Pragmatica-Lung Cancer Treatment Trial

Optimizing Public-Private Partnerships for Clinical Cancer Research

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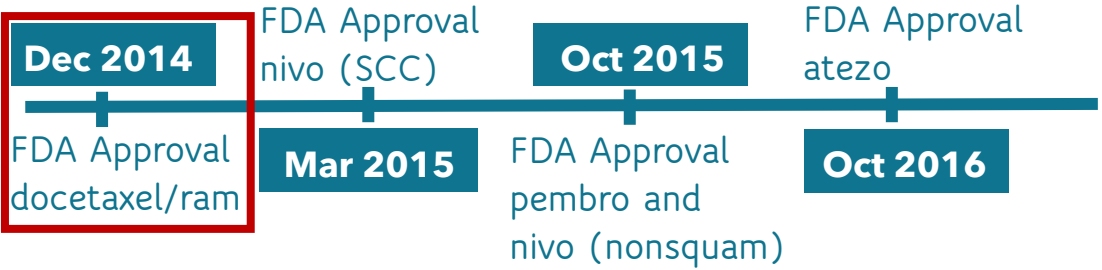
Pragmatica-Lung

A real-world clinical trial for patients whose non-small cell lung cancer has returned after chemo- and immuno-therapy

S2302 Pragmatica-Lung Timeline

Second-line therapy for advanced NSCLC



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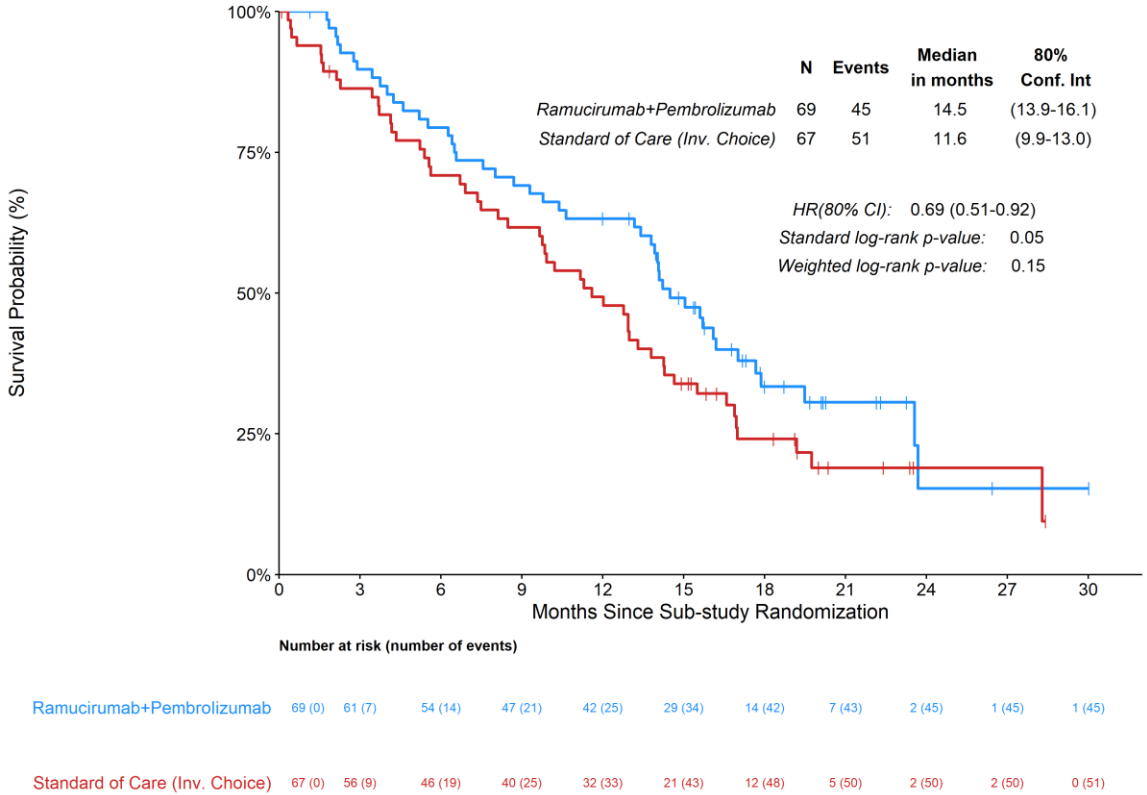
S1800A—Overall survival



