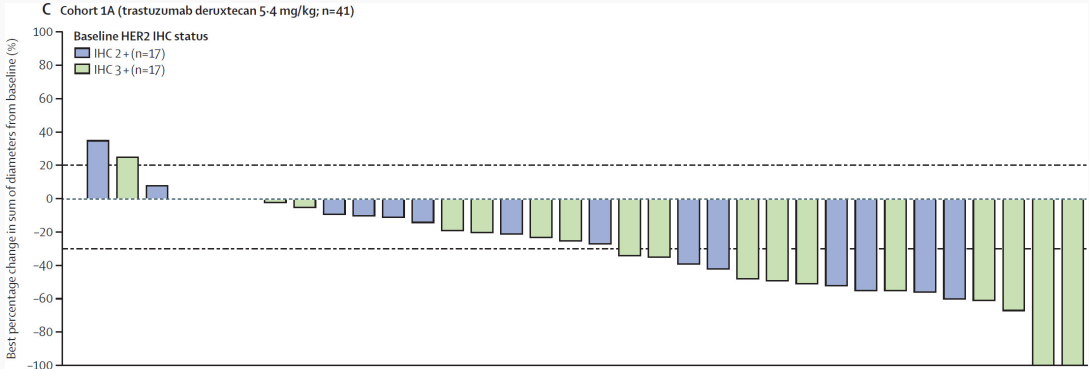
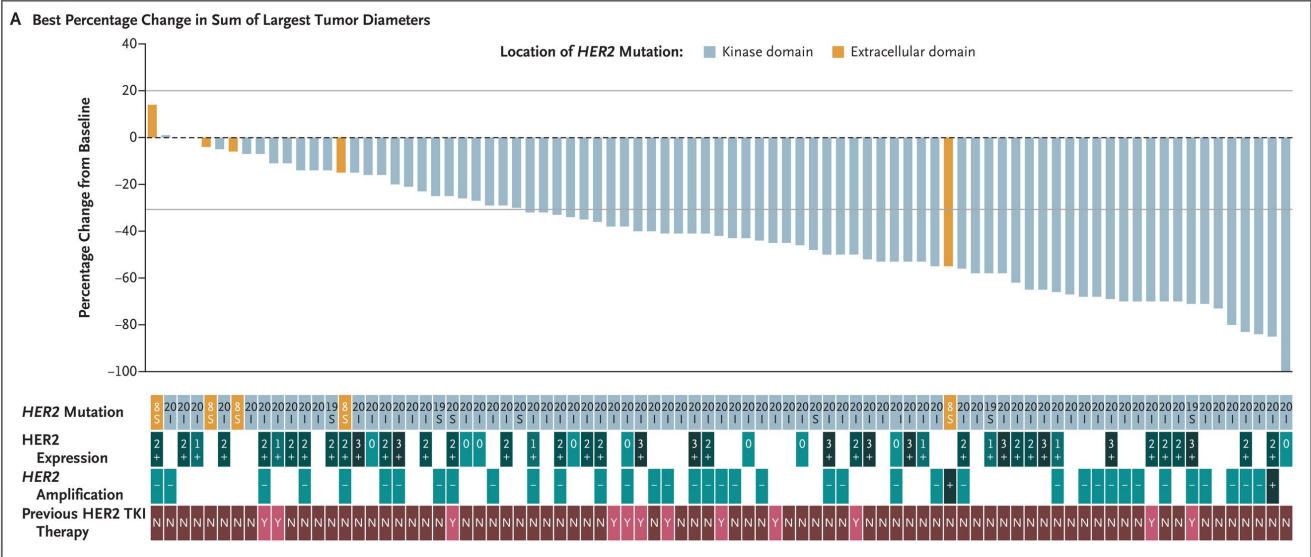
ZONGERTINIB

- Selective HER2 tyrosine kinase inhibitor
- Covalently binds to C805 causing irreversible inhibition of HER2 phosphorylation

