Caring Ambassadors Lung Cancer Program
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Literature Review

SCREENING, COMPREHENSIVE BIOMARKER TESTING, DIAGNOSIS AND STAGING

Implementing lung cancer screening in primary care: needs assessment and implementation strategy design Transl Behav Med. 2022 Feb 16;12(2):187-197. doi: 10.1093/tbm/ibab115. Thomas J Reese 1 , Chelsey R Schlechter 2   3 , Heidi Kramer 4 , et al.

Lung cancer screening with low-dose computed tomography (CT) could help avert thousands of deaths each year. Since the implementation of screening is complex and underspecified, there is a need for systematic and theory-based strategies. Explore the implementation of lung cancer screening in primary care, in the context of integrating a decision aid into the electronic health record. Design implementation strategies that target hypothesized mechanisms of change and context-specific barriers. The study had two phases. The Qualitative Analysis phase included semi-structured interviews with primary care physicians to elicit key task behaviors (e.g., ordering a low-dose CT) and understand the underlying behavioral determinants (e.g., social influence). The Implementation Strategy Design phase consisted of defining implementation strategies and hypothesizing causal pathways to improve screening with a decision aid. Three key task behaviors and four behavioral determinants emerged from 14 interviews. Implementation strategies were designed to target multiple levels of influence. Strategies included increasing provider self-efficacy toward performing shared decision making and using the decision aid, improving provider performance expectancy toward ordering a low-dose CT, increasing social influence toward performing shared decision making and using the decision aid, and addressing key facilitators to using the decision aid. This study contributes knowledge about theoretical determinants of key task behaviors associated with lung cancer screening. We designed implementation strategies according to causal pathways that can be replicated and tested at other institutions. Future research is needed to evaluate the effectiveness of these strategies and to determine the contexts in which they can be effectively applied.

Improved motivation and readiness to quit shortly after lung cancer screening: Evidence for a teachable moment Cancer. 2022 Feb 10. doi: 10.1002/cncr.34133. Online ahead of print. Randi M Williams 1 , Marisa Cordon 1 , Ellie Eyestone 1 , Laney Smith 1 , et al.

BACKGROUND: For patients at high risk for lung cancer, screening using low-dose computed tomography (lung cancer screening [LCS]) is recommended. The purpose of this study was to examine whether screening may serve as a teachable moment for smoking-related outcomes. **METHODS:** In a smoking-cessation trial, participants (N = 843) completed 2 phone interviews before randomization: before LCS (T0) and after LCS (T1). By using logistic and linear regression, the authors examined teachable moment variables (perceived risk, lung cancer worry) and outcomes (readiness, motivation, and cigarettes per day [CPD]). **RESULTS:** Participants were a mean ± SD age of 63.7 ± 5.9 years, had 47.8 ± 7.1 pack-years of smoking, 35.2% had a high school diploma or General Educational Development (high school equivalency) degree or less, and 42.3% were undergoing their first scan. Between T0 and T1, 25.7% of participants increased readiness to quit, 9.6% decreased readiness, and 64.7% reported no change (P < .001). Motivation to quit increased (P < .05) and CPD decreased between assessments (P < .001), but only 1.3% self-reported quitting. Compared with individuals who reported no lung cancer worry/little worry, extreme worry was associated with readiness to quit in the next 30 days (odds ratio, 1.8; 95% CI, 1.1-3.0) and with higher motivation (b = 0.83; P < .001) at T1. Individuals undergoing a baseline (vs annual) scan were more ready to quit in the next 30 days (odds ratio, 1.8; 95% CI, 1.3-2.5). **CONCLUSIONS:** During the brief window between registering for LCS and receiving the results, the authors observed that very few participants quit smoking, but a significant proportion improved on readiness and motivation to quit, particularly among individuals who were undergoing their first scan and those who were extremely worried about lung cancer. These results indicate that providing evidence-based tobacco treatment can build upon this teachable moment.

[Geographic access to lung cancer screening among eligible adults living in rural and urban environments in the United States](#) Liora Sahar 1 , Vanhvilai L Douangchai Wills 1 , Ka Kit Antonio Liu 1 , Stacey A Fedewa 2 , Lauren Rosenthal 3 , Ella A Kazerooni 4   5 , Debra S Dyer 6 , Robert A Smith 3

BACKGROUND: Although recommended lung cancer screening with low-dose computed tomography scanning (LDCT) reduces mortality among high-risk adults, annual screening rates remain low. This study complements a previous nationwide assessment of access to lung cancer screening within 40 miles by evaluating differences in accessibility across rural and urban settings for the population aged 50 to 80 years and a subset eligible population based on the 2021 US Preventive Services Task Force LDCT lung screening recommendations. **METHODS:** Distances from population centers to screening facilities (American College of Radiology Lung Cancer Screening Registry) were calculated, and the number of individuals who had access within graduating distances, including 10, 20, 40, 50, and 100 miles, were estimated. Census tract results were aggregated to counties, and both geographies were classified with rural-urban schemas. **RESULTS:** Approximately 5% of the eligible population did not have access to lung cancer screening facilities within 40 miles; however, different patterns of accessibility were observed at different distances, between regions, and across rural-urban environments. Across all distances and geographies, there was a larger percentage of the population in rural geographies with no access. Although the rural population represented approximately 8% of the eligible population, the larger percentage of the rural population with no access was noteworthy and translated into a larger number of individuals with no access at longer distance thresholds (≥40 miles). **CONCLUSIONS:** Disparities in access should be examined as both percentages of the population and numbers of individuals with no access in order to tailor interventions to communities and increase access. Geospatial analysis at the census tract level is recommended to help to identify optimal focus areas and reach the most people. **LAY SUMMARY:** As annual lung cancer screening rates remain low, this study examines access to lung cancer screening nationwide and across rural and urban settings. A geographic information system network analysis of census tract-level populations is used to estimate access at different distances, including 10, 20, 40, 50, and 100 miles, and the results are aggregated to counties. Approximately 5% of

the eligible population does not have access to screening facilities within 40 miles; however, different patterns of accessibility are observed at different distances, between regions, and across rural-urban environments. Across all distances and geographies, there is a larger percentage of the population in rural geographies with no access.

[Management of Lung Cancer Screening Results Based on Individual Prediction of Current and Future Lung Cancer Risks](#) J Thorac Oncol. 2022 Feb;17(2):252-263. doi: 10.1016/j.jtho.2021.10.001. Epub 2021 Oct 11. Hilary A Robbins 1 , Li C Cheung 2 , Anil K Chaturvedi 2 , David R Baldwin 3 , Christine D Berg 2 , Hormuzd A Katki 2

OBJECTIVES: We propose a risk-tailored approach for management of lung cancer screening results. This approach incorporates individual risk factors and low-dose computed tomography (LDCT) image features into calculations of immediate and next-screen (1-y) risks of lung cancer detection, which in turn can recommend short-interval imaging or 1-year or 2-year screening intervals. **METHODS:** We first extended the "LCRAT+CT" individualized risk calculator to predict lung cancer risk after either a negative or abnormal LDCT screen result. To develop the abnormal screen portion, we analyzed 18,129 abnormal LDCT results in the National Lung Screening Trial (NLST), including lung cancers detected immediately (n = 649) or at the next screen (n = 235). We estimated the potential impact of this approach among NLST participants with any screen result (negative or abnormal). **RESULTS:** Applying the draft National Health Service (NHS) England protocol for lung screening to NLST participants referred 76% of participants to a 2-year interval, but delayed diagnosis for 40% of detectable cancers. The Lung Cancer Risk Assessment Tool+Computed Tomography (LCRAT+CT) risk model, with a threshold of less than 0.95% cumulative lung cancer risk, would also refer 76% of participants to a 2-year interval, but would delay diagnosis for only 30% of cancers, a 25% reduction versus the NHS protocol. Alternatively, LCRAT+CT, with a threshold of less than 1.7% cumulative lung cancer risk, would also delay diagnosis for 40% of cancers, but would refer 85% of participants for a 2-year interval, a 38% further reduction in the number of required 1-year screens beyond the NHS protocol. **CONCLUSIONS:** Using individualized risk models to determine management in lung cancer screening could substantially reduce the number of screens or increase early detection.

[Missed Opportunities? An Observational Analysis of Lung Cancer Screening Utilization Amongst Patients With Lung Cancer](#) Cancer Control. Jan-Dec 2022;29:10732748221077959. doi: 10.1177/10732748221077959. Coral Olazagasti 1 , Matthew Ehrlich 2 , Nina Kohn 3 , Karen Aviles 4 , Aldane Hoilett 4 , Nagashree Seetharamu 4

Lung cancer (LC) is the leading cause of cancer-related deaths worldwide. The U.S. Preventive Services Task Force (USPSTF) and National Comprehensive Cancer Network (NCCN) recommend annual low-dose CT chest (LDCT) for LC screening in high-risk adults who meet appropriate criteria, which primarily focus on age and smoking history. Despite this, screening rates remain low and patients with LC are typically diagnosed at a later stage. We conducted a single-center retrospective analysis of patients with an established diagnosis of lung cancer to evaluate if screening guidelines were appropriately followed before the cancer diagnosis. Patients diagnosed with LC between 2016 and 2019 were included in the analysis. Charts were reviewed for demographics, detailed smoking history, as well as histology and stage of LC. Associations between categorical factors and screening were examined using the chi-square test. Associations between continuous and ordinal factors and screening were examined using the Mann-Whitney test.A total of 530 charts were reviewed, of which 52% met NCCN criteria and 35% met USPSTF criteria. Only 4.0% and 4.8% of patients who met NCCN and USPSTF criteria, respectively, underwent screening. There was a significant association between staging at diagnosis and screening with LDCT. All the patients who had screening CT scans were diagnosed at localized stages of lung cancer in both NCCN and USPSTF groups compared to 49.1% and 48% in eligible subjects that did not undergo

screening, respectively. Our study showed that despite established guidelines for LC screening and insurance coverage, a vast majority of screening-eligible LC patients have never had LDCT. We found that patients who underwent screening as per guidelines were diagnosed at earlier stages of the disease. Ongoing efforts to increase awareness and adherence to LC screening guidelines are needed to improve early detection and reduce LC mortality.

[Implementation and Uptake of Rural Lung Cancer Screening](#) J Am Coll Radiol. 2022 Feb 7;S1546-1440(22)00014-X. doi: 10.1016/j.jacr.2021.12.003. Online ahead of print. Tri Le 1 , Stacie Miller 2 , Emily Berry 3 , Sarah Zamarripa 4 , Aurelio Rodriguez 5 , Benjamin Barkley 6 , Asha Kandathil 7 , Cecelia Brewington 8 , Keith E Argenbright 9 , David E Gerber 10

OBJECTIVE: Given the higher rates of tobacco use along with increased mortality specific to lung cancer in rural settings, low-dose CT (LDCT)-based lung cancer screening could be particularly beneficial to such populations. However, limited radiology facilities and increased geographical distance, combined with lower income and education along with reduced patient engagement, present heightened barriers to screening initiation and adherence. **METHODS:** In collaboration with community leaders and stakeholders, we developed and implemented a community-based lung cancer screening program, including telephone-based navigation and tobacco cessation counseling support, serving 18 North Texas counties. Funding was available to support clinical services costs where needed. We collected data on LDCT referrals, orders, and completion. **RESULTS:** To raise awareness for lung cancer screening, we leveraged our established collaborative network of more than 700 community partners. In the first year of operation, 107 medical providers referred 570 patients for lung cancer screening, of whom 488 (86%) were eligible for LDCT. The most common reasons for ineligibility were age (43%) and insufficient tobacco history (20%). Of 381 ordered LDCTs, 334 (88%) were completed. Among screened patients, 61% were current smokers and 36% had insurance coverage for the procedure. The program cost per patient was $430. **DISCUSSION:** Implementation, uptake, and completion of LDCT-based lung cancer screening is feasible in rural settings. Community outreach, health promotion, and algorithm-based navigation may support such efforts. Given low lung cancer screening rates nationally and heightened lung cancer risk in rural populations, similar programs in other regions may be particularly impactful.

[Clinical Reliability of Genomic Data Obtained from Spinal Metastatic Tumor Samples](#) Neuro Oncol. 2022 Jan 6;noac009. doi: 10.1093/neuonc/noac009. Online ahead of print. Ori Barzilai 1 , Axel Martin 2 , Anne S Reiner 2 , Ilya Laufer 3 , Adam Schmitt 4 , Mark H Bilsky 1 5

PURPOSE: The role of tumor genomic profiling is rapidly growing as it results in targeted, personalized, cancer therapy. Though routinely used in clinical practice, there are no data exploring the reliability of genomic data obtained from spine metastases samples often leading to multiple biopsies in clinical practice. This study compares the genomic tumor landscape between spinal metastases and the corresponding primary tumors as well as between spinal metastases and visceral metastases. Patients and **METHODS:** Spine tumor samples, obtained for routine clinical care from 2013 to 2019, were analyzed using MSK-IMPACT, a next generation sequencing assay. These samples were matched to primary or metastatic tumors from the corresponding patients. A concordance rate for genomic alterations was calculated for matching sample pairs within patients for the primary and spinal metastatic tumor samples as well as for the matching sample pairs within patients for the spinal and visceral metastases. For a more robust and clinically relevant estimate of concordance, a subgroup analyses of previously established driver mutations specific to the main primary tumor histologies was performed. **RESULTS:** Eighty-four patients contributed next generation sequencing from a spinal metastasis and at least one other site of disease: 54 from the primary tumor, 39 had genomic tumor data from another, non-spinal metastasis, 12 patients participated in both subsets. For the cohort of matched primary tumors and spinal metastases (n = 54) comprised of mixed histologies, we found an average concordance rate of 96.97% for all genetic

events, 97.17% for mutations, 100% for fusions, 89.81% for deletions, and 97.01% for amplifications across all matched samples. Notably, >25% of patients harbored at least one genetic variant between samples tested, though not specifically for known driver mutations. The average concordance rate of driver mutations was 96.99% for prostate cancer, 95.69% (p = 0.0004513) for lung cancer and 96.43% for breast cancer. An average concordance of 99.02% was calculated for all genetic events between spine metastases and non-spinal metastases (n=41) and, more specifically, a concordance rate of 98.91% was calculated between spine metastases and liver metastases (n=12) which was the largest represented group of non-spine metastases. **CONCLUSION:** Sequencing data performed on spine tumor samples demonstrate a high concordance rate for genetic alterations between the primary tumor and spinal metastasis as well as between spinal metastases and other, visceral metastases, particularly for driver mutations. Spine tumor samples may be reliably used for genomic based decision making in cancer care, particularly for prostate, NSCLC and breast cancer.

[Smoking cessation services and shared decision-making practices among lung cancer screening facilities: A cross-sectional study](#) Cancer. 2022 Feb 14. doi: 10.1002/cncr.34145. Online ahead of print. Lisa M Lowenstein 1 , Shawn P E Nishi 2 , Maria A Lopez-Olivo 1 , Laura Covarrubias Crocker 1 , Noah Choi 1   3 , Bumyang Kim 1   4 , Ya-Chen Tina Shih 1 , Robert J Volk 1

BACKGROUND: Little is known about how screening facilities are meeting the requirements for the reimbursement of lung cancer screening from the Centers for Medicare & Medicaid Services (CMS), including 1) the collection and submission of data to the CMS-approved registry (American College of Radiology [ACR] Lung Cancer Screening Registry), 2) the verification of a counseling and shared decision-making (SDM) visit having occurred as part of the written order for lung cancer screening with low-dose computed tomography, and 3) the offering of smoking cessation interventions. **METHODS:** The authors identified facilities in a southwestern state that were listed by either the ACR Lung Cancer Screening Registry or the GO2 Foundation Centers of Excellence. To select facilities, they used 2 purposive sampling approaches: maximum variation sampling and snowball sampling. They surveyed facilities from February to November 2019. **RESULTS:** There were 87 facilities contacted, and a total of 63 facilities representing 32 counties across Texas completed the survey. Nearly all facilities used Lung-RADS to classify nodules (92%; n = 58) and submitted data to a CMS-approved registry (92%; n = 57). Most facilities verified that the counseling and SDM visit had occurred (86%; n = 54). Although slightly more than half of the facilities reported always providing self-help cessation materials (68%; n = 42), similar or higher proportions of facilities reported that they never referred smokers to onsite cessation services (68%; n = 42) or quitlines (77%; n = 47), provided cessation counseling (81%; n = 50), or recommended medications (85%; n = 52). **CONCLUSIONS:** In general, screening facilities are meeting CMS requirements for screening, but they are struggling to offer smoking cessation interventions other than providing self-help materials.

[Liquid Biopsy, Diagnostic Imaging, and Future Synergies](#) J Am Coll Radiol. 2022 Feb;19(2 Pt B):336-343. doi: 10.1016/j.jacr.2021.11.001.Milena Petranovic 1 , Sana Raoof 2 , Subba R Digumarthy 3 , 777 Imaging plays an integral role in the initial diagnosis and longitudinal care of patients with cancer. Liquid biopsies, which most commonly involve genetic analysis of circulating free DNA, have emerged as important complementary tools in cancer care with the potential to interface with imaging at each step of the cancer care continuum. Here, the authors use non-small-cell lung cancer as a paradigm to elucidate factors driving the need for liquid biopsy in the spectrum of lung cancer care, demonstrate ways in which liquid biopsy has already changed standard clinical practice, and discuss anticipated synergies of liquid biopsy and imaging in screening and early detection and in monitoring of disease.

[**Low-dose CT lung cancer screening uptake: A rural-urban comparison**](#) J Rural Health. 2022 Jan;38(1):40-53. doi: 10.1111/jrh.12568. Epub 2021 Mar 18. Anja Zgodic 1   2 , Whitney E Zahnd 2 , Shailesh Advani 3   4 , Jan M Eberth 1   2

PURPOSE: The US Preventive Services Task Force recommends lung cancer screening with Low-Dose Computed Tomography (LDCT) in high-risk individuals. Our objective was to identify demographic, health, and financial factors associated with screening uptake, with a focus on urban-rural differences. **METHODS:** We analyzed data from the 2018 and 2019 Behavioral Risk Factor Surveillance System and its optional Lung Cancer Screening Module to examine factors associated with screening uptake among 20 states that administered the optional module. We compared differences in factors associated with uptake overall and by geographical regions and conducted multivariable logistic mixed-effects regression, accounting for participant clustering by state to assess the impact of these factors on uptake. **FINDINGS:** Overall 1,268 participants underwent LDCT screening with no significant differences observed between rural (16.3%) and urban residents (17.7%, p = 0.67). In multivariable models, rural residents did not differ significantly in their LDCT screening uptake (OR = 0.85; 95% CI: 0.67-1.09, p = 0.20), but uptake was significantly higher for participants with underlying chronic respiratory conditions, veterans, those with higher pack-year history, and those with poor/fair general health and prior history of cancer. Uptake declined with age, higher education level, concerns about paying for medical care, and lack of primary care. **CONCLUSIONS:** Modifiable targets can be leveraged to increase LDCT screening. Based on significant predictors of screening uptake, clinicians should prioritize interventions that effectively consider smoking history as well as those identified as effective in veterans' health settings. Additionally, reducing structural barriers to care related to insurance and income will be key to reducing disparities.

