Pragmatica-Lung:

A New Paradigm for Practical Clinical Trials

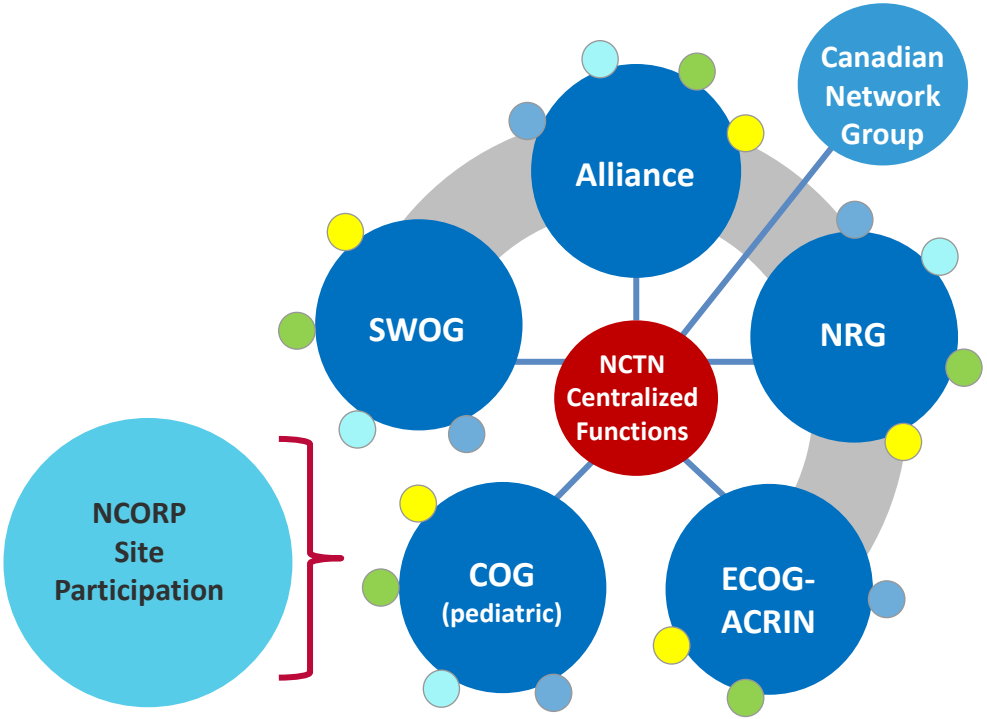
NIH NATIONAL CANCER INSTITUTE

16th Joint Meeting of NCI BSA/NCAB Clinical Investigations Subcommittee
June 11, 2024

Chair: Nilofer Azad, MD
Executive Secretary: Meg Mooney, MD

NCI National Clinical Trials Network (NCTN)

Established in 2014 from former Cooperative Group Program to provide support with an infrastructure designed to harmonize processes & promote collaborations to focus on questions not well supported in commercial environment



LEGEND:

Centralized Functions:
- NCI Central IRB with 4 Boards
- Cancer Trials Support Unit for Administrative & Regulatory Functions
- RT/Imaging Core Center
- NCI Disease Steering Review Committees
- Common Data Mgt w/ Central Hosting

Lead Academic Participating Sites (LAPS)