Median OS for RP 14.5 months v. SOC 11.6 months

HR= 0.69; SLR p-value 0.05

Standard of care therapy received:

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

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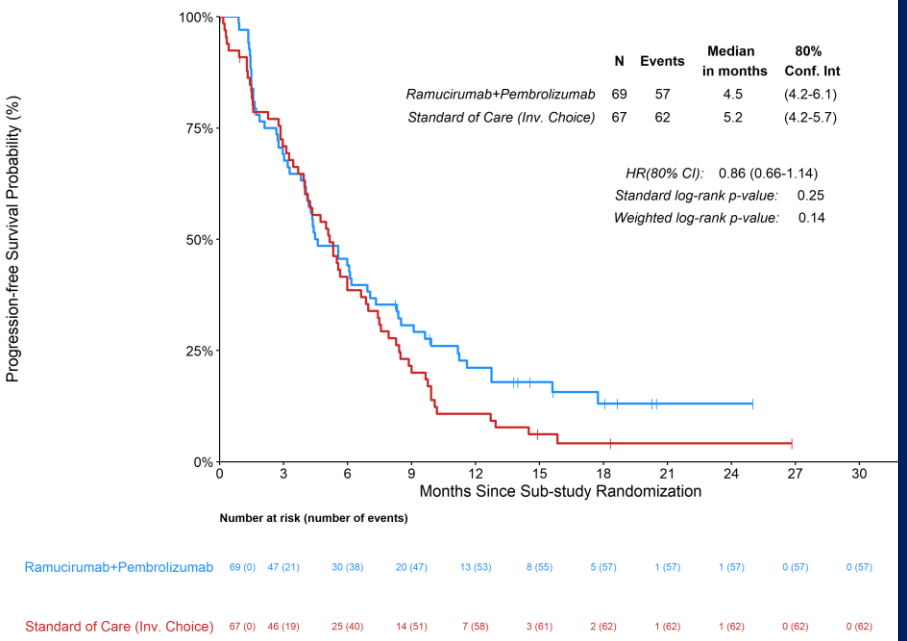
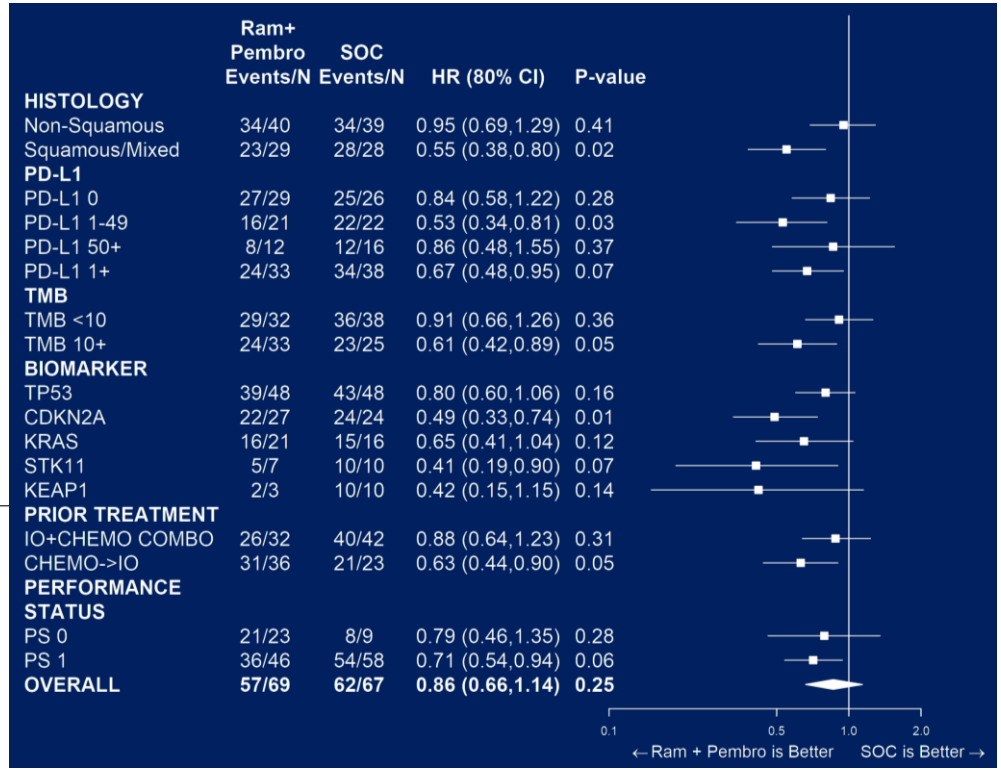
LUNG-MAP