[**Lung Cancer Screening by Race and Ethnicity in an Integrated Health System in Hawaii**](#) JAMA Netw Open. 2022 Jan 4;5(1):e2144381. doi: 10.1001/jamanetworkopen.2021.44381.
Caryn E S Oshiro 1 , Timothy B Frankland 1 , Joanne Mor 1 , Carmen P Wong 1 , Yannica Theda Martinez 1 , Cheryl K K Aruga 2 , Stacey Honda 1   2

IMPORTANCE: Racial and ethnic differences in lung cancer screening (LCS) completion and follow-up may be associated with lung cancer incidence and mortality rates among high-risk populations. Aggregation of Asian American, Native Hawaiian, and Pacific Islander racial and ethnic groups may mask the true underlying disparities in screening uptake and diagnostic follow-up, creating barriers for targeted, preventive health care. **OBJECTIVE:** To examine racial and ethnic differences in LCS completion and follow-up rates in a multiethnic population. Design, setting, and participants: This population-based cohort study was conducted at a health maintenance organization in Hawaii. LCS program participants were identified using electronic medical records from January 1, 2015, to December 31, 2019. Study eligibility requirements included being aged 55 to 79 years, a 30 pack-year smoking history, a current smoker or having quit within the past 15 years, at least 5 years past any lung cancer diagnosis and treatment, and cancer free. Data analysis was performed from June 2019 to October 2020. Exposure: Eligible for LCS. Main outcomes and measures: Screening rates were analyzed by self-reported race and ethnicity and completion of a low-dose computed tomography (LDCT) test. Diagnostic follow-up results were based on the Lung Imaging Reporting and Data System (Lung-RADS) staging system. **RESULTS:** A total of 1030 eligible LCS program members had an order placed; their mean (SD) age was 65.5 (5.8) years, and 633 (61%) were men. The largest racial and ethnic groups were non-Hispanic White (381 participants [37.0%]), Native Hawaiian or part Native Hawaiian (186 participants [18.1%]), and Japanese (146 participants [14.2%]). Men and Filipino, Chinese, Japanese, and non-Hispanic White individuals had a higher proportion of screen orders for LDCT compared with women and individuals of the other racial and ethnic groups. The overall LCS completion rate was 81% (838 participants). There was a 14% to 15% screening completion rate gap among groups. Asian individuals had the highest screening completion rate (266 participants [86%]) followed by Native Hawaiian (149 participants [80%])

and non-Hispanic White individuals (305 participants [80%]), Pacific Islander (50 participants [79%]) individuals, and individuals of other racial and ethnic groups (68 participants [77%]). Within Asian subgroups, Korean (31 participants [94%]) and Japanese (129 participants [88%]) individuals had the highest completion rates followed by Chinese individuals (28 participants [82%]) and Filipino individuals (78 participants [79%]). Of the 54 participants with Lung-RADS stage 3 disease, 93% (50 participants) completed a 6-month surveillance LDCT test; of 37 individuals with Lung-RADS stage 4 disease, 35 (97%) were followed-up for additional procedures. **CONCLUSIONS AND RELEVANCE:** This cohort study found racial and ethnic disparities in LCS completion rates after disaggregation of Native Hawaiian, Pacific Islander, and Asian individuals and their subgroups. These findings suggest that future research is needed to understand factors that may be associated with LCS completion and follow-up behaviors among these racial and ethnic groups.

[Procedural complications associated with invasive diagnostic procedures after lung cancer screening with low-dose computed tomography](#) Lung Cancer. 2022 Jan 4;165:141-144. doi: 10.1016/j.lungcan.2021.12.020. Online ahead of print. Shuang Yang 1 , Ya-Chen Tina Shih 2 , Jinhai Huo 3 , Hiren J Mehta 4 , Yonghui Wu 1 , Ramzi G Salloum 1 , Michelle Alvarado 5 , Dongyu Zhang 6 , Dejana Braithwaite 6 , Yi Guo 7 , Jiang Bian 8

INTRODUCTION: Although the National Lung Screening Trial (NLST) has proven low-dose computed tomography (LDCT) is effective for lung cancer screening, little is known about complication rates from invasive diagnostic procedures (IDPs) after LDCT in real-world settings. In this study, we used the real-world data from a large clinical research network to estimate the complication rates associated with IDPs after LDCT. **METHODS:** Using 2014-2021 electronic health records and claims data from the OneFlorida clinical research network, we identified case individuals who underwent an IDP (i.e., cytology or needle biopsy, bronchoscopy, thoracic surgery, and other surgery) within 12 months of their first LDCT. We matched each case with one control individual who underwent an LDCT but without any IDPs. We calculated 3-month incremental complication rates as the difference in the complication rate between the case and control groups by IDP and complication severity. **RESULTS:** Among 7,041 individuals who underwent an LDCT, 301 (4.3%) subsequently had an IDP within 12 months following the LDCT. The overall 3-month incremental complication rate was 16.6% (95% confidence interval [CI]: 9.9% - 23.1%), higher than that reported in the NLST (9.4%). The overall incremental complication rate was 5.6% (95% CI: 1.9% - 9.6%) for major, 8.6% (95% CI: 3.1% - 14.1%) for intermediate, and 13.2% (95% CI: 8.1% - 18.5%) for minor complications. **CONCLUSIONS:** It is important to ensure adherence to clinical guidelines for nodule management and downstream work-up to minimize potential harms from screening.

[Real-world patterns of biomarker testing and targeted therapy in de novo metastatic non-small cell lung cancer patients in the US oncology network](#) Cancer Treat Res Commun. 2022 Jan 29;31:100522. doi: 10.1016/j.ctarc.2022.100522. Online ahead of print. Eric Nadler 1 , Anupama Vasudevan 2 , Yunfei Wang 3 , Sarika Ogale 4

BACKGROUND: This study investigated biomarker testing and biomarker-guided treatment among patients with metastatic NSCLC in a real-world setting. **METHODS:** This retrospective study examined adult patients diagnosed with de novo mNSCLC between 01-Jan-2016 and 30-Sep-2019, with follow-up through 31-Dec-2019 using The US Oncology Network structured electronic health records data, with chart review for a subset. **RESULTS:** Of 2257 patients, 76.3% had results for ≥1 driver mutation (DM) or programmed death ligand-1 (PD-L1) during the study observation period. The proportion with results for all 4 DM before 1L initiation increased from 2017 to 2019. Over 40% had results for anaplastic lymphoma kinase (ALK), epidermal growth factor receptor (EGFR), and c-ros oncogene 1 (ROS1) and 22% for B-Raf proto-oncogene (BRAF) before 1L initiation by structured data. In the chart review subset

(n = 197), >70% had results for ALK, EGFR, or ROS1 with 44% for BRAF. Of the 42 ALK+ patients, 5 had results before 1L treatment and 3 received 1L ALK inhibitors. Similar, for the other biomarkers, not all who tested positive for a DM received 1L targeted therapy. The proportion of biomarker-positive patients receiving 1L targeted therapy was higher in chart review versus structured data. However, in both analyses, a substantial proportion did not have results for all 4 DM plus PD-L1 tests for appropriate biomarker-directed 1L treatment selection. **CONCLUSIONS:** Despite increasing biomarker testing rates, reduced turnaround times, and availability of promising biomarker-based therapies, inadequate testing in the community oncology setting means that not all eligible patients are receiving the most effective therapies up front.

[**Developing a clinical and PET/CT volumetric prognostic index for risk assessment and management of NSCLC patients after initial therapy**](#) Front Biosci (Landmark Ed). 2022 Jan 12;27(1):16. doi: 10.31083/j.fbl2701016. Liu Liu 1   2 , Jingmian Zhang 3 , Mark K Ferguson 4 , Daniel Appelbaum 5 , James X Zhang 6 , Yonglin Pu 5

BACKGROUND: Currently, individual clinical prognostic variables are used sequentially with risk-stratification after TNM staging in clinical practice for the prognostic assessment of patients with NSCLC, which is not effective for estimating the collective impact of multiple individual variables on patient outcomes. Here, we developed a clinical and PET/CT volumetric prognostic (CPVP) index that integrates the prognostic power of multiple clinical variables and metabolic tumor volume from baseline FDG-PET, for use immediately after definitive therapy. Patients and **METHODS:** This retrospective cohort study included 998 NSCLC patients diagnosed between 2004 and 2017, randomly assigned to two cohorts for modeling the CPVP index using Cox regression models examining overall survival (OS) and subsequent validation. **RESULTS:** The CPVP index generated from the model cohort included pretreatment variables (whole-body metabolic tumor volume [MTVwb], clinical TNM stage, tumor histology, performance status, age, race, gender, smoking history) and treatment type. A clinical variable (CV) index without MTVwb and PET/CT volumetric prognostic (PVP) index without clinical variables were also generated for comparison. In the validation cohort, univariate Cox modeling showed a significant association of the index with overall survival (OS; Hazard Ratio [HR] 3.14; 95% confidence interval [95% CI] = 2.71 to 3.65, p < 0.001). Multivariate Cox regression analysis demonstrated a significant association of the index with OS (HR = 3.13, 95% CI = 2.66 to 3.67, p < 0.001). The index showed greater prognostic power (C-statistic = 0.72) than any of its independent variables including clinical TNM stage (C-statistic ranged from 0.50 to 0.69, all p < 0.003), CV index (C-statistic = 0.68, p < 0.001) and PVP index (C-statistic = 0.70, p = 0.006). **CONCLUSIONS:** The CPVP index for NSCLC patients has moderately strong prognostic power and is more prognostic than its individual prognostic variables and other indices. It provides a practical tool for quantitative prognostic assessment after initial treatment and therefore may be helpful for the development of individualized treatment and monitoring strategy for NSCLC patients.

CLINICAL TRIALS, COHORT STUDIES, PILOT STUDIES

NSCLC - SURGERY

[**Effect of Upper Arm Position Changes on the Occurrence of Ipsilateral Shoulder Pain After Single-Operator Port Thoracoscopy**](#) Front Surg. 2022 Feb 2;9:823259. doi: 10.3389/fsurg.2022.823259. eCollection 2022. Dian Ren 1 , Bo Zhang 1 , Jie Xu 2 , Renwang Liu 1 , et al.

BACKGROUND: The aim of this study was to explore the factors associated with the occurrence of ISP after VATS to reduce the incidence of ISP and improve patients' quality of life. **METHODS:** The data of patients were collected between June 2020 and August 2020 in the Department of Lung Cancer Surgery,

Tianjin Medical University General Hospital. The angle of upper arm was measured intraoperatively. The patient's postoperative shoulder function was quantified using the Constant-Murley shoulder function rating score. The proportional hazards model was applied to identify multiple influence factors. **RESULTS:** A total of 140 eligible patients met criteria. At postoperative day 3, only the age influenced patients' shoulder pain. At postoperative day 14, univariate and multivariate logistic regression analyses showed that age (odds ratio [OR]: 1.098 [1.046-1.152]; P < 0.001) and upper arm Angle A (OR: 1.064 [1.011-1.121]; P = 0.018) were independent risk factors for low shoulder function scores. However, height was its protective factor (OR: 0.923 [0.871-0.977]; P = 0.006). At postoperative day 42, univariate and multivariate logistic regression analyses showed that age (OR: 1.079 [1.036-1.124]; P < 0.001) was a risk factor for low shoulder function scores, and height (OR: 0.933 [0.886-0.983]; P = 0.009) was its protective factor. In contrast, upper arm Angle B was not statistically associated with low shoulder function scores (P>0.05). In addition, the reduction in ipsilateral Shoulder scores after surgery was higher in patients with more than 113° of angle A (P = 0.025). **CONCLUSION:** ISP was closely related to the angle of anterior flexion of the upper arm on the patient's operative side intraoperatively. The increase in the degree of postoperative shoulder injury is more pronounced for an anterior flexion angle of >113°. Therefore, we recommend that the angle of anterior flexion of the upper extremity should be <113° intraoperatively.

[Does Operative Duration of Lobectomy for Early Lung Cancer Increase Perioperative Morbidity?](#)
Ann Thorac Surg. 2022 Feb 17;S0003-4975(22)00192-8. doi: 10.1016/j.athoracsur.2022.01.040. Online ahead of print. Elisabeth Dexter 1 , Kristopher Attwood 2 , Todd Demmy 3 , Sai Yendamuri 3
BACKGROUND: Longer bariatric, colorectal, plastic, spine, and urologic operations increase complications and lengths of stay. We aimed to determine whether this is a risk factor for lung lobectomy morbidity. **METHODS:** The STS GTS Database was queried for early-stage non-small cell lung cancer lobectomy with surgical duration treated as a continuous variable. Univariate and multivariate analyses compared patient and clinical characteristics with perioperative outcomes and procedure durations. Robotic were combined with thoracoscopic cases for duration analyses into minimally invasive group. All analyses were conducted in SAS v9.4 (Cary, NC) at a significance level of 0.05. **RESULTS:** In 17,852 patients mean duration of thoracotomy, thoracoscopy, and robotic lobectomies were 170± 80, 181 ± 80, and 211 ± 80 minutes respectively (p<0.001). The most common complications were prolonged air leak (12.3%), atrial fibrillation (12%), pneumonia (4.4%). and atelectasis requiring bronchoscopy (4.1%). Procedure duration was associated with increased odds of intraoperative PRBC (p <0.001), and length of stay (LOS) > 5 days (p<0.001) for both thoracotomy and minimally invasive lobectomy. Increased odds of pneumonia (p<0.001), atelectasis (p<0.001),and unexpected intensive care (ICU) admission (p=0.006) for thoracotomy lobectomy were associated with longer procedure duration. Increased lobectomy duration was not associated with readmission (p=0.549) or 30-day mortality (p=0.208). **CONCLUSIONS:** Longer early-stage lung cancer lobectomy durations are associated with postoperative morbidity and increased LOS. Although protracted operation effects on long-term survival are unknown, short-term mortality differences were not detected. Measures that decrease operative durations without sacrificing safety and oncologic outcome should be undertaken by surgeons and hospital systems.

[Impact of COVID-19 on the Delivery of Care for Thoracic Surgical Patients](#) JTCVS Open. 2022 Feb 17. doi: 10.1016/j.xjon.2021.11.015. Online ahead of print. Dao M Nguyen 1 , Karishma Kodia 1 , Joanne Szewczyk 1 , Ahmed Alnajar 1 , Joy A Stephens-McDonnough 1 , Nestor R Villamizar 1
OBJECTIVE: This study aims to determine the impact of the COVID-19 pandemic on the delivery of care for thoracic surgical patients at an urban medical center. **METHODS:** A retrospective analysis of all thoracic surgical cases from 5/1/2019 to 12/31/2020 was conducted. Demographics, pre-operative surgical indications, procedures, final pathologic diagnoses, and perioperative outcomes were recorded. A census

of operative cases, relevant ancillary services, and outpatient thoracic clinics were obtained from our institutional database. **RESULTS:** 619 cases were included in this study (329 pre-COVID-19 and 290 COVID-19, representing an 11.8% reduction). There were no differences in type of thoracic procedures or peri-operative outcomes between the two cohorts. Prolonged reduction of thoracic surgical cases (50% of baseline) during the first half of the COVID-19 period was followed by a resurgence of surgical volumes to 110% of baseline in the second half. Similar incidence of cases were performed for oncologic indications during the first half while more benign cases were performed in the second half coinciding with the launch of our robotic foregut surgery program. After undergoing surgery during the pandemic, none of our patients reported COVID-19 symptoms within 14 days of discharge. **CONCLUSION:** During the initial surge of COVID-19, while there was temporary closure of operative services, our healthcare system continued to provide safe care for thoracic surgery patients, particularly those with oncologic indications. Since phased reopening, we have experienced a rebound of surgical volume and case mix, ultimately mitigating the initial negative impact of the pandemic on delivery of thoracic surgical care.

High-grade tumor classified by new system is a prognostic predictor in resected lung adenocarcinoma

Gen Thorac Cardiovasc Surg. 2022 Jan 20. doi: 10.1007/s11748-021-01758-3. Online ahead of print. Chihiro Yoshida 1 , Hiroyasu Yokomise 1 , Emi Ibuki 2 , Tetsuhiko Go , Reiji Haba 2 , Kyuichi Kadota 3

OBJECTIVES: A grading system for pulmonary adenocarcinoma has not been established; hence, the International Association for the Study of Lung Cancer (IASLC) pathology panel developed a new grading system for invasive adenocarcinoma. We aimed to evaluate the prognostic significance of the IASLC grading system for invasive pulmonary adenocarcinoma. **METHODS:** We conducted a retrospective analysis of 471 Japanese patients with resected lung adenocarcinoma. Tumors were classified in accordance with the IASLC grading system and 2015 World Health Organization classification. We analyzed recurrence-free probability (RFP) and overall survival (OS) using the log-rank test and compared the two grading systems using the Cox proportional hazards model. **RESULTS:** Grade 3 tumors of the IASLC system and high-grade tumors of the 2015 World Health Organization classification were present in 38% and 17% of patients, respectively. The 5-year RFP was lower in patients with IASLC Grade 3 tumors (45%) than in patients with IASLC Grade 1 and 2 tumors (91% and 83%, respectively). The 5-year RFP of patients with IASLC Grade 2 tumors (83%) was higher than of those with 2015 World Health Organization intermediate tumors (69%). On multivariate analysis for recurrence, IASLC Grade 3 was an independent prognostic factor of worse RFP. We showed similar results on analysis for the OS. **CONCLUSIONS:** The prognostic significance of IASLC Grade 3 tumors on recurrence-free probability was confirmed through both univariate and multivariate analyses. Thus, the IASLC Grade 3 tumor is an independent factor of poor prognosis in patients with resected lung adenocarcinoma.

The Effect of Major and Minor Complications After Lung Surgery on Length of Stay and Readmission

J Patient Exp. 2022 Feb 1;9:23743735221077524. doi: 10.1177/23743735221077524. eCollection 2022. Christian J Finley 1 , Housne A Begum 1 , Kendra Pearce 1 , John Agzarian 1 , Waël C Hanna 1 , Yaron Shargall 1 , Noori Akhtar-Danesh 2

The effect of post-operative adverse events (AEs) on patient outcomes such as length of stay (LOS) and readmissions to hospital is not completely understood. This study examined the severity of AEs from a high-volume thoracic surgery center and its effect on the patient postoperative LOS and readmissions to hospital. This study includes patients who underwent an elective lung resection between September 2018 and January 2020. The AEs were grouped as no AEs, 1 or more minor AEs, and 1 or more major AEs. The effects of the AEs on patient LOS and readmissions were examined using a survival analysis and

logistic regression, respectively, while adjusting for the other demographic or clinical variables. Among 488 patients who underwent lung surgery, (Wedge resection [n = 100], Segmentectomy [n = 51], Lobectomy [n = 310], Bilobectomy [n = 10], or Pneumonectomy [n = 17]) for either primary (n = 440) or secondary (n = 48) lung cancers, 179 (36.7%) patients had no AEs, 264 (54.1%) patients had 1 or more minor AEs, and 45 (9.2%) patients had 1 or more major AEs. Overall, the median of LOS was 3 days which varied significantly between AE groups; 2, 4, and 8 days among the no, minor, and major AE groups, respectively. In addition, type of surgery, renal disease (urinary tract infection [UTI], urinary retention, or acute kidney injury), and ASA (American Society of Anesthesiology) score were significant predictors of LOS. Finally, 58 (11.9%) patients were readmitted. Readmission was significantly associated with AE group (P = 0.016). No other variable could significantly predict patient readmission. Overall, postoperative AEs significantly affect the postoperative LOS and readmission rates.

[Comparison of the long-term oncologic outcomes of robotic-assisted and video-assisted thoracoscopic lobectomy for resectable non-small cell lung carcinoma](#) J Robot Surg. 2022 Jan 15. doi: 10.1007/s11701-022-01368-y. Online ahead of print. Robert E Merritt 1 , Mahmoud Abdel-Rasoul 2 , Desmond M D'Souza 3 , Peter J Kneuertz 3
The current oncologic outcomes of robotic-assisted lobectomy compared to video-assisted thoracoscopic lobectomy are currently not well defined. This study compares the overall survival and recurrence-free survival rates between the two approaches for patients with resectable non-small cell lung carcinoma. This is a retrospective review of 200 patients diagnosed with resectable primary lung carcinoma who underwent minimally invasive lobectomy from March 2014 to May 2018. A total of 100 patients underwent thoracoscopic lobectomy and 100 patients underwent robotic-assisted lobectomy by a single surgeon. The data collected included patient demographics, tumor characteristics, surgical margin status, total number of lymph nodes harvested, lymph node upstaging rate, and overall survival and recurrence-free survival. The patients in each group were similar in age, gender, smoking status, pulmonary function, tumor histology, and pathologic stage. The postoperative mortality and complication rates were similar as well. The median number of total lymph nodes and N2 lymph nodes were significantly higher in the robotic lobectomy group (p < 0.0001). The Kaplan-Meier survival rates of overall survival (p = 0.097) and recurrence-free survival (p = 0.769) were similar between the two surgical approaches. The results of this report suggest that thoracoscopic and robotic-assisted lobectomy have similar long-term oncologic outcomes. There may be an advantage for robotic-assisted lobectomy in the total number of lymph nodes harvested during lobectomy.