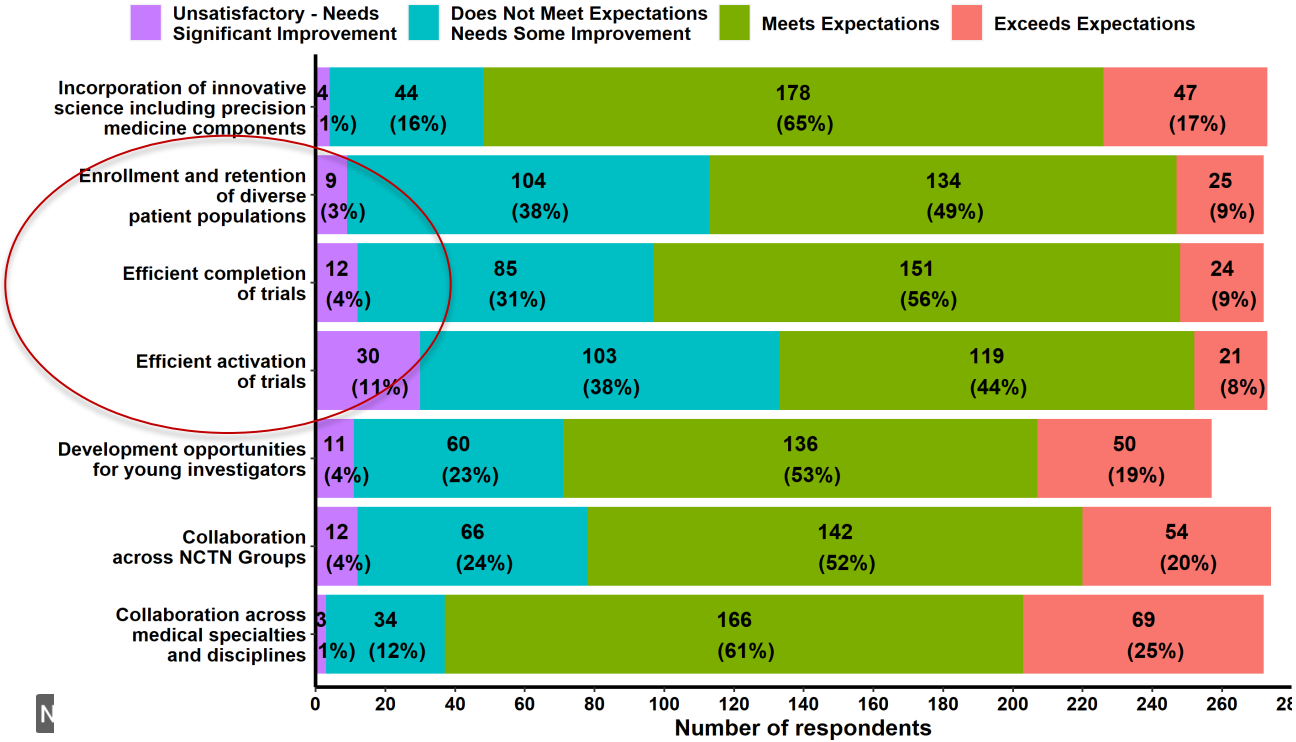
Operations Centers

Statistics & Data Management

Tumor Banks

Increasing Concerns with Clinical Trials related to Cost, Complexity & Site Burden for Trial Conduct

Survey Question in Summer/Fall 2022 to Key NCTN Participants: *Overall, how satisfied are you with the degree to which the NCTN is achieving the following goals? (n~270)*



Also, in response to question on satisfaction of the funding provided for accrual:

- **23% rating funding as "inadequate**
- **44% rated it as "does not meet expectations/ & needs some improvement"**

NCI Strategic Vision for Clinical Trials: 2030 and Beyond

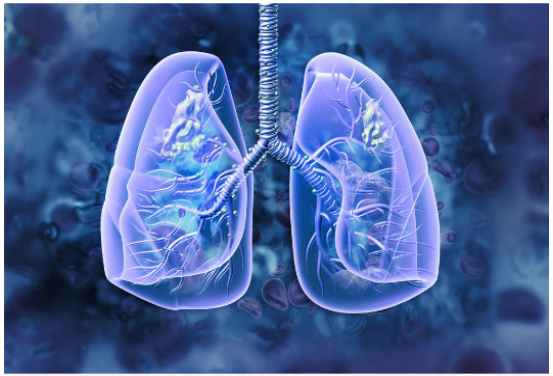
Develop **flexible**, **faster**, **simpler**, **less expensive**, **high-impact** clinical trials that seamlessly integrate with clinical practice

- Streamline processes for trial design and execution
- Focus on essential endpoints
- Decrease regulatory hurdles and broaden trial access
- Increase efficiency of data collection

Pragmatica-Lung Treatment Trial: A streamlined model for future cancer trials

- Uses a trial design that removes many of the barriers that prevent people from joining clinical trial, provides a model to increase diversity of participants in trials and reduces the burden on sites for conducting the trial

- Is part of a broader effort by NIH and FDA to modernize clinical trials with fewer & simpler eligibility criteria while still ensuring the quality of data and safety of the patients.



Credit: iStock

Pragmatica-Lung Treatment Trial: A streamlined model for future cancer trials

- This approach is most appropriate for trials in which the agents being studied have already been approved by FDA for an indication & their side effects are well understood.
- The research question in Pragmatica-Lung fits with this approach and is designed for potential registration by the FDA for a new indication in advanced non-small cell lung cancer (NSCLC) with overall survival as the primary endpoint.

The hope is this type of simplified trial can be less burdensome to patients & Investigators, accrue study participants faster, be more representative of real-world patient population, & serve as a model for future cancer clinical trials.

https://www.nih.gov/news-events/news-releases/pragmatica-lung-study-streamlined-model-future-cancer-clinical-trials-begins-enrolling-patients

S2302: Pragmatica-Lung Treatment Trial

A Prospective Randomized Study of Ramucirumab Plus Pembrolizumab vs Standard of Care for Participants Previously Treated with Immunotherapy for Stage IV or Recurrent Non-Small Cell Lung Cancer

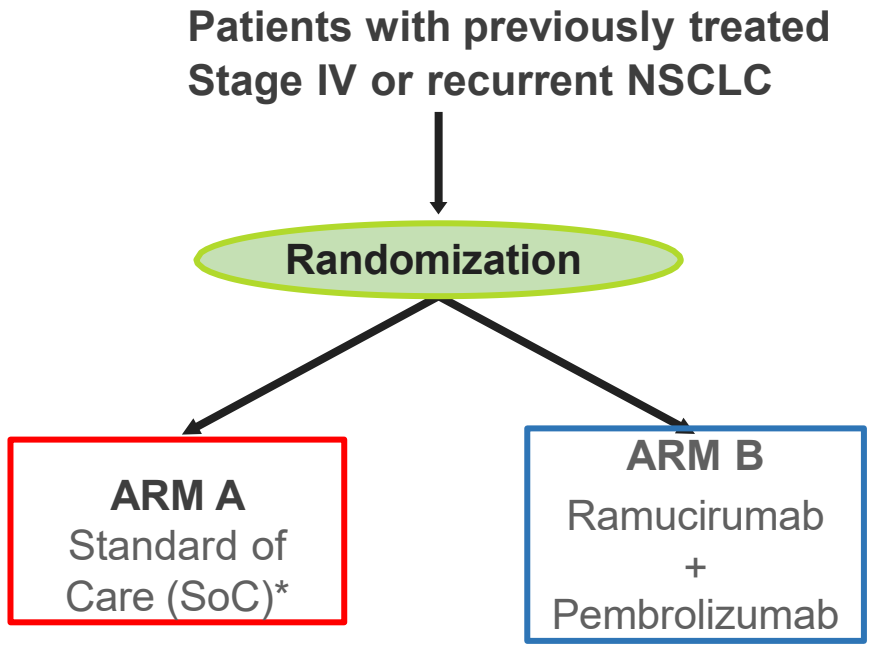
Chair: Karen Reckamp, MD (SWOG)
Co-Chair: Konstantin Dragnev, MD (Alliance)

