Lung-MAP Update Meeting

SWOG FALL MEETING
OCTOBER 21, 2022

Agenda

- Welcome & Leadership Update Announcement – *Jhanelle E. Gray, MD*
- Lung-MAP Accomplishments– *Roy Herbst, MD, PhD*
- Manuscript Updates– *Mary Redman, PhD*
- Accrual Review & Update on Future Direction of S1800A– *Karen Reckamp, MD, MS*
- S1900G Site Initiation Training – *Sarah Goldberg, MD, MPH*
- LUNGMAP Revision #7 – *Jyoti Patel, MD*
- S1900F Update – *Jhanelle E. Gray, MD*
- S1800D Update – *John Wrangle, MD*
- S1900E Update – *Sukhmani Padda, MD*
- Translational Medicine Committee Updates –*David Kozono, MD, PhD*
- Drug Selection Committee Updates – *Hossein Borghaei, DO, MS & Saiama Waqar, MD*

There will be a Q & A session at the end of the presentation.

Welcome & Leadership Announcement

JHANELLE E. GRAY, MD

LUNG COMMITTEE CHAIR

SWOG

LUNG-MAP

Lung-MAP Accomplishments

ROY HERBST, MD, PHD

LUNGMAP EMERITUS STUDY CHAIR & SENIOR ADVISOR

SWOG

LUNG-MAP

Lung-MAP Publications:

Manuscripts, Abstracts, and Presentations

MARY REDMAN, PHD

LEAD STATISTICIAN

SWOG

LUNG-MAP

Lung-MAP Publications Fall 2021-2022

- **S1800A**: A Phase II Randomized Study of Ramucirumab and Pembrolizumab Versus Standard of Care in Advanced Non-Small-Cell Lung Cancer Previously Treated With Immunotherapy-Lung-MAP S1800A. Reckamp KL, Redman MW, Dragnev KH, Minichiello K, Villaruz LC, Faller B, Al Baghdadi T, Hines S, Everhart L, Highleyman L, Papadimitrakopoulou V, Gandara DR, Kelly K, Herbst RS. J Clin Oncol 2022
  - Presented at ASCO and co-published in JCO, June 2022.

Lung-MAP Presentations and Pending Publications

- **S1900A** A phase II study of rucaparib in patients with high genomic LOH and/or BRCA 1/2 mutated stage IV non-small cell lung cancer Jonathan W. Riess, Mary Weber Redman, Paul Wheatley-Price, Bryan A. Faller, Liza C. Villaruz, Larry R. Corum, Aruna C. Gowda, Gordan Srkalovic, Raymond U. Osarogiagbon, Megan Ann Baumgart, Lu Qian, Katherine Minichiello, David R. Gandara, Roy S. Herbst, Karen Kelly
  - Presented at ASCO 2021. Study team finalizing manuscript
- **S1900C**: A Phase II Study of avelumab and talazoparib in Patients with STK11/LKB1-MUTANT positive STAGE IV Non-small Lung Cancer Ferdinandos Skoulidis, Mary Weber Redman, Jennifer Marie Suga, Tareq Al Baghdadi, John L. Villano, Sarah B. Goldberg, Liza C Villaruz, Katherine Minichiello, David R. Gandara, Roy S. Herbst, Karen Kelly
  - Presented at ASCO 2022. Study team finalizing manuscript

S1400 Series Publications

Sub-study ID	Biomarker/ Population	Investigational Therapy	SoC/Control Arm	Publication, 1st author
S1400	All patients: screening study	N/A	N/A	Lancet 12/2020, Redman
S1400A	Non-Match, immunotherapy naïve	Durvalumab	Docetaxel	Clinical Lung Cancer 2020, Borghaei
S1400B	PI3KCA alteration by FMI	Taselisib	Docetaxel	JTO 2019, Edelman
S1400C	Cell Cycle Gene Alterations by FMI	Palbociclib	Docetaxel	JTO 2019, Langer
S1400D	FGFR Alteration by FMI	AZD4547	Docetaxel	JTO 2019, Aggarwal
S1400F	Non-Match, immunotherapy exposed	Durvalumab + Tremelimumab	N/A	Journal for Immunotherapy of Cancer 2021, Leighl
S1400G	Homologous recombinant repair deficiency (HRRD) genes by FMI	Talazoparib	N/A	Clinical Lung Cancer 2021, Owonikoko
S1400I	Non-Match, immunotherapy naïve	Nivolumab + Ipilimumab	Nivolumab	JAMA Oncology 2021, Gettinger
S1400K	c-MET by IHC (Ventana Rabbit SP44 Antibody c-MET Assay)	ABBV-399	N/A	Clinical Lung Cancer 2020, Waqar
S1400GEN	N/A ancillary study for physician and patients thoughts on genomic screening	N/A	N/A	JCO Oncol. Practice 2021, Roth

Lung-MAP Translational Medicine Efforts

- **Lung Master Protocol (Lung-MAP) Next Generation Sequencing Analysis of Advanced Squamous Cell Cancers (SWOG S1400)** D. Kozono, X. Hua,2 M. Wu, K. Tolba, S. Waqar, K. Dragnev, H. Cheng, F. Hirsch, P. Mack,7 K. Kelly, R. Herbst, D. Gandara, M. Redman
  - World Conference on Lung Cancer 2020 January 28-31, 2021. Manuscript under preparation for submission.
- **LUNGMAP Master Protocol (LUNGMAP): Concordance Between Plasma ctDNA and Tissue Molecular Analysis** P. Mack, K. Minichiello, M. Redman, K. Tolba, D. Kozono, S. Waqar, A. Chowdhury, A. Dowlati, J. Neal, K. Dragnev, C. Aggarwal, F. Hirsch, K. Kelly, D. Gandara, R. Herbst
  - World Conference on Lung Cancer 2020 January 28-31, 2021. Updating analyses underway and manuscript anticipated for 2022
- **Tumor Mutation Burden (TMB) by Next Generation Sequencing (NGS) Associates with Survival (OS) in Lung-MAP Immunotherapy Trials S1400I and S1400A** F. Hirsch,X. Hua, M. Wu, J. Neal, H. Cheng, S. Gettinger, L. Bazhenova, V. Papadimitrakopoulou, H. Borghaei, P. Mack, K. Kelly, R. Herbst, D. Gandara, Redman, D. Kozono
  - World Conference on Lung Cancer 2020 January 28-31, 2021. Manuscript being finalized for submission.
- **CIMAC projects on S1400I**
  - Dynamic changes in circulating protein levels reveal an association between ipilimumab and nivolumab combination treatment (SWOG Lung-MAP S1400I trial) with outcomes in squamous cell lung cancer
  - Immune gene expression signatures associated clinical benefit from nivolumab and ipilimumab for previously treated patients with stage IV squamous cell lung cancer: An immune biomarker analysis of phase III SWOG LungMAP S1400I trial
  - Infiltration and spatial distribution of immune cells are associated clinical benefit from Nivolumab and Ipilimumab for previously treated patients with stage IV squamous cell lung cancer: an immune biomarker analysis of Phase III SWOG LungMAP S1400I trial
  - Multiomics profiling reveals molecular and immune features associated with benefit from immunotherapy for Previously Treated Stage IV or recurrent Squamous Cell Lung Cancer patients from the Phase III SWOG LungMAP S1400I trial
  - Presented at AACR and ASCO 2022 and publications are underway, led by the Mt. Sinai and MDACC CIMAC groups

Accrual review & Future direction for S1800A

KAREN RECKAMP, MD, MS

LUNGMAP VICE CHAIR (SWOG)

DIVISION DIRECTOR, MEDICAL ONCOLOGY

CEDARS-SINAI

LUNG-MAP

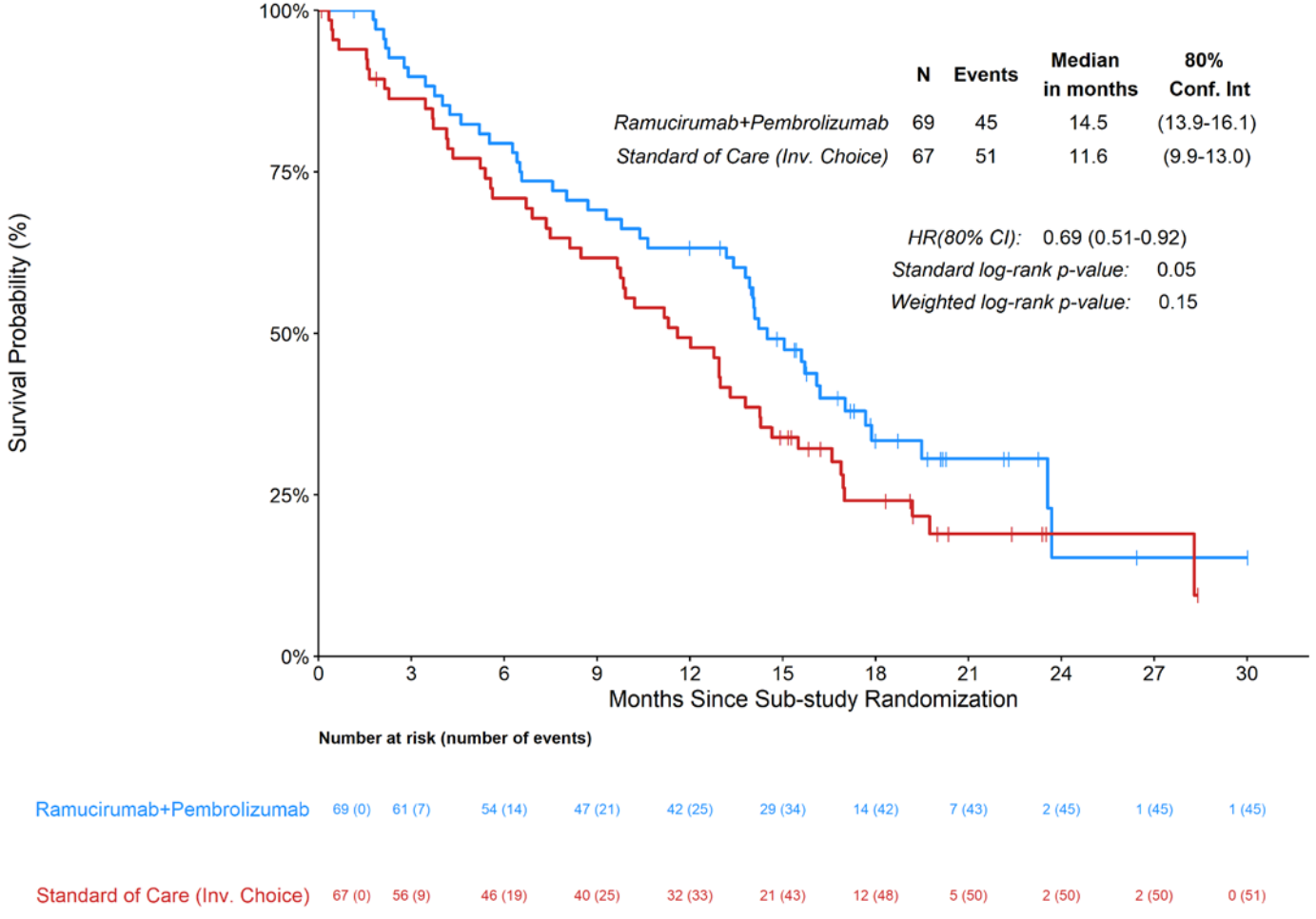
Lung MAP Accrual (as of September 2022)

	ACCR GOAL	TOTAL REGS.	REGS. LAST 12 Month	REGS. LAST 6 Month	REGS. LAST 3 Month	REGS. LAST 30 DAYS	REGS. LAST 7 DAYS
LUNGMAPScreening Protocol Registrations							
Total		2706	516	326	151	52	8
Screened at PD		996	162	112	58	25	5
Pre-Screened prior to PD		1710	354	214	93	27	3
ctDNA Specimen Submission		291	26	18	7	2	1
Re-analysis Requests		223	182	107	48	20	5
Sub-Study Assignments							
LUNGMAP Sub-Study Assignments		1460	460	173	96	35	11
Screened at PD		832	191	99	50	22	5
Pre-Screened prior to PD		580	247	71	45	13	6
After PD on a Lung_MAP Sub-Study		48	22	3	1	0	0
Sub-Study Assignments (open studies only)							
S1800D		401	401	142	80	29	9
S1900E		152	74	31	16	6	2