SEVABERTINIB

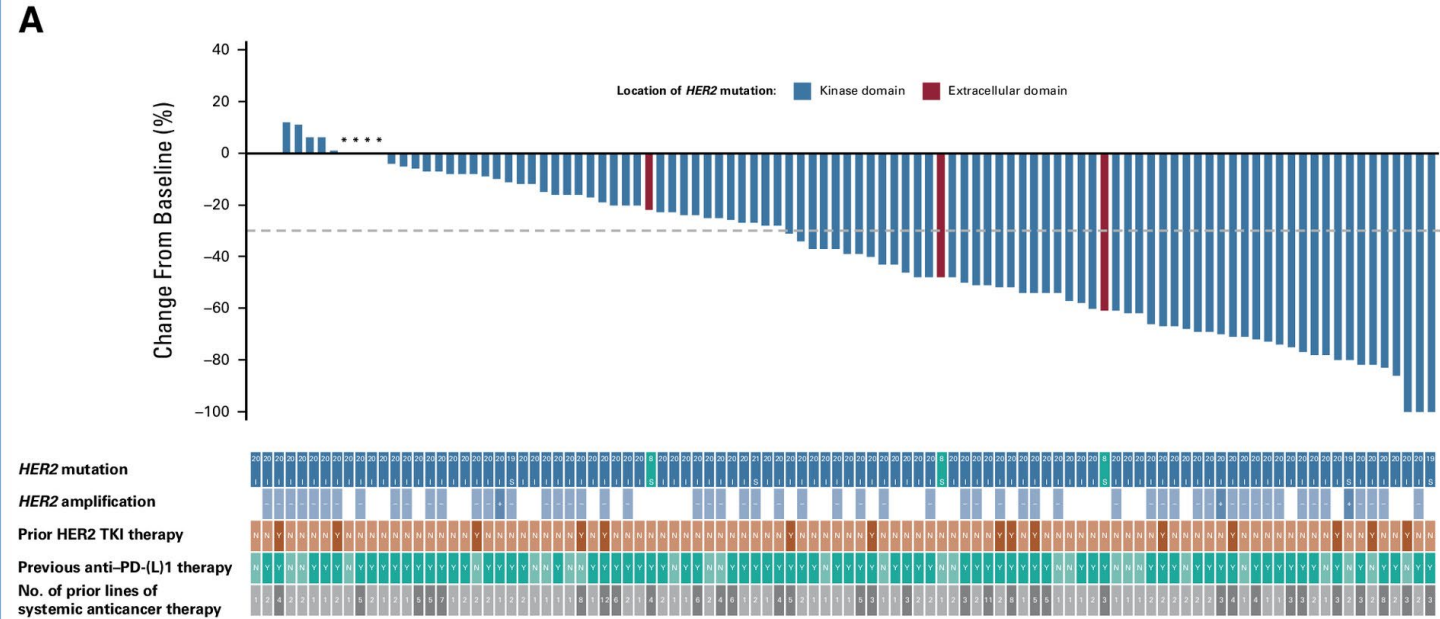
- Mutant HER2 and EGFR tyrosine kinase inhibitor
- Reversible inhibition of HER2