[Robotic-assisted lobectomy for malignant lung tumors](#) J Minim Access Surg. 2022 Jan 4. doi: 10.4103/jmas.jmas_266_21. Online ahead of print. Jessica Emilia Wahi 1 , Navid Ajabshir 1 , Roy Williams 2 , Harlee Bustamante 2 , Fernando Martin Safdie 2
OBJECTIVES: For patients with lung cancer, surgical resection remains the best curative option and is associated with the longest disease-free survival. We present our institutional outcomes treating pulmonary malignancy with robotic lobectomy over the course of 1 year. **METHODS:** A retrospective review was conducted on patients who underwent robotic pulmonary lobectomy for malignancy at a single institution in 2018. **RESULTS:** Over the course of 1 year, 166 patients underwent robotic lobectomy for pulmonary neoplasm. The mean age of the patients was 75 years; 73% were current or prior smokers and 52% of the patients were male. The mean body mass index was 28 kg/m2. Conversion to open thoracotomy occurred in 7% of patients. The mean total hospital length of stay (LOS) was 3 days. Histopathological examination revealed a mean tumour size of 2.7 cm with 11 lymph nodes harvested. Left-sided tumours had a significantly higher number of lymph nodes harvested when compared to right-sided tumours (11.6 vs. 9.8, P = 0.01), despite sampling the recommended minimum of three N2 stations. The most common pathology was adenocarcinoma (65%), followed by squamous cell carcinoma (17%)

The 30-day operative mortality was 0.6%. **CONCLUSIONS:** Robotic video-assisted thoracoscopic surgery is a safe, feasible and oncologically adequate procedure for lung malignancies. Comparison of our outcomes to previously reported national averages suggests a similar hospital LOS, lymph node harvest, conversion rate to open thoracotomy and 30-day mortality rate. We acknowledge the limitations of this non-randomised, retrospective study. Future research on robotic lobectomies is encouraged.

[Extent of Resection Influences Survival in Early-Stage Lung Cancer with Occult Nodal Disease](#) Ann Thorac Surg. 2022 Feb 15;S0003-4975(22)00189-8. doi: 10.1016/j.athoracsur.2022.01.038. Online ahead of print.Nathan Mynard 1 , Abu Nasar 1 , Mohamed Rahouma 1 , Benjamin Lee 1 , Sebron Harrison 1 , Oliver Chow 1 , Jonathan Villena-Vargas 1 , Nasser Altorki 1 , Jeffrey Port 2

BACKGROUND: Minimal literature exists evaluating the impact of the extent of resection on survival in patients with small, early-stage non-small cell lung cancer (NSCLC) found to have occult nodal disease (OND). We hypothesized that sublobar resection has comparable overall survival to patients undergoing lobectomy for clinical Stage IA NSCLC that harbors OND. **METHODS:** The National Cancer Database was reviewed for identification of patients with clinical Stage IA NSCLC who underwent wedge resection, segmentectomy or lobectomy and were found to have OND. Overall survival was compared between groups and a multivariate Cox-Regression model identified factors associated with worse survival. **RESULTS:** OND occurred in 6.1% of all patients with clinical Stage IA disease undergoing resection. Patients undergoing wedge resection and segmentectomy found to have OND were older (67.6 $\pm$ 9.6 vs. 66.1 $\pm$ 9.3 vs. 65.6 $\pm$ 9.5, p=0.004), and had more advanced pathologic stage (pStage III: 68.7% vs. 50.5% vs. 41.5%, p<0.001) than those receiving lobectomy. There was no difference in the median overall survival between segmentectomy and lobectomy (68.5 months vs. 57.6, p=0.200.) However, wedge resection was independently associated with worse overall survival when controlling for other preoperative variables, hazard ratio: 1.23 (1.01 - 1.51), p=0.042. **CONCLUSIONS:** Review of the National Cancer Database suggests that there is no improvement in overall survival in patients undergoing lobectomy versus segmentectomy in carefully selected patients with clinical Stage IA NSCLC harboring occult nodal disease. However, those undergoing wedge resection may have worse overall survival than those undergoing both lobectomy and segmentectomy.

[Comparison of operative and postoperative characteristics and outcomes between thoracoscopic segmentectomy and lobectomy for non-small-cell lung cancer: a propensity score matching study from the Italian VATS Group Registry](#) Eur J Cardiothorac Surg. 2022 Feb 18;61(3):533-542. doi: 10.1093/ejcts/ezab430. Andrea Dell'Amore 1 , Ivan Lomangino 1 , Giorgio Cannone 1 , et al.

OBJECTIVES: Only few studies compared the surgical morbidity and mortality of thoracoscopic segmentectomy versus lobectomy for non-small-cell lung cancer, in particular, by relating the segmental resections with the corresponding anatomical lobes. **METHODS:** We enrolled a total of 7487 patients who underwent VATS lobectomy (7269) or segmentectomy (218) from January 2014 to July 2019. A propensity score matching approach was used to account for potential confounding factors between the 2 groups. After matching, 349 lobectomies and 208 segmentectomies were included in the analysis. We analysed the operative and postoperative outcomes of video-assisted anatomical segmentectomy compared with video-assisted lobectomy and, in details, the results of segmentectomy with its corresponding lobectomy in a large cohort of patients from the Italian VATS Group Registry. **RESULTS:** The overall conversion rate to thoracotomy was not statistically different between the groups (27 patients 8% vs 7 patients 3%, P = 0.1). The lobectomy group had a greater number of resected lymph nodes (median 11 vs 8, P = 0.006). No significant differences were detected in 30-day mortality (1.4%, 5 patients vs 0.9%, 2 patients), overall complications (18%, 62 patients vs 14%, 29 patients) and prolonged air leakage (31 patients, 9% vs 12 patients, 6%) between lobectomy and segmentectomy, respectively. No statistical differences were found regarding the median duration of drainage (3.2 days, P = 1) and the

overall median length of hospital stay (6.4 days, P = 0.1) between the 2 groups. In the context of segmentectomy versus corresponding lobectomy, the right upper lobectomy compared with right upper segmentectomy showed a higher number of resected lymph nodes (P = 0.027). No statistical differences were reported in terms of conversion rate and postoperative complication and mortality.
CONCLUSIONS: Segmentectomy could be considered a safe procedure without significant differences compared to thoracoscopic lobectomy in terms of postoperative morbidity and mortality.

[Open, Video- and Robot-Assisted Thoracoscopic Lobectomy for Stage II-IIIA Non-Small Cell Lung Cancer](#) Ann Thorac Surg. 2022 Feb 8;S0003-4975(22)00173-4. doi: 10.1016/j.athoracsur.2022.01.026. Online ahead of print. Larisa Shagabayeva 1 , Beverly Fu 1 , Nikhil Panda 1 , Alexandra Potter 1 , Hugh Auchincloss 1 , Arian Mansur 1 , Chi-Fu Jeffrey Yang 2 , Lana Schumacher 3
BACKGROUND: The study's objective is to compare the short- and long-term outcomes of open vs robotic vs video-assisted thoracoscopic (VATS) lobectomy for stage II-IIIA non-small-cell lung cancer. **METHODS:** Outcomes of patients with stage II and IIIA NSCLC (excluding T4 tumors) who received open and minimally invasive (MIS) lobectomy in the National Cancer Data Base from 2010-2017 were assessed using propensity score-matched analysis. **RESULTS:** A propensity score-matched analysis of 4,502 open and 4,502 MIS patients demonstrated a decreased median length of stay associated with MIS lobectomy as compared to open lobectomy (5 vs 6 days; p<0.001). There were no significant differences in 30-day mortality, 30-day readmission, or 5-year survival between the open and MIS groups. A propensity score-matched analysis of 1,088 VATS and 1,088 robotic patients showed that when compared to VATS, the robotic approach was associated with no significant difference in 30-day mortality, 30-day readmission and 5-year survival. However, the robotic group had a decreased median length of stay when compared to VATS (4 vs 5 days; p=0.002). The conversion rate was also significantly lower for robotic when compared to VATS (9.1% vs 15.9%, p<0.001). **CONCLUSIONS:** In this national analysis, no significant differences were found in long-term survival between open and MIS lobectomy and between VATS and robotic lobectomy for stage II-IIIA NSCLC. However, the MIS approach was associated with a decreased length of stay when compared to the open approach. The robotic approach was associated with decreased length of stay and decreased conversions when compared to the VATS approach.

[Surgical outcomes after nivolumab or nivolumab with ipilimumab treatment in patients with non-small cell lung cancer](#) J Thorac Cardiovasc Surg. 2022 Jan 23;S0022-5223(22)00089-7. doi: 10.1016/j.jtcvs.2022.01.019. Online ahead of print. Boris Sepesi 1 , Nicolas Zhou 2 , William N William Jr 3 , et al.
BACKGROUND: Surgical outcomes for non-small cell lung cancer after neoadjuvant immune checkpoint inhibitors continue to be debated. We assessed perioperative outcomes of the Nivolumab With or Without Ipilimumab or Chemotherapy in Treating Patients With Previously Untreated Stage I-IIIA Non-Small Cell Lung Cancer (NEOSTAR) trial patients after immunotherapy. **METHODS:** Forty-four patients with stage I to IIIA non-small cell lung cancer (American Joint Committee on Cancer Staging Manual, seventh edition) were randomized to nivolumab (N; 3 mg/kg intravenously on days 1, 15, and 29; n = 23) or nivolumab with ipilimumab (NI; 1 mg/kg intravenously on day 1; n = 21). Curative-intent operations were planned between 3 and 6 weeks after the last dose of neoadjuvant N. Patients who completed resection upfront or after chemotherapy from the same time period were used as comparison. **RESULTS:** In the N arm, 21 (91%) were resected in the trial, 1 underwent surgery outside of the trial, and one was not resected (toxicity-related). In the NI arm, 16 (76%) resections were in trial, one outside of the trial, and 4 were not resected (none toxicity-related). Median time to operation was 31 days, and consisted of 2 (5%) pneumonectomies, 33 (89%) lobectomies, and 1 (3%) each of segmentectomy and wedge resection. The approach was 27 (73%) thoracotomy, 7 (19%) thoracoscopy, and 3 (8%) robotic-assisted. Conversion occurred in 17% (n = 2/12) of minimally invasive cases. All 37 achieved R0

resections. Pulmonary, cardiac, enteric, neurologic, and wound complications occurred in 9 (24%), 4 (11%), 2 (5%), 1 (3%), and 1 (3%) patient, respectively. The 30- and 90-day mortality rate was 0% and 2.7% (n = 1), respectively. Postoperative complications rates were comparable with lung resection upfront or after chemotherapy. **CONCLUSIONS:** Operating after neoadjuvant N or NI is safe and effective and yields perioperative outcomes similar to those achieved after chemotherapy or upfront resection.

[Long-Term Functional Outcomes Among Older Adults Undergoing Video-Assisted Versus Open Surgery for Lung Cancer: A Population-Based Cohort Study](#) Ann Surg. 2022 Jan 21. doi: 10.1097/SLA.0000000000005387. Online ahead of print. Julie Hallet 1 , Mathieu Rousseau, Vaibhav Gupta, et al.

OBJECTIVE: To examine the long-term healthcare dependency outcomes of older adults undergoing video-assisted thoracic surgery (VATS) compared to open lung cancer resection. **SUMMARY BACKGROUND:** data: While the benefits of video-assisted thoracoscopic surgery (VATS) for lung cancer resection have been reported, there is a knowledge gap related to long-term functional outcomes central to decision-making for older adults. **METHODS:** We conducted a population-based retrospective comparative cohort study of patients > 70 years old undergoing lung cancer resection between 2010-2017 using linked administrative health databases. VATS was compared to open surgery for lung cancer resection. Outcomes were receipt of homecare and high time-at-home, defined as <14 institution-days within one year, in 5 years after surgery. We used time-to-event analyses. Homecare was analyzed as recurrent dichotomous outcome with Andersen-Gill multivariable models, and high time-at-home with Cox multivariable models. **RESULTS:** Of 4,974 patients, 2,951 had VATS (59.3%). In the first three months postoperatively, homecare use ranged from 17.5-34.4% for VATS and 23.0-36.6% for open surgery. VATS was independently associated with lower need for postoperative homecare over 5 years (hazard ratio - H R 0.82, 95%CI 0.74-0.92). 1- and 5-year probability of high "time-at-home" were superior for VATS (74.4% vs. 66.7% and 55.6% vs. 45.4%, p<0.001). VATS was independently associated with higher probability of high "time-at-home" (HR 0.81, 95%CI 0.74-0.89) compared to open surgery. **CONCLUSIONS:** Compared to open surgery, VATS was associated with lower homecare needs and higher probability of high "time-at-home", indicating reduced long-term functional dependence. Those important patient-centred endpoints reflect the overall long-term treatment burden on mortality and morbidity that can inform surgical decision-making.

NSCLC – SYSTEMIC THERAPIES (CHEMOTHERAPY, TARGETED THERAPY, AND IMMUNOTHERAPY)

[Association of Hypokalemia Incidence and Better Treatment Response in NSCLC Patients: A Meta-Analysis and Systematic Review on Anti-EGFR Targeted Therapy Clinical Trials](#)
Front Oncol. 2022 Jan 5;11:757456. doi: 10.3389/fonc.2021.757456. eCollection 2021. Jiawei Zhou 1 , Jianling Bai 1 , Yuanping Yue 1 , Xin Chen 1 , Theis Lange 2 , Dongfang You 1 , Yang Zhao 1 3
BACKGROUND: This meta-analysis was designed to explore the relationship between the level of serum potassium and the treatment effect of epidermal growth factor receptor (EGFR) antagonist in advanced non-small cell lung cancer (aNSCLC). **METHODS:** We searched phase II/III prospective clinical trials on treatment with EGFR antagonists for aNSCLC patients. The objective response rate (ORR) and/or the disease control rate (DCR) and the incidence of hypokalemia of high grade (equal to or greater than grade 3) were summarized from all eligible trials. Heterogeneity, which was evaluated by Cochran's Q-test and the I2 statistics, was used to determine whether a random effects model or a fixed effects model will be used to calculate pooled proportions. Subgroup analysis was performed on different interventions, line types, phases, and drug numbers. **RESULTS:** From 666 potentially relevant articles, 36 clinical trials with a total of 9,761 participants were included in this meta-analysis. The pooled ORR was 16.25% (95%CI = 12.45-21.19) when the incidence of hypokalemia was 0%-5%, and it increased to

34.58% (95%CI = 24.09-45.07) when the incidence of hypokalemia was greater than 5%. The pooled DCR were 56.03% (95%CI = 45.03-67.03) and 64.38% (95%CI = 48.60-80.17) when the incidence rates of hypokalemia were 0%-5% and greater than 5%, respectively. The results of the subgroup analysis were consistent with the results of the whole population, except for not first-line treatment, which may have been confounded by malnutrition or poor quality of life in long-term survival. **CONCLUSION:** The efficacy of anti-EGFR targeted therapy was positively associated with the hypokalemia incidence rate. Treatment effects on the different serum potassium strata need to be considered in future clinical trials with targeted therapy.

[**Treatment of Choroidal Metastasis from Epidermal Growth Factor Mutant Non-Small Cell Lung Cancer with First-line Osimertinib Therapy**](#) J Ophthalmic Vis Res. 2022 Jan 21;17(1):130-134. doi: 10.18502/jovr.v17i1.10178. eCollection Jan-Mar 2022. Anderson N Vu 1 , Urmi V Mehta 1   2 , Paul Israelsen 1 , Sai-Hong Ignatius Ou 3   4 , Andrew W Browne 5   6
PURPOSE: To illustrate the regression of a metastatic lesion through ophthalmic imaging and correlating findings with standard chest imaging and treatment with osimertinib, an oral chemotherapy agent specific to Epidermal Growth Factor Receptor + Non-small Cell Lung Cancer (EGFR+ NSCLC). Case report: A 63-year-old Asian male presented to ophthalmology with a complaint of left blurry vision. Initial ophthalmic exam revealed a choroidal lesion and imaging results highlighted a spiculated lung mass with brain and bony metastases. Osimertinib was chosen for its specificity and ability to cross the blood-brain barrier. Follow-up ophthalmic and radiographic imaging were repeated over the course of treatment. **CONCLUSION:** After the initiation of osimertinib, ophthalmic and computed tomography imaging highlighted the regression of the ocular metastatic disease and primary malignancy, respectively. Osimertinib is an effective first-line treatment of EGFR+ NSCLC and corresponding metastatic sites. Additionally, ophthalmic imaging can be used to monitor general response to chemotherapy agents when ocular metastasis is identified.

[**First-Line Immunotherapy for Non-Small-Cell Lung Cancer**](#) J Clin Oncol. 2022 Feb 20;40(6):586-597. doi: 10.1200/JCO.21.01497. Epub 2022 Jan 5. Martin Reck 1 , Jordi Remon 2 , Matthew D Hellmann 3
For patients with metastatic non-small-cell lung cancer (mNSCLC), the last decade has been characterized by critical progress that has contributed to substantially improved survival. In particular, the development of specific antibodies against the programmed death (PD-1) receptor, programmed death-ligand 1 (PD-L1), and the cytotoxic T-lymphocyte-associated protein 4 receptor in the therapeutic strategy of mNSCLC either in first- or in second-line settings have led to unprecedented prolonged survival for a proportion of these patients. Although clinical development of immune checkpoint inhibitors with anti-PD-1 and PD-L1 therapies largely began as monotherapy in the second-line setting, the more recent progress has shifted toward combination approaches in first-line settings as well as the integration of immunotherapy into the clinical paradigm in earlier stages. Today, with the exception of mNSCLC harboring targetable oncogenes, nearly all patients with mNSCLC receive PD-1 or PD-L1 therapy in first-line settings. Here we report the current status of first-line immunotherapy in mNSCLC together with current challenges in selecting the best immunotherapeutic approach for the individual patient.

[**Adjuvant Chemotherapy for T4 Non-Small Cell Lung Cancer with Additional Ipsilateral Lung Nodules**](#) Ann Thorac Surg. 2022 Feb;113(2):421-428. doi: 10.1016/j.athoracsur.2021.02.042. Epub 2021 Mar 6. Andrew X Li 1 , Kaitlin Flores 2 , Maureen E Canavan 3, Daniel J Boffa 1 , Justin D Blasberg 4
BACKGROUND: Adjuvant chemotherapy is indicated for patients with resectable stage II and IIIa non-small cell lung cancer. With the revised definition of T4 tumors with nodules in a different ipsilateral lobe, the survival advantage imparted by adjuvant chemotherapy has yet to be defined. We evaluated the

role of adjuvant chemotherapy in patients with T4 disease characterized by additional tumor nodules in a different ipsilateral lobe treated with surgical resection. **METHODS:** We identified patients with T4 disease and additional tumor nodules in a different ipsilateral lobe treated with surgical resection alone or with adjuvant chemotherapy in the National Cancer Database between 2010 and 2016. The primary outcome was 3-year overall survival (OS). **RESULTS:** A total of 920 patients with T4 tumors and additional tumor nodules in a different ipsilateral lobe were identified. We excluded patients with lymph node metastases, tumors 4 cm or greater, and local invasion. Of the remaining 373 patients, 152 received surgery and adjuvant multiagent chemotherapy whereas 221 received surgery alone. When adjusted for patient, tumor, and treatment factors, the use of adjuvant chemotherapy was associated with improved 3-year OS compared with surgery alone (hazard ratio = 0.572; 95% confidence interval, 0.348-0.940; P = .03). **CONCLUSIONS:** Adjuvant chemotherapy in patients with T4 non-small cell lung cancer with additional tumor nodules in a different ipsilateral lobe is associated with improved 3-year OS. Accurate identification of T4 disease is important to define patients in whom adjuvant chemotherapy should be considered. Further prospective study is needed to delineate further the use of adjuvant chemotherapy for this patient population.

[ASCEND-7: Efficacy and Safety of Ceritinib Treatment in Patients With ALK-Positive Non-Small Cell Lung Cancer Metastatic to the Brain and/or Leptomeninges](#) Clin Cancer Res. 2022 Jan 28;clincanres.1838.2021. doi: 10.1158/1078-0432.CCR-21-1838. Online ahead of print. Laura Q M Chow 1 , Fabrice Barlesi 2 , Erin M Bertino 3 , Martin J van den Bent 4 , Heather A Wakelee 5 , Patrick Y Wen 6 , Chao-Hua Chiu 7 , et al.