Sub-Study Registrations							
LUNGMAP Sub-Study Registrations		386	81	54	24	11	2
Initial sub-study registrations		376	80	53	24	11	2
Subsequent sub-study registrations		10	1	1	0	0	0
Patients Registered to a Sub-Study (open studies only)							
S1800D: Non-Match: N-803 + Pembro vs SoC	478	40	40	39	16	7	2
Primary Resistance		3	3	2	1	0	0
Acquired Resistance		37	37	37	15	7	2
S1900E: KRAS G12C: Sotorasib (AMG 510)	116	72	41	15	8	4	0
Cohort 1: TP53		32	21	9	4	2	0
Cohort 2: STK11		16	9	3	1	0	0
Cohort 3: All Others		24	11	3	3	2	0

Future direction for S1800A

S1800A—Overall survival



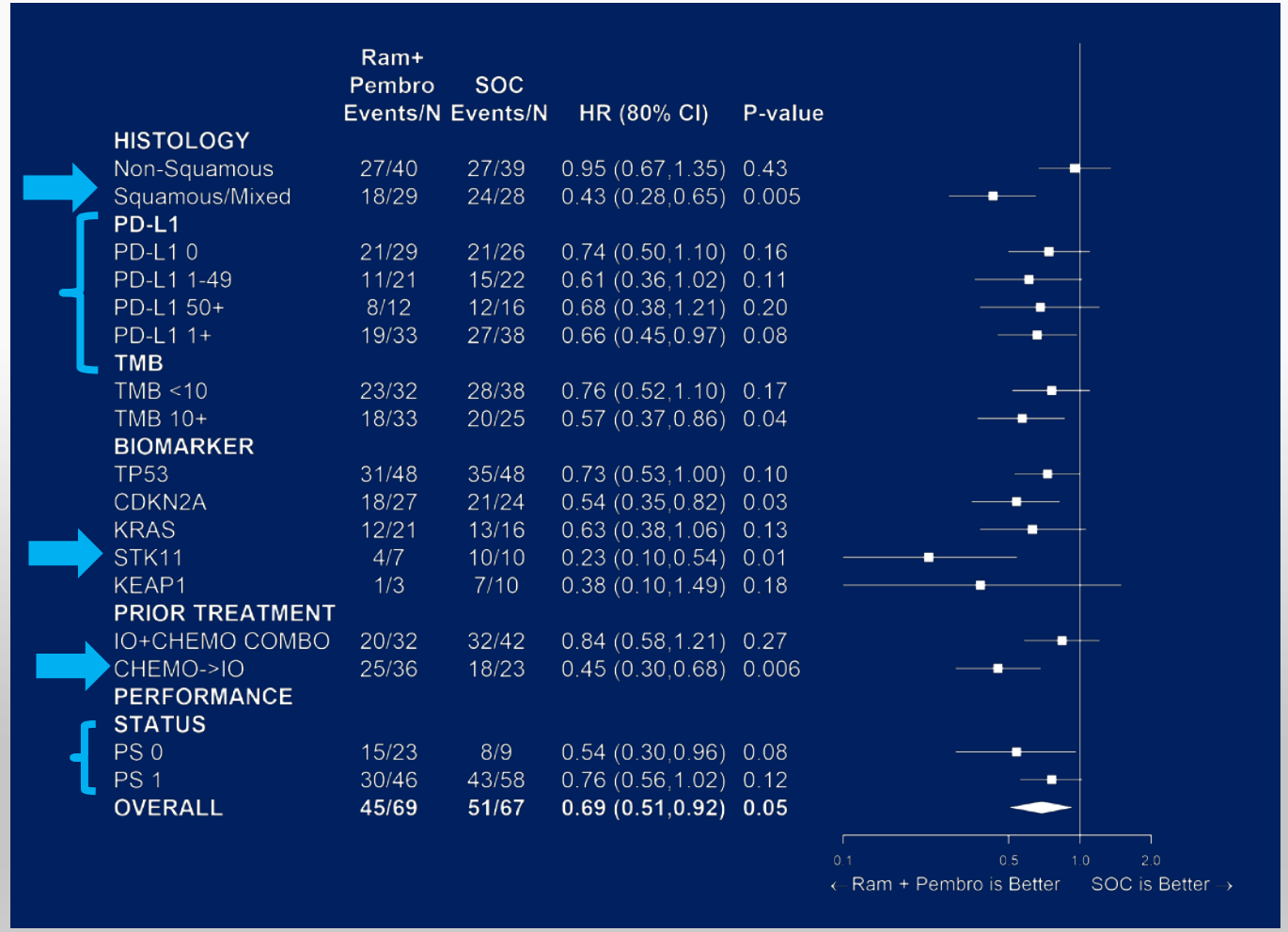
- HR= 0.69; SLR p-value 0.05
- Median OS for RP 14.5 months v. SOC 11.6 months

Standard of care therapy received:

- Docetaxel + Ramucirumab (n = 45)
- Docetaxel (n = 3)
- Gemcitabine (n = 12)
- Pemetrexed (n = 1)
- No treatment (n = 6)

Reckamp KL et al ASCO 2022; J Clin Oncol 2022

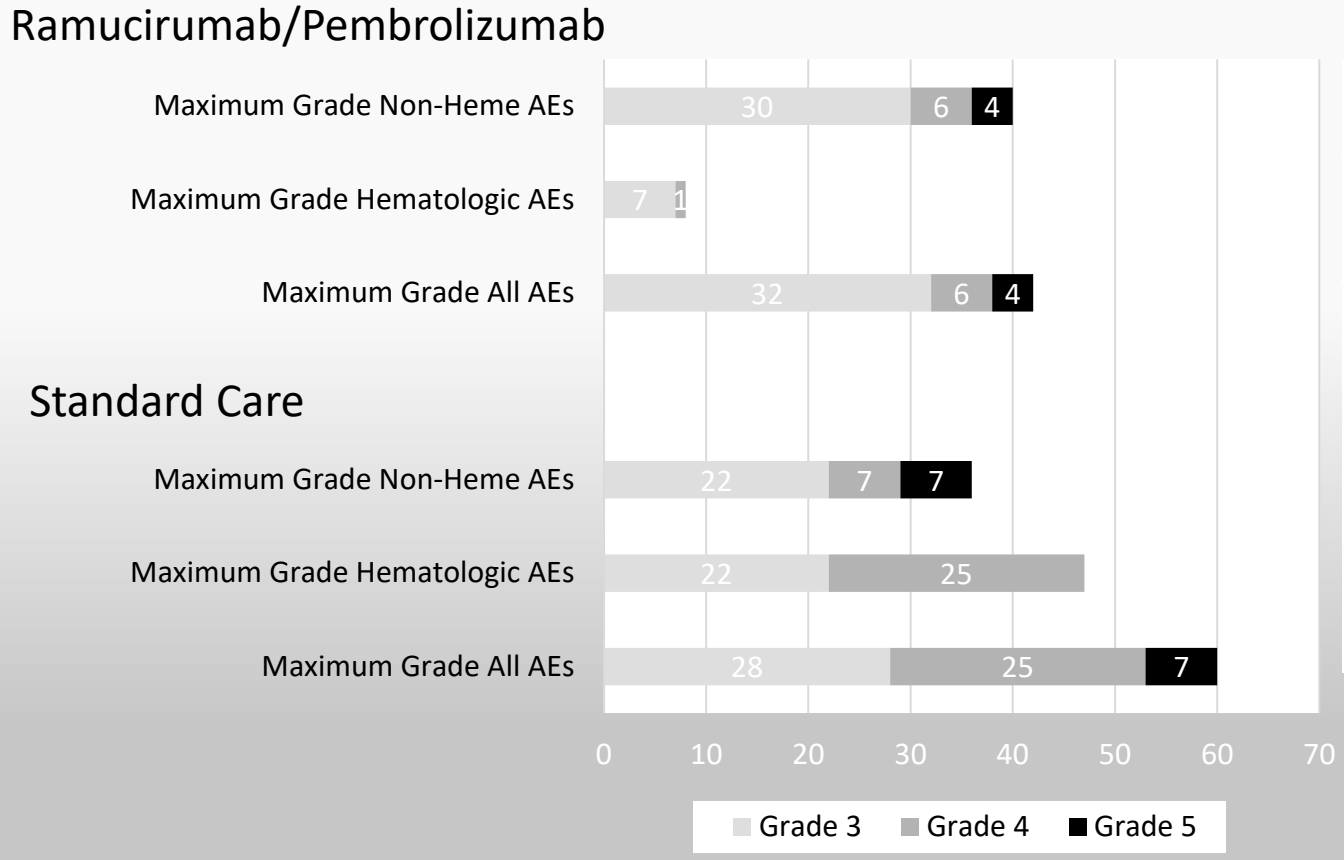
S1800A Overall survival—subgroup analysis

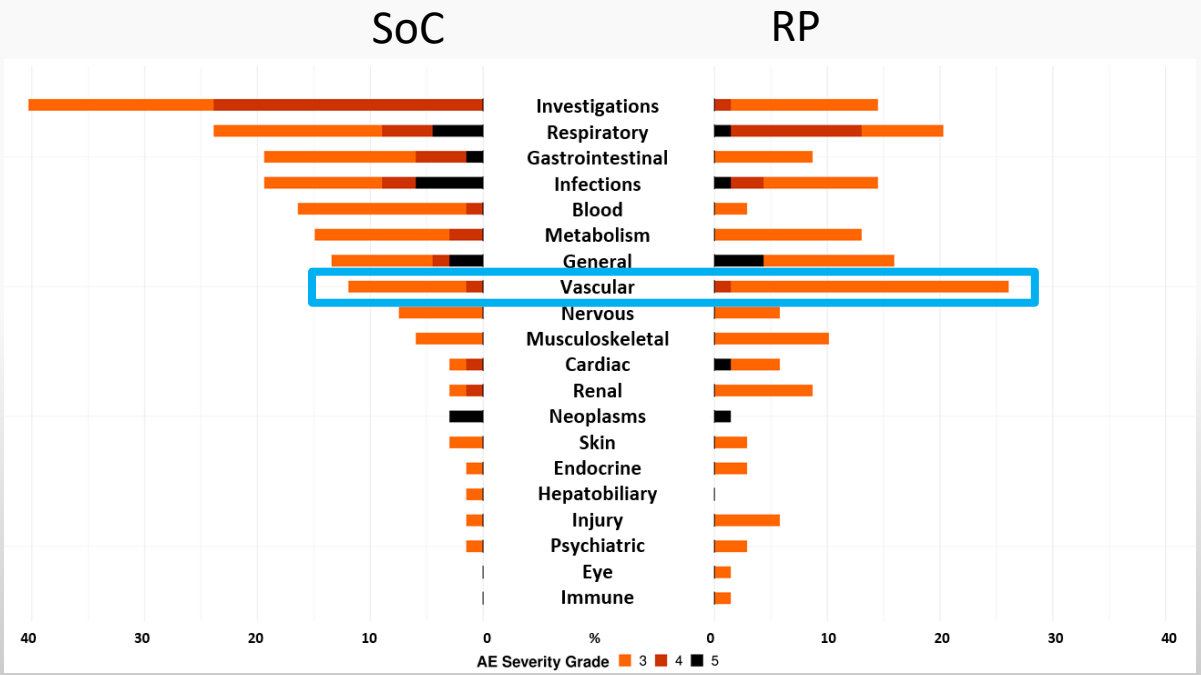


- All subgroup HRs < 1
- HRs by PD-L1 does not appear to vary
- Pronounced benefit in SCC/mixed histology
- Benefit seen with PS 0 and 1
- Co-mutations did not affect OS improvement

Reckamp KL et al ASCO 2022; J Clin Oncol 2022

S1800A Safety summary—Percentage of patients with Grade 3-5 AEs





- Grade ≥3 TRAEs: 42% on RP; 60% on SOC
- Nine (31%) Grade 3–5 irAEs on RP

Reckamp KL et al ASCO 2022; J Clin Oncol 2022

LUNG-MAP

Phase III Rationale

- Springboard from Lung MAP and unique partnership with FDA to provide a platform for NCTN to perform registrational trials in collaboration with industry.
- Effective therapy following frontline ICI for NSCLC is needed with limited FDA-approved options.
- We propose a pragmatic clinical trial design to promote diversity and inclusion in clinical trials.
- The aim of the trial is to validate the improvement in overall survival demonstrated in S1800A.
- The purpose is to empower investigators to treat patients as would be done in real world practice.
- The design is novel and potentially paradigm-changing to decrease barriers to enrollment and minimize the data collection burden.