Reckamp KL et al ASCO 2022; J Clin Oncol 2022

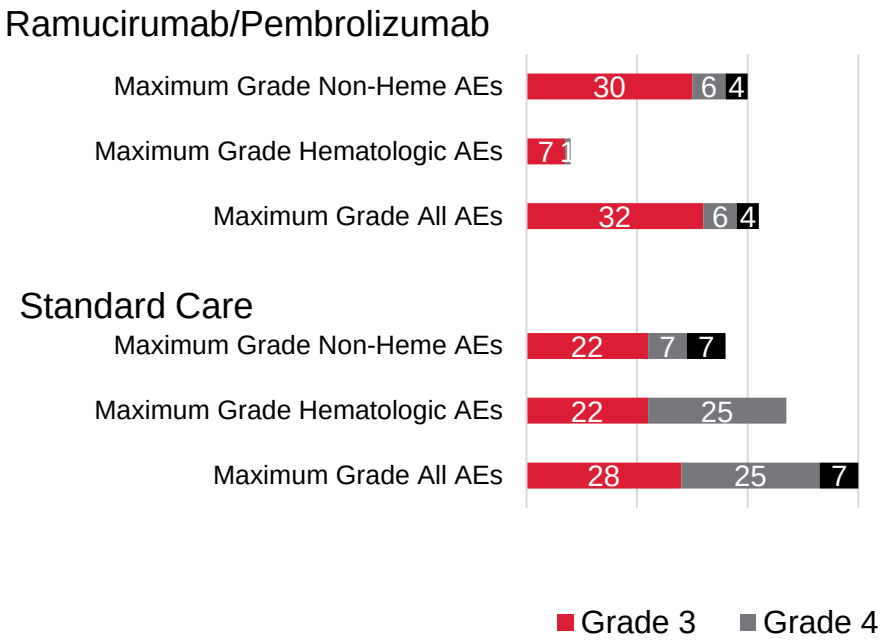
Progression free survival with subgroup analysis