Statistical Chair: Mary Redman, PhD
Co-statisticians: Jieling Miao, MD, James Moon, MS

Study Champions: Wade Iams, MD (ECOG-ACRIN)
Brian S. Henick (NRG Oncology)

Lung Community Engagement Subcommittee Rep:
Daniel Carrizosa, MD, MS

Company Collaborators:
Eli Lilly & Co. and Merck



Primary endpoint:
Overall Survival

Accrual Goal:
700 participants

* 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."

Pragmatica-Lung Treatment Trial

- Based on randomized phase 2 trial with promising results conducted by within the NCTN program under the Lung-MAP Initiative (*a public-private collaboration among NCI, SWOG/NCTN, FOCR, FNIH with pharmaceutical & diagnostic companies for biomarker-driven IND trials in advanced NSCLC*)
- Simplified study proposal reviewed / approved through the NCI Thoracic Malignancy Steering Committee
- Use of existing NCI DCTD/CTEP Cooperative Research & Development Agreements w/ company partners (Eli Lilly & Merck & Co. Inc.) for drug supply and distribution
- Led by SWOG with broad support by the NCTN Group network

Pragmatica-Lung Treatment Trial:

Practical Approach for a Registration-Intent Phase 3 IND Trial

- Simplified design with reduced data collection & primary endpoint of Overall Survival (no imaging, biospecimen, QOL/Pros instruments collection)
- Eligibility (Broadening eligibility for diverse patient population)
- Treatment (Physician's choice for standard of care control arm per NCCN / FDA approved treatments)
- Streamlined Toxicity/AE collection (Only SAEs, Unexpected Gr 3-4, Treatment-Related and All Gr 5s require reporting in Data Mgt System) & Simplified Study Calendar standard of care follow-up
- Standard NCTN Auditing Program (Q 3 yr) instead of on-site or central monitoring

Pragmatica-Lung Treatment Trial

- Timeline from study trial concept submission to activation with NCI Central IRB approval: 200 days
  - compared to absolute deadline for Phase 3 studies of 540 days (w/ target being around 300 days although most phase 3 IND studies exceed the 300-day target)

- Protocol: 28 pages (plus Administrative Appendix of 19 pages)
  - Compared to 108 pages for the predecessor phase S1800A phase 2 trial; other phase 3 trial w/ more complexities, secondary endpoints may be much longer

  - Pragmatica-Lung Appendix includes contact information, including contacts for the Centralized Trials Support Unit (CTSU); Staging criteria; Registration guidelines, Data submission procedures, Ethics/Regulatory considerations; QA Auditing & Monitoring; Recruitment & retention plan; and Remote Consent Procedures

Pragmatica-Lung Treatment Trial

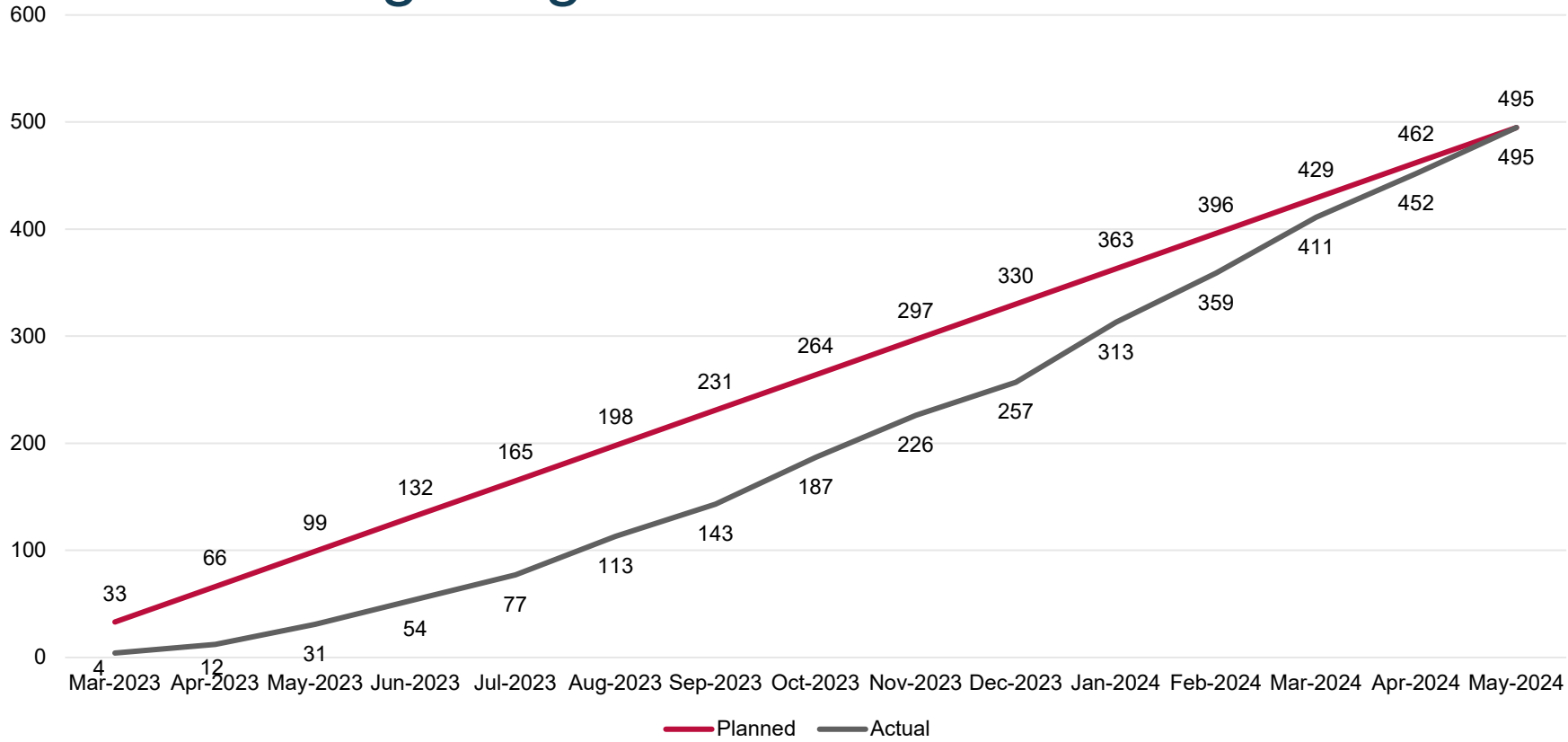
- Informed Consent Document: 11 pages (*includes summary of ICD of 3 pages per the Common Rule and 1 signature page*)
  - compared to 24 pages for the predecessor phase S1800A phase 2 trial; other phase 3 trial w/ more complexities & secondary endpoints in same general range