S2302 Project Pragmatica Treatment/Schema

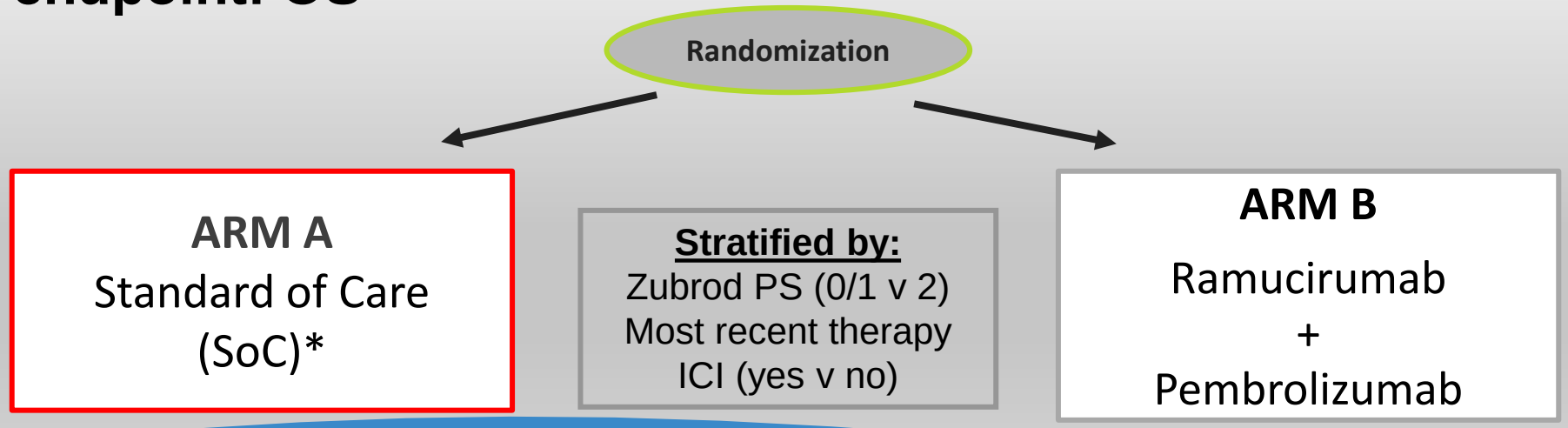
A PROSPECTIVE RANDOMIZED STUDY OF RAMUCIRUMAB (NSC 749128) PLUS PEMBROLIZUMAB (MK-3475; NSC 776864) VERSUS STANDARD OF CARE FOR PARTICIPANTS PREVIOUSLY TREATED WITH IMMUNOTHERAPY FOR STAGE IV OR RECURRENT NON-SMALL CELL LUNG CANCER

Chair: Karen Reckamp, MD; Co-chairs: Konstantin Dragnev, MD; Wade Iams, MD
Statistician: Mary Redman PhD, Jieling Miao, M.S.
Lung community engagement subcommittee representative: Daniel Carrizosa, MD, MS

*SoC treatment is to be determined by the treating investigator and participant. It is recommended that the choice of SoC drug(s) is based on NCCN guidelines for a "systemic therapy for advanced or metastatic disease-subsequent."

Primary endpoint: OS

N= 700 patients



LUNG-MAP

Objectives

- **Primary study objective:** To compare overall survival (OS) between participants previously treated with platinum-based chemotherapy and immunotherapy for Stage IV or recurrent NSCLC randomized to pembrolizumab and ramucirumab versus SOC.

- **Secondary study objective:** To summarize reports of serious and unexpected high-grade (≥ Grade 3) treatment-related adverse events determined by the treating physician within each treatment arm.

Eligibility

The eligibility criteria are notable for items that have been removed from historical eligibility lists to increase inclusion and generalizability.

- Stage IV or recurrent non-small cell lung cancer
- Received at least one line of anti-PD-1 or anti-PD-L1 therapy for any stage of NSCLC, alone or combination therapy
- No more than one line of anti-PD-1 or anti-PD-L1 for Stage IV or recurrent disease
- Disease progression (in the opinion of the treating physician) more than (>) 84 days following initiation (Cycle 1 Day 1) of their most recent anti-PD-1 or PD-L1 therapy
- Best response on anti-PD-1 or anti-PD-L1 therapy of stable, partial response or complete response for stage IV/recurrent NSCLC (in the opinion of the treating physician)
- Disease progression within (<=) 365 days from initiation (Cycle 1 Day 1) of anti-PD-1 or PD-L1 therapy as neoadjuvant, adjuvant, and/or consolidation if only line of anti-PD-1 or anti-PD-L1 therapy
- Received platinum-based chemotherapy and experienced disease progression (in the opinion of the treating physician) during or after this regimen
- Known sensitizing mutation for which an FDA-approved targeted therapy for NSCLC exists (e.g., EGFR, ALK, ROS1, BRAF, RET, NTRK, KRAS, HER2 and MET sensitizing mutations), must have previously received at least one of the approved therapy(s)
- Ability to safely receive the investigational drug combination and the investigator's choice of standard of care regimens per the current FDA-approved package insert(s), treating investigator's discretion, and institutional guidelines
- Zubrod Performance Status of 0-2

Statistical Considerations

Sample Size Justification

- Accrual goal—700 participants
- Based on a design with 85% power to detect a hazard ratio of 0.77, using a 1-sided 2.5% level log-rank test.
- Total number of OS events is 526 events
- Estimated duration of accrual: 24 months (~ 29 participants/month)
- Primary analysis ~ 12 months after completion of accrual

Analysis Plan

- Primary analysis will include all randomized patients (ITT, includes those not meeting eligibility)
- Analyses:
  - 1st interim evaluating early stopping for futility alone at 210 OS events (40% information)
  - 2nd interim evaluating early stopping for futility or efficacy at 315 events (60% information)
  - Primary analysis at 526 events.
- If study reaches full accrual/information – statistical significance associated with observed ~ HR = 0.84 or 19% improvement in median OS.

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)

Jhanelle E. Gray, MD
Lung Committee Chair
(SWOG)

Jyoti D. Patel, MD
LUNGMAP Study Champion Lead
(Alliance)

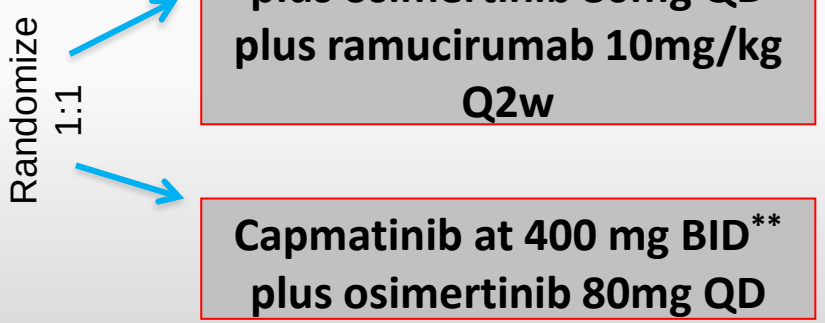
Mary Redman, PhD
Lead Statistician
(SWOG)

LUNG-MAP

S1900G Schema

KEY ELIGIBILITY

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



Primary Endpoints:

- **Progression-free survival**

Secondary Endpoints:

- **Toxicity by CTCAE**
- **Response**
- **Duration of response**
- **Overall survival**

N = 60 eligible (66 total)

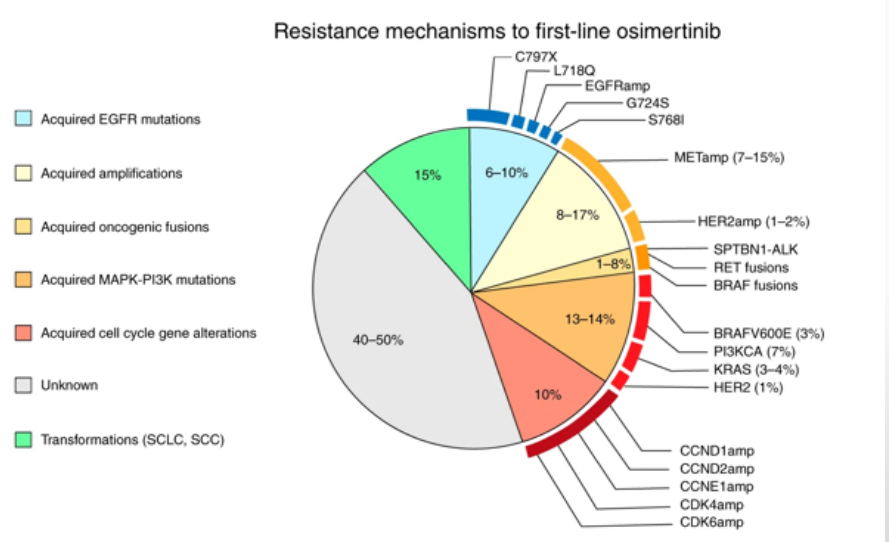
Stratification factors: Brain metastases and 2L vs 3+L prior lines of therapy

* *MET* amplification as determined by tissue-based or blood-based (ctDNA) NGS assay obtained at the time of progression on osimertinib. Tissue testing may be done by FMI through the LUNGMAP screening protocol or using testing results completed outside of the study.

** 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

Background/Overview

- Participants with advanced EGFR-mutant NSCLC often respond well to EGFR inhibitors but resistance eventually develops
- One mechanism of resistance to EGFR inhibitors is MET amplification
- Combining a MET inhibitor with an EGFR inhibitor can overcome resistance to EGFR TKIs driven by MET amplification



- 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, and the dual inhibition of VEGFR and MET may be able to delay or overcome resistance to EGFR TKIs

Primary Objectives

- To compare investigator-assessed progression-free survival (IA-PFS) between participants with EGFR mutated, MET amplified NSCLC randomized to capmatinib and osimertinib with or without ramucirumab

Secondary Objectives

- To evaluate if the combination of capmatinib, osimertinib and ramucirumab or capmatinib and osimertinib during the first cycle of treatment has an acceptable toxicity rate.
- To evaluate the frequency and severity of toxicities within the arms.
- To compare IA-PFS between the arms, in the following subsets:
  - Participants with centrally-confirmed MET amplification in tissue
  - Participants with centrally-confirmed MET amplification based on ctDNA
  - Participants with and without history of brain metastases
  - Participants who have received only 1 prior line of therapy and those who have received 2 or more prior lines of therapy
- To compare the objective response rate between the arms among participants with measurable disease at baseline.
- To evaluate duration of response among responders within each arm.
- To compare overall survival between the arms.

Translational Medicine Objectives

- To collect, process, and bank cell-free deoxyribonucleic acid (ctDNA) prior to treatment and throughout treatment for future development of a proposal to evaluate comprehensive next-generation sequencing of circulating tumor deoxyribonucleic acid (ctDNA).
- To establish a tissue/blood repository from participants with refractory non-small cell lung cancer (NSCLC).

Overview of Treatments

- Osimertinib is an EGFR tyrosine kinase inhibitor.
  - Approved for first-line treatment of participants with EGFR-mutant NSCLC.
- Capmatinib is a kinase inhibitor that targets MET.
  - FDA-approved for participants with MET exon 14 skipping mutations.
- Ramucirumab is a VEGFR2 antagonist that results in inhibition of angiogenesis.
  - FDA-approved in combination with erlotinib or docetaxel.
- Concomitant therapy:
  - No concomitant systemic cancer therapies are permitted while on trial.
  - Radiation for symptomatic metastases (e.g. bone) is permitted.
- Recommended pre-medication:
  - Pre-medication associated with standard drug administration and supportive care (including anti-diarrheals, antibiotics, diuretics, growth factors, or other medications) may be given as indicated by the current ASCO guidelines.
  - Pre-medication with a histamine H1 antagonist such as diphenhydramine hydrochloride is recommended prior to infusion of ramucirumab.