PURPOSE: Central nervous system (CNS) metastases are a prominent cause of morbidity and mortality in patients with ALK-positive (ALK+) non-small cell lung cancer (NSCLC). The phase 2 ASCEND-7 (NCT02336451) study was specifically designed to assess the efficacy and safety of ALK inhibitor (ALKi) ceritinib in patients with ALK+ NSCLC metastatic to the brain and/or leptomeninges.
EXPERIMENTAL DESIGN: Patients with active brain metastases were allocated to study arms 1-4 based on prior exposure to an ALKi and/or prior brain radiation (arm 1: prior radiotherapy/ALKi-pretreated; arm 2: no radiotherapy/ALKi-pretreated; arm 3: prior radiotherapy/ALKi-naive; arm 4: no radiotherapy/ALKi-naive). Arm 5 included patients with leptomeningeal carcinomatosis. Patients received ceritinib 750 mg once daily (fasted condition). Primary endpoint was investigator-assessed whole-body overall response rate (ORR) per RECIST v1.1. Secondary endpoints included disease control rate (DCR) and intracranial/ extracranial responses. **RESULTS:** Per investigator assessment, in arms 1 (n=42), 2 (n=40), 3 (n=12), and 4 (n=44), respectively: whole-body ORRs (95% CI) were 35.7% (21.6-52.0), 30.0% (16.6-46.5), 50.0% (21.1-78.9), and 59.1% (43.2-73.7); whole-body DCR (95% CI): 66.7% (50.5-80.4), 82.5% (67.2-92.7), 66.7% (34.9-90.1), and 70.5% (54.8-83.2); intracranial ORRs (95% CI): 39.3% (21.5-59.4), 27.6% (12.7-47.2), 28.6% (3.7-71.0), and 51.5% (33.5-69.2). In arm 5 (n=18), whole-body ORR was 16.7% (95% CI, 3.6-41.4) and DCR was 66.7% (95% CI, 41.0-86.7). Paired cerebrospinal fluid and plasma sampling revealed that ceritinib penetrated the human blood-brain barrier.
CONCLUSIONS: Ceritinib showed antitumor activity in patients with ALK+ NSCLC with active brain metastases and/or leptomeningeal disease, and could be considered in the management of intracranial disease.

[Afatinib Treatment Alone or with Bevacizumab in a Real-World Cohort of Non-Small Cell Lung Cancer Patients with Epidermal Growth Factor Receptor Mutation](#) ancers (Basel). 2022 Jan 9;14(2):316. doi: 10.3390/cancers14020316. Chih-Hsi Scott Kuo 1 2 3 , Tzu-Hsuan Chiu 1 , Pi-Hung Tung 1 , et al.

BACKGROUND: Treatment outcome between afatinib alone or with bevacizumab in non-small cell lung cancer (NSCLC) patient with epidermal growth factor receptor (EGFR) mutation remains

insufficiently reported. **METHODS:** A total of 405 advanced NSCLC patients with sensitizing-EGFR mutation receiving first-line single-agent afatinib or with bevacizumab were grouped and propensity score-matched. Progression-free survival (PFS), overall survival (OS) and secondary T790M mutation were analyzed. **RESULTS:** In the original cohort, 367 (90.6%) patients received afatinib treatment alone and 38 (9.4%) patients received afatinib plus bevacizumab. Patients who received bevacizumab combination were significantly younger (54.6 ± 10.9 vs. 63.9 ± 11.5; $p < 0.001$) compared to the afatinib alone group. After propensity score matching, the afatinib alone and afatinib plus bevacizumab groups contained 118 and 34 patients, respectively. A non-significantly higher objective response was noted in the afatinib plus bevacizumab group (82.4% vs. 67.8%; $p = 0.133$). In the propensity score-matched cohort, a bevacizumab add-on offered no increased PFS (16.1 vs. 15.0 months; $p = 0.500$), risk reduction of progression (HR 0.85 [95% CI, 0.52-1.40]; $p = 0.528$), OS benefit (32.1 vs. 42.0 months; $p = 0.700$), nor risk reduction of death (HR 0.85 [95% CI, 0.42-1.74] $p = 0.660$) compared to the single-agent afatinib. The secondary T790M rate in afatinib plus bevacizumab and afatinib alone groups was similar (56.3% vs. 49.4%, $p = 0.794$). Multivariate analysis demonstrated that EGFR L858R (OR 0.51 [95% CI, 0.26-0.97]; $p = 0.044$), EGFR uncommon mutation (OR 0.14 [95% CI, 0.02-0.64]; $p = 0.021$), and PFS longer than 12 months (OR 2.71 [95% CI, 1.39-5.41]; $p = 0.004$) were independent predictors of secondary T790M positivity. **CONCLUSION:** Bevacizumab treatment showed moderate efficacy in real-world, afatinib-treated NSCLC patients with EGFR-sensitizing mutation.

[**Clinical efficacy of atezolizumab plus bevacizumab and chemotherapy in KRAS- mutated non-small cell lung cancer with STK11, KEAP1, or TP53 comutations: subgroup results from the phase III IMpower150 trial**](#) J Immunother Cancer. 2022 Feb;10(2):e003027. doi: 10.1136/jitc-2021-003027. Howard Jack West 1 , Mark McCleland 2 , Federico Cappuzzo 3 , et al.
BACKGROUND: The efficacy of atezolizumab (A) and/or bevacizumab (B) with carboplatin/paclitaxel (CP) chemotherapy was explored in the phase III, randomized IMpower150 study in patients with non-squamous non-small cell lung cancer (NSCLC) according to KRAS mutations (mKRAS) and co-occurring STK11, KEAP1, or TP53 mutations. **METHODS:** Mutation status was determined by circulating tumor DNA next-generation sequencing. Overall survival (OS) and progression-free survival (PFS) were analyzed in a mutation-evaluable intention-to-treat population (MEP; n=920) and SP263 (programmed cell death ligand 1 (PD-L1)) biomarker-evaluable population (n=774). **RESULTS:** Within the mKRAS population (24.5% of MEP), ABCP showed numerical improvements vs BCP in median OS (19.8 vs 9.9 months; HR 0.50; 95% CI 0.34 to 0.72) and PFS (8.1 vs 5.8 months; HR 0.42; 95% CI 0.29 to 0.61)-greater than with ACP (OS: 11.7 vs 9.9 months; HR 0.63; 95% CI 0.43 to 0.91; PFS: 4.8 vs 5.8 months; HR 0.80; 95% CI 0.56 to 1.13) vs BCP. Across PD-L1 subgroups in mKRAS patients, OS and PFS were longer with ABCP vs BCP, but OS with ACP was similar to BCP in PD-L1-low and PD-L1-negative subgroups. Conversely, in KRAS-WT patients, OS was longer with ACP than with ABCP or BCP across PD-L1 subgroups. KRAS was frequently comutated with STK11, KEAP1, and TP53; these subgroups conferred different prognostic outcomes. Within the mKRAS population, STK11 and/or KEAP1 mutations were associated with inferior OS and PFS across treatments compared with STK11-WT and/or KEAP1-WT. In mKRAS patients with co-occurring mSTK11 and/or mKEAP1 (44.9%) or mTP53 (49.3%), survival was longer with ABCP than with ACP or BCP. **CONCLUSIONS:** These analyses support previous findings of mutation of STK11 and/or KEAP1 as poor prognostic indicators. While clinical efficacy favored ABCP and ACP vs BCP in these mutational subgroups, survival benefits were greater in the mKRAS and KEAP1-WT and STK11-WT population vs mKRAS and mKEAP1 and mSTK11 population, suggesting both prognostic and predictive effects. Overall, these results suggest that atezolizumab combined with bevacizumab and chemotherapy is an efficacious first-line treatment in metastatic NSCLC subgroups with mKRAS and co-occurring STK11 and/or KEAP1 or TP53 mutations and/or high PD-L1 expression.

PURPOSE: The phase III PACIFIC trial compared durvalumab with placebo in patients with unresectable, stage III non-small-cell lung cancer and no disease progression after concurrent chemoradiotherapy. Consolidation durvalumab was associated with significant improvements in the primary end points of overall survival (OS; stratified hazard ratio [HR], 0.68; 95% CI, 0.53 to 0.87; P = .00251) and progression-free survival (PFS [blinded independent central review; RECIST v1.1]; stratified HR, 0.52; 95% CI, 0.42 to 0.65; P < .0001), with manageable safety. We report updated, exploratory analyses of survival, approximately 5 years after the last patient was randomly assigned. **METHODS:** Patients with WHO performance status 0 or 1 (any tumor programmed cell death-ligand 1 status) were randomly assigned (2:1) to durvalumab (10 mg/kg intravenously; administered once every 2 weeks for 12 months) or placebo, stratified by age, sex, and smoking history. Time-to-event end point analyses were performed using stratified log-rank tests. Medians and landmark survival rates were estimated using the Kaplan-Meier method. **RESULTS:** Seven hundred and nine of 713 randomly assigned patients received durvalumab (473 of 476) or placebo (236 of 237). As of January 11, 2021 (median follow-up, 34.2 months [all patients]; 61.6 months [censored patients]), updated OS (stratified HR, 0.72; 95% CI, 0.59 to 0.89; median, 47.5 v 29.1 months) and PFS (stratified HR, 0.55; 95% CI, 0.45 to 0.68; median, 16.9 v 5.6 months) remained consistent with the primary analyses. Estimated 5-year rates (95% CI) for durvalumab and placebo were 42.9% (38.2 to 47.4) versus 33.4% (27.3 to 39.6) for OS and 33.1% (28.0 to 38.2) versus 19.0% (13.6 to 25.2) for PFS. **CONCLUSION:** These updated analyses demonstrate robust and sustained OS and durable PFS benefit with durvalumab after chemoradiotherapy. An estimated 42.9% of patients randomly assigned to durvalumab remain alive at 5 years and 33.1% of patients randomly assigned to durvalumab remain alive and free of disease progression, establishing a new benchmark for standard of care in this setting.

INTRODUCTION: Immunotherapy has prolonged the time that NSCLC patients are off platinum-based (PB) chemotherapy. However, the significance of the platinum-free-interval (PFI) is unclear. We evaluated whether an optimal PFI exists in NSCLC for PB re-exposure in contemporary treatment settings. **METHODS:** We conducted a retrospective cohort study of patients with metastatic NSCLC treated with 1st-line PB chemotherapy with or without immunotherapy. Using multivariable Cox models stratified by treatment strategies, we evaluated whether salvage PB vs. nonPB chemotherapy resulted in superior outcomes and whether this was modulated by the PFI. **RESULTS:** A total of 751 patients treated with salvage chemotherapy after PB chemoimmunotherapy were identified in 2 treatment strategy cohorts: 3rd-line after sequential chemotherapy and immunotherapy (Sequential Chemo IO, n = 604); 2ndline after chemoimmunotherapy (Concurrent ChemoIO, n = 147). An optimal PFI of 5 and 6 months was identified in the Sequential Chemo IO and Concurrent ChemoIO cohorts, respectively, but there was no overall survival or progression free survival advantage for PB vs. nonPB chemotherapy in long or short PFI groups. **CONCLUSION:** An optimal PFI was identified in this contemporary NSCLC cohort

treated with two common immunotherapy-containing treatment approaches, but PFI threshold did not predict benefit from platinum re-exposure as it has in other malignancies.

FDA Approval Summary: Pembrolizumab, Atezolizumab, and Cemiplimab-rwlc as single agents for first-line treatment of advanced/metastatic PD-L1 high NSCLC Clin Cancer Res. 2022 Jan 31;clincanres.3844.2021. doi: 10.1158/1078-0432.CCR-21-3844. Online ahead of print. Oladimeji Akinboro 1 , Erin Larkins 2 , et al.

FDA's approval of cemiplimab-rwlc on February 22, 2021 follows prior approvals of pembrolizumab and atezolizumab for similar indications - as first-line treatment for patients with programmed death ligand-1 (PD-L1)-high advanced non-small cell lung cancer (NSCLC). Approvals of these anti-PD-(L)-1 agents were supported by statistically significant and clinically meaningful improvements in overall survival (OS) in international, multi-center, active-controlled randomized trials. In KEYNOTE-024, the OS hazard ratio (HR) was 0.60 (95% [CI]: 0.41, 0.89; p=0.005) favoring pembrolizumab over platinum-doublet chemotherapy. In IMpower110, the OS HR was 0.59 (95% CI: 0.40, 0.89; p=0.0106) favoring atezolizumab over platinum-doublet chemotherapy. In Study 1624, the OS HR was 0.68 (95% CI: 0.53, 0.87; p=0.0022) favoring cemiplimab-rwlc over platinum-doublet chemotherapy. The PFS effect sizes for these anti-PD-(L)-1 antibodies were also comparable across their respective registrational trials, and their safety profiles were consistent with the anti-PD-(L)-1 class adverse event profile. The consistent survival benefits and manageable toxicity profiles of these single agent anti-PD-(L)-1 antibodies have established them as important treatment options in the PD-L1 high NSCLC treatment landscape. FDA approvals of these anti-PD-(L)-1 antibodies, based on their favorable benefit-risk profiles, present effective chemotherapy-free therapeutic options for patients with advanced PD-L1 high NSCLC in the United States.

First-Line Treatment of Advanced Non-Small-Cell Lung Cancer with Immune-Checkpoint Inhibitors: New Combinations and Long-Term Data BioDrugs. 2022 Feb 11. doi: 10.1007/s40259-022-00515-z. Online ahead of print. Maxime Bossageon 1 , Aurélie Swalduz 1 , Christos Chouaïd 2 3 , Olivier Bylicki 4

Treatment of metastatic non-small-cell lung cancers (NSCLCs) has long been based on cytotoxic chemotherapy. Immune checkpoint inhibitors (ICIs), notably monoclonal antibodies directed against programmed cell death protein-1 (PD-1) or its ligand (PD-L1), have transformed therapeutic standards in thoracic oncology. These ICIs are now the reference first-line therapy, and numerous phase III trials have established their efficacy in treatment-naïve patients. First-line pembrolizumab monotherapy was validated for patients with ≥ 50% of tumor cells expressing PD-L1 and, in the USA, for patients with ≥ 1% PD-L1 positivity. More recently, cemiplimab as monotherapy was also validated for patients whose tumors expressed ≥ 50% PD-L1. Several ICIs (pembrolizumab, atezolizumab, nivolumab, and recently durvalumab) in combination with chemotherapy achieved overall survival gains among "all comers", compared with chemotherapy alone. The results were more contrasting for paired immunotherapies combining anti-PD-L1 and anti-cytotoxic T-lymphocyte antigen-4 agents, with the benefit/risk balance not yet fully established. Recently, nivolumab-ipilimumab and two chemotherapy cycles limited patient exposure to chemotherapy and obtained positive results compared with the latter alone. However, those phase III trials included selected patients in good general condition and without active brain metastases. Little is known about immunotherapy and combination immunotherapy-chemotherapy efficacies in never-smokers or patients with tumors harboring an epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) translocation. In this review, we report our analysis of the main results available on first-line ICI use, as monotherapy or combined or in combination with chemotherapy, to treat metastatic NSCLCs in general and also for specific populations: the elderly, never-smokers, patients with brain metastases, and those with an EGFR mutation or ALK translocation.

[Pretreatment neutrophil-to-lymphocyte ratio and cigarette smoking as prognostic factors in patients with advanced NSCLC treated with osimertinib](#) Tuberc Respir Dis (Seoul). 2022 Jan 20. doi: 10.4046/trd.2021.0139. Online ahead of print. Ji Young Park 1   2 , Seung Hun Jang 1   2 , Chang Youl Lee 2   3 , et al.

BACKGROUND: The remarkable efficacy of osimertinib in non-small cell lung cancer (NSCLC) with acquired T790M mutation has widely been documented in clinical trials and real-world practice. However, some patients show primary resistance to the drug and even those patients who initially show a favorable response have inconsistent clinical outcomes. Therefore, this study aimed to identify additional clinical predictive factors for osimertinib efficacy. **METHODS:** We analyzed a prospective cohort of patients with acquired T790M positive stage IV lung adenocarcinoma treated with osimertinib salvage therapy in the Hallym University Medical Center. **RESULTS:** Sixty-one eligible patients were analyzed. The mean age was 63.3 years, 38 (62%) were women, and 39 (64%) never smoked. The median follow-up after treatment with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) was 36.0 months (IQR 24.7-50.2); 45 (74%) patients were deceased. Based on univariate analysis, factors including low baseline neutrophil-to-lymphocyte ratios (NLR), age ($\geq$50 years), never-smoking history, stage IVA at osimertinib initiation, and prolonged response to previous TKIs ($\geq$10 months) were associated with a significantly longer progression-free survival (PFS). Multivariate analysis showed that never-smoking status (hazard ratio [HR], 0.54, 95% CI 0.30-0.98, p = 0.041) and a baseline NLR less than or equal to 3.5 (HR 0.23, 95% CI 0.12-0.45, p < 0.001) were independently associated with a prolonged PFS with osimertinib. **CONCLUSIONS:** Smoking history and high NLR were independent negative predictors of osimertinib PFS in patients with advanced NSCLC developing EGFR T790M resistance after the initial EGFR-TKI treatment.

[Real-World Treatment Patterns and Outcomes Among Patients With Metastatic NSCLC Previously Treated With Programmed Cell Death Protein-1/Programmed Death-Ligand 1 Inhibitors](#) JTO Clin Res Rep. 2022 Jan 1;3(2):100275. doi: 10.1016/j.jtocrr.2021.100275. eCollection 2022 Feb. Savreet Bains 1 , Anu Kalsekar 1 , Katayoun I Amiri 1 , Jared Weiss 2

INTRODUCTION: Programmed cell death protein-1 (PD-1)/programmed death-ligand 1 (PD-L1) inhibitors are standard-of-care treatment for metastatic NSCLC (mNSCLC). Intolerance to treatment/disease progression warrants additional lines of therapy. Real-world treatment patterns and efficacy outcomes after PD-1/PD-L1 use are insufficiently characterized to inform treatment decisions. **METHODS:** Electronic health records of adults with stage IV NSCLC initiating PD-1/PD-L1 inhibitors as first-line monotherapy (cohort 1), first-line combination therapy (cohort 2), or second-line monotherapy (cohort 3) who received a subsequent line of therapy (i.e., index therapy) in the Flatiron NSCLC Core Registry Dataset were identified. Patient characteristics, types of index treatments/therapies, and associated index treatment outcomes were extracted. **RESULTS:** A total of 1061 patients with mNSCLC were included in this analysis. In cohort 1 (n = 242), median real-world overall survival (mrwOS) with index therapies for the overall population was 9.18 months (95% confidence interval: 7.54-12.13); platinum-based chemotherapy was the most common index therapy (39.3%) with mrwOS of 12.52 months (8.39-not applicable). In cohort 2 (n = 145), mrwOS for the overall population was 6.43 months (5.34-7.61); vascular endothelial growth factor inhibitor plus chemotherapy was the most common index therapy (32.4%) with mrwOS of 5.97 months (4.95-7.34). In cohort 3 (n = 647), mrwOS for the overall population was 7.21 months (6.39-7.80); single-agent chemotherapy was the most common index therapy (45.4%) with mrwOS of 6.59 months (5.64-7.61). **CONCLUSIONS:** Real-world treatment patterns and survival outcomes of index therapies in mNSCLC after PD-1/PD-L1 use are variable. These analyses provide insights to optimize post-PD-1/PD-L1 treatments and inform standards of care.

[**Sugemalimab versus placebo, in combination with platinum-based chemotherapy, as first-line treatment of metastatic non-small-cell lung cancer (GEMSTONE-302): interim and final analyses of a double-blind, randomised, phase 3 clinical trial**](#) Lancet Oncol. 2022 Feb;23(2):220-233. doi: 10.1016/S1470-2045(21)00650-1. Epub 2022 Jan 14. Caicun Zhou 1 ; Ziping Wang 2 , Yuping Sun 3 , et al.

BACKGROUND: PD-1 inhibitor plus chemotherapy had been shown to be an effective first-line treatment for patients with metastatic non-small-cell lung cancer (NSCLC). However, there was no robust evidence showing a PD-L1 inhibitor combined with chemotherapy benefited patients with squamous and non-squamous NSCLC. GEMSTONE-302 aimed to evaluate the efficacy and safety of a PD-L1 inhibitor, sugemalimab, plus chemotherapy for patients with metastatic squamous or non-squamous NSCLC.