T-Dxd Efficacy Data

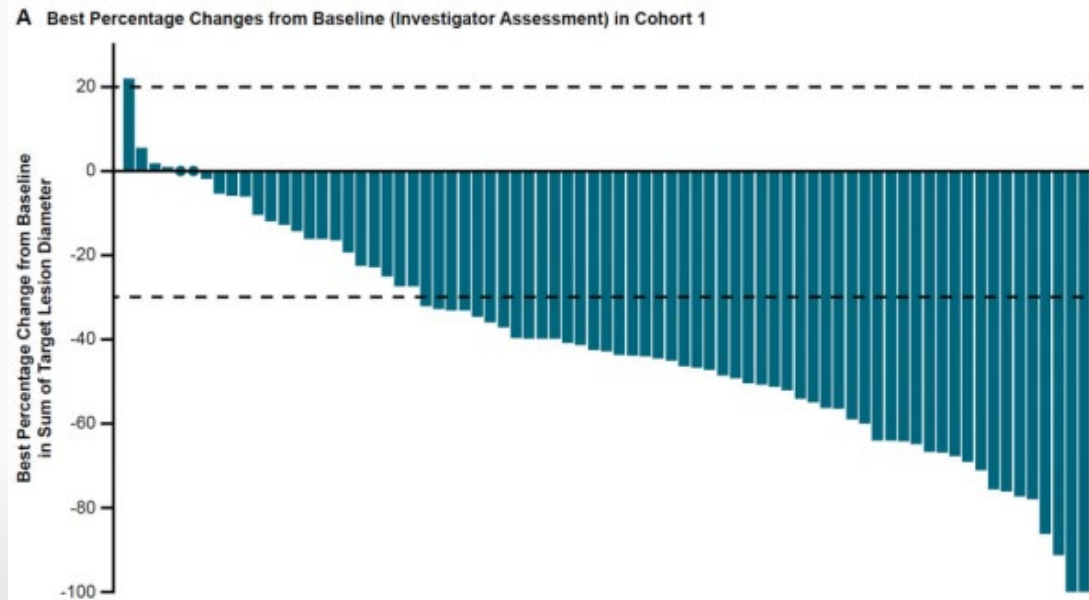


	Her2 mt	Her2 OE
ORR	58%	34.1%
PFS	9.9 m	6.7 m
DOR	16.8 m	6.2 m

Li et al, NEJM 2021
Goto et al, JCO 2023
Smit et al, Lancet Oncol 2024



Zongertinib efficacy data – Beamion Lung-1



	HER2 naïve	Prior ADC
ORR	75%	44%
PFS	12.4 m	6.8 m
DOR	14.1 m	5.3 m

FDA grants accelerated approval to zongertinib for non-squamous NSCLC with HER2 TKD activating mutations

On August 8, 2025, the Food and Drug Administration granted accelerated approval to zongertinib (Hernexeos, Boehringer Ingelheim Pharmaceuticals, Inc.), a kinase inhibitor, for adults with unresectable or metastatic non-squamous non-small cell lung cancer (NSCLC) whose tumors have HER2 (ERBB2) tyrosine kinase domain (TKD) activating mutations, as detected by an FDA-approved test, and who have received prior systemic therapy.

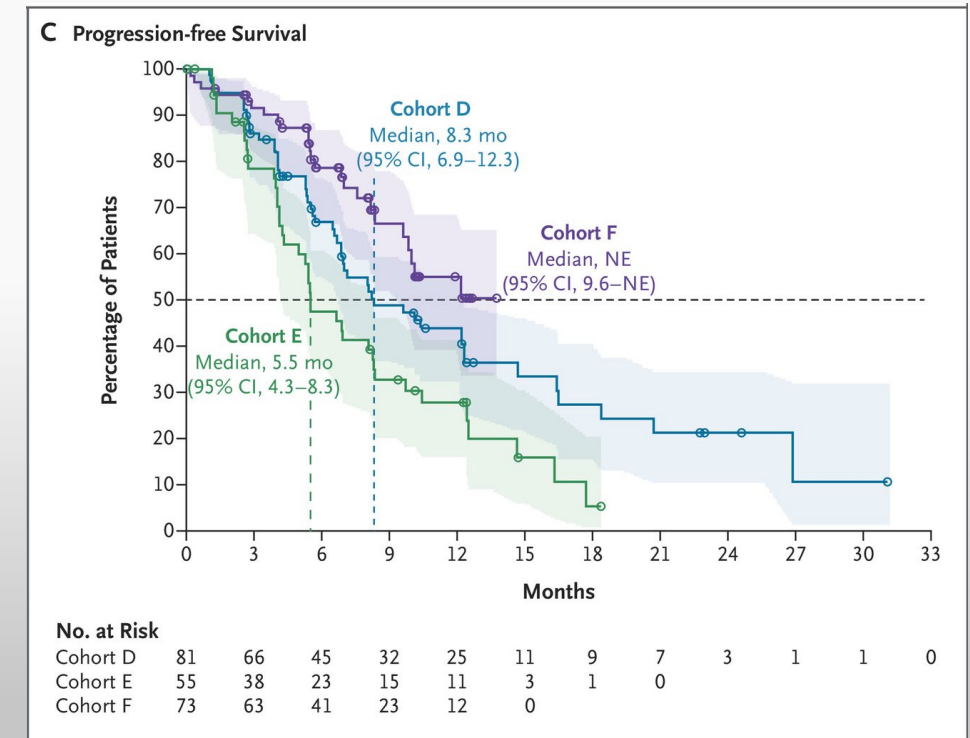
Cohort 3 (N = 20)			
HER2 non-TKD mutation type — no. (%)	Activating mutation	Objective response — no. (%)	
Extracellular domain	-	3 (25)	
S310F*	Known	3 (50)	
S310Y	Known	0	
D277Y	Known	0	
S113F	Unknown	0	
Transmembrane domain	-	3 (43)	
V659E	Known	3 (50)	
G660D	Likely	0	
Intracellular domain	-	0	
P1199S	Unknown	0	