Treatment Administration

	Osimertinib	Capmatinib	Ramucirumab
Route:	PO	PO	IV
Dose:	80mg	400mg	10 mg/kg
Cycle duration:	28 days	28 days	28 days
Administration:	Daily	Twice daily	Day 1 and 15
Premedication:	None	None	Histamine H1 antagonist recommended
Supportive care:	See Section 8 of the protocol		
Disease assessment:	CT scans +/- brain MRI every 8 weeks		
Prohibited medications:	Strong inducers of CYP3A4 (including herbal supplements such as St. John's Wort); CYP3A4 inhibitors; CYP1A2 substrates; P-gp and BCRP substrates; sensitive substrates of MATE1 and MATE2K; or drugs that are known to prolong QT interval.		

Key Eligibility (1)

- Documentation of NSCLC with a sensitizing EGFR mutation and have radiologically or clinically progressed (in the opinion of the treating physician) on osimertinib, alone or in combination with other agent(s), as their most recent line of therapy. Any number of prior lines of therapy is allowed.
- MET amplification determined by tissue-based or blood-based (circulating tumor DNA [ctDNA]) NGS assay. MET amplifications may have been determined based on tissue submitted for testing by FMI through the **LUNGMAP** screening protocol or using test results completed outside of the study. Tissue or blood must be obtained after disease progression on osimertinib. The testing must be done within a laboratory with CLIA, ISO/IEC, CAP, or similar certification.
- Participants must have either measurable disease or non-measurable disease documented by CT or MRI.
- Participants with symptomatic CNS metastasis (brain metastases or leptomeningeal disease) must be neurologically stable and have a stable or decreasing corticosteroid requirement for at least 5 days before sub-study randomization.

Key Eligibility (2)

- Participants must not have received an anti-VEGF or VEGFR inhibitor or MET inhibitor.
- Zubrod performance status must be 0-1.
- ECG performed, with a QTcF ≤ 470 msec.
- Participant must have a urinary protein ≤1+ on dipstick or routine urinalysis (UA).
- Participants must have adequate cardiac function.
- Participants must not have received strong inducers of CYP3A4 (including herbal supplements such as St. John's Wort); CYP3A4 inhibitors; CYP1A2 substrates; P-gp and BCRP substrates; sensitive substrates of MATE1 and MATE2K; or drugs that are known to prolong QT interval within 7 days prior to sub-study registration and must not be planning to use any of these throughout protocol treatment.
- Participants must not have uncontrolled blood pressure and hypertension.

Anticipated Adverse Events/ Serious Adverse Events

- All study drugs are FDA-approved and not anticipated to result in toxicity outside of what is typically expected.

Dose Modifications/Interruptions

- Dose reductions of ramucirumab are allowed for proteinuria only.
- Osimertinib and capmatinib may be dose-reduced as necessary.
- The maximum dose delay for any treatment-related toxicity or unforeseen circumstance unrelated to toxicity is 28 days.
- Missed doses will not be made up.
- Dose interruptions and discontinuations are allowed to manage toxicity.
- If multiple toxicities are experienced, dose modifications will be based on the toxicity requiring the largest dose reduction.
- Reductions are based on the dose being given at the end of the preceding cycle and are based on toxicities observed since the prior toxicity evaluation.
- If osimertinib or capmatinib must be permanently discontinued, the participant must be removed from protocol therapy. If ramucirumab must be discontinued the participant may remain on osimertinib and capmatinib as long as they are well tolerated and according to the treatment physician, the participant is still deriving clinical benefit.

Dose Modifications Table

DRUG	DOSE LEVEL	DOSE
osimertinib		
	Full	80 mg
	-1 Level	40 mg
INC280 (capmatinib)		
	Full	400 mg BID
	-1 Level	300 mg BID
	-2 Level	200 mg BID
Ramucirumab		
	Full	10 mg/kg
	-1 Level	6 mg/kg

Criteria for Removal from Treatment

- Progression of disease or symptomatic deterioration. However, a participant may continue protocol treatment as long as the participant is continuing to clinically benefit form treatment in the opinion of the treating investigator.
- Unacceptable toxicity.
- Treatment delay > 28 days.
- Participants may withdraw from protocol treatment at any time for any reason.

LUNGMAP Registration (Screening Step): Identification of MET amplification

This will occur during **LUNGMAP** screening prior to sub-study assignment to **S1900G**:

THREE POSSIBLE SCENARIOS:

- Note: The specimen that identifies MET amplification must have been obtained after radiographic or clinical progression on osimertinib as the most recent line of therapy.

1. Participant with EGFR-mutant NSCLC progressing on osimertinib (alone or in combination with another therapy) and repeat molecular testing at progression has not yet been performed:

    - Submit new biopsy material for on-study biomarker profiling on **LUNGMAP** *(standard **LUNGMAP** procedure)*

LUNGMAP Registration (Screening Step): Identification of MET amplification cont.

2. Participant with EGFR-mutant NSCLC progressing on osimertinib (alone or in combination with another therapy) and MET amplification was **detected at the time of progression** using commercial FoundationOne CDx tissue-based (not liquid) tumor testing:

   - Submit request for reanalysis of commercial FoundationOne CDx results via the SWOG Specimen Tracking System *(standard **LUNGMAP** procedure)*

   - Additional submission of tissue on **LUNGMAP** is not needed.

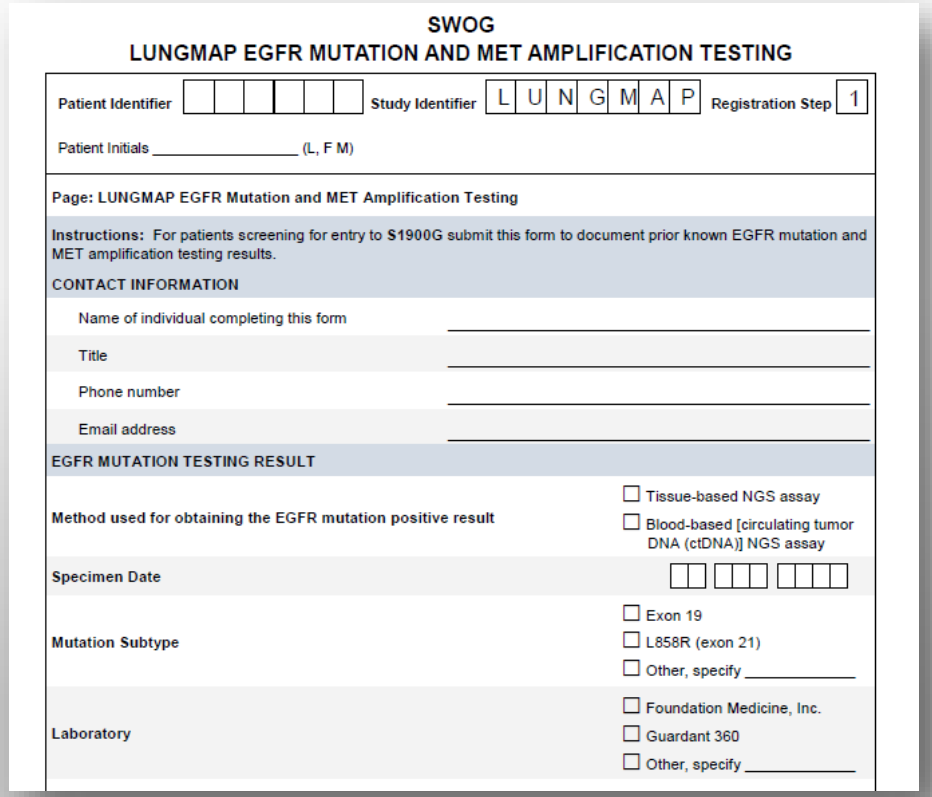
LUNGMAP Registration (Screening Step): Identification of MET amplification cont.

3. Participant with EGFR-mutant NSCLC progressing on osimertinib (alone or in combination with another therapy) and MET amplification was **detected at the time of progression** using other tissue OR blood-based assay results

   - Acceptable assays:
     - Tissue-based: Any assay performed in a laboratory with CLIA, ISO/IEC, CAP or similar certification

       Note: If results are from commercial FoundationOne CDx (tissue) assay, refer to #2 on the previous slide.
     - Blood-based: Foundation Medicine or Guardant 360 cfDNA assays only
   - Indicate this during **LUNGMAP** registration and then submit results in **LUNGMAP** Rave EDC on the EGFR Mutation and MET Amplification Testing Form (new with activation of S1900G)
   - Submit tissue if available (not required)

Email LungMAPquestion@crab.org or call 206-652-2267 with questions



SWOG
LUNGMAP EGFR MUTATION AND MET AMPLIFICATION TESTING

Patient Identifier ☐☐☐☐☐☐ Study Identifier L U N G M A P Registration Step 1

Patient Initials _____ (L, F M)

Page: LUNGMAP EGFR Mutation and MET Amplification Testing

Instructions: For patients screening for entry to S1900G submit this form to document prior known EGFR mutation and MET amplification testing results.

CONTACT INFORMATION

Name of individual completing this form _____

Title _____

Phone number _____

Email address _____

EGFR MUTATION TESTING RESULT

Method used for obtaining the EGFR mutation positive result
☐ Tissue-based NGS assay
☐ Blood-based [circulating tumor DNA (ctDNA)] NGS assay

Specimen Date ☐☐ ☐☐☐ ☐☐☐☐

Mutation Subtype
☐ Exon 19
☐ L858R (exon 21)
☐ Other, specify _____

Laboratory
☐ Foundation Medicine, Inc.
☐ Guardant 360
☐ Other, specify _____

Has patient been tested for and determined to have EGFR-mutated, MET-amplified NSCLC? ☐Yes ☐No

LUNG-MAP

Tissue Submission for LUNGMAP – if using known test results

- Participants must submit tumor tissue if available when screening on the LUNGMAP protocol with known test results.
- The tissue must be from a biopsy performed at the time of disease progression on the most recent line of therapy.
- An additional biopsy is not required to obtain this tissue if it is not already available.
- Participants with prior commercial FoundationOne CDx tissue-based (not liquid) tumor test results [obtained after radiographic or clinical disease progression on osimertinib] do not need to submit tumor tissue

Registration for **S1900G**

- The **LUNGMAP** screening protocol has a Protocol Specific Requirement (PSR) as noted in Section 13.2 of **LUNGMAP**.
- The **S1900G** sub-study has additional optional training materials available through the Compliance, Learning, and SOP Solutions (CLASS) website. Online training is not required to register participants to **S1900G**.
- A Delegation Task Log is required for this sub-study.

Data Submission

- Data must be submitted according to the protocol requirements for ALL participants registered, whether or not assigned treatment is administered, including participants deemed to be ineligible. Participants for whom documentation is inadequate to determine eligibility will generally be deemed ineligible. See Protocol Section 14.0 for Data Submission Requirements, Procedures and Timepoints.

Specimen Submission on S1900G

- **ctDNA Assay – Peripheral Whole Blood (Required for Participants)**
  - Sites must contact Foundation Medicine, Inc. – Blood Samples, Lab #232, to order kits
    - Kits include: two Roche Cell-Free DNA blood collection tubes, collection instructions, FedEx return bags, and pre-printed FedEx airway bills.
  - Collection timepoints: Cycle 1 Day 1 (prior to treatment); Cycle 1 Day 15; Cycle 3 Day 1; First Progression
  - The translational medicine proposal to use these specimens will be submitted as a revision to CTEP for approval, prior to the SWOG Statistical and Data Management Center review of assay results.
- **Buffy Coat and Plasma Banking (Required If Participant Consents)**
  - Participants must be offered the opportunity to participate in banking of specimens for future research.
  - Collection timepoints: Pre-treatment, Cycles 2-4 (same day as other labs), first progression.
  - Collect approximately 8-10 mL of blood in EDTA tubes.
  - See Protocol Section 15.5 for additional specimen processing instructions.
  - Frozen plasma and buffy coat specimens must be shipped to the SWOG Biospecimen Bank – Solid Tissue, Myeloma and Lymphoma Division, Lab #201.
  - Specimen collection kits are not being provided for this submission; sites must use institutional supplies.

Quality Control – Routine Data Monitoring

S1900G includes routine SWOG Centralized Data Coordinator Monitoring and Safety-specific monitoring (standard for all SWOG trials, Lung-MAP and Lung-MAP substudies), including:

- Data submission review for missing data, submission errors and protocol deviations.
- Institutional Performance Review processes.
- Source data (pathology, radiology and lab reports) review for confirmation of disease classification and response assessment.
- Routine monitoring of SAE reporting.