METHODS: This randomised, double-blind, phase 3 trial was done in 35 hospitals and academic research centres in China. Eligible patients were aged 18-75 years, had histologically or cytologically confirmed stage IV squamous or non-squamous NSCLC without known EGFR sensitising mutations, ALK, ROS1, or RET fusions, no previous systemic treatment for metastatic disease, and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Patients were randomly assigned (2:1) to receive sugemalimab (1200 mg, intravenously, every 3 weeks) plus platinum-based chemotherapy (carboplatin [area under the curve (AUC) 5 mg/mL per min, intravenously] and paclitaxel [175 mg/m2, intravenously] for squamous NSCLC, or carboplatin [AUC 5 mg/mL per min, intravenously] and pemetrexed [500 mg/m2, intravenously] for non-squamous NSCLC; sugemalimab group) or placebo plus the same platinum-based chemotherapy regimens for squamous or non-squamous NSCLC as in the sugemalimab group; placebo group) for up to four cycles, followed by maintenance therapy with sugemalimab or placebo for squamous NSCLC, and intravenous sugemalimab 500 mg/m2 or matching placebo plus pemetrexed for non-squamous NSCLC. Randomisation was done by an interactive voice-web-response system via permuted blocks (block size was a mixture of three and six with a random order within each stratum) and stratified by ECOG performance status, PD-L1 expression, and tumour pathology. The investigators, patients, and the sponsor were masked to treatment assignment. The primary endpoint was investigator-assessed progression-free survival in the intention-to-treat population. Safety was analysed in all patients who received at least one treatment dose. Results reported are from a prespecified interim analysis (ie, when the study met the primary endpoint) and an updated analysis (prespecified final analysis for progression-free survival) with a longer follow-up. This study is registered with ClinicalTrials.gov (NCT03789604), is closed to new participants, and follow-up is ongoing. Findings: Between Dec 13, 2018, and May 15, 2020, 846 patients were assessed for eligibility; 367 were ineligible, and the remaining 479 patients were randomly assigned to the sugemalimab group (n=320) or placebo group (n=159). At the preplanned interim analysis (data cutoff June 8, 2020; median follow-up 8·6 months [IQR 6·1-11·4]), GEMSTONE-302 met its primary endpoint, with significantly longer progression-free survival in the sugemalimab group compared with the placebo group (median 7·8 months [95% CI 6·9-9·0] vs 4·9 months [4·7-5·0]; stratified hazard ratio [HR] 0·50 [95% CI 0·39-0·64], p<0·0001]). At the final analysis (March 15, 2021) with a median follow-up of 17·8 months (IQR 15·1-20·9), the improvement in progression-free survival was maintained (median 9·0 months [95% CI 7·4-10·8] vs 4·9 months [4·8-5·1]; stratified HR 0·48 [95% CI 0·39-0·60], p<0·0001). The most common grade 3 or 4 any treatment-related adverse events were neutrophil count decreased (104 [33%] of 320 with sugemalimab vs 52 [33%] of 159 with placebo), white blood cell count decreased (45 [14%] vs 27 [17%]), anaemia (43 [13%] vs 18 [11%]), platelet count decreased (33 [10%] vs 15 [9%]), and neutropenia (12 [4%] vs seven [4%]). Any treatment-related serious adverse events occurred in 73 (23%) patients in the sugemalimab group and 31 (20%) patients in the placebo group. Any treatment-related deaths were reported in ten (3%) patients in the sugemalimab group (pneumonia with respiratory failure in one patient; myelosuppression with septic shock in one patient; pneumonia in two patients; respiratory failure, abdominal pain, cardiac failure, and immune-mediated pneumonitis in one patient each; the other

two deaths had an unspecified cause) and in two (1%) patients in the placebo group (pneumonia and multiple organ dysfunction syndrome). **INTERPRETATION:** Sugemalimab plus chemotherapy showed a statistically significant and clinically meaningful progression-free survival improvement compared with placebo plus chemotherapy, in patients with previously untreated squamous and non-squamous metastatic NSCLC, regardless of PD-L1 expression, and could be a newfirst-line treatment option for both squamous and non-squamous metastatic NSCLC.

[**Durvalumab plus tremelimumab alone or in combination with low-dose or hypofractionated radiotherapy in metastatic non-small-cell lung cancer refractory to previous PD(L)-1 therapy: an open-label, multicentre, randomised, phase 2 trial**](#) Lancet Oncol. 2022 Feb;23(2):279-291. doi: 10.1016/S1470-2045(21)00658-6. Epub 2022 Jan 13. Jonathan D Schoenfeld 1, Anita Giobbie-Hurder 2, Srinika Ranasinghe 3, Katrina Z Kao 3, et al.

BACKGROUND: Patients with non-small-cell lung cancer (NSCLC) that is resistant to PD-1 and PD-L1 (PD[L]-1)-targeted therapy have poor outcomes. Studies suggest that radiotherapy could enhance antitumour immunity. Therefore, we investigated the potential benefit of PD-L1 (durvalumab) and CTLA-4 (tremelimumab) inhibition alone or combined with radiotherapy. **METHODS:** This open-label, multicentre, randomised, phase 2 trial was done by the National Cancer Institute Experimental Therapeutics Clinical Trials Network at 18 US sites. Patients aged 18 years or older with metastatic NSCLC, an Eastern Cooperative Oncology Group performance status of 0 or 1, and progression during previous PD(L)-1 therapy were eligible. They were randomly assigned (1:1:1) in a web-based system by the study statistician using a permuted block scheme (block sizes of three or six) without stratification to receive either durvalumab (1500 mg intravenously every 4 weeks for a maximum of 13 cycles) plus tremelimumab (75 mg intravenously every 4 weeks for a maximum of four cycles) alone or with low-dose (0·5 Gy delivered twice per day, repeated for 2 days during each of the first four cycles of therapy) or hypofractionated radiotherapy (24 Gy total delivered over three 8-Gy fractions during the first cycle only), 1 week after initial durvalumab-tremelimumab administration. Study treatment was continued until 1 year or until progression. The primary endpoint was overall response rate (best locally assessed confirmed response of a partial or complete response) and, along with safety, was analysed in patients who received at least one dose of study therapy. The trial is registered with ClinicalTrials.gov, NCT02888743, and is now complete. **FINDINGS:** Between Aug 24, 2017, and March 29, 2019, 90 patients were enrolled and randomly assigned, of whom 78 (26 per group) were treated. This trial was stopped due to futility assessed in an interim analysis. At a median follow-up of 12·4 months (IQR 7·8-15·1), there were no differences in overall response rates between the durvalumab-tremelimumab alone group (three [11·5%, 90% CI 1·2-21·8] of 26 patients) and the low-dose radiotherapy group (two [7·7%, 0·0-16·3] of 26 patients; p=0·64) or the hypofractionated radiotherapy group (three [11·5%, 1·2-21·8] of 26 patients; p=0·99). The most common grade 3-4 adverse events were dyspnoea (two [8%] in the durvalumab-tremelimumab alone group; three [12%] in the low-dose radiotherapy group; and three [12%] in the hypofractionated radiotherapy group) and hyponatraemia (one [4%] in the durvalumab-tremelimumab alone group vs two [8%] in the low-dose radiotherapy group vs three [12%] in the hypofractionated radiotherapy group). Treatment-related serious adverse events occurred in one (4%) patient in the durvalumab-tremelimumab alone group (maculopapular rash), five (19%) patients in the low-dose radiotherapy group (abdominal pain, diarrhoea, dyspnoea, hypokalemia, and respiratory failure), and four (15%) patients in the hypofractionated group (adrenal insufficiency, colitis, diarrhoea, and hyponatremia). In the low-dose radiotherapy group, there was one death from respiratory failure potentially related to study therapy. **INTERPRETATION:** Radiotherapy did not increase responses to combined PD-L1 plus CTLA-4 inhibition in patients with NSCLC resistant to PD(L)-1 therapy. However, PD-L1 plus CTLA-4 therapy could be a treatment option for some patients. Future studies should refine predictive biomarkers in this setting.

INTRODUCTION: Biological therapies such as bevacizumab have improved survival in patients with NSCLC. This study was conducted to confirm the equivalent efficacy of the biosimilar candidate BI 695502 to the bevacizumab reference product (RP). **METHODS:** In this phase 3, multicenter, randomized, double-blind trial of adult patients with recurrent or metastatic NSCLC received up to 18 weeks of induction treatment with BI 695502 or bevacizumab RP 15 mg/kg plus paclitaxel and carboplatin. Subsequent maintenance therapy comprised BI 695502 or bevacizumab RP monotherapy until disease progression or unacceptable toxicity. The primary end point was the best overall response rate (ORR) per Response Evaluation Criteria in Solid Tumors version 1.1 assessed by central imaging review, until 18 weeks after the start of treatment. **RESULTS:** In total, 671 patients were randomized at one-to-one ratio to BI 695502 or bevacizumab RP, of whom 335 and 328, respectively, received treatment. Of these, 228 (68.1%) and 256 (78.0%), respectively, proceeded to maintenance monotherapy. A manufacturing issue led to a small number of patients treated with BI 695502 switching to bevacizumab RP late in the study. The primary end point, best ORR, was 54.0% in the BI 695502 group and 63.1% in the bevacizumab RP group. The 90% confidence interval for the between-group ratio of best ORR (0.770 to 0.951) was within the prespecified range for equivalence (0.736-1.359). Adverse events were class-related and similar between the two treatment arms. **CONCLUSIONS:** This study revealed equivalent ORR after 18 weeks of treatment with BI 695502 or bevacizumab RP, with similar adverse event profiles.

BACKGROUND: At the primary data cut-off, the ALUR study demonstrated significantly improved progression-free survival (PFS) and central nervous system (CNS) objective response rate (ORR) with alectinib versus chemotherapy in pretreated, advanced anaplastic lymphoma kinase (ALK)-positive non-small-cell lung cancer. We report final efficacy and safety data, and exploratory molecular profiling. Patients and **METHODS:** Patients who received prior platinum-doublet chemotherapy and crizotinib were randomized 2 : 1 to receive alectinib 600 mg twice daily (n = 79) or chemotherapy (pemetrexed 500 mg/m2 or docetaxel 75 mg/m2, every 3 weeks; n = 40) until progressive disease, death or withdrawal. The primary endpoint was investigator-assessed PFS. Secondary endpoints included ORR, CNS ORR and safety. Plasma samples were collected at baseline, then every 6 weeks until progressive disease; molecular factors detected by next-generation sequencing were correlated with outcomes. **RESULTS:** Investigator-assessed PFS was significantly longer with alectinib than chemotherapy (median 10.9 versus 1.4 months; hazard ratio 0.20, 95% confidence interval 0.12-0.33; P < 0.001). ORR was 50.6% with alectinib versus 2.5% with chemotherapy (P < 0.001). In patients with measurable CNS metastases at baseline, CNS ORR was 66.7% with alectinib versus 0% with chemotherapy (P < 0.001). No new safety signals were seen. ALK rearrangement was identified in 69.5% (n = 41/59) of baseline plasma samples. Confirmed partial responses were observed with alectinib in 6/11 patients with a secondary ALK mutation and 4/6 patients with a non-EML4-ALK (where EML4 is echinoderm microtubule-associated protein-like 4) fusion. Detection of mutant TP53 in baseline plasma resulted in numerically shorter PFS with alectinib (hazard ratio 1.88, 95% confidence interval 0.9-3.93). **CONCLUSIONS:** Final efficacy data from ALUR confirmed the superior PFS, ORR and CNS ORR of alectinib versus chemotherapy in pretreated,

advanced ALK-positive non-small-cell lung cancer. Alectinib prolonged PFS versus chemotherapy in patients with wild-type or mutant TP53; however, alectinib activity was considerably decreased in patients with mutant TP53.

[Carboplatin and nab-paclitaxel chemotherapy with or without atezolizumab as front-line management for treatment-naïve metastatic nonsquamous non-small cell lung cancer with PD-L1 staining: a retrospective study](#)

J Cancer Res Clin Oncol. 2022 Jan 1. doi: 10.1007/s00432-021-03873-3. Online ahead of print. Bo Xu # 1 , Huihui Cheng # 2 , Kunhong Li # 3 4 , Yukai Lv 5 , Xianshang Zeng 6 , Tao Liu 7 8 , Weiguang Yu 6 , Wenbo Guo 9

PURPOSE: The aim of this retrospective review was to compare the efficacy and safety of the atezolizumab plus carboplatin and nab-paclitaxel regimen versus the carboplatin and nab-paclitaxel regimen as front-line management for treatment-naïve, metastatic nonsquamous programmed death-ligand 1 (PD-L1)-positive non-small cell lung cancer (NSCLC) in a selected population. **METHODS:** Consecutive patients with untreated, metastatic nonsquamous PD-L1-positive NSCLC who initially received the atezolizumab plus carboplatin and nab-paclitaxel (ACN) regimen or carboplatin and nab-paclitaxel (CN) regimen were retrospectively identified in two medical institutions from 2017 to 2020. The co-primary end points were overall survival (OS) and progression-free survival (PFS); secondary end point was the rate of key adverse events (AEs). **RESULTS:** In sum, 171 patients were retrospectively analysed, 47 of whom were excluded according to the criteria used in this study, leaving 124 patients (ACN: n = 60, median age 64 years [range 46-75]; CN: n = 64, 63 years [47-72]). The median duration of follow-up was 27 months [range 1-37]. At the final follow-up, the median OS was 19.9 months (95% confidence interval [CI], 16.3-22.5) in the ACN group vs. 14.8 months (95% CI 12.5-17.2) in the CN group (hazard ratio [HR] 0.51, 95% CI 0.33-0.77; p = 0.001). A marked distinction in the median PFS was seen (8.5 months [95% CI 6.7-9.4] in the ACN group vs. in the CN group [5.1 months [95% CI 3.6-6.8; HR 0.60; 95% CI 0.38-0.95; p = 0.005]). The rates of the key AEs (neutropenia and anaemia) were greater in the ACN group than in the CN group (all p < 0.05), but these AEs were manageable. **CONCLUSION:** Among selected populations of individuals with treatment-naïve, metastatic nonsquamous PD-L1-positive NSCLC, atezolizumab combined with carboplatin and nab-paclitaxel chemotherapy might have encouraging anticancer activity, with a tolerable safety profile.

[Sintilimab with chemotherapy as first-line treatment for locally advanced or metastatic squamous non-small-cell lung cancer: a real-world data study](#)

Cancer Res Clin Oncol. 2022 Feb 10. doi: 10.1007/s00432-021-03903-0. Online ahead of print. Xinqing Lin # 1 , Haiyi Deng 1 , Suyang Li # 1 , et al.

PURPOSE: The ORIENT-12 study demonstrated the promising results of sintilimab combined with gemcitabine and platinum (GP) therapy in squamous non-small-cell lung cancer (sqNSCLC) patients. However, the efficacy of sintilimab plus paclitaxel/nab-paclitaxel and platinum (TP) in sqNSCLC is not yet known. **METHODS:** Real-life data were retrospectively collected from patients with untreated locally advanced or metastatic sqNSCLC who were treated with sintilimab plus TP (arm A) or sintilimab plus GP (arm B) between January 2019 and January 2021. Baseline characteristics, the efficacy of sintilimab, and adverse events were analyzed. **RESULTS:** A total of 52 patients were included (arm A, n = 32 and arm B, n = 20). The overall response rate was 59.4% in arm A and 40.0% in arm B. The median progression-free survival was 13.9 months (95% confidence interval [CI], 6.9-21.0) in arm A and 8.5 months (95% CI, 6.9-10.2) in arm B (hazard ratio [HR], 0.61; 95% CI, 0.30 to 1.25; p = 0.18). The median overall survival was 21.3 months (95% CI, 13.4-29.3) in arm A and 13.3 months (95% CI, 9.1-17.5) in arm B (HR, 0.62; 95% CI, 0.28-1.36; p = 0.23). Adverse events of grade 3 or higher occurred in 37.5% of the patients in arm A and 55.0% of the patients in arm B. **CONCLUSIONS:** Sintilimab-TP may have similar clinical

benefits compared with sintilimab-GP in patients with untreated advanced or metastatic sqNSCLC. These results require further validation by prospective randomized controlled studies.

[Timing of Adjuvant Durvalumab Initiation Is Not Associated With Outcomes in Stage III Non-small Cell Lung Cancer](#) Int J Radiat Oncol Biol Phys. 2022 Jan 31;S0360-3016(22)00002-5. doi: 10.1016/j.ijrobp.2021.12.176. Online ahead of print. Alex K Bryant 1 , Kamya Sankar 2 , Garth W Strohbehn 3 , Lili Zhao 4 , David Elliott 1 , Victoria Daniel 5 , Nithya Ramnath 6 , Michael D Green 7
PURPOSE: It is unclear whether time from radiation therapy (RT) completion to durvalumab initiation influences the outcomes of stage III non-small cell lung cancer (NSCLC) treated with definitive chemoradiation and adjuvant durvalumab. **METHODS AND MATERIALS:** Using the US Veterans Health Administration database, we retrospectively identified 728 patients with stage III NSCLC treated with definitive chemoradiation who started durvalumab within 120 days of radiation completion. Time between the last radiation treatment and first durvalumab infusion was analyzed in multivariable Cox regression models for the primary outcomes of progression-free survival (PFS) and overall survival (OS), adjusting for baseline patient and disease characteristics. The primary analysis used a 120-day landmark, measuring OS and PFS from 120 days after radiation completion. **RESULTS:** Among 728 patients, the median time from RT completion to durvalumab start was 41 days (interquartile range 30-58). In multivariable Cox regression, time from RT completion to durvalumab start showed no association with PFS (adjusted hazard ratio [aHR] 1.01 per week, 95% confidence interval [CI] 0.98-1.04, P = .4) or OS (aHR 1.02 per week, 95% CI 0.98-1.06, P = .3). Starting durvalumab ≤14 days after RT was also not associated with improved PFS or OS. Results were robust in sensitivity analyses varying analytical technique. **CONCLUSIONS:** Timing of durvalumab initiation up to 120 days after RT completion is not associated with PFS or OS in this real-world patient cohort.

[Investigating the efficacy of osimertinib and crizotinib in phase 3 clinical trials on anti-cancer treatment-induced cardiotoxicity: are real-world studies the way forward?](#) J Oncol Pharm Pract. 2022 Feb 15;10781552221077417. doi: 10.1177/10781552221077417. Online ahead of print. Hasan Kobat 1 , Islam Elkonaissi 2 , Emma Foreman 3 , Mary O'Brien 4 , Mehmet Tevfik Dorak 5 , Shereen Nabhani-Gebara 1
BACKGROUND: Oncology clinical trials demonstrate the risk of cardiotoxicity but are not sufficient to reveal the true risk. In this article, we compared the incidence of cardiotoxicity of crizotinib and osimertinib from a real-world study to data reported by phase 3 clinical trials. **METHODS:** Data from an ongoing real-world lung cancer study was used as a comparator. Patients were recruited retrospectively with the criteria of being diagnosed with non-small cell lung cancer and having received at least a course of treatment of tyrosine-kinase inhibitor and/or immune check-point inhibitor. Characteristics of the patients who developed cardiotoxicity associated with osimertinib and crizotinib in the real-world lung cancer study were analysed against the inclusion criteria of the corresponding phase 3 clinical trials. Variations of cardiotoxicity incidence among the real-world lung cancer study and clinical trials were investigated. **RESULTS:** 18%, n = 37/206, of the patients developed cardiotoxicity. QTc prolongation was the most frequently observed cardiotoxicity (n = 12/37). Osimertinib and crizotinib were the most cardiotoxic agents, each responsible for seven cases of cardiotoxicity. FLAURA, AURA3, PROFILE 1007 and PROFILE 1014 were the included clinical trials for analysis. None of the patients who developed cardiotoxicity in the real-world study would have been eligible to participate in FLAURA and PROFILE 1014 study whereas n = 4/7 and n = 5/7 patients were eligible to participate in AURA3 and PROFILE 1007 trials, respectively. **CONCLUSION:** Although phase 3 clinical trials play an important role in understanding the effectiveness and give insights on side-effect profiles, real-world studies can show the real risk of cardiotoxicity more accurately and realistically.

[**Primary systemic therapy for patients with brain metastases from lung cancer ineligible for targeted agents**](#) J Cancer Res Clin Oncol. 2022 Jan 12. doi: 10.1007/s00432-022-03919-0. Online ahead of print. Carsten Nieder 1   2 , Siv G Aanes 3 , Ellinor Haukland 3   4   5
PURPOSE: The purpose of this study was to evaluate overall survival after systemic therapy, largely chemotherapy, in patients with small cell or non-small cell lung cancer and brain metastases. After completion of systemic therapy, some patients received planned brain irradiation, while others were followed. **METHODS:** Retrospective cohort study. **RESULTS:** Thirty-eight patients were included (28 small cell, 20 followed with imaging). Six of these 20 patients (30%) received delayed radiotherapy during follow-up. Planned radiotherapy (n = 18, intention-to-treat) was associated with longer survival from diagnosis of brain metastases, median 10.8 versus 6.1 months, p = 0.025. Delayed radiotherapy still resulted in numerically better survival than no radiotherapy at all (median 8.8 versus 5.3 months, not significant). If calculated from the start of delayed radiotherapy, median survival was only 2.7 months. In a multivariable analysis, both Karnofsky performance status ≥ 70 (p = 0.03) and planned radiotherapy (p = 0.05) were associated with better survival. **CONCLUSION:** In patients ineligible for targeted agents, planned radiotherapy in a modern treatment setting was associated with longer survival compared to no radiotherapy. Timing and type of radiotherapy in such patients should be evaluated in prospective trials to identify patients who might not need planned radiotherapy.