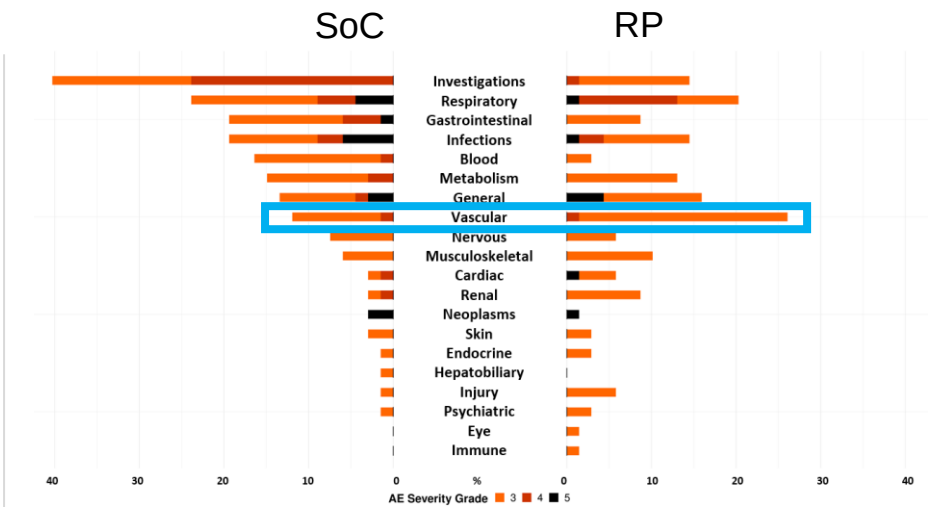




Reckamp KL et al ASCO 2022; J Clin Oncol 2022

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

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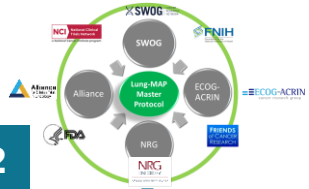

July 2022

Discussions start for Pragmatica-Lung

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Background/Overview

- Effective therapy following frontline ICI for NSCLC is needed with limited FDA-approved options.
- S1800A was a Phase II randomized study of ramucirumab plus pembrolizumab versus standard of care for NSCLC patients previously treated with immunotherapy performed within the Lung-MAP platform.
- **Overall survival was significantly improved with a hazard ratio 0.69**, median OS of 14.5 and 11.6 months, for pembrolizumab and ramucirumab vs. standard of care, respectively.
- Collaborative relationships made within Lung-MAP set the foundation for next steps.
- Pembrolizumab and ramucirumab are approved in multiple tumors (including NSCLC) with well known safety and efficacy profiles
- Design a simple trial to answer the specific question of overall survival benefit (challenge: 12-page protocol and 5-page consent)

Timing is everything

- Growing number of complex studies in cancer in the -omics era
- Increasing awareness that clinical research needs to adjust to become more inclusive and representative
- NCI and FDA with initiatives to promote pragmatic trial designs
- Strong support from FOCR and FNIH
- Post-COVID realities: Clinical trial offices at sites challenged by high turnover and staff burnout
- Niche population trials limit patient accrual in a single trial
- Cancer centers and clinical research sites interested in finding ways to enhance patient accrual

S2302 Pragmatica-Lung

Pragmatica-Lung
A real-world clinical trial for patients whose non-small cell lung cancer has returned after chemo- and immuno-therapy

NCT05633602

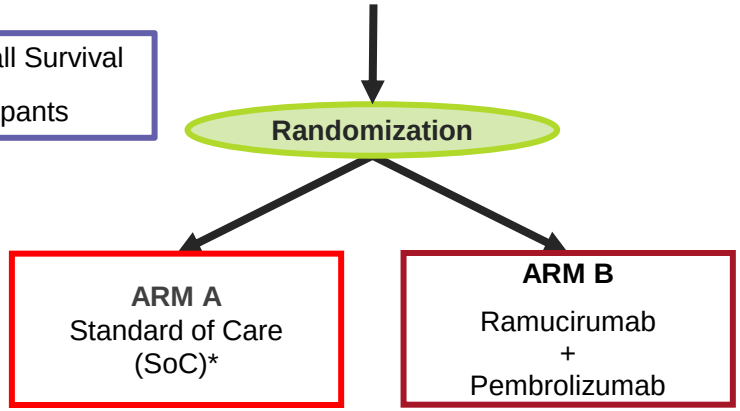
A Prospective Randomized Study of Ramucirumab plus Pembrolizumab v Standard of Care for Participants Previously Treated with Immunotherapy for Stage IV or Recurrent NSCLC

Previously treated Stage IV or recurrent non-small cell lung cancer

Primary endpoint: Overall Survival

Accrual Goal: 700 participants

Current Accrual: 138 participants (9/22/23)



*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."

Chair: Karen Reckamp, MD (SWOG); Co-chair: Konstantin Dragnev, MD (Alliance); Statistical Chair: Mary Redman, PhD
Co-statisticians: Jieling Miao, MS, James Moon, MS Study Champion(s): Wade Iams, MD (ECOG), Brian Henick, MD (NRG); Lung community engagement subcommittee representative: Daniel Carrizosa, MD, MS

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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.**

This is an FDA Registration Trial.