S1900G substudy does NOT have potential to be utilized for FDA registration.
Herein, S1900G does NOT require:

1) Participating site maintenance of a Trial Master File,
2) Upload of documents into the Source Document Portal (SDP), or
3) Central Monitoring Review by the SDMC Monitors
4) Blinded independent central review of response and Progression-Free Survival (PFS) Endpoint.

Quality Control – Additional On-Site Monitoring

Consistent with Lung-MAP Protocol Section 18.2 and all Lung-MAP substudies, S1900G includes On-Site Monitoring, as follows:

- First on-site monitoring visit at each institution within 3 months of first patient registration to a LUNGMAP sub-study.
- Subsequent on-site visits for all sites with patients registered to a sub-study twice per year. Additional visits may be scheduled in response to several factors such as high rate of accrual, previous monitoring visit results, centralized monitoring outcome, change in staff, etc.
- An exception to the onsite audit requirement may be allowed in the following circumstances:
  - Sites that use a centralized pharmacy and data management team may be monitored at this central location.
  - Sites that had an acceptable on-site pharmacy audit in the last year may be audited off site.
  - Covid visitor restrictions

Funding

- Capmatinib and ramucirumab will be provided; osimertinib is commercially available and should be purchased by a third party.
- Available site payments are included in the table below. Payments to offset the cost of research-directed laboratory tests are pending. Complete and detailed funding information, including Study-Specific Notes, will be available in the approved funding memorandum posted via CTSU.org at time of activation.

Funding Source and Study Component		Collect Type	Enter Date in Open?	NCTN Funding per Patient Std/HP LAPS	NCORP Funding per Patient Std/HP
Federal	Base Intervention – Standard / High Performance LAPS & NCORP	Mandatory	No	$2,500/$4,100	$2,500/$4,100
Federal	Biospecimen – Whole Blood Whole blood for ctDNA at multiple timepoints	Mandatory	Yes	$200	$200
Federal	Biospecimen – Blood (Multiple) Buffy coat and plasma collections at multiple timepoints	Mandatory Request	Yes	$200	$200
Total Potential Federal Funds				**$2,900/$4,500**	**$2,900/$4,500**
Non-Federal	Additional capitation resources from industry partners	Mandatory	No	$2,610/$1,010	$2,610/$1,010
Total Potential Non-Federal Funds				**$2,610/$1,010**	**$2,610/$1,010**
Total Potential Funds				**$5,510/$5,510**	**$5,510/$5,510**
Additional Support for Site Auditing					
Non-Federal	Additional capitation resources from industry partners for additional site auditing /monitoring.	Mandatory Event	No	$1,333 (per audit)	**$1,333 (per audit)**
All sites will be audited a minimum of twice per year as recommended by the FDA for this study. Sites will be reimbursed for any extra effort associated with increased auditing at $1,333 per additional audit above the FDA recommendation.					

Resources and Materials

- **S1900G** patient-friendly plain language trial summary and accompanying social media toolkit (tweets and graphics).
  - The patient-friendly trial summary and social media toolkit will be available for participating site use on SWOG.org and via the S1900G protocol abstract page on CTSU.org.

S1900G Contacts

Study Chairs:

- Dr. Sarah Goldberg (SWOG)
  Yale School of Medicine
- Dr. Ross Camidge (SWOG)
  University of Colorado School of Medicine

Questions:

Medical Questions for Study Chairs:

S1900GMedicalQuery@swog.org

Eligibility/Specimen/Data Submissions:
LUNGMAPquestion@crab.org

General Protocol/Regulatory:
lgildner@swog.org

LUNGMAP Revision #7

JYOTI PATEL, MD

LUNGMAP MEDICAL ONCOLOGY CHAIR/CHAMPION

ALLIANCE

LUNG-MAP

S1900F

A Randomized Phase II Study of Carboplatin and Pemetrexed with or without Selpercatinib (LY3527723) in Participants with Non-Squamous RET Fusion-Positive Stage IV Non-Small Cell Lung Cancer and Progression of Disease on Prior RET Directed Therapy (Lung-MAP Sub-Study)

JHANELLE GRAY, MD
Study Chair (SWOG)
Lung Committee Chair

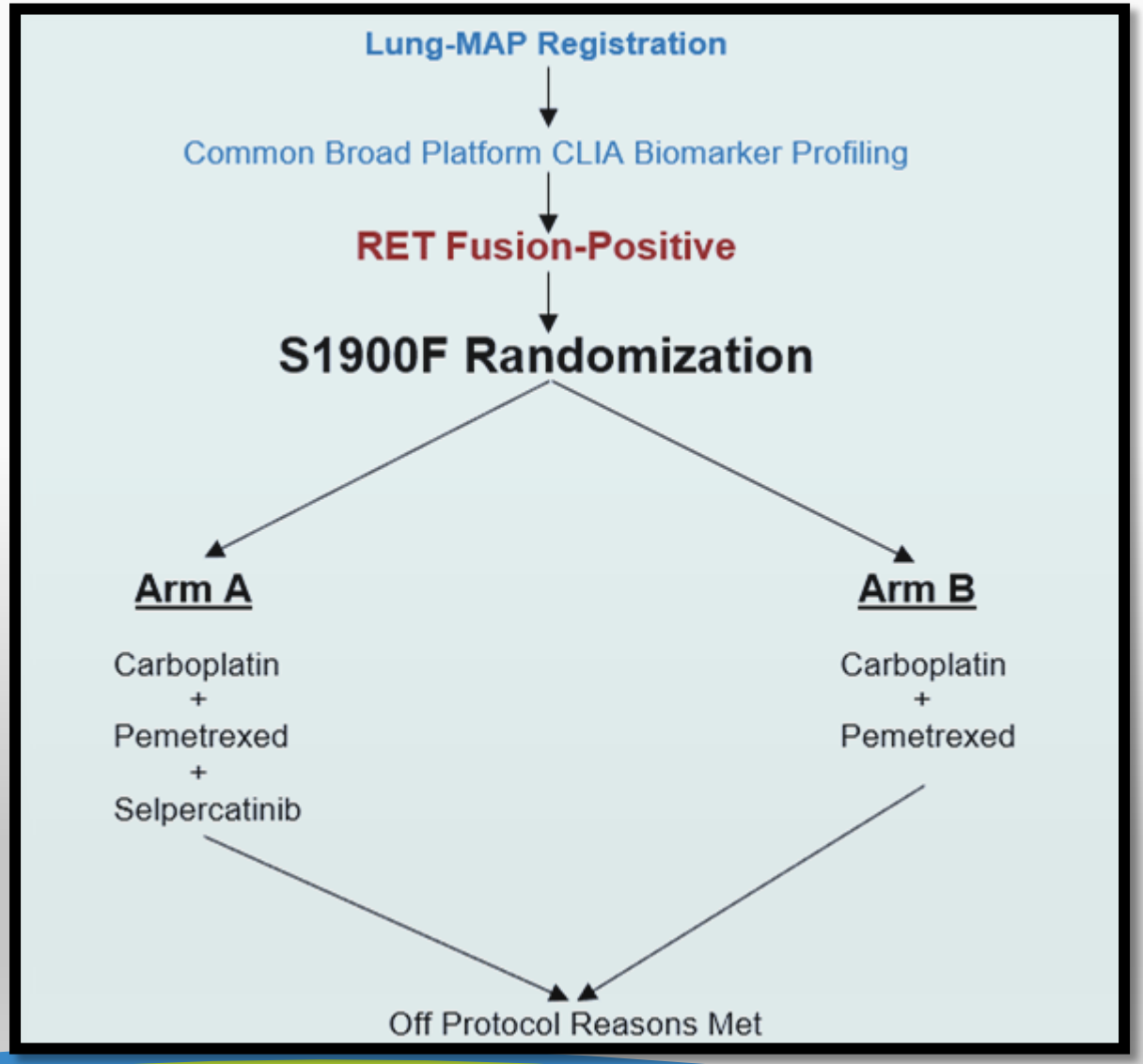
YASIR ELAMIN, MD
Study Co-chair (SWOG)

DAVID GANDARA, MD
LUNGMAP Study Champion Lead (SWOG)

Mary Redman, PhD
Lead Statistician (SWOG)

LUNG-MAP

S1900F Schema



S1900F Contacts

Study Chairs:

- Dr. Jhanelle E. Gray (SWOG)
  - Moffit Cancer Center

- Dr. Yasir Y. Elamin (SWOG)
  - UT/MD Anderson Cancer Center

Questions:

Medical Questions for Study Chairs:

S1900FMedicalQuery@swog.org

Eligibility/Specimen/Data Submissions:
LUNGMAPquestion@crab.org

General Protocol/Regulatory:
jbeeler@swog.org

S1800D

A Phase II/III Study of N-803 (ALT-803) plus Pembrolizumab versus Standard of Care in Participants with Stage IV or Recurrent Non-Small Cell Lung Cancer Previously Treated with Anti-PD-1 or Anti-PD-L1 Therapy (Lung-MAP Non-Match Sub-Study)

John Wrangle, MD, MPH
Study Chair (SWOG)

Hatim Husain, MD
Study Co-chair (SWOG)

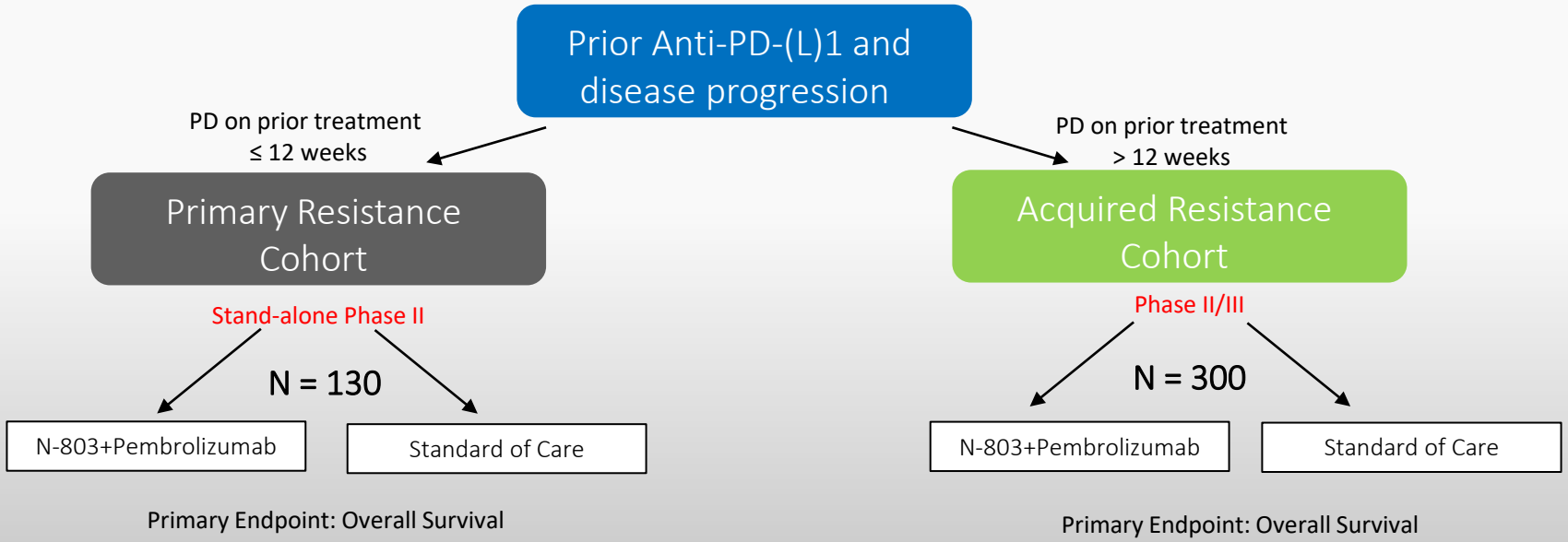
Jhanelle E. Gray, MD
Lung Committee Chair
(SWOG)

Roy Herbst, MD, PhD
LUNGMAP Study Champion Lead
(SWOG)

Mary Redman, PhD
Lead Statistician
(SWOG)