- Launch of trial coordinated with:
  - Communications plan at national level and locally
  - Extensive Recruitment & Retention Plan
  - Patient Educational
  - Engaging Sites with Diverse Populations
  - Connecting with Patient Advocacy Groups
  - Community Engagement
  - Recognitions for Sites in Email & NCTN Group Meetings

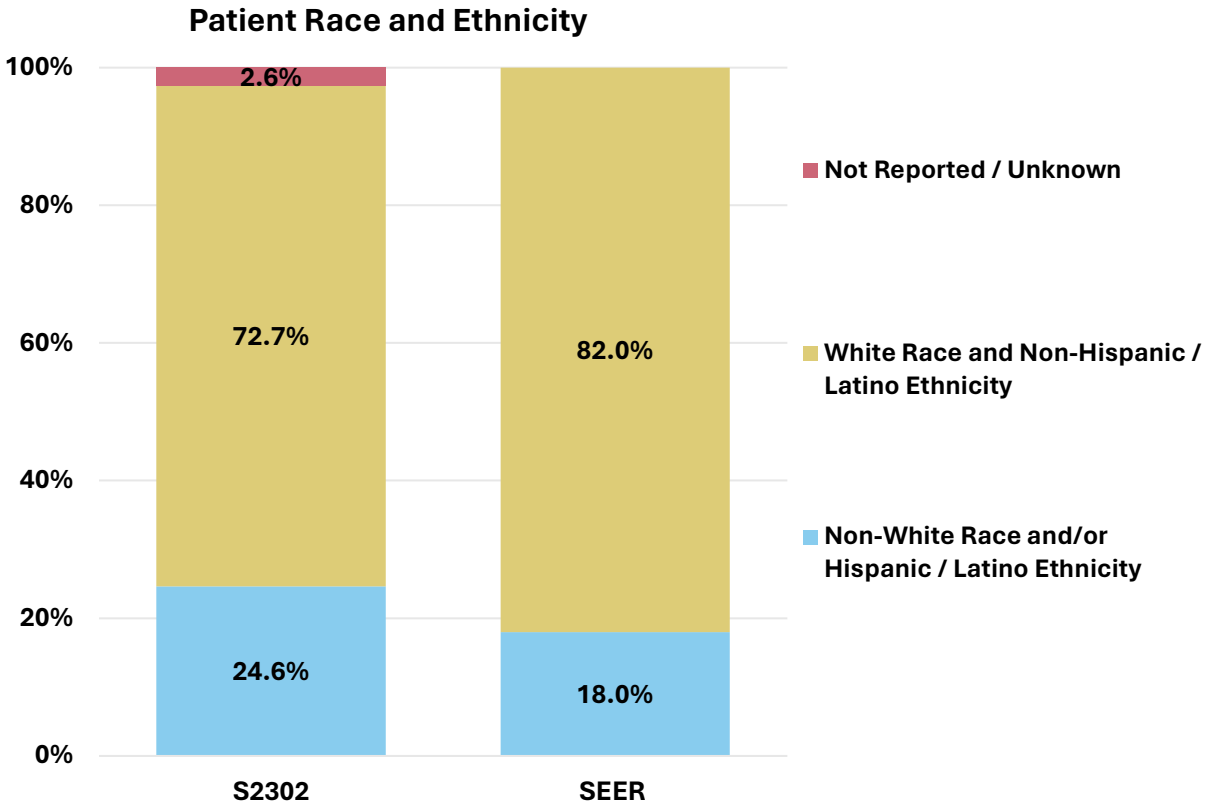
Pragmatica-Lung Treatment Trial

- Trial Activated on March 6, 2023
- Total Sample Size: 700 patients
- Estimated Accrual Timeline: 24 months (2 years)
- Accrual 6/6/2024 (12 PM ET): 505 patients (72% of total sample size) with a total of 219 sites enrolling 1 or more patients
- Amendment recently submitted to increase accrual to 800 patients and still finish trial within the same estimated 2-year timeline initially conceived for the trial