Sevabertinib efficacy data – SOHO-01

	Prior chemo (n=81)	Prior ADC (n=55)	Rx naïve (n=73)
ORR	64%	38%	71%
PFS	8.3 m	5.5 m	NE
DOR	9.2 m	8.5 m	11.0 m

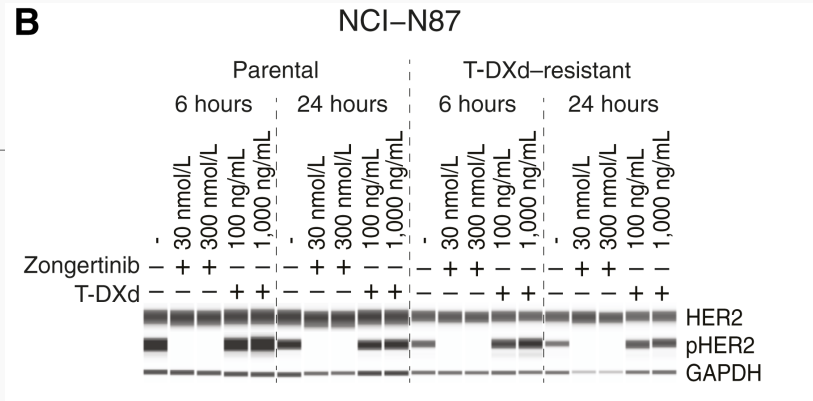
FDA grants accelerated approval to sevabertinib for non-squamous non-small cell lung cancer

On November 19, 2025, the Food and Drug Administration granted accelerated approval to sevabertinib (Hymuo, Bayer HealthCare Pharmaceuticals Inc.), a kinase inhibitor, for adults with locally advanced or metastatic, non-squamous non-small cell lung cancer (NSCLC) whose tumors have *HER2* (*ERBB2*) tyrosine kinase domain (TKD) activating mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy.