S2302 Goals

- Empowerment of investigators to treat patients as would be done in real world practice.
- To decrease barriers to enrollment.
- To minimize the data collection burden and monitoring.
- Reduce reporting of unnecessary data.
- Shift resources used for data collection and reporting to increasing representativeness
- Designed to reduce the burden of clinical trial participation and to promote the inclusion of all participants with the disease.

Eligibility

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

At least 18 yrs old with 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) > 8 cent anti-PD-1 or PD-L1 therapy.

Best response on anti-PD-1 or anti-PD-L1 therapy of stable tage IV/recurrent NSCLC (in the opinion of the treating physician).

Disease progression </= 365 days from initiation (C1/D1) of anti-P d/or consolidation if only line of anti-PD-1 or anti-PD-L1 therapy.

Received platinum-based chemotherapy and experienced disease ian) during or after this regimen.

- **Stage IV or Recurrent**
- **Prior Treatment**
- **Performance Status**
- **Safety**

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). Prior targeted therapy allowed for pts. with targetable alterations if all other criteria met.

Ability to safely receive the investigational drug combination and the investigator's choice of SoC regimens per the current FDA-approved package insert(s), treating investigator's discretion, and institutional guidelines.

Zubrod Performance Status of 0-2.

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** With consent, there are no other eligibility criteria.

Study Calendar

— Per Institution Standard and FDA-approved package insert(s)

REQUIRED	Cycle Length (+/- 3 days) Cycle 1	Cycle 2	Cycle 3	Cycle 4	Subsequent Cycles	At Off Tx	Off Tx FU
PHYSICAL							
Vital Status Assessment	X	X	X				
SAE Assessment	X	X	X				
LABORATORY							
Participants must be able to safely receive the investigatc pembrolizumab described in protocol Section 7.2, per the discretion, and institutional guidelines.							
TREATMENT							
Arm A: Investigator's Choice of Standard of Care (So							
Chosen SoC drug(s) should be administered according to the current FDA-approved package insert(s). Arm A cycle length may vary.							
Arm B: Ramucirumab plus Pembrolizumab (21-day cycle)							
Ramucirumab	X	X	X	X	X		
Pembrolizumab	X	X	X	X	X (up to 35 cycles)		

- **No protocol required disease assessment (CT, imaging)**
- **No protocol required lab tests**
- **No specimen collection**
- **Only report all Grade 5 and Unexpected Reportable Gr 3-4 AE**

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Pragmatic Design
Eligibility and study calendar

PRAGMATIC

Limited eligibility criteria

- Items focus on stage, prior therapy, PS and safety

Enroll and treat patients as would be done in real world practice with institutional guidelines and investigator discretion.

Minimal items on study calendar.

- No labs
- No imaging or RECIST

STANDARD

- Extensive, complex eligibility.
- Specifics of treatment may vary from institutional standards.
- Complicated study calendar with labs/imaging/biomarker testing.

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Data Submission Schedule and Requirements

Baseline (within 15 days after randomization):

- **S2302 Vital Status Form**
- **S2302 Onstudy Forms**
- **S2302 Eligibility Criteria Form**
- **S2302 PD-L1 Results Form**
- **S2302 Genomic Alterations Form**
- **Pathology Report**

No Cycle based Treatment Form
No Disease Assessment Form (BTA, FUTA)

On Treatment (within 30 days after every treatment cycle):

- **S2302 Vital Status Form**
- **S2302 Adverse Event Form**

Off Treatment (within 30 days after discontinuation of treatment):

- **S2302 Vital Status Form**
- **S2302 Treatment Summary Form**

Follow Up (within 60 days after each follow-up visit):

- **S2302 Vital Status Form**
- **Late Adverse Events**

No Detailed Follow Up form, only vital status (alive or not)

Within 30 days after knowledge of death:

- **S2302 Notice of Death**

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Pragmatic Design
Data capture