Monthly Planned and Actual Accrual to S2302 Lung-Pragmatica – as of 5/31/2024

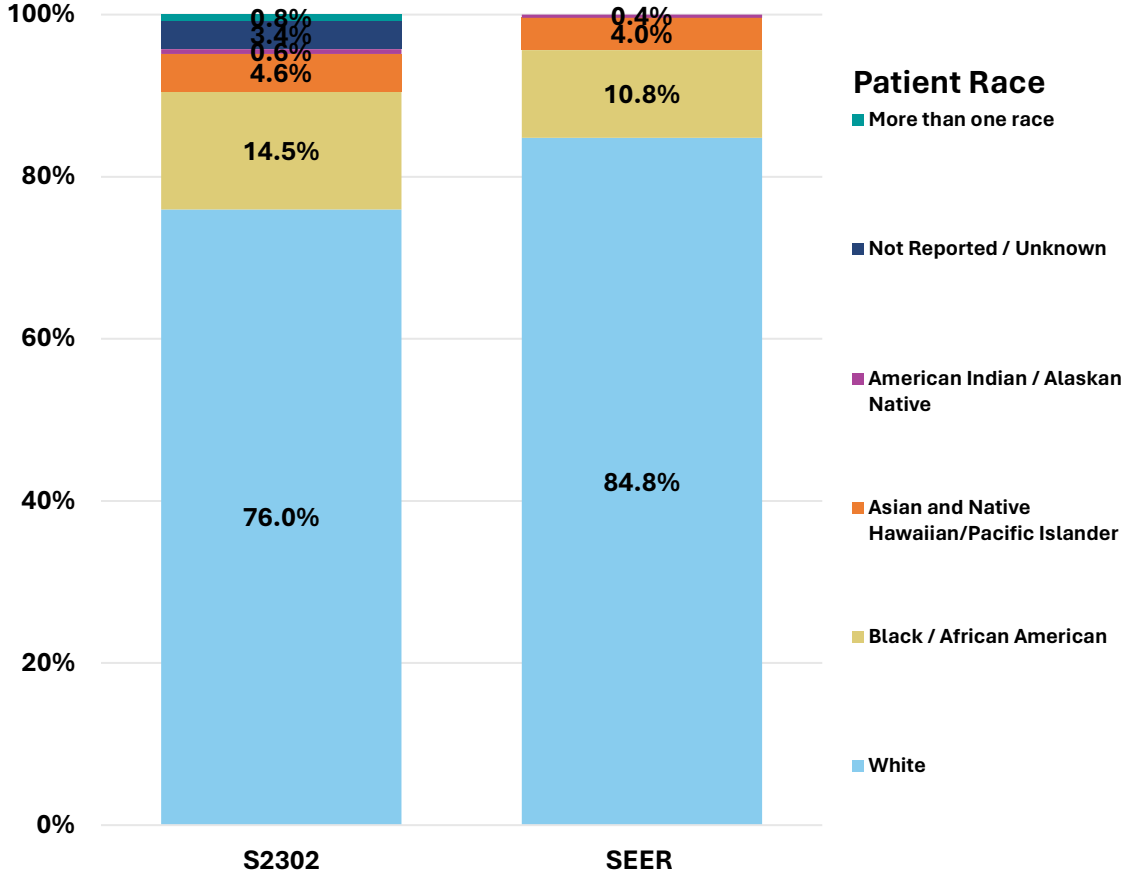


Race and Ethnicity of Patients Enrolled on S2302 Lung-Pragmatica Compared to SEER Lung Cancer Population Incidence Data



Based on S2302 enrollments as of 5/31/2024. Census-adjusted SEER incidence rates for 2017-2021 diagnosis years.