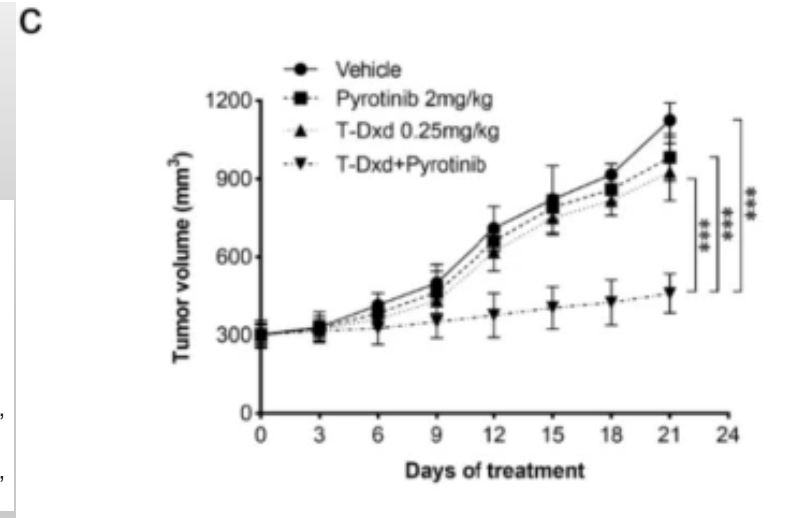
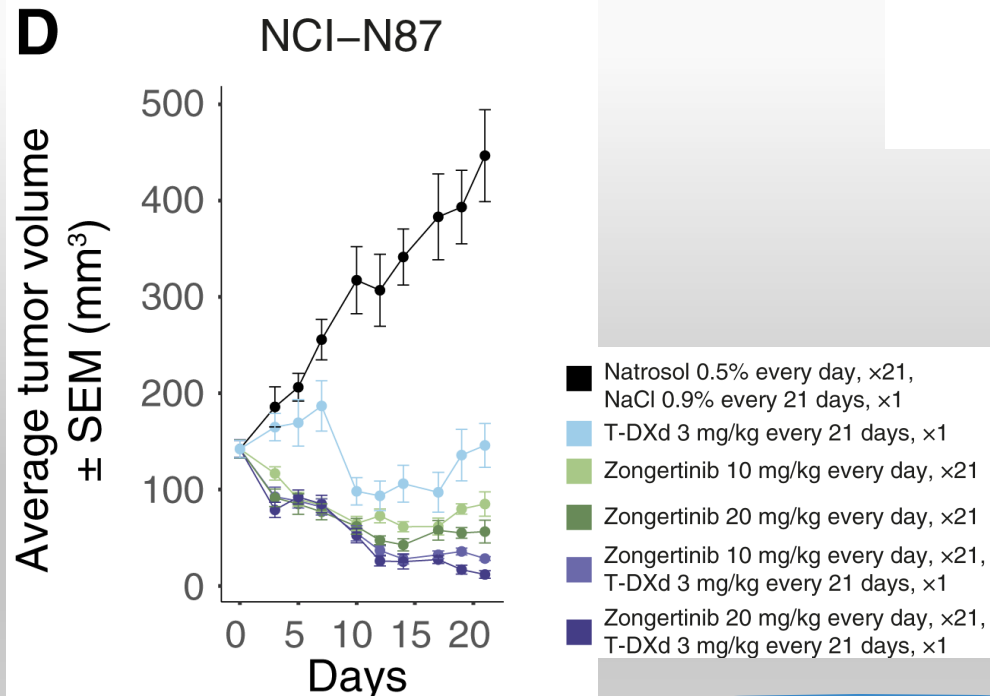
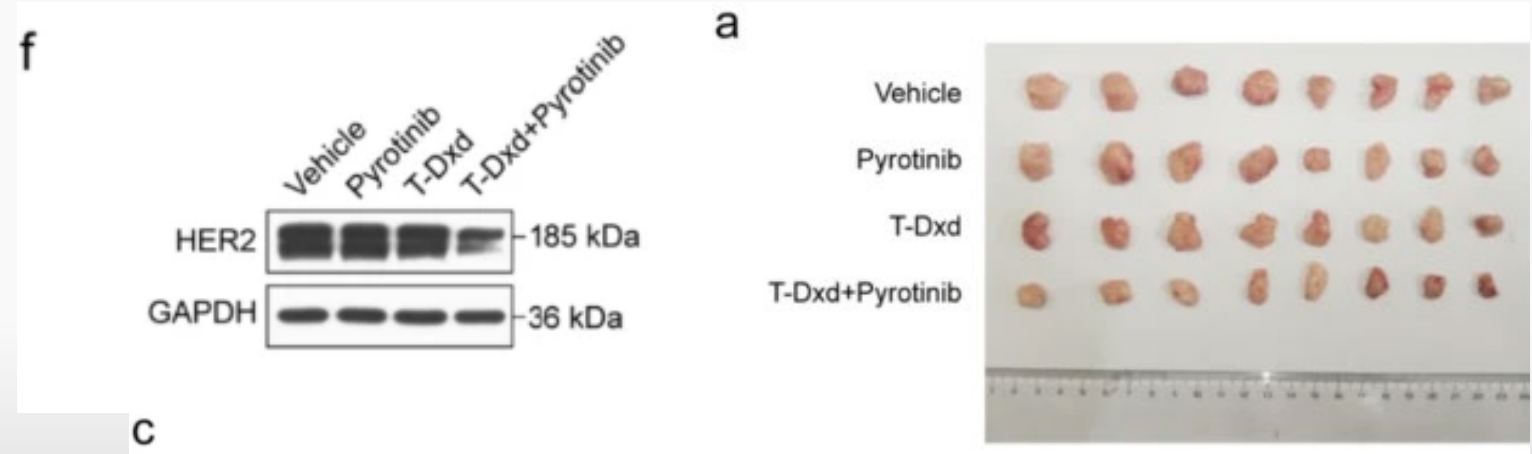