LUNG-MAP

S1800D Schema



Standard of Care Options: Docetaxel + Ramucirumab, Docetaxel, Gemcitabine, Pemetrexed

Accrual Update October 16, 2022

- 43 Total
- 7 in the las 30 days
- 5 to Primary Resistance Cohort

S1800D Contacts

Study Chairs:

- Dr. John Wrangle (SWOG)
  - Medical University of South Carolina

- Dr. Hatim Husain (SWOG)
  - University of California San Diego

Questions:

Medical Questions for Study Chairs:

S1800DMedicalQuery@swog.org

Eligibility/Specimen/Data Submissions:
LUNGMAPquestion@crab.org

General Protocol/Regulatory:
lgildner@swog.org

S1900E

A Phase II Study Of Sotorasib (AMG 510) In Participants With Previously Treated Stage IV Or Recurrent KRAS G12C Mutated Non-squamous Non-small Cell Lung Cancer (ECOG-ACRIN Lung-MAP Sub-study)

Sukhmani K. Padda, MD
Study Chair (ECOG-ACRIN)

David Gerber, MD
Study Co-chair (ECOG-ACRIN)

Julie R. Brahmer, MD
Lung Committee Chair
(ECOG-ACRIN)

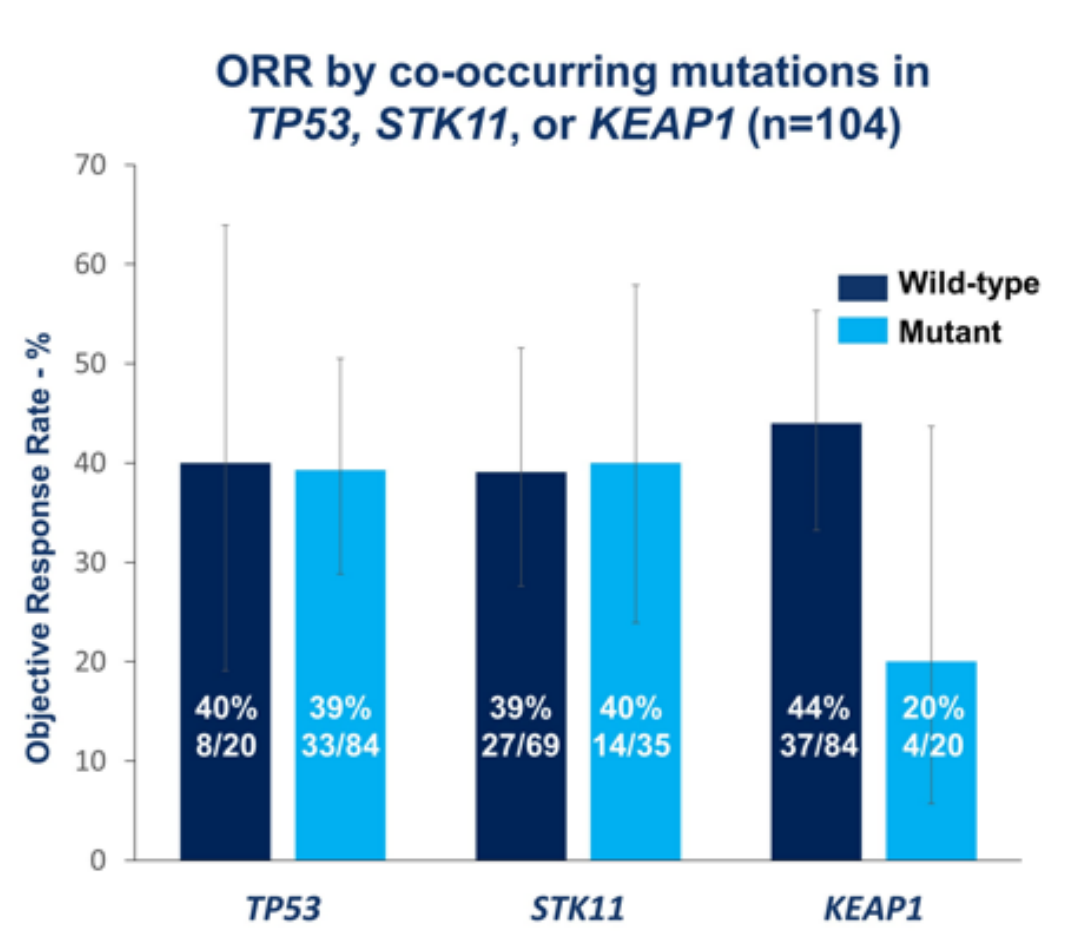
Joel Neal, MD, PhD
LUNGMAP Study Champion Lead
(ECOG-ACRIN)

Mary Redman, PhD
Lead Statistician
(SWOG)

LUNG-MAP

Sotorasib efficacy across *KRAS* G12C co-mutation subsets

FDA accelerated approval May 2021
CodeBreaK 100 (n=126): ORR 37.1%, DCR 80.6%
mDOR 11.1 mo, mPFS 6.8 mo, mOS 12.5 mo



PFS and OS by co-occurring mutations in both *STK11* and *KEAP1* (n=104)

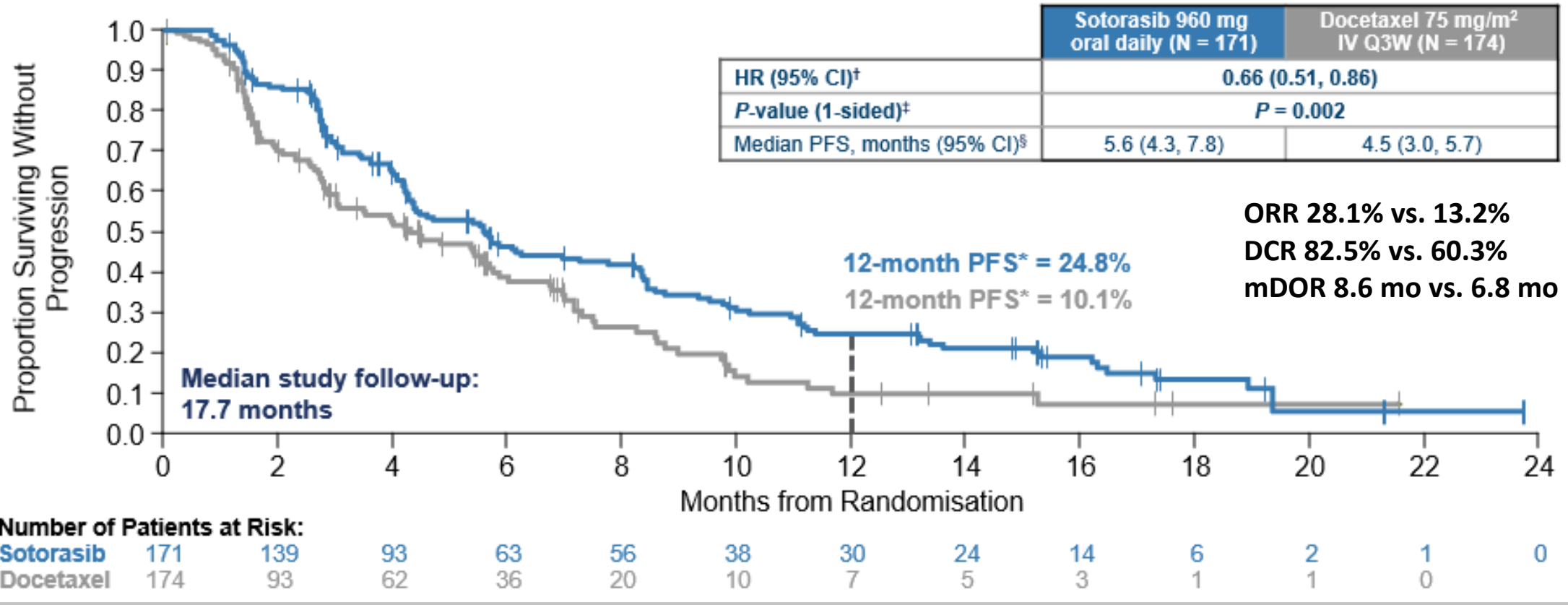
STK11 status	*KEAP1* status	n	mPFS month (95% CI)	mOS month (95% CI)
MUT	MUT	13	2.6 (1.4, 11.1)	4.8 (2.1, 10.8)
MUT	WT	22	11.0 (2.8, NE)	15.3 (4.8, NE)
WT	MUT	7	5.5 (0, 7.0)	7.5 (0, NE)
WT	WT	62	6.8 (4.0, 11.0)	NE (NE, NE)
All evaluable	All evaluable	104	6.3 (4.1, 8.3)	13.1 (9.5, NE)

LUNG-MAP

F Skoulidis et al. ASCO 2021. N Engl J Med 2021;384:2371-2381.

CodeBreaK 200 RP3 Study Sotorasib vs. Docetaxel Previously Treated *KRAS* G12C NSCLC

PRIMARY ENDPOINT: PFS by BICR



	Sotorasib 960 mg oral daily (N = 171)	Docetaxel 75 mg/m² IV Q3W (N = 174)
HR (95% CI)†	0.66 (0.51, 0.86)	
P-value (1-sided)‡	*P* = 0.002	
Median PFS, months (95% CI)§	5.6 (4.3, 7.8)	4.5 (3.0, 5.7)

ORR 28.1% vs. 13.2%
DCR 82.5% vs. 60.3%
mDOR 8.6 mo vs. 6.8 mo

No difference in OS sotorasib vs. docetaxel
HR 1.01 (95% CI 0.77-1.33); P=0.53
Median 10.6 mo vs. 11.3 mo
34% Crossover docetaxel to sotorasib

IG-MAP

Johnson ML et al. ESMO 2022.

S1900E Schema

Primary Endpoint

- **Objective response rate**

Secondary Endpoints

- Duration of response
- Progression free survival
- Overall survival
- Safety

Treatment Period
until disease progression, intolerance, or consent withdrawal
Clinic visits/labs every 3 weeks
Imaging every 6 weeks

If Progression
Liquid biopsy to determine resistance mechanism

[a]**other co-mutations (e.g., *KEAP1, NFE2L2, CUL3*), double or triple co-mutations (e.g., *STK11/TP53, STK11/TP53/KEAP1*), or no co-mutations**

LUNG-MAP

Status Update

- **72/116** participants enrolled (**32** *TP53*, **16** *STK11*, **24** Others) since 04/02/2021 activation
  - 4 in last 30 days; 0 in last 7 days as of 10/04/2022
  - *TP53 & STK11*- meeting accrual goals (15-25 pts/year & 6-11 pts/year)
  - *Others*- meeting conservative accrual goals (14-24 pts/year)

- Re-assessment…
  - Re-examining further liberalization of protocol after Revision #3 Amendment (CIRB & NCI CTEP Approved)
  - Social media tool kit & patient language friendly handouts
    - Led by Amanda Stamplis and Frank DeSanto (SWOG Communications)
    - Also partner with Upal Basu Roy PhD from LUNGevity and Kim Norris from Lung Cancer Foundation of America
  - Seeking further input on pt concerns from Judy Johnson (Patient Advocate SWOG)
  - Review by SWOG ops office and SWOG Site Coordinators Committee to address any logistical issues

S1900E Contacts

Study Chairs:

- Dr. Sukhmani K. Padda (ECOG-ACRIN)
  - Cedars-Sinai Medical Center
- Dr. David E. Gerber (ECOG-ACRIN)
  - UT Southwestern Medical Center

Questions:

Medical Questions for Study Chairs:

S1900EMedicalQuery@swog.org

Eligibility/Specimen/Data Submissions:
LUNGMAPquestion@crab.org

General Protocol/Regulatory:
jbeeler@swog.org

Lung-MAP Translational Medicine

DAVID KOZONO, MD, PHD

TRANSLATIONAL MEDICINE & SCIENTIFIC LEADERSHIP COMMITTEE CHAIR

ALLIANCE

LUNG-MAP

Teleconferences

- Monthly, 3rd Tuesday at 11 am PT / 2 pm ET
  - Recent topics: FoundationOne CDx Tissue Baitset Update (June), S1900F biomarker definitions update (March), prevalence of co-mutations (Jan)
  - Sub-study discussions: S1900G study team (May), S1900C study team (April)
  - Guests: Ionpath: proteomic assays/IO benefit (July), GenPro: immuno-methylome epimarkers (Feb), Nucleai: H&E slide image analysis (Jan)
- Smaller meetings to discuss specific initiatives, projects, and publications

Letter of Intent

- Goal: to promote TM research by simplifying initial inquiries
- One to two pages
- Preliminary information on proposed retrospective use of banked specimens and/or data
- Send to TM committee chair for review and advice: lungmaptm@gmail.com

Letter of Intent for a **Lung-MAP** Translational Medicine Study Using Banked Specimens and/or Data
(Please limit to not more than 1-2 pages)

The purpose of this LOI is to provide preliminary information to the Lung-MAP Translational Medicine/Scientific Leadership (TM/SL) Committee on proposed retrospective use of banked specimens and/or data, to obtain feedback on feasibility and suitability for development into full proposals for SWOG then CTEP submission.