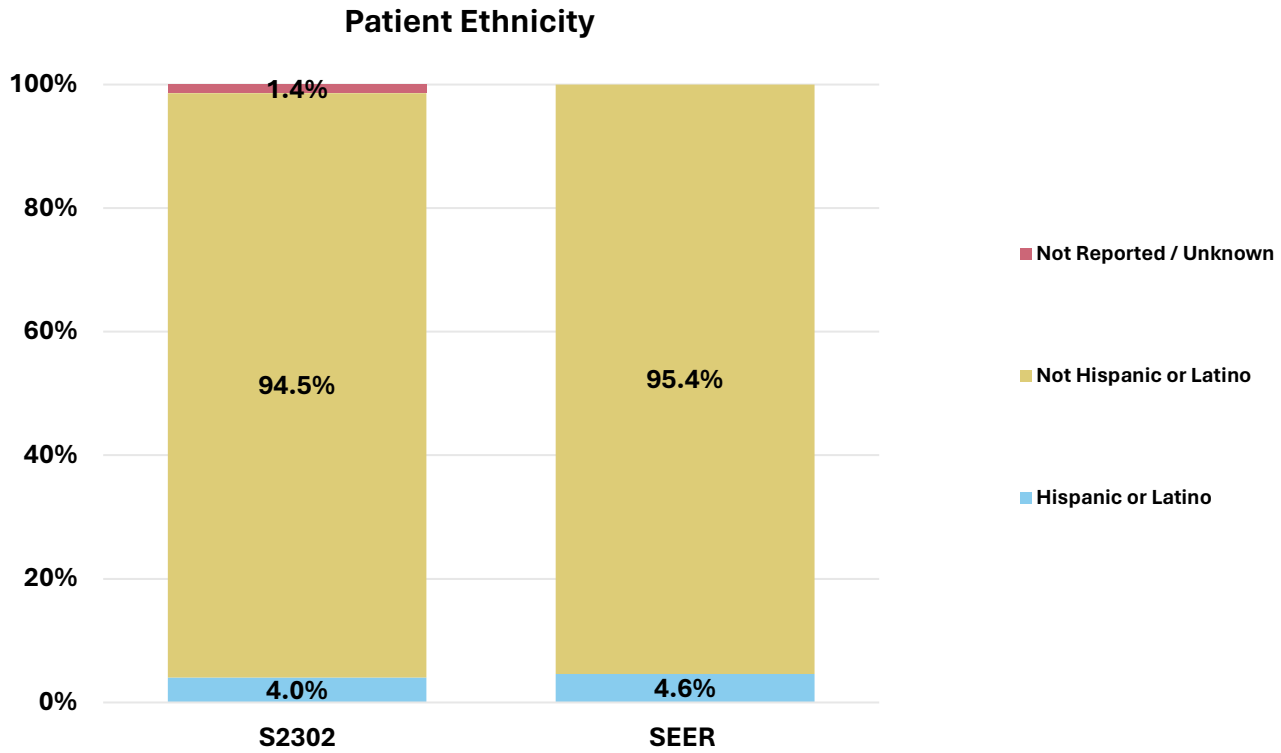
Race of Patients Enrolled on S2302 Lung-Pragmatica Compared to SEER Lung Cancer Population Incidence Data



Patient Race	S2302	SEER
More than 1 Race	0.8%	
Not Reported	3.4%	
American Indian/ Alaskan Native	0.6%	0.4%
Asian & Native Hawaiian/Pacific Islander	4.6%	4.0%
Black/African American	14.5%	10.8%
White	76.0%	84.8%

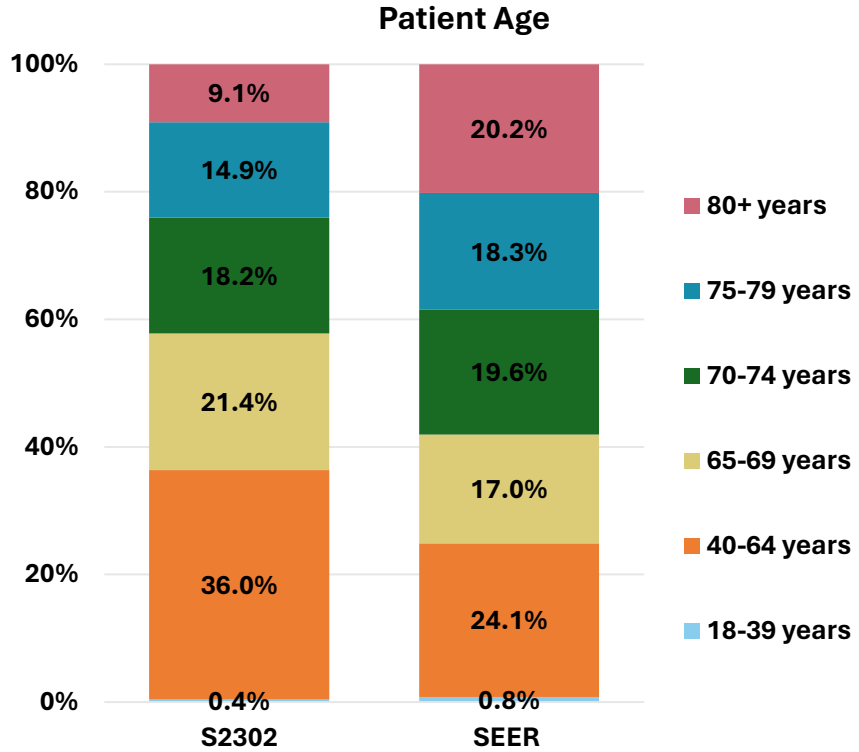
Based on S2302 enrollments as of 5/31/2024. Census-adjusted SEER incidence rates for 2017-2021 diagnosis years.