NSCLC - RADIOTHERAPY

[**A Phase 1 Trial of Concurrent or Sequential Ipilimumab, Nivolumab, and Stereotactic Body Radiotherapy in Patients With Stage IV NSCLC Study**](#) J Thorac Oncol. 2022 Jan;17(1):130-140. doi: 10.1016/j.jtho.2021.08.019. Epub 2021 Sep 6. Christine M Bestvina 1 , Kelli B Pointer 2 , Theodore Karrison 3 , et al.
INTRODUCTION: Previous studies have evaluated stereotactic body radiotherapy (SBRT) in oligometastatic patients with NSCLC, including multimodality treatment with anti-programmed cell death protein-1 monotherapy. Questions remain regarding the timing of SBRT and immunotherapy, safety with dual checkpoint blockade, and the utility in widely metastatic patients. This randomized phase 1 trial combined nivolumab and ipilimumab with sequential or concurrent multisite SBRT in patients with stage IV NSCLC to evaluate safety and obtain preliminary activity data. **METHODS:** Treatment-naive patients with metastatic NSCLC were randomized to concurrent (SBRT with immunotherapy) or sequential (SBRT followed by immunotherapy) treatment. A maximum of four treatment fields received SBRT. Nivolumab and ipilimumab were continued until clinical progression, development of toxicity, or after 2 years. Dose-limiting toxicity was defined as greater than or equal to grade 3 toxicity to the relevant organ system attributed to SBRT and immunotherapy occuring within 3 months. **RESULTS:** A total of 37 patients were assessable. No dose-limiting toxicity occurred in the concurrent cohort (n = 18). The sequential cohort required a dose reduction in the central lung group owing to two grade 4 pneumonitis events (2 of 19). Overall best response was as follows: 5.4% (2 of 37) complete response, 40.5% (15 of 37) partial response, 16.2% (6 of 37) stable disease, and 37.8% (14 of 37) progressive disease. Median progression-free survival was 5.8 months (95% confidence interval: 3.6-11.4 mo), with median follow-up of 17.0 months. Median overall survival was not reached. **CONCLUSIONS:** Concurrent nivolumab, ipilimumab, and SBRT were not more toxic than sequential therapy, and multisite SBRT was well tolerated in widely metastatic patients. Multimodality therapy resulted in durable metastasis control and encouraging early overall survival.

[**The Michigan Radiation Oncology Quality Consortium: A Novel Initiative to Improve the Quality of Radiation Oncology Care**](#) Int J Radiat Oncol Biol Phys. 2022 Feb 3;S0360-3016(22)00094-3. doi: 10.1016/j.ijrobp.2022.01.048. Online ahead of print. Reshma Jagsi 1 , Matthew Schipper 2 , Melissa Mietzel 2 , et al.

PURPOSE: Numerous quality measures have been proposed in radiation oncology, and initiatives to improve access to high-complexity care, quality, and equity are needed. We describe the design and evaluate impact of a voluntary statewide collaboration for quality improvement in radiation oncology initiated a decade ago. **METHODS AND MATERIALS:** We evaluate compliance before and since implementation of annual metrics for quality improvement, using an observational dataset with information from over 20,000 patients treated in the 28 participating radiation oncology practices. At thrice-yearly meetings, experts have spoken regarding trends within the field and inspired discussions regarding potential targets for quality improvement. Blinded data on practices at various sites have been provided. Following Standards for Quality Improvement Reporting Excellence (SQUIRE) guidelines, we describe the approach and measures the program has implemented. To evaluate impact, we compare compliance at baseline and now with active measures using mixed effects regression models with site-level random effects. **RESULTS:** Compliance has increased, including use of guideline-concordant hypofractionated radiotherapy, doses to targets/normal tissues, motion management, and consistency in delineating and naming contoured structures (a precondition for quality evaluation). For example, use of guideline-concordant hypofractionation for breast cancer increased from 47% to 97%, adherence to target coverage goals and heart dose limits for dose increased from 46% to 86%, motion assessment in patients with lung cancer increased from 52% to 94%, and use of standard nomenclature increased from 53% to 82% for lung patients and from 80% to 94% for breast patients (all p<0.001). **CONCLUSIONS:** Although observational analysis cannot fully exclude secular trends, contextual data revealing slow uptake of best practices elsewhere in the US and qualitative feedback from participants suggests that this initiative has improved the consistency, efficiency, and quality of radiation oncology care in its member practices and may be a model for oncology quality improvement more generally.

[**Factors associated with progression and mortality among patients undergoing stereotactic radiosurgery for intracranial metastasis: results from a national real-world registry**](#) J Neurosurg. 2022 Jan 14;1-14. doi: 10.3171/2021.10.JNS211410. Online ahead of print. Mohammed Ali Alvi 1 2 , Anthony L Asher 3 , Giorgos D Michalopoulos 1 2 , et al.

OBJECTIVE: Stereotactic radiosurgery (SRS) has been increasingly employed in recent years to treat intracranial metastatic lesions. However, there is still a need for optimization of treatment paradigms to provide better local control and prevent progressive intracranial disease. In the current study, the authors utilized a national collaborative registry to investigate the outcomes of patients with intracranial metastatic disease who underwent SRS and to determine factors associated with lesion treatment response, overall progression, and mortality. **METHODS:** The NeuroPoint Alliance SRS registry was queried for all patients with intracranial metastatic lesions undergoing single- or multifraction SRS at participating institutions between 2016 and 2020. The main outcomes of interest included lesion response (lesion-level analysis), progression using Response Assessment for Neuro-Oncology criteria, and mortality (patient-level analysis). Kaplan-Meier analysis was used to report time to progression and overall survival, and multivariable Cox proportional hazards analysis was used to investigate factors associated with lesion response, progression, and mortality. **RESULTS:** A total of 501 patients (1447 intracranial metastatic lesions) who underwent SRS and had available follow-up were included in the current analyses. The most common primary tumor was lung cancer (49.5%, n = 248), followed by breast (15.4%, n = 77) and melanoma (12.2%, n = 61). Most patients had a single lesion (44.9%, n = 225), 29.3% (n = 147) had 2 or 3 lesions, and 25.7% (n = 129) had > 3 lesions. The mean sum of baseline measurements of the lesions according to Response Evaluation Criteria in Solid Tumors (RECIST) was

35.54 mm (SD 25.94). At follow-up, 671 lesions (46.4%) had a complete response, 631 (43.6%) had a partial response (≥ 30% decrease in longest diameter) or were stable (< 30% decrease but < 20% increase), and 145 (10%) showed progression (> 20% increase in longest diameter). On multivariable Cox proportional hazards analysis, melanoma-associated lesions (HR 0.48, 95% CI 0.34-0.67; p < 0.001) and larger lesion size (HR 0.94, 95% CI 0.93-0.96; p < 0.001) showed lower odds of lesion regression, while a higher biologically effective dose was associated with higher odds (HR 1.001, 95% CI 1.0001-1.00023; p < 0.001). A total of 237 patients (47.3%) had overall progression (local failure or intracranial progressive disease), with a median time to progression of 10.03 months after the index SRS. Factors found to be associated with increased hazards of progression included male sex (HR 1.48, 95% CI 1.108-1.99; p = 0.008), while administration of immunotherapy (before or after SRS) was found to be associated with lower hazards of overall progression (HR 0.62, 95% CI 0.460-0.85; p = 0.003). A total of 121 patients (23.95%) died during the follow-up period, with a median survival of 19.4 months from the time of initial SRS. A higher recursive partitioning analysis score (HR 21.3485, 95% CI 1.53202-3.6285; p < 0.001) was found to be associated with higher hazards of mortality, while single-fraction treatment compared with hypofractionated treatment (HR 0.082, 95% CI 0.011-0.61; p = 0.015), administration of immunotherapy (HR 0.385, 95% CI 0.233-0.64; p < 0.001), and presence of single compared with > 3 lesions (HR 0.427, 95% CI 0.187-0.98; p = 0.044) were found to be associated with lower risk of mortality.
CONCLUSIONS: The comparability of results between this study and those of previously published clinical trials affirms the value of multicenter databases with real-world data collected without predetermined research purpose.

[Improving Outcomes in NSCLC: Optimum Dose Fractionation in Radical Radiotherapy Matters](#)
J Thorac Oncol. 2022 Jan 31;S1556-0864(22)00051-X. doi: 10.1016/j.jtho.2022.01.006. Online ahead of print. Michael Brada 1 , Helen Forbes 2 , Susan Ashley 3 , John Fenwick 4
INTRODUCTION: We analyzed a comprehensive national radiotherapy data set to compare outcomes of the most frequently used moderate hypofractionation regimen (55 Gy in 20 fractions) and conventional fractionation regimen (60-66 Gy in 30-33 fractions). **METHODS:** A total of 169,863 cases of NSCLC registered in England from January 2012 to December 2016 obtained from the Public Health England were divided into cohort 1 (training set) diagnosed in 2012 to 2013 and cohort 2 (validation set) diagnosed in 2014 to 2016. Radiotherapy data were obtained from the National Radiotherapy Dataset and linked by National Health Service number to survival data from the Office of National Statistics and Hospital Episode Statistics, from which surgical data and Charlson comorbidity index were obtained. Of 73,186 patients with stages I to III NSCLC, 12,898 received radical fractionated radiotherapy (cohort 1-4894; cohort 2-8004). The proportional hazards model was used to investigate overall survival from time of diagnosis. Survival was adjusted for the prognostic factors of age, sex, stage of disease, comorbidity, other radical treatments, and adjuvant chemotherapy, and the difference between the treatment schedules was summarized by hazard ratio (HR) and 95% confidence interval. The significance of any difference was evaluated by the log likelihood test. **RESULTS:** Of patients with stages I to III NSCLC, 17% to 18% received radical fractionated radiotherapy. After adjustment for independent prognostic factors of age, stage, comorbidity, and other radical and adjuvant treatments, patients in cohort 1 treated with the 2.75 Gy per fraction regimen had a median survival of 25 months compared with 29 months for patients treated with the 2 Gy per fraction regimen (HR = 1.16, p = 0.001). Similarly, in cohort 2, the respective median survival values were 25 and 28 months (HR = 1.10, p = 0.02). **CONCLUSIONS:** Big data analysis of a comprehensive national cohort of patients with NSCLC treated in England suggests that compared with a 4-week regimen of 55 Gy in 20 fractions, a 6-week regimen of conventional daily fractionation to a dose of 60 to 66 Gy at 2 Gy per fraction is associated with a survival benefit. Within the limitations of the retrospective big data analysis with potential selection bias and in the absence of randomized trials, the results suggest that conventional fractionation regimens should remain the standard of care.

[**Radiomic Phenotypes for Improving Early Prediction of Survival in Stage III Non-Small Cell Lung Cancer Adenocarcinoma after Chemoradiation**](#) Cancers (Basel). 2022 Jan 29;14(3):700. doi: 10.3390/cancers14030700. José Marcio Luna 1 2 3 , Andrew R Barsky 4 , Russell T Shinohara 1 5 , et al. We evaluate radiomic phenotypes derived from CT scans as early predictors of overall survival (OS) after chemoradiation in stage III primary lung adenocarcinoma. We retrospectively analyzed 110 thoracic CT scans acquired between April 2012-October 2018. Patients received a median radiation dose of 66.6 Gy at 1.8 Gy/fraction delivered with proton (55.5%) and photon (44.5%) beam treatment, as well as concurrent chemotherapy (89%) with carboplatin-based (55.5%) and cisplatin-based (36.4%) doublets. A total of 56 death events were recorded. Using manual tumor segmentations, 107 radiomic features were extracted. Feature harmonization using ComBat was performed to mitigate image heterogeneity due to the presence or lack of intravenous contrast material and variability in CT scanner vendors. A binary radiomic phenotype to predict OS was derived through the unsupervised hierarchical clustering of the first principal components explaining 85% of the variance of the radiomic features. C-scores and likelihood ratio tests (LRT) were used to compare the performance of a baseline Cox model based on ECOG status and age, with a model integrating the radiomic phenotype with such clinical predictors. The model integrating the radiomic phenotype (C-score = 0.69, 95% CI = (0.62, 0.77)) significantly improved (p<0.005) upon the baseline model (C-score = 0.65, CI = (0.57, 0.73)). Our results suggest that harmonized radiomic phenotypes can significantly improve OS prediction in stage III NSCLC after chemoradiation.

[**A Comparative Study of Patients With Early-Stage Non-Small Cell Lung Cancer Treated With Stereotactic Body Radiation Therapy Using CyberKnife and Linear Accelerator-Based Volumetric Modulated Arc Therapy**](#) Pract Radiat Oncol. 2022 Feb 14;S1879-8500(22)00001-7. doi: 10.1016/j.prro.2021.12.011. Online ahead of print. Saarang R Deshpande 1 , William R Grubb 2 , Michael Kharouta 3 , et al.

PURPOSE: Stereotactic body radiation therapy (SBRT) has become the standard of care for medically inoperable early-stage non-small cell lung cancer. We investigated 2 modalities of lung SBRT, CyberKnife (CK) and volumetric modulated arc therapy (VMAT), for differences in dosimetric parameters, tumor control, and clinical outcomes. **METHODS AND MATERIALS:** Patients who underwent SBRT for T1-2N0M0 non-small cell lung cancer from 2012 to 2018 were included. Dosimetric parameters for target volume coverage and organ-at-risk dose distribution were collected. Survival outcomes were evaluated using the Kaplan-Meier method with log-rank test. A multivariate Cox proportional hazards model was analyzed for local, regional, and distant tumor control; overall survival (OS) and progression-free survival; and radiation pneumonitis. **RESULTS:** Two hundred twenty-seven patients (142 CK, 85 VMAT SBRT) met inclusion criteria. Overall, the local, regional, and distant control rates were 89.3%, 86.3%, and 87.4% at 2 years, and the OS was 67.5% and 32.8% at 2 and 5 years, respectively. VMAT delivered higher maximum doses to the gross tumor volume and planning target volume and had a lower lung and heart V5. Although there was no difference in local or distant failure, progression-free survival, or OS, VMAT was associated with superior freedom from regional failure (adjusted hazard ratio, 0.26; P = .045). With no difference between treatment modalities, 11.9% of patients developed grade 1 to 2 radiation pneumonitis. There were no grade 3+ events of radiation pneumonitis. **CONCLUSIONS:** This study revealed that VMAT and CK provided comparable local and distant control and survival outcomes; however, VMAT exhibited better regional control. Further study in this regard is imperative.

[Addition of Immune Checkpoint Inhibitors to Chemotherapy vs Chemotherapy Alone as First-Line Treatment in Extensive-Stage Small-Cell Lung Carcinoma: A Systematic Review and Meta-Analysis](#) Oncol Ther. 2022 Jan 15. doi: 10.1007/s40487-021-00182-0. Online ahead of print. Edurne Arriola 1 , María González-Cao 2 , Manuel Domine 3 , Javier De Castro 4 , Manuel Cobo 5 , Reyes Bernabé 6 , Alejandro Navarro 7 , Ivana Sullivan 8 , José Manuel Trigo 9 , Joaquín Mosquera 10 , Leonardo Crama 11 , Dolores Isla 12

INTRODUCTION: The addition of immune checkpoint inhibitors (ICIs) to conventional chemotherapy (CT) as first-line treatment improves survival in extensive-stage small-cell lung cancer (ES-SCLC). The aim of this meta-analysis was to determine the relative efficacy of first-line ICIs compared with CT in patients with ES-SCLC. **METHODS:** Two independent reviewers extracted relevant data according to PRISMA guidelines and assessed the risk of bias using the Cochrane Collaboration's risk-of-bias tool. Meta-analysis was conducted using random-effects models to calculate an average effect size for overall survival (OS), progression-free survival (PFS), and safety outcomes in the overall populations and clinically relevant subgroups. **RESULTS:** A literature search of PubMed and Embase was performed. Six randomized controlled clinical trials (IMpower133, CHECKMATE-451, CASPIAN, KEYNOTE-604, and phase II and III ipilimumab plus CT trials) with a total of 3757 patients were included. Compared with CT alone, ICIs plus CT showed a favourable effect on OS (hazard ratio [HR] 0.85; 95% confidence intervals [CI] 0.79-0.96) and PFS (HR 0.78; 95% CI 0.72-0.83) but a non-significant increase in the risk of experiencing any adverse event (relative risk, 1.05; 95% CI 0.99-1.11). The estimated HR for OS favoured ICI combinations in all planned subgroups according to age (< 65 years/≥ 65 years), sex (men/women), and ECOG performance status (0/1). Analysis by specific ICI revealed significant improvements in OS only for atezolizumab + CT (HR 1.36; 95% CI 1.09-1.69) and durvalumab + CT (HR 1.35; 95% CI 1.12-1.62) compared with CT alone. **CONCLUSION:** Combining anti-programmed cell death ligand 1 antibodies with platinum/etoposide is a superior therapeutic approach compared to CT alone for the first-line treatment of patients with ES-SCLC.

[Evolving Role of Immunotherapy in Small Cell Lung Cancer](#) Semin Cancer Biol. 2022 Feb 19;S1044-579X(22)00048-7. doi: 10.1016/j.semcancer.2022.02.021. Online ahead of print. Elizabeth D Barrows 1 , Matthew J Blackburn 1 , Stephen V Liu 2

Small cell lung cancer (SCLC) is a highly lethal subtype of lung cancer with a particularly poor prognosis. For decades, the best available systemic therapy was platinum plus etoposide chemotherapy, which offered frequent but transient responses. Survival gains were finally realized with the addition of immune checkpoint inhibitors to first-line chemotherapy. The phase III IMpower 133 trial showed that the addition of atezolizumab to chemotherapy improved survival. The subsequent CASPIAN trial demonstrated a similar benefit with durvalumab. These results quickly established chemo-immunotherapy as the preferred initial treatment for advanced SCLC, but outcomes remain poor for most patients. Here, we review the current and evolving role of immunotherapy in SCLC and outline emerging strategies poised to further elevate the standard of care.

[A phase II, open-label, single-arm trial of carboplatin plus etoposide with bevacizumab and atezolizumab in patients with extended-stage small-cell lung cancer (CeLEBrATE study): BACKGROUND:, design and rationale](#) Future Oncol. 2022 Mar;18(7):771-779. doi: 10.2217/fon-2021-1027. Epub 2022 Jan 24. Elisa Andrini 1 , Giuseppe Lamberti 1   2 , Francesca Mazzoni 3 , et al.
Based on improved survival from the addition of PD-L1 inhibitors in phase III trials, the combination of immunotherapy and platinum-doublet chemotherapy has become the new standard treatment for extended-stage small-cell lung cancer (ES-SCLC). Furthermore, the antiangiogenetic agent bevacizumab

showed a longer progression-free survival by targeting VEGF that has pleiotropic effects, including immunosuppressive ones. We, therefore, hypothesized that targeting angiogenesis would improve the efficacy of chemoimmunotherapy. The CeLEBrATE trial is an open-label, multicenter, phase II study designed to assess the efficacy and safety of the combination of carboplatin and etoposide plus bevacizumab and atezolizumab in treatment-naive patients with ES-SCLC. The primary end point is overall survival rate at 1 year, while secondary end points include overall response rate, progression-free survival and toxicity. **PLAIN LANGUAGE SUMMARY:** Lay abstract Extended-stage small-cell lung cancer (ES-SCLC) is a highly aggressive lung cancer subtype, accounting for 13–15% of all lung cancers. For several years, the standard treatment for this disease was based on polychemotherapy, with a rapid disease response but with an equally rapid disease progression. The new standard treatment has recently been changed, based on the results of two large clinical trials, which showed the efficacy and safety of the combination of chemotherapy with immunotherapy compared to chemotherapy alone. Nevertheless, prognosis of ES-SCLC remains poor, and new treatment strategies are urgently needed. Therefore, we designed the CeLEBrATE trial to investigate whether the combination of chemotherapy with antiangiogenetic therapy and immunotherapy is safe and could improve survival in patients with ES-SCLC.

[Apatinib as maintenance therapy following standard first-line chemotherapy in extensive disease small cell lung cancer: A phase II single-arm trial](#) Thorac Cancer. 2022 Feb;13(4):557-562. doi: 10.1111/1759-7714.14298. Epub 2022 Jan 14. Fei Teng 1 , Puyuan Xing 1 , Ke Yang 2 , Lizhen Gao 2 , Zhongqiu Tian 2 , Junling Li 1
BACKGROUND: There is a need for the development of therapies to delay cancer progression and prolong survival after initial chemotherapy for the treatment of small cell lung cancer (SCLC). Since apatinib has been found to exert promising effects on cancer patients after standard first-line chemotherapy, this study aimed to investigate apatinib as a maintenance treatment following first-line chemotherapy in extensive disease (ED)-SCLC. **METHODS:** The primary endpoints were overall survival (OS) and progression-free survival (PFS). The secondary endpoints included toxicity and safety. Apatinib (250 mg/day) was administered during the chemotherapy interval and as maintenance therapy after 4-6 cycles until the patient's disease progressed, the patient died, or became intolerant to the drug's toxicity. **RESULTS:** The patients who received apatinib maintenance treatment had a median PFS of 3.7 months (95% CI: 1.3-6.2 months). The median OS was 16.3 months (95% CI: 9.7-22.8 months). The objective response rate and disease control rate were 50.0% and 66.7%, respectively. Two patients required dose reduction due to adverse effects (AEs). The most common AEs included hypertension (n = 4, 33.3%) and hand-foot-skin reaction (n = 2, 16.7%). One patient developed diarrhea, while another patient developed hemoptysis. The most serious AE was intestinal obstruction. **CONCLUSIONS:** Apatinib maintenance therapy showed promising efficacy and safety to extend the OS/PFS of patients with ED-SCLC, thus making it a potent therapeutic option in future clinical practice. Given the small sample size of this study, further studies with large sample sizes are needed to validate the findings of the present study.

[Effectiveness and Safety of Anlotinib Monotherapy for Patients with Extensive-stage Small-Cell Lung Cancer Who Progressed to Chemotherapy: A Real-world Exploratory Study](#) Clin Med Insights Oncol. 2022 Jan 24;16:11795549211067184. doi: 10.1177/11795549211067184. eCollection 2022. Yonghui Li 1 , Zhenqing Sun 1 , Wei Sun 2 , Haibo Wang 1 , Jinchi Zu 1
BACKGROUND: Anlotinib demonstrated promising efficacy for patients with extensive-stage small-cell lung cancer (ES-SCLC) in clinical trials. However, the real-world evidence of anlotinib monotherapy in ES-SCLC was still limited currently. Therefore, present study was to investigate the effectiveness and safety of anlotinib for patients with ES-SCLC who progressed to chemotherapy in real-world and the

potential biomarker during anlotinib monotherapy. **METHODS:** A total of 89 patients with ES-SCLC who failed the previous chemotherapy treatment were recruited. All the patients were administered with anlotinib monotherapy. Demographic data of the patients were collected; effectiveness and safety profile during anlotinib monotherapy were documented through electronic medical record system in the hospital. Progression-free survival (PFS) and overall survival (OS) were presented using Kaplan-Meier survival curves and multivariate analysis was adjusted by Cox regression analysis. **RESULTS:** All the 89 patients with ES-SCLC who progressed to chemotherapy were available for the assessment of effectiveness and safety profile. Best overall response indicated that partial response was observed in 6 patients (6.7%), stable disease was noted in 61 patients (68.5%), and progressive disease was found in 22 patients (24.7%). Therefore, the objective response rate (ORR) and disease control rate (DCR) of the 89 patients with ES-SCLC was 6.7% (95% confidence interval [CI]: 2.5%-14.1%) and 75.3% (95% CI: 65.0%-83.8%), respectively. The prognostic data suggested that the median PFS of the 89 patients was 3.1 months (95% CI: 2.10-4.10), and the median OS was 8.6 months (95% CI: 7.42-9.78). In addition, the most common adverse reactions of the patients who received anlotinib monotherapy were hypertension (34.8%), hand-foot syndrome (30.3%), fatigue (29.2%), loss of appetite (27.0%), and hematological toxicity (21.3%). Association analysis between biomarker (hypertension status) and prognosis indicated that the median PFS of patients with hypertension and patients with non-hypertension was 5.5 and 3.0 months, respectively ($\chi^2 = 4.64$, P = .031). Furthermore, multivariate Cox analysis for PFS suggested that hypertension status was an independent factor for PFS (hazard ratio [HR] = 0.71, P = .035]. **CONCLUSION:** Anlotinib monotherapy showed encouraging effectiveness and acceptable safety profile for patients with ES-SCLC in real world. Hypertension induced by anlotinib administration might be used as a potential biomarker to predict superior PFS for patients with ES-SCLC.

PALLIATIVE AND SUPPORTIVE CARE

[Patient-reported distress as an early warning sign of unmet palliative care needs and increased healthcare utilization in patients with advanced cancer](#) Support Care Cancer. 2022 Apr;30(4):3419-3427. doi: 10.1007/s00520-021-06727-3. Epub 2022 Jan 8. Jordan D Hildenbrand 1 , Hee S Park 2 , David J Casarett 3 4 5 , et al.
INTRODUCTION: Cancer patients' sources of distress are often unaddressed, and patient-reported distress data could be utilized to identify those with unmet and impending care needs. We explored the association between moderate/severe distress and healthcare utilization in a large sample of non-small cell lung cancer (NSCLC) and non-colorectal gastrointestinal cancer patients. **METHODS AND MATERIALS:** Adult patients treated between July 2013 and March 2019. Data from the NCCN Distress Thermometer (DT) and the accompanying "Problem List" were extracted from the EHR. A DT score of $\geq$ 4 indicates "actionable distress." Statistical analysis was performed using descriptive analysis for patient characteristics, clinical outcomes, and sources of distress. Generalized linear mixed models were fit to determine the relationship between distress and healthcare utilization (hospitalization, emergency department (ED) visit, or both). **RESULTS:** The ten most frequently reported problems were from the Physical and Emotional domains of the Problem List. Distress was mostly related to physical symptoms (pain, fatigue) and emotional issues (worry, fears, sadness, nervousness). Patients with actionable distress generally reported more problems across all their visits. Actionable distress was associated with higher odds of the composite outcome measure of hospitalization or visiting the ED, within both the next 3 months (OR = 1.37; 95% CI = 1.19, 1.58; p < 0.001) and 6 months (OR = 1.19; 95% CI = 1.03, 1.37; p = 0.019). **CONCLUSION:** Patients with significant distress had marked utilization of ED and inpatient services. DT scores are a source of untapped data in the EHR that can highlight patients in need of intervention, including palliative care and cancer support services.

Patient-Centered Palliative Care for Patients With Advanced Lung Cancer J Clin Oncol. 2022 Feb 20;40(6):626-634. doi: 10.1200/JCO.21.01710. Epub 2022 Jan 5. Jennifer S Temel 1   2 , Laura A Petrillo 1   3 , Joseph A Greer 1   4

The evidence base demonstrating the benefits of an early focus on palliative care for patients with serious cancers, including advanced lung cancer, is substantial. Early involvement of specialty-trained palliative care clinicians in the care of patients with advanced lung cancer improves patient-reported outcomes, such as quality of life, and health care delivery, including hospice utilization. Since the time that many of these palliative care trials were conducted, the paradigm of cancer care for many cancers, including lung cancer, has changed dramatically. The majority of patients with advanced lung cancer are now treated with immune checkpoint inhibitors or targeted therapies, both of which have had a significant impact on patient's experience and outcomes. With this changing landscape of lung cancer therapeutics, patients are facing new and different challenges, including dealing with novel side effect profiles and coping with greater uncertainty regarding their prognosis. Patients who are living longer with their advanced cancer also struggle with how to address survivorship issues, such as sexual health and exercise, and decision making about end-of-life care. Although palliative care clinicians remain well-suited to address these care needs, they may need to learn new skills to support patients treated with novel therapies. Additionally, as the experience of patients with advanced lung cancer is becoming more varied and individualized, palliative care research interventions and clinical programs should also be delivered in a patient-centered manner to best meet patient's needs and improve their outcomes. Tailored and technology-based palliative care interventions are promising strategies for delivering patient-centered palliative care.

Disparities in Supportive Care Needs Over Time Between Racial and Ethnic Minority and Non-Minority Patients With Advanced Lung Cancer J Pain Symptom Manage. 2022 Jan 11;S0885-3924(21)00670-9. doi: 10.1016/j.jpainsymman.2021.12.007. Online ahead of print. Melissa B Mazor 1 , Lihua Li 2 , Jose Morillo 3 , Olivia S Allen 4 , Juan P Wisnivesky 3 , Cardinale B Smith 5

CONTEXT: Little is known about inequities in supportive care needs among diverse patients with advanced lung cancer. **OBJECTIVES:** We aimed to examine differences in supportive care needs between racial/ethnic minority and non-minority patients with lung cancer and identify how these needs change over time. **METHODS:** We performed a prospective cohort study of patients newly diagnosed with advanced lung cancer (stage III and IV). Patients completed a validated survey at baseline, 4-, 8- and 12-months post-diagnosis, assessing supportive care needs: medical communication/information, psychological/emotional support, daily living, financial concerns, physical symptoms, and spiritual and social needs. Univariable and multivariable regression analyses compared differences in supportive care needs between minority (Black and Latinx) and non-minority patients. A mixed effect model with minority status, follow-up time and the interaction between minority status and time assessed the association between each need and minority status with changes over time. **RESULTS:** We enrolled 99 patients; 55 (56%) were minorities and 44 (44%) were non-minorities. At baseline, minorities reported significantly higher needs across each domain except medical communication/information. Over time, these reported differences remained consistent except for medical communication. After adjustment, the needs of both minorities and non-minorities increased significantly in the psychological/emotional, daily living and physical symptom domains. **CONCLUSION:** Minority patients with advanced lung cancer are more likely to have higher baseline and persistent supportive care needs relatives to non-minority patients. Clinicians caring for minority patients with lung cancer should provide targeted supportive care evaluation and treatment to ensure health equity.

Psychological Symptom Trajectories and Non-Small Cell Lung Cancer Survival: A Joint Model Analysis Psychosom Med. 2022 Feb-Mar 01;84(2):215-223. doi: 10.1097/PSY.0000000000001027.

Barbara L Andersen 1 , Joseph P McElroy, David P Carbone, Carolyn J Presley, Rachel M Smith, Peter G Shields, Guy N Brock

OBJECTIVE: Lung cancer remains the number one cause of cancer-related mortality worldwide, but less known is that lung cancer patients are among the most psychologically disabled of all cancer groups. Patients with stage IV non-small cell lung cancer (NSCLC) were studied to test the hypothesis that trajectories of depression and/or anxiety symptoms after diagnosis would show an adverse relationship with survival, beyond relevant controls. **METHODS:** Patients with stage IV NSCLC (n = 157) were enrolled (ClinicalTrials.gov Identifier: NCT03199651) at diagnosis and completed validated measures for depressive symptoms (Patient Health Questionnaire-9) and anxiety symptoms (Generalized Anxiety Disorder-7). Patients were reassessed every 1 to 2 months through 24 months (16 assessments; 80% average completion rate) and survival monitored. Joint statistical models provided simultaneous modeling of longitudinal (psychological) and time-to-event (survival) processes. Control variables were age, sex, marital status, education, smoking status, cancer type, and treatment received. **RESULTS:** Depression and anxiety symptoms significantly decreased with time since diagnosis. The 2-year trajectory of depressive symptoms was significantly associated with cancer survival after adjustment for covariates (hazard ratio = 1.09 per unit increase in the Patient Health Questionnaire-9, 95% confidence interval = 1.03-1.15, p = .002). Anxiety was marginally significant in the unadjusted (p = .053) but not the adjusted (p = .39) model. **CONCLUSIONS:** For the first time, joint model analyses test the interaction of a longitudinal trajectory of psychological symptoms, assessed from diagnosis to 24 months, and cancer survival. New data show the continuation of depressive and anxiety symptoms through treatment and thereafter. Immunotherapy and targeted therapies have dramatically improved survival for patients with advanced NSCLC; however, novel data suggest their benefit may be constrained by depressive symptoms.

"You have to be sure that the patient has the full picture": Adaptation of the Best Case/Worst Case communication tool for geriatric oncology J Geriatr Oncol. 2022 Feb 2;S1879-4068(22)00015-7. doi: 10.1016/j.jgo.2022.01.014. Online ahead of print. Melisa L Wong 1 , Francesca M Nicosia 2 , Alexander K Smith 3 , et al.

BACKGROUND: Shared decision making (SDM) is especially important for older adults with cancer given the risks of over- and undertreatment, uncertainty regarding benefits/harms worsened by research underrepresentation, and individual preferences. We aimed to adapt the Best Case/Worst Case (BC/WC) communication tool, which improves SDM in geriatric surgery, to geriatric oncology. **METHODS:** We conducted focus groups with 40 stakeholders (fourteen older adults with lung cancer, twelve caregivers, fourteen medical oncologists) to elicit perspectives on using the BC/WC tool for geriatric oncology and to identify components needing refinement. During each focus group, participants viewed a BC/WC demonstration video and answered questions modified from the Decision Aid Acceptability Scale. We analyzed transcripts using deductive and inductive thematic analyses. **DISCUSSION:** Participants believed that the BC/WC tool could help patients understand their cancer care choices, explore tradeoffs and picture potential outcomes, and deliberate about decisions based on their goals, preferences, and values. Oncologists also reported the tool could guide conversations to address points that may frequently be skipped (e.g., alternative options, treatment goals). Participant preferences varied widely regarding discussion of the worst-case scenario and desire for statistical information. **CONCLUSION:** The BC/WC tool is a promising strategy that may improve SDM in geriatric oncology and patient understanding of alternative options and treatment goals. Based on participant input, adaptations will include framing cancer care as a series of decisions, eliciting patient preferences and asking permission before offering the worst-case scenario, and selection of the two most relevant options to present if multiple exist.

Trends in Opioid Use Among Cancer Patients in the United States: 2013-2018 JNCI Cancer Spectr. 2021 Dec 23;6(1):pkab095. doi: 10.1093/jncics/pkab095. eCollection 2022 Feb. Yingxi Chen 1 , Susan

Spillane 1 , Meredith S Shiels 1 , Lauren Young 2 , David Quach 2 , Amy Berrington de González 1 , Neal D Freedman 1

BACKGROUND: In response to the US opioid epidemic, the Centers for Disease Control and Prevention updated their guideline on prescription opioids for chronic pain management in March 2016. The aim of this study was to provide detailed analysis of trends in opioid claims among cancer patients in the United States during 2013-2018. **METHODS:** We analyzed pharmaceutical dispensing data from Symphony Health's Integrated Dataverse database, which covers approximately 80% of the US population. We examined annual trends in dispensed opioids in cancer patients during 2013-2018. We examined quarterly trends of the prevalence, mean number of days, and dose (stated as morphine milligram equivalents) of opioid dispensing in cancer patients. **RESULTS:** Dispensing records of an average of over 3.7 million cancer patients contributed to the study annually in 2013-2018. The annual prevalence of opioid dispensing claims declined from 40.2% in 2013 to 34.5% in 2018. Annual declines occurred across cancer sites, and particularly among patients with metastatic cancer (decline of 19.8%), breast cancer (18.2%), and lung cancer (13.8%). By quarter, the prevalence of opioid claims declined statistically significantly from 26.6% in Q1 2013 to 21.2% in Q4 2018; this decline was more pronounced after Q3 2016 (2-sided P =.004). Both quarterly trends in mean days and morphine milligram equivalents of opioids supplied showed a gradual decline from 2013 to 2018, with a slightly larger decline after 2016. **CONCLUSIONS:** We observed a decline in opioid use among cancer patients, particularly after 2016, coinciding with the publication of the Centers for Disease Control and Prevention's guideline on prescription opioids for chronic pain management.

[Patient and Caregiver Preferences for First-Line Treatments of Metastatic Non-Small Cell Lung Cancer: A Discrete Choice Experiment](#) Patient Prefer Adherence. 2022 Jan 15;16:123-135. doi: 10.2147/PPA.S338840. eCollection 2022. Candice Yong 1 , M Janelle Cambron-Mellott 2 , Brian Seal 1 , Oliver Will 2 , Martine C Maculaitis 2 , Kelly Clapp 2 , Emily Mulvihill 2 , Ion Cotarla 1 , Ranee Mehra 3

PURPOSE: The approval of immune checkpoint inhibitors for metastatic non-small-cell lung carcinomas (mNSCLC) treatment has presented more care options. Therefore, it is important to identify the benefit-risk trade-offs patients and caregivers are willing to make among potential treatment options. This study quantified the preferences of patients and caregivers for attributes of mNSCLC treatment. **METHODS:** Patients with mNSCLC and caregivers completed an online survey assessing preferences using a discrete choice experiment. Respondents chose between hypothetical treatment profiles, with varying levels for 7 attributes associated with first-line treatment, including overall survival (OS), progression-free survival, select adverse events (AEs), and regimen (caregivers). Hierarchical Bayesian modeling was used to estimate attribute-level preference weights. **RESULTS:** Patients (n = 308) and caregivers (n = 166) most valued increasing OS from 11 to 30 months, followed by decreasing the risk of a serious AE (grade 3/4) that may lead to hospitalization from 70% to 18%. These attributes were over twice as important to both sets of respondents as the other attributes measured. Patients and caregivers would accept increases in the risks of a serious AE (grade 3/4) from 18% to 70% and all grades nausea from 10% to 69% if OS increased by 16.8 and 4.0 months, respectively. The least valued attributes were all grades of pneumonitis (patients) and all grades of skin rash (caregivers). **CONCLUSION:** Patients and caregivers are willing to make trade-offs between efficacy and toxicity and may require up to 1.5 years of increased OS to accept a higher risk of AEs. These results can provide guidance to oncologists when engaging in shared-decision making discussions.

[Evidence-based nursing intervention can improve the treatment compliance, quality of life and self-efficacy of patients with lung cancer undergoing radiotherapy and chemotherapy](#) Am J Transl Res. 2022 Jan 15;14(1):396-405. eCollection 2022. Tianjie Zhang 1, Jierong Lu 2, Yanmei Fan 3 , Li Wang 1

OBJECTIVE: To investigate the improvement effect of evidence-based nursing intervention on treatment compliance, quality of life and self-efficacy of patients with lung carcinoma (LC) undergoing radiotherapy and chemotherapy. **METHODS:** From May 2018 to August 2019, 183 patients with LC who received radiotherapy and chemotherapy in our hospital were selected and divided into two groups in accordance with different nursing methods. Among them, 85 patients who received routine nursing intervention were included in the control group (CG), and 98 patients who received evidence-based nursing intervention were included in the research group (RG). The improvement of pulmonary function indexes [(FVC), forced expiratory volume in one second (FEV1), ratio of forced expiratory volume in one second to forced vital capacity (FEV1/FVC)] was observed before and after nursing. The pain degree was evaluated by the visual analogue scale (VAS). The treatment compliance between groups was compared. The psychological emotions of the patients were evaluated by a self-rating anxiety scale (SAS) and a self-rating depression scale (SDS). The General Self-efficacy Scale (GSES) was applied to assess the self-efficacy and the Quality of Life (SF-36) scale was applied to evaluate the quality of life. The incidence of secondary infection was observed in the two groups. The nursing satisfaction was evaluated by a nursing satisfaction questionnaire made by our hospital. **RESULTS:** After nursing, the improvement of FEV1, FVC and FEV1/FVC levels in the RG were obviously better than that in the CG; The scores of VAS, SAS and SDS and total incidence of secondary infection in the RG were obviously lower than those in the CG; The treatment compliance, GSES and SF-36 scores, and nursing satisfaction scores of patients in the RG were obviously higher than that in the CG. **CONCLUSION:** Evidence-based nursing intervention can improve treatment compliance, lung function, self-efficacy and quality of life for patients with LC undergoing radiotherapy and chemotherapy.

[Study protocol for a randomised trial evaluating the non-inferiority of stepped palliative care versus early integrated palliative care for patients with advanced lung cancer](#) BMJ Open. 2022 Feb 10;12(2):e057591. doi: 10.1136/bmjopen-2021-057591. Kathryn E Post 1 , Lauren B Heuer 2 , Arif H Kamal 3 , Pallavi Kumar 4 , Madeleine Elyze 2 , Sarah Griffith 2 , Jacqueline Han 2 , Fred Friedman 3 , Ashley Jackson 4 , Chardria Trotter 2 , Rachel Plotke 2 , Charu Vyas 2 , Vicki Jackson 2 , Dustin J Rabideau 2 , Joseph A Greer 5 , Jennifer S Temel 2

INTRODUCTION: Integrating palliative care (PC) early in the illness course for patients with serious cancers improves their outcomes and is recommended by national organisations such as the American Society of Clinical Oncology. However, monthly visits with PC clinicians from the time of diagnosis can be challenging to implement due to the lack of specialty-trained PC clinicians and resources. Therefore, we developed a stepped care model to triage PC service based on patients' needs. Methods and analysis: We are conducting a non-blinded, randomised trial to evaluate the non-inferiority of a stepped PC model compared with an early integrated PC model for improving patients' quality of life (QOL) at 24 weeks (primary outcome). Patients assigned to early integrated PC meet with PC every 4 weeks throughout their illness. Patients assigned to stepped PC have PC visits only at clinically significant points in their illness (eg, cancer progression) unless their QOL decreases, at which time they are 'stepped up' and meet with PC every 4 weeks throughout the remainder of their illness. Secondary aims include assessing whether stepped PC is non-inferior to early integrated PC regarding patient-clinician communication about end of life care and length of stay on hospice as well as comparing resource utilisation. Patients are recruited from the Massachusetts General Hospital Cancer Center, Boston, Massachusetts; Duke Cancer Center, Durham, North Carolina and University of Pennsylvania Abramson Cancer Center, Philadelphia, Pennsylvania. The target sample size is 510 patients. Ethics and dissemination: The study is funded by the National Cancer Institute, approved by the Dana-Farber/Harvard Cancer Center Institutional Review Board and will be reported in accordance with the Consolidated Standards of Reporting Trials statement. We will disseminate results through professional society meetings, peer-reviewed publications and presentations to patient organisations.

Psychological Dimensions of Palliative Care Consultation: Approaches to Seriously Ill Patients at the End of Life J Clin Psychiatry. 2022 Feb 22;83(2):22ct14391. doi: 10.4088/JCP.22ct14391. Leah B Rosenberg 1   2 , Anne K Fishel 3 , Rebecca Harley 4 , Theodore A Stern 5 , Linda Emanuel 6 , Jonah N Cohen 7

Mental health clinicians often hear seriously ill patients ask the unanswerable: Why did this happen? What is the meaning of my suffering? In the inpatient setting, general medical ward, or oncology unit, patients are confronted with their mortality in new, urgent ways. Palliative medicine, or the specialized, comprehensive care of patients facing a life-limiting illness, occupies a unique and liminal space. Although often practiced by clinicians with non-mental health training backgrounds, there exists ample psychological content to be explored in the palliative care encounter. In this article, we present the case of a husband and international businessperson who experienced terminal complications from an advanced stage lung cancer. His illness was not responsive to multiple cancer-directed treatments, and he developed respiratory failure requiring high levels of supplemental oxygen support, from which he was unable to wean. Palliative care consultation was sought with the multiple objectives of ameliorating his severe death anxiety and persistent dyspnea as well as assisting in the clarification of his end-of-life wishes. Our goal with this case presentation and related discussion is to introduce the psychological aspects of palliative medicine to psychiatrists and psychotherapists.

Duration of palliative care involvement and immunotherapy treatment near the end of life among patients with cancer who died in-hospital Support Care Cancer. 2022 Feb 22. doi: 10.1007/s00520-022-06901-1. Online ahead of print. Juline Auclair 1 , Stéphane Sanchez 2 , Jan Chrusciel 2 , et al.

BACKGROUND: Immune checkpoint inhibitors (ICIs) have revolutionised cancer treatment, but their use near the end of life in patients with advanced cancer is poorly documented. This study investigated the association between administration of ICI therapy in the last month of life and the duration of involvement of the palliative care (PC) team, among patients with advanced cancer who died in-hospital. **METHODS:** In a retrospective, multicentre study, we included all patients who died in 2018 of melanoma, head and neck carcinoma, non-small cell lung cancer or urothelial or renal cancer, in 2 teaching hospitals and one community hospital in France. The primary outcome was the association between ICI therapy in the last month of life and duration of involvement of the PC team in patient management. **RESULTS:** Among 350 patients included, 133 (38%) received anti-cancer treatment in the last month of life, including 71/133 (53%) who received ICIs. A total of 207 patients (59%) received palliative care, only 127 (36%) 30 days before death. There was a significant association between ongoing ICI therapy in the last month of life and shorter duration of PC management (p = 0.04). Receiving ICI therapy in the last month of life was associated with an increased risk of late PC initiation by multivariate regression analysis (hazard ratio 1.668; 95% CI 1.022-2.722). **CONCLUSION:** ICI therapy is frequently used close to the end of life in patients with advanced cancer. Innovative new anti-cancer treatments should not delay PC referral. Improved collaboration between PC and oncological teams is needed to address this issue.

Integrating Quality of Life in the Care Pathway of Cancer Patients Undergoing Immunotherapy Treatment: Descriptive, Cross-sectional Survey of an Online Patient Community's Experiences and Expectations J Med Internet Res. 2022 Jan 11;24(1):e25792. doi: 10.2196/25792. Ophélie Wilczynski #
1 , Anthony Boisbouvier 1 , Lise Radoszycki 1 , François-Emery Cotté 2 , Anne-Françoise Gaudin 2 , Hervé Lemasson 2

BACKGROUND: New cancer treatments, such as immune checkpoint inhibitors (ICIs), can improve survival and health-related quality of life (HRQoL) in patients with cancer. Although long-term

monitoring of HRQoL has been shown to improve survival, integration of HRQoL into everyday practice remains poorly documented. **OBJECTIVE:** This study describes experiences and expectations of patients treated with ICIs regarding a discussion of HRQoL with health care professionals (HCPs) in cancer management. **METHODS:** This cross-sectional study was conducted in an online patient community (Carenity) in France. Patients treated with ICIs for cancer, included between September 2018 and January 2019, completed a questionnaire to assess the involvement of HCP in a discussion of HRQoL and when and what was discussed. **RESULTS:** Of 82 patients included (mean age: 56.9 years, 95% CI 54.2-59.6; 46 [56%] male; 34 [41%] with lung cancer), 62 (76%) reported discussing HRQoL at least once with HCPs, mainly general practitioners (54/82, 66%), oncologists (53/82, 65%), and hospital nurses (50/82, 61%). Around half (45/82, 55%) of the patients were satisfied with these discussions. Discussions with the oncologist were at the patient's initiative (34/53, 64%). Discussions occurred primarily during follow-up visits (40/62, 65%), when adverse events occurred (30/62, 48%), and at treatment initiation (27/62, 32%). The most discussed dimensions were symptoms (48/62, 77%) and physical well-being (43/62, 69%). With respect to expectations, 54/82 (66%) patients considered oncologists as the most important HCPs for discussing HRQoL. These discussions were desirable throughout the care pathway, particularly at diagnosis (63/82, 77%) and when treatment was initiated (75/82, 92%) or changed (68/82, 83%). All HRQoL dimensions were considered important to discuss. **CONCLUSIONS:** With only around half of the patients satisfied with HRQoL discussions, impactful HRQoL integration in clinical practice is critical. According to patients, this integration should involve mainly oncologists and general practitioners, should happen at every step of the care pathway, and should be extended to dimensions that are currently rarely addressed.

COMPLEMENTARY & ALTERNATIVE THERAPY

[Comparative efficacy of 10 Chinese herbal injections combined with GP regimen chemotherapy for patients with advanced NSCLC a systematic review and network meta-analysis](#) J Cancer. 2022 Jan 1;13(2):465-480. doi: 10.7150/jca.66410. eCollection 2022. Juan Li 1   2 , Guang-Hui Zhu 1   2 , Tong-Tong Liu 1 , Bo-Wen Xu 1   2 , Jie Li 1

BACKGROUND: Numerous studies have indicated that some Chinese herbal injections (CHIs) might have a beneficial treatment effect when used in combination with chemotherapy. However, the results of these studies have been inconsistent. The aim of this network meta-analysis (NMA) was to evaluate and compare the clinical efficacy and safety of different CHIs combined with gemcitabine plus cisplatin (GP) regimen chemotherapy with that of GP regimen chemotherapy alone in the treatment of patients with advanced non-small cell lung cancer (NSCLC). Materials and **METHODS:** Eight databases were systematically searched to identify randomized clinical trials (RCTs) from the date of inception of the database to August 11, 2021. The primary outcome measures were the objective response rate (ORR) and adverse reactions (including nausea and vomiting, and leukopenia). The secondary outcome measures were median survival time (MST) and quality of life (QOL). The quality of the included studies was assessed using the Cochrane risk of bias tool. Standard pair-wise and Bayesian NMAs were carried out to compare the effectiveness and safety of different CHIs combined with GP regimen chemotherapy using WinBUGS 14 and Stata 15.1 software. Sensitivity analysis and Egger's test were also performed to check robust. **RESULTS:** A total of 92 eligible RCTs involving 7,728 patients and 10 CHIs were included. The results showed that Kangai injection (KAI), Kanglaite injection (KLT), Aidi injection and Compound Kushen (CKSI) injection displayed obvious advantages in both efficacy and safety. Aidi+GP (79.0%) showed great advantages of ORR, and KAI+GP and KLT+GP had the lowest probability in terms of leukopenia (4.4%) and nausea and vomiting (24.2%). Besides, KLT+GP was shown to positively affect MST. According to the subgroup analyses, CHIs might have a limited effect in reducing adverse reactions, and have a similar effect in squamous cell carcinoma and adenocarcinoma. **CONCLUSIONS:**

KAI+GP of adjuvant drugs, Aidi+GP and CKSI+GP of anticancer drugs appeared to be the advantageous treatment options for patients with advanced NSCLC, owing to its superior therapeutic performance and reduced adverse reactions. KLT+GP might prolong survival. Nevertheless, additional results from multicenter trials and high-quality studies will be pivotal in supporting our findings.

MISCELLANEOUS WORKS

Mortality Among Adults With Cancer Undergoing Chemotherapy or Immunotherapy and Infected With COVID-19 JAMA Netw Open. 2022 Feb 1;5(2):e220130. doi: 10.1001/jamanetworkopen.2022.0130. Csilla Várnai 1   2   3 , Claire Palles 2 , Roland Arnold 2 , et al.
IMPORTANCE: Large cohorts of patients with active cancers and COVID-19 infection are needed to provide evidence of the association of recent cancer treatment and cancer type with COVID-19 mortality. **OBJECTIVE:** To evaluate whether systemic anticancer treatments (SACTs), tumor subtypes, patient demographic characteristics (age and sex), and comorbidities are associated with COVID-19 mortality. Design, setting, and participants: The UK Coronavirus Cancer Monitoring Project (UKCCMP) is a prospective cohort study conducted at 69 UK cancer hospitals among adult patients (≥18 years) with an active cancer and a clinical diagnosis of COVID-19. Patients registered from March 18 to August 1, 2020, were included in this analysis. Exposures: SACT, tumor subtype, patient demographic characteristics (eg, age, sex, body mass index, race and ethnicity, smoking history), and comorbidities were investigated. Main outcomes and measures: The primary end point was all-cause mortality within the primary hospitalization. **RESULTS:** Overall, 2515 of 2786 patients registered during the study period were included; 1464 (58%) were men; and the median (IQR) age was 72 (62-80) years. The mortality rate was 38% (966 patients). The data suggest an association between higher mortality in patients with hematological malignant neoplasms irrespective of recent SACT, particularly in those with acute leukemias or myelodysplastic syndrome (OR, 2.16; 95% CI, 1.30-3.60) and myeloma or plasmacytoma (OR, 1.53; 95% CI, 1.04-2.26). Lung cancer was also significantly associated with higher COVID-19-related mortality (OR, 1.58; 95% CI, 1.11-2.25). No association between higher mortality and receiving chemotherapy in the 4 weeks before COVID-19 diagnosis was observed after correcting for the crucial confounders of age, sex, and comorbidities. An association between lower mortality and receiving immunotherapy in the 4 weeks before COVID-19 diagnosis was observed (immunotherapy vs no cancer therapy: OR, 0.52; 95% CI, 0.31-0.86). **CONCLUSIONS AND RELEVANCE:** The findings of this study of patients with active cancer suggest that recent SACT is not associated with inferior outcomes from COVID-19 infection. This has relevance for the care of patients with cancer requiring treatment, particularly in countries experiencing an increase in COVID-19 case numbers. Important differences in outcomes among patients with hematological and lung cancers were observed.

Cancer disparities among non-Hispanic urban American Indian and Alaska Native populations in the United States, 1999-2017 Cancer. 2022 Feb 4. doi: 10.1002/cncr.34122. Online ahead of print. Stephanie C Melkonian 1 , Melissa A Jim 1 , Dornell Pete 2 , Amy Poel 2 , Adrian E Dominguez 2 , Abigail Echo-Hawk 2 , Stephanie Zhang 3 , Reda J Wilson 4 , Donald Haverkamp 1, Lindsey Petras 5 , Ashley Pohlenz 5
BACKGROUND: Disparities in cancer incidence have not been described for urban American Indian/Alaska Native (AI/AN) populations. The purpose of the present study was to examine incidence rates (2008-2017) and trends (1999-2017) for leading cancers in urban non-Hispanic AI/AN (NH AI/AN) compared to non-Hispanic White (NHW) populations living in the same urban areas. **METHODS:** Incident cases from population-based cancer registries were linked with the Indian Health Service patient registration database for improved racial classification of NH AI/AN populations. This study was limited to counties in Urban Indian Health Organization service areas. Analyses were conducted by geographic

region. Age-adjusted rates (per 100,000) and trends (joinpoint regression) were calculated for leading cancers. **RESULTS:** Rates of colorectal, liver, and kidney cancers were higher overall for urban NH AI/AN compared to urban NHW populations. By region, rates of these cancers were 10% to nearly 4 times higher in NH AI/AN compared to NHW populations. Rates for breast, prostate, and lung cancer were lower in urban NH AI/AN compared to urban NHW populations. Incidence rates for kidney, liver, pancreatic, and breast cancers increased from 2% to nearly 7% annually between 1999 to 2017 in urban NH AI/AN populations. **CONCLUSIONS:** This study presents cancer incidence rates and trends for the leading cancers among urban NH AI/AN compared to urban NHW populations for the first time, by region, in the United States. Elevated risk of certain cancers among urban NH AI/AN populations and widening cancer disparities highlight important health inequities and missed opportunities for cancer prevention in this population.

[Financial distress and its associated burden in couples coping with an advanced cancer](#) Support Care Cancer. 2022 Feb 3. doi: 10.1007/s00520-021-06758-w. Online ahead of print. Juliet L Kroll 1 , Seokhun Kim 2 , Dalnim Cho 3 , Shiao-Pei Weathers 4 , Aileen B Chen 5 , Grace Smith 3 5 , Eduardo Bruera 6 , Kathrin Milbury 2

PURPOSE: In efforts to understand financial distress (FD) associated with advanced cancer care from the perspective of both patients with incurable disease and their spousal caregivers, we assessed FD in both members of the couple, identified symptom and quality of life (QOL) correlates, and examined the potential role of illness communication. **METHODS:** Patients undergoing treatment for stage III/IV lung cancer or a grade III/IV primary brain tumor and their spousal caregivers (n = 76 dyads) completed measures of somatic and affective symptoms including FD, physical and mental QOL, and ease of engaging in illness communication. Patients and caregivers additionally rated their perception of each other's symptoms, including FD. **RESULTS:** FD was endorsed by both patients (any FD 62.7%; high FD 24%) and spousal caregivers (any FD 64.7%; high FD 32.3%). Self-reported FD was significantly correlated (partial r = .52, p < .001) within couples. FD was associated with greater symptoms of anxiety (r = .29, p = .01; r = .31, p = .01), depression (r = 29, p = 01; r = .39, p = .001), and poorer physical QOL(r = - .25, p = .03; r = - .25, p = .001) for patients and caregivers, respectively. For patients, FD was additionally associated with poorer mental QOL(r = - .44, p < .001). Caregivers accurately perceived patient FD, yet patients tended to underreport their caregiver's FD by almost an entire point (t = 2.8, p = .007). A 3-way interaction (FD X role X illness communication) revealed (b = .40, p = .041) that illness communication moderated the association between FD and physical QOL for spouses so that spouses who reported less ease of illness communication demonstrated a stronger association between financial distress and physical QOL (b = - 2.08, p < .001) than those reporting greater ease of engaging in illness communication (b = .49, p = .508). **CONCLUSION:** In the advanced cancer setting, FD is prevalent in both patients and their spousal caregivers and associated with psychological distress and poor physical QOL. Results suggest that optimal FD assessment should include patients and spouses, and spouse's ease of engaging with illness communication may be a potential target for future intervention studies.

[Representation and Outcomes of Older Adults in Practice-Changing Oncology Trials in the Era of Novel Therapies: A Guideline Appraisal](#) Natl Compr Canc Netw. 2022 Jan;20(1):37-44. doi: 10.6004/jnccn.2021.7055. Ronald Chow 1 , Daniel E Lage 1 , Grant R Williams 2 , Mina S Sedrak 3 , Joseph A Greer 4 , Jennifer S Temel 1 , Ryan D Nipp 1

BACKGROUND: Older adults account for 70% of cancer-related deaths, but previous studies have shown that they are underrepresented in cancer clinical trials. We sought to analyze the representation and outcomes of older adults in trials conducted in the era of novel targeted therapy and immunotherapy. **METHODS:** We searched the 2020 NCCN Clinical Practice Guidelines in Oncology and retrieved trials from the past 10 years leading to category 1 recommendations in the first-line metastatic setting for the 5

most common causes of cancer death. We categorized trials by cancer type, single-agent versus multiagent approach, and therapeutic class. We described the percentage of older adults (according to each trial's definition) and used a Mantel-Haenszel random-effects meta-analysis model to compare overall and progression-free survival by age. **RESULTS:** We identified 30 trials consisting of 24,416 patients. Across all trials, 44% of enrolled patients were older adults. Representation of older adults by cancer type within trials was 49% prostate cancer, 38% pancreatic cancer, 37% breast cancer, and 34% non-small cell lung cancer. Representation of older adults also varied by therapeutic class: 20% received immunotherapy, 44% received cytotoxic chemotherapy, 54% received targeted/hormonal therapy, and 34% received combination therapy (P<.001 for all comparisons). For each year since 2010, the percentage of older adults enrolled in trials increased by 1.9%, although this difference was not significant. We observed no difference in overall or progression-free survival between older and younger adults. In our analysis of practice-changing clinical trials, we found that 44% of clinical trial participants were older adults. Trials that included immunotherapy or a combination of therapeutic classes had a lower representation of older adults (<40%). **CONCLUSIONS:** We found that >40% of patients in practice-changing trials are older adults. Although they remain underrepresented in clinical trials compared with the general population, older adults in practice-changing trials seem to be better represented than in previously reported analyses of cooperative group trials.

[Impact of Diagnostic Delays on Lung Cancer Survival Outcomes: A Population Study of the US SEER-Medicare Database](#) JCO Oncol Pract. 2022 Feb 4;OP2100485. doi: 10.1200/OP.21.00485. Online ahead of print. Perrin E Romine 1 , Qin Sun 2 , Catherine Fedorenko 2 , Li Li 2 , Mariel Tang , Keith D Eaton 1 4 , Bernardo H L Goulart 5 , Renato G Martins 1 4

PURPOSE: Time from diagnosis to treatment has been associated with worse survival outcomes in non-small-cell lung cancer (NSCLC). However, little is known about the impact of delay in time to diagnosis. We aimed to evaluate the impact of time from radiographic suspicion to histologic diagnosis on survival outcomes using the US SEER-Medicare population database. **METHODS:** We identified patients from the SEER-Medicare data set diagnosed with any stage NSCLC between January 1, 2011, and December 31, 2015, who received stage-appropriate treatment and had a computed tomography scan within 1 year of diagnosis. Time to confirmation was determined as the interval between most recent computed tomography imaging and date of histologic diagnosis. Our primary outcome was overall survival (OS). **RESULTS:** In total, 10,824 eligible patients were identified. The median time to confirmation was 20 (range 0-363) days. Using multivariate Cox regression models, longer time to confirmation was associated with improved OS in all comers driven by stage IV patients after adjustment for age, sex, diagnosis year, histology, and comorbidity index. In a separate landmark analysis excluding patients deceased within 6 months of diagnosis, the association between time to diagnosis and survival was no longer evident. **CONCLUSION:** Time to confirmation of NSCLC was inversely associated with OS in this US SEER population study. This association was lost when patients deceased within 6 months of diagnosis were excluded, suggesting that retrospective registry-claims databases may not be the optimal data source to study time to diagnosis as a quality metric because of the unaccounted confounding effects of tumor behavior. Prospective evaluations of clinically enriched data sources may better serve this purpose.

[Cancer Treatment During COVID-19: Resilience of Individuals With Advanced Non-Small Cell Lung Cancer Versus Community Controls](#) J Natl Compr Canc Netw. 2022 Feb;20(2):118-125. doi: 10.6004/jnccn.