Translational medicine study title:

Translational medicine study objective(s):

Lung-MAP studies from which data and/or specimens are requested:

	Study	Specify
☐	S1400 sub-studies	
☐	S1800/S1900 sub-studies	
☐	S1400 (original squamous cell screening study)	
☐	LUNGMAP (current screening study)	

Data requested, or required to identify applicable specimens:

	Data type	Specify
☐	Specific gene alterations	
☐	T5/F1CDx sequencing data	
☐	Patient/disease characteristics	
☐	Outcomes (from published studies)	
☐	Other	

Specimens requested: ☐ **none**

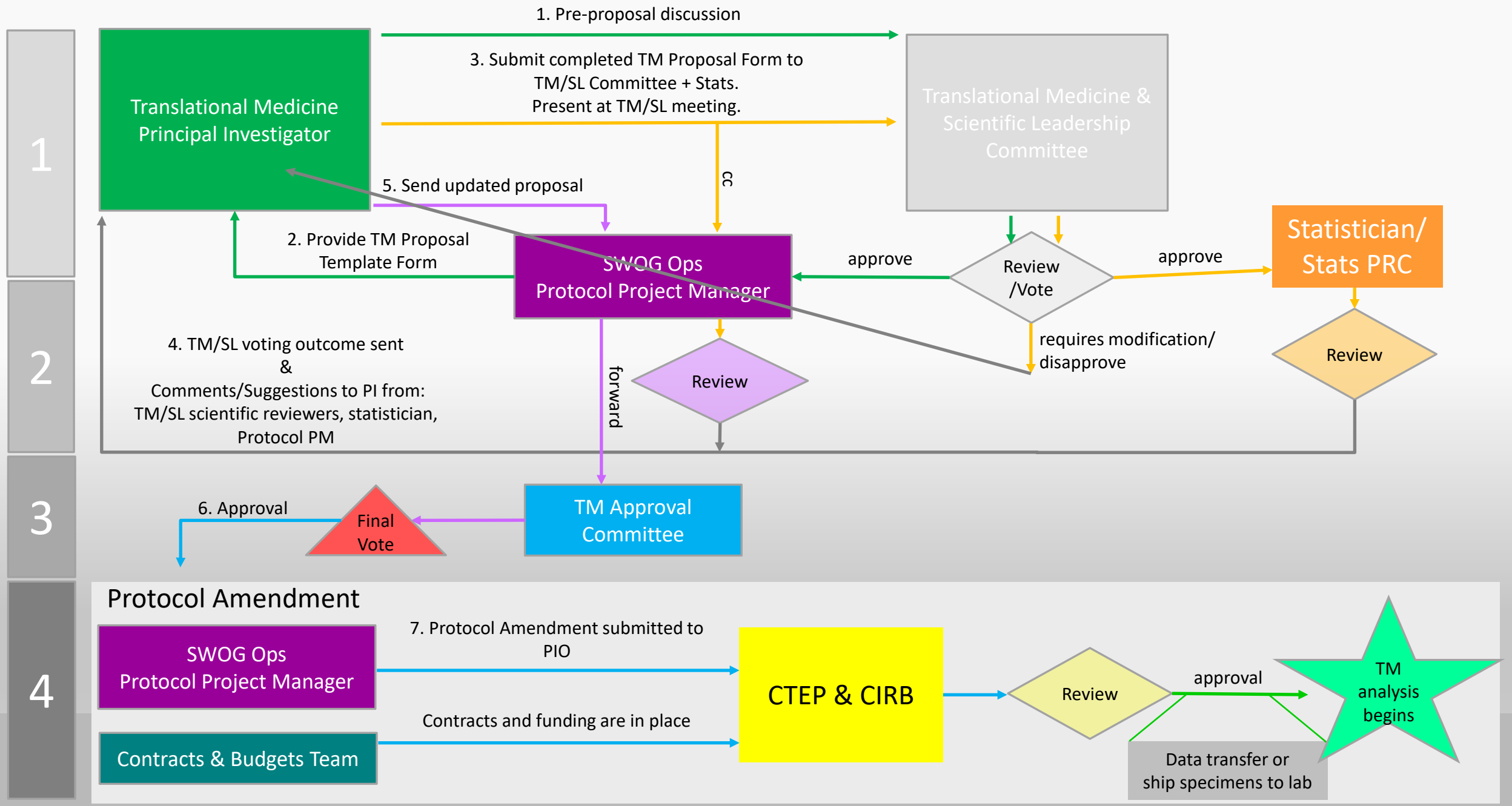
	Specimen type	# of subjects/study (e.g., 25/S1400A, 75/S1400I)	Time points (e.g., baseline, C3D1)	Amount (# of slides, ml per sample)	Processing (if needed)
☐	FFPE				
☐	Buffy coat				
☐	EDTA plasma				
☐	cfDNA plasma				
☐	Other				

Proposed assays:

Other considerations (including plan for financial support, grant submission, etc.):

Name of Principal Investigator (TM Study) _____ Date _____

Email _____


1
2
3
4
1. Pre-proposal discussion
Translational Medicine Principal Investigator
3. Submit completed TM Proposal Form to TM/SL Committee + Stats. Present at TM/SL meeting.
Translational Medicine & Scientific Leadership Committee
cc
5. Send updated proposal
2. Provide TM Proposal Template Form
SWOG Ops Protocol Project Manager
approve
Review /Vote
approve
Statistician/ Stats PRC
requires modification/ disapprove
Review
4. TM/SL voting outcome sent & Comments/Suggestions to PI from: TM/SL scientific reviewers, statistician, Protocol PM
forward
Review
6. Approval
Final Vote
TM Approval Committee
Protocol Amendment
SWOG Ops Protocol Project Manager
7. Protocol Amendment submitted to PIO
CTEP & CIRB
Review
approval
TM analysis begins
Contracts and funding are in place
Contracts & Budgets Team
Data transfer or ship specimens to lab

TM proposals and funding

- Priority for use of biospecimens: validation studies and hypothesis-based research vs. exploratory analyses
- Secondary use of data (genomic, digital pathology, etc.) has a lower bar since resources are not being exhausted
- Proposals with funding secured or available are favored
  - Example funding opportunity: NIH/NCI FOA PAR-20-313 and 314

Proposed Projects

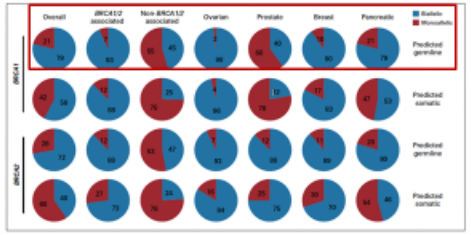
- Tumor fraction and ctDNA in LM sub-studies (Gandara, Mack) – CTEP/CIRB approval needed for ctDNA analyses in sub-studies
- ctDNA in S1900C (Nandos Skoulidis) – protocol amendment pending
- H&E slide image analysis in LM IO Sub-Studies: Predicting IO therapy responses by analyzing spatial arrangement of immune cells using deep learning (Ori Zelichov @Nucleai) – TM proposal pending

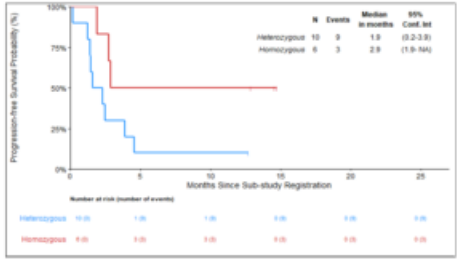
Approved: S1900A TM analyses (J. Riess)

Significance of *BRCA 1/2* Mono-Allelic vs Bi-Allelic mutation in PARP Inhibitor Response –S1900A

Best response	Total (N=59)	Squamous (n=25)	Non-squamous (n=34)
Partial response	6	2	4
Stable disease	31	14	17
Progressive disease	15	7	8
Symptomatic deterioration	5	1	4
Assessment inadequate	2	1	1
RR by RECIST (95% CI)	10% (2, 18)	8% (0, 19)	12% (0, 23)
DCR (95% CI)	63%, (50, 75)	64% (45, 83)	62% (45, 78)

Outcome	*BRCA 1/2* total[a] (n=16)	*BRCA 1/2* heterozygous (n=10)	*BRCA 1/2* homozygous (n=6)
Partial response	4	1	3
Stable disease	8	5	3
Increasing disease	4	4	0
RR by RECIST (95% CI)	25% (4, 46)	10% (0, 29)	50%[b] (10, 90)
DCR (95% CI)	75% (54, 96)	60% (29, 90)	100% (100, 100)
6-month PFS (95% CI)	25% (4, 46)	10% (0, 29)	50% (10, 90)





Presented by J. Riess –ASCO 2021

- CTEP approved amendment to analyze:
  - Frequency of reversion mutations in BRCA1/2 and other homologous recombination deficiency (HRD) genes
  - Concordance of BRCA1/2 and other HRD gene mutations in plasma and tissue
  - Clinical outcomes of homozygous or heterozygous BRCA1/2 and other HRD gene mutations detected by ctDNA
  - Association of reversion mutations with de novo or acquired resistance to rucaparib
  - Changes in ctDNA variant allele frequency
  - Association of clinical outcomes with the FM HRDv2 signature and gene mutations
- Met on 7/26/22 to discuss analyses

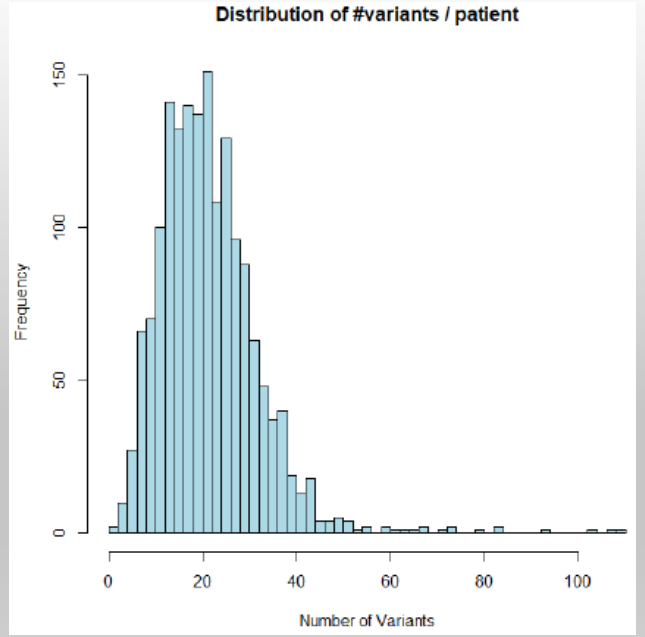
Approved: KRAS in LUNGMAP

- Evaluation of KRAS mutation sub-types and co-mutation detected by NGS in the LUNGMAP screening protocol (S. Padda)
- Abstract submitted to ASCO, but only given online presentation and therefore withdrawn
- Next step is to characterize rare KRAS and driver mutations, DNA repair and MAPK/PI3K/AKT alterations for additional analyses

Lung-MAP TM resources

- Sequencing data from S1400 (Jun 16, 2014 – Jan 28, 2019)
  - Enrolled 1864 patients with stage IV or recurrent squamous cell lung cancer
  - Next Generation Sequencing (NGS) data available for 1672 patients using the FoundationOne T5 research platform
  - T5 = exons and/or introns of 313 cancer-related genes
  - 36,677 variants identified
  - Largest NGS dataset of advanced squamous cell lung cancers of previously treated patients

Type \ Impact	Known	Likely	Ambiguous	Unknown	Total
Copy number alteration (CNA)	5144	0	926	3955	10025
Gene rearrangement (REARR)	18	262	0	396	676
Short variant (SV)	3051	2597	0	20328	25976
Total	8213	2859	926	24679	36677



LUNG-MAP

Samples for liquid biopsy analyses

- ctDNA in LUNGMAP
  - 277 registrations to submit ctDNA, 25 in most recent 12 months – being removed in next protocol revision
  - 166 with ctDNA and matched tissue results
- Studies with plasma collection at multiple timepoints:
  - S1900B (RET fusion, LOXO-292): baseline, progression, end of treatment
  - S1900C (STK11m+, talazoparib + avelumab): baseline, C3D1, progression, end of treatment
  - S1800A (non-match, pembro + ramucirumab): baseline, relapse/progression

Composite ICI Signature (D. Gandara)

- Composite Immune Checkpoint Inhibitor (ICI) Signature for Efficacy of ICI Therapy in Advanced Squamous Cell Lung Cancer (SCC)
- Accepted at WCLC 2022 for poster presentation
- Resubmitted for SITC 2022 Nov 8-12

Upcoming priorities

- Adding ctDNA analyses to Lung-MAP sub-study protocols
  - S1900C, S1900E, S1800A: protocol-specific
  - Generalized template for future sub-studies
- Streamlining TM research in Lung-MAP
  - While maintaining required regulatory oversight and high quality scientific, statistical and operations review

LungMap
Drug Selection Committee

Hossein Borghaei, MS, DO
Professor and Chief, Thoracic Oncology
The Gloria and Edmund M. Dunn Chair in Thoracic Oncology
Fox Chase Cancer Center

Saiama Waqar, MBBS, MSCI
Associate Professor of Medicine
Director, Hematology and Oncology Fellowship Program
Washington University School of Medicine

LUNG-MAP

Disclosures for Dr. Borghaei

- **Research Support (Clinical Trials):**
  - Millennium, Merck/Celgene, BMS/Lilly
- **Advisory Board/Consultant:**
  - BMS, Lilly, Genentech, Celgene, Pfizer, Merck, EMD-Serono, Boehringer Ingelheim, Astra Zeneca, Novartis, Genmab, Regeneron, BioNTech, Cantargia AB, Amgen, Abbvie, Axiom, PharmaMar, Takeda, Huya Bio, GLG, Daiichi, Guardant, Natera, Oncocyte, Beigene
- **Scientific Advisory Board:**
  - Sonnetbio (Shares), Rgenix (Shares), Nucleai (Shares)
- **Data and Safety Monitoring Board:**
  - University of Pennsylvania, CAR T Program, Takeda, Incyte
- **Employment:**
  - Fox Chase Cancer Center

Disclosures for Dr. Waqar

Research Grant support

- SWOG-Clinical Trials Partnership
- Research Support to institution for clinical trials (site PI): AbbVie Inc, Ariad Pharmaceuticals, Genentech, Immunomedics, Inc., Millennium Pharmaceuticals Inc, Roche, Astellas Pharma Inc, Daiichi Sankyo, Cullinan Pearl, Verastem Inc, GlaxoSmithKline/GSK , Janssen Research & Development, LLC ,Elevation Oncology, Genentech, Loxo Oncology, Takeda Pharmaceuticals

Data and Safety Monitoring Board:

- Hoosier Cancer Research Network- Chair of Data Safety Monitoring Board for study

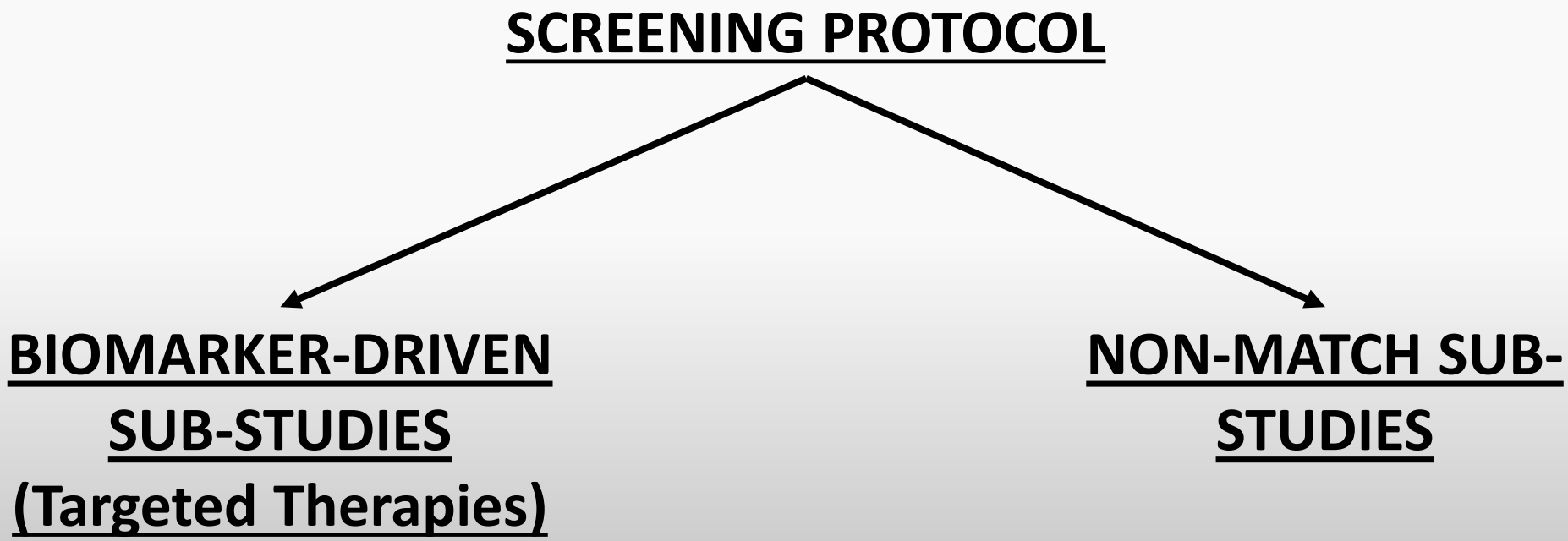
Drug Selection Committee

- Sources
  - Investigators/Drug Selection Committee Initiated
  - Pharmaceutical company initiated
- Initial Qualification
  - Investigational drug/biomarker combination with preclinical & clinical data supporting safety & potential efficacy as a targeted therapy or “non-match” therapy in lung SCC.
  - Ready or near ready to enter the Lung-MAP phase 2 clinical protocol
- Candidates are evaluated by the Lung-MAP Drug Selection Committee (DSC), comprised of:
  - Key investigators & clinical researchers
  - Biomarker & molecular target experts from academia, NCI & FDA
  - Non-conflicted industry-based drug developers
- Candidates are scored based on:
  - Target appropriateness for Lung-MAP
  - Drug/Biomarker preclinical & clinical data
  - PK/PD data

Process

- Sub-study suggestions come from Lung-MAP PIs, outside investigators, or pharma
- Initial discussions are internal with a PIs, followed by informal presentation from investigator/pharma to internal drug selection committee
- Next step is decision to proceed to full Drug Selection Committee (DSC)
  - Completion of Drug Selection application, summarizing preclinical and PK/PD data, prior human experience and safety profile, especially in lung cancer, and status of assay if proposed sub-study includes biomarker selection
  - DSC presentation by investigator/pharma, Q&A, and committee closed session discussion
- Formal voting by DSC members; 6 criteria for evaluation, each scored on 1-9 scale
  - Target/target appropriateness to NSCLC; Drug/biomarker understanding; Preclinical data; PK/PD; Toxicity; Clinical data
- PIs have final decision if vote is close or issues are brought up
- Acceptance/deferral letters sent to pharma
- Upon acceptance, kick-off call and regular teleconferences are set up with FNIH and SWOG Operations, for concept/protocol development, including regulatory aspects and FDA requirements, confirmation of drug supply, and contractual agreements

Studies Under Development



Studies under development
Targeted therapies

- **S1900G** (Novartis/Lilly): *A Randomized Phase II Study of Osimertinib and Capmatinib with or without Ramucirumab in Patients with Met Amplified and EGFR Mutated Stage IV Non-Small Cell Lung Cancer after Progression of Disease on Prior Osimertinib-Containing Therapy*.
  - Study chairs Sarah Goldberg, Ross Camidge. The protocol documents were resubmitted to CTEP on 9/13/22 to address their Consensus Review Comments. Contracts and budget are underway. Activation targeted for Q1/2023.

- **S1900I:** *EGFR TKI ± anti-VEGFR in EGFR Exon 20 Insertion Mutations*. Study chair Deborah Doroshow, co-chair Sandip Patel.
  - The revised concept and responses to the CTEP Consensus Review comments were submitted to CTEP on 9/9/22. Protocol is underway, RaPID call is scheduled for 10/12/22. Contract and budget are underway. Activation targeted for Q2-3 2023

- **S1900J**: *Phase II of EGFR-MET bispecific antibody in Participants with Stage IV or Recurrent Non-Small Cell Lung Cancer Previously Treated with High MET Amplification.* Study chair Christian Rolfo, co-chair Shirish Gadgeel.
  - The DSC approved the proposal on 8/30/22 and the company accepted. Study team is working on the concept and the kick-off call is being scheduled. Activation targeted for Q1 2024.

- **S1900K**: *A Randomized Phase II Study of MET TKI with or without anti-VEGFR2 in Participants with Met Exon 14 Skipping Positive Stage IV or Recurrent NSCLC.* Study chairs Paul Paik, Xiuning Le.
  - Revised study concept was sent to the company for their review and approval on 9/14/22. Contract is underway. Activation is TBD.

Studies under development
Non-Matched Arm

- **S1800E: A Randomized Phase II/III Study of anti-PDL1 Plus Docetaxel and anti-VEGFR2 versus Standard of Care Docetaxel and Ramucirumab for Participants Previously Treated with Immunotherapy for Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Non-Match Sub-Study). Study chair Karen Reckamp, co-chairs Konstantin Dragnev and Saiama Waqar.**
  - **DSC approved 4/1/22. Activation initially targeted for Q2-3 2023.**
  - **Pre-look concept submitted to CTEP on 7/22/22, communication from CTEP 9/8/22 that studies in same space as PRAGMATICA are on hold due to accrual concerns. Lung-MAP team to discuss with CTEP**

- **S1800F: anti-TIGIT + anti-PD1 + VEGFR-TKI for Patients Previously Treated with Immunotherapy. Study chair Erminia Massarelli, co-chair Tina Li.**
  - **DSC approved 4/26/22. Activation initially targeted for Q3 2023**
  - **Pre-look concept submitted to CTEP on 8/18/22, communication from CTEP 9/8/22 that studies in same space as PRAGMATICA are on hold due to accrual concerns. Lung-MAP team to discuss with CTEP**

Summary

- Significant potential for benefiting patients
- A unique opportunity to explore drugs or combinations in patients with metastatic non-small cell lung cancer
- Ability to explore efficacy in rare patient populations
- Great support from NCI, FDA and industry
- Significant opportunity to collect biosample for correlative studies
- Opportunity for participation of all thoracic oncologists, translational scientists and other interested parties around the country

Virtual attendees -
Place your questions in the chat box and a team member will read it out loud for the study team to answer

Closing Announcements & General Q & A Session

HOSSEIN BORGHAEI, MS, DO, LUNGMAP CHAIR

ALL ATTENDEES

Contact Us

Site Coordinators Committee

LUNGMAPSCC@crab.org

Protocol & Regulatory Questions

lgildner@swog.org or

jbeeler@swog.org

Eligibility & Data Submission Questions

LUNGMAPQuestion@crab.org

Funding Questions

Funding@swog.org

General Medical Questions

LUNGMAP@swog.org

S1900E Medical Questions

S1900EMedicalQuery@swog.org

S1800D Medical Questions

S1800DMedicalQuery@swog.org

S1900F Medical Questions

S1900FMedicalQuery@swog.org

Accrual Enhancement Committee

lungmapAEC@swog.org

Acknowledgements

Thank you for supporting the Lung-MAP Trial!

Patients and Sites

Lung-MAP Site Coordinators Committee

Patient Advocate

Diversity, Equity, and Inclusion Champion

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.

Summary & Adjourn

Thank you joining us!

The slides will be available on the SWOG & CTSU websites