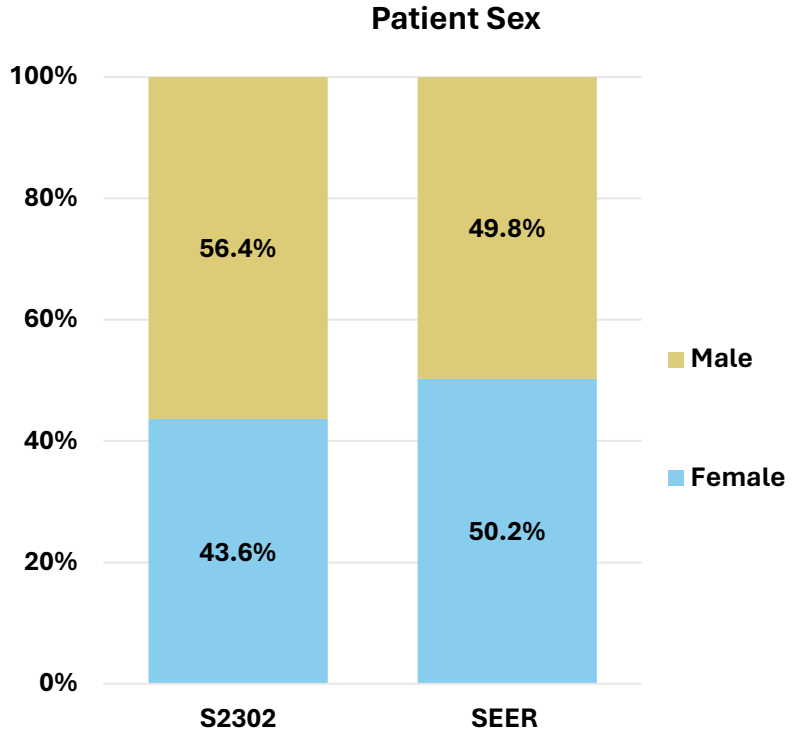
Ethnicity of Patients Enrolled on S2302 Lung-Pragmatica Compared to SEER Lung Cancer Population Incidence Data



Based on S2302 enrollments as of 5/31/2024. Census-adjusted SEER incidence rates for 2017-2021 diagnosis years.

Age and Sex of Patients Enrolled on S2302 Lung-Pragmatica Compared to SEER Lung Cancer Population Incidence Data



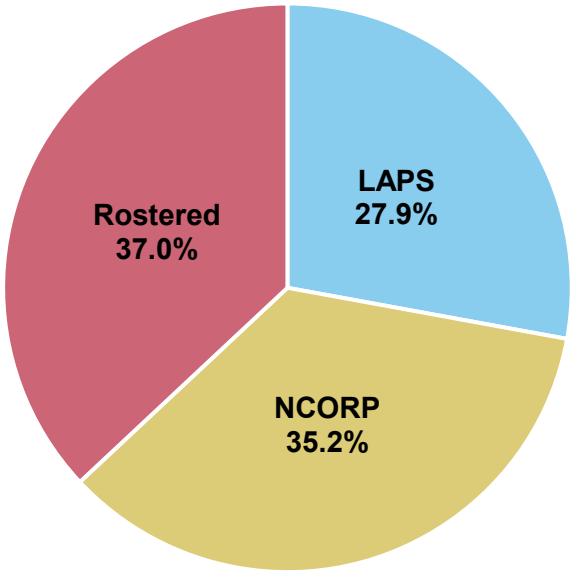


Based on S2302 enrollments as of 5/31/2024. Census-adjusted SEER incidence rates for 2017-2021 diagnosis years.

Site Type and Rurality for Patients Enrolled on S2302 Lung-Pragmatica

Based on S2302 enrollments as of 5/31/2024

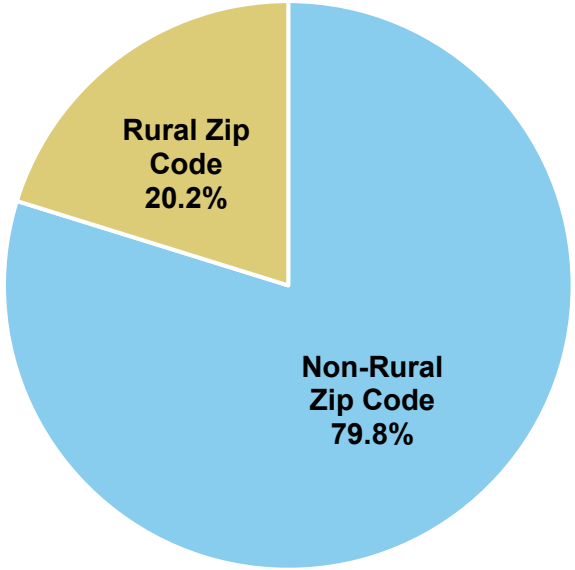
Accrual by Site Type



% of Total Sites as of 5/8/2023:

LAPs: 24%; NCORPs: 43%; Rostered: 33%

Rurality by Patient Zip Code



Note: Rurality defined using USDA ERS Rural-Urban Commuting Area (RUCA) Codes, with codes 1-3 considered non-rural and codes 4-10 considered rural. **According to HRSA, the US Census definition of rural includes 19.3% of the US population (likely an overestimate), while the OMB definition of rural includes 15% of the population (likely an underestimate)**. https://www.hrsa.gov/rural-health/about-us/what-is-rural