PRAGMATIC

Minimize the data collection burden

- Reduced time points for data submitted
- Reduced number of forms
- Reduced number of data elements

No protocol required disease assessment (CT, imaging)

No protocol required lab tests

No specimen collection

Grade 5 and unexpected, related Grade 3-4 AE (~90% fewer AEs reported)

No conmed collection

Reduced data to monitor and audit

STANDARD

- Extensive, complex electronic data capture
- Collection of labs
- Collection of RECIST and associated queries
- Conmed collection and dates
- Extensive study monitoring and auditing

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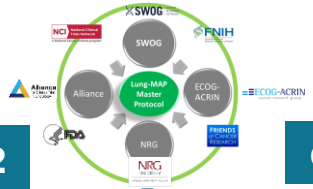

Oct 2022

FDA grants BTD for pembro/ram

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S2302 Enhanced Recruitment Efforts: Representativeness

- **Special focus: Enhanced outreach and support to sites with high % of patients from historically underrepresented groups**
- Will place initial calls to support activation
- Will develop community engagement package with outreach strategies and materials
- **Monthly monitoring of representativeness of enrolled population throughout trial**
- Will provide targeted additional outreach and support based on these percentages
- Possibility of additional funds for targeted sites to support community engagement events

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Resources and Materials

- **Enhanced set of resources to aid sites with outreach and patient recruitment.**
- **S2302 patient-friendly plain language trial summary and accompanying social media toolkit (tweets and graphics).**
  - **Available for participating site use on SWOG.org and via the S2302 protocol abstract page on CTSU.org.**
- **For S2302, CTSU will provide a template to assist with EMR implementation.**
  - Institutions that choose to utilize the EMR template are responsible for the verification and modification of the EMR in compliance with local institutional guidelines.

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S2302 Pragmatica-Lung Activation

Mar 2023

MERCK Lilly

Pragmatica-Lung

A real-world clinical trial for patients whose non-small cell lung cancer has returned after chemo- and immuno-therapy

Current Accrual 160+

Oct 2023

Accrual rate 30-40/month

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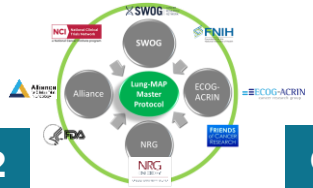

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Accrual rate 30-40/month

Second-line therapy for advanced NSCLC

Dec 2014

FDA Approval docetaxel/ram

FDA Approval nivo (SCC)

Mar 2015

Oct 2015

FDA Approval pembro and nivo (nonsquam)

FDA Approval atezo

Oct 2016

OS negative

Dec 2022

cabozantinib/ nivo vs doce

sitravatinib/ nivo vs doce

May 2023

Sept 2023

lenvatinib/ pembro vs doce

S2302 Pragmatica-Lung Acknowledgments

SWOG: Roy Herbst, M.D., Ph.D.; Jhanelle Gray, M.D.; Charles Blanke, M.D.
Judy Johnson, MBA (Patient Advocate); Lucy Gansauer, MSN, RN, OCN, CCRP (DEI Champion)
FDA: Rick Pazdur, M.D., Harpreet Singh, M.D.
NCI CTEP: Jim Doroshow, M.D.; Meg Moony, M.D., M.S.; Shakun Malik, M.D.
NCTN partners: Alliance; ECOG-ACRIN; NRG Oncology
Foundation for the National Institutes of Health (FNIH): Stacey Adam, Ph.D.
Friends of Cancer Research (FoCR): Ellen Sigal, Ph.D.
Funding: Merck and Lilly

SWOG Operations Office and Statistics and Data Management Center (SDMC):
SWOG Statisticians: Mary Redman, Ph.D., Jieling Miao, M.S., James Moon, M.S.
Data Coordinators: Louise Highleyman, Pasarlai Ahmadzai
SDMC Project Management: Dani Weatherbee; Study Build: Greg Auger
Protocol Project Manager: Mariah Norman**,** Justine Trevino

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Thank You!

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