Le, NEJM 2025
FDA.gov

Preclinical evidence for HER2 TKI+ADC

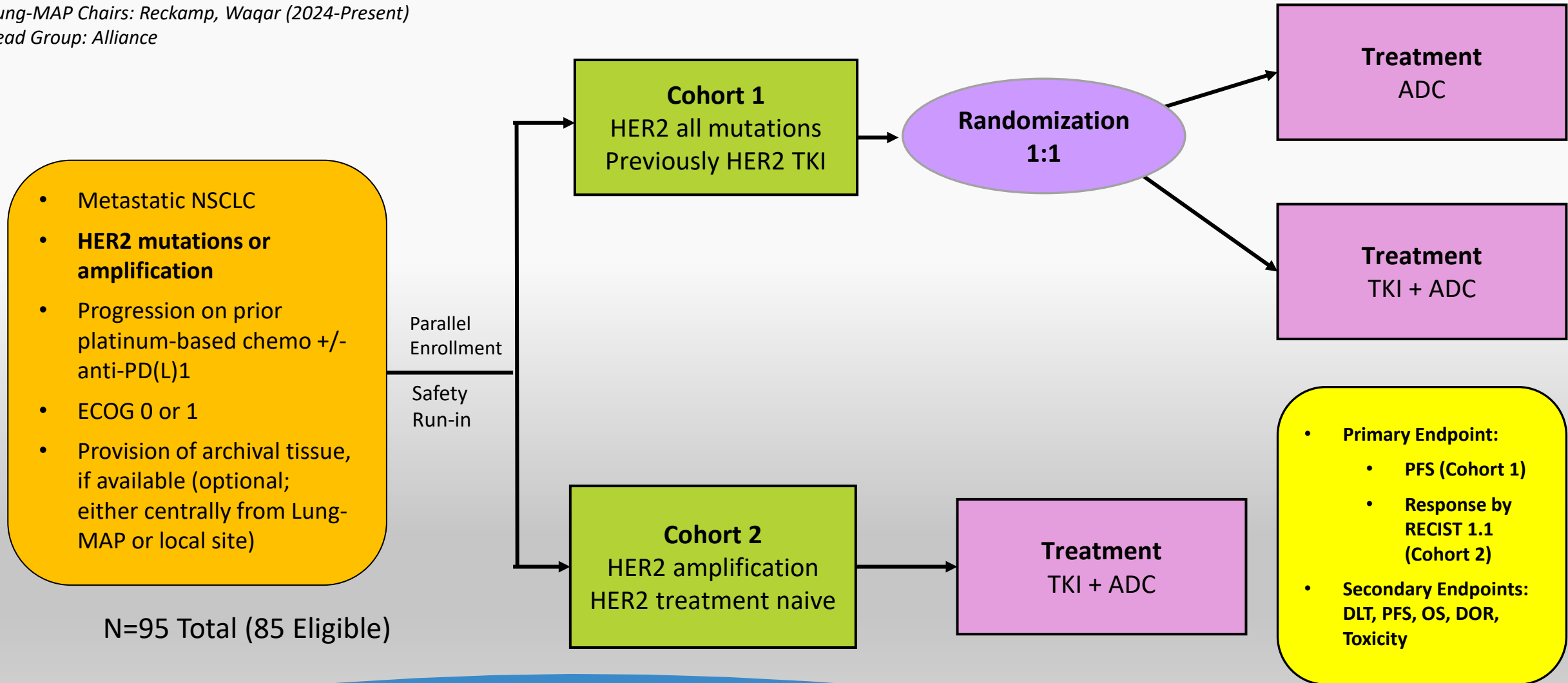


Synergism seen in PDX models against combined ADC + TKI



Liu et al. Gastric Cancer 2024

Study Chairs: Parikh, Doroshow
Statisticians: Redman, Minichiello
Data Coordinator: TBD
Protocol Project Manager: Chadwell
Study Champion: Dragnev
Lung-MAP Chairs: Reckamp, Waqar (2024-Present)
Lead Group: Alliance



Virtual attendees–

Place your questions in the chat box and a team member will read it out loud for the Lung-MAP team to answer.

Q & A Session

KAREN RECKAMP, MD,MS, CHAIR, LUNG-MAP (SWOG)

ALL ATTENDEES

Contact Us

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Acknowledgements

Thank you for supporting the Lung-MAP Trial!

Patients and Sites

Lung-MAP Site Coordinators Committee

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Participant Engagement Coordinator

Accrual Enhancement Committee

Trial Oversight Committee

Study Chairs

Statistical Team

Pharmaceutical Collaborators

Data Coordinators & Protocol Project Managers

Applications Development Team

Quality Assurance Team

Funding & Contracts Team

NCI, CTEP, CIRB, CTSU

Foundation for the National Institutes of Health

Friends of Cancer Research

CCS Associates Inc.



Thank you for joining us!

The slides will be available on the SWOG & CTSU websites.