Sites With Enrollments to S2302 Lung-Pragmatica

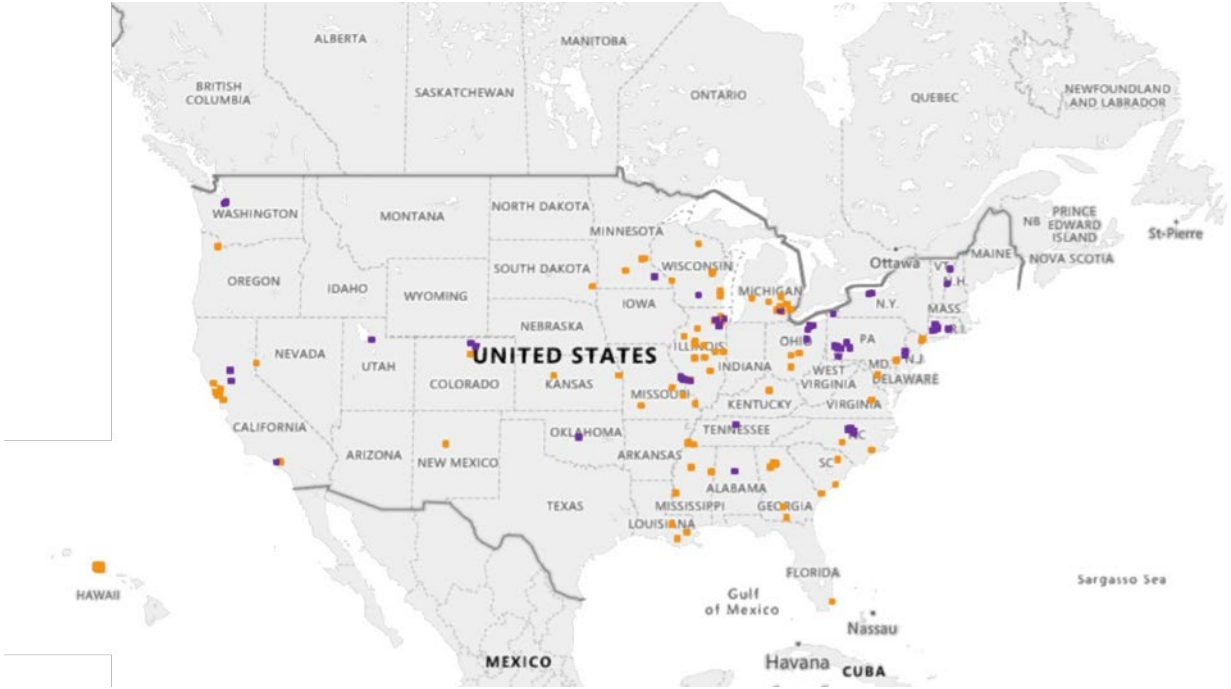
NCTN LAPS Sites

Based on S2302 enrollments as of 5/8/2024

Sites With Enrollments to S2302 Lung-Pragmatica

NCTN LAPS Sites

NCORP Sites



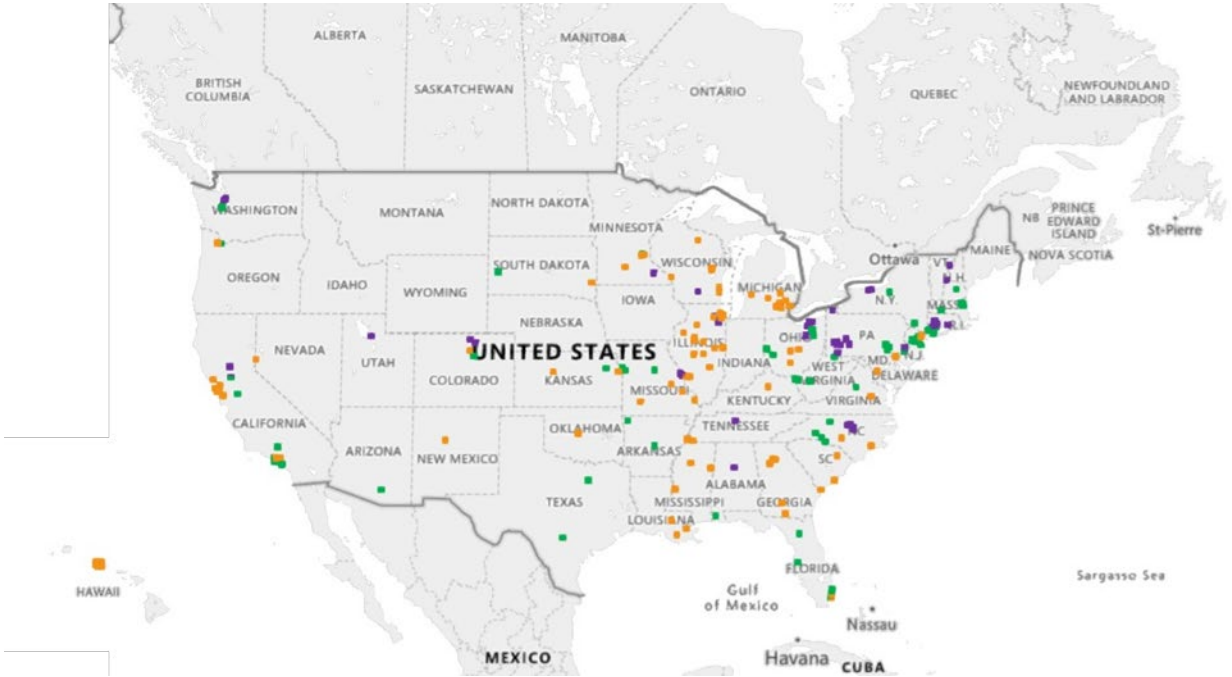
Based on S2302 enrollments as of 5/8/2024

Sites With Enrollments to S2302 Lung-Pragmatica

NCTN LAPS Sites

NCORP Sites

NCTN Rostered Member Sites



Based on S2302 enrollments as of 5/8/2024

www.cancer.gov

www.cancer.gov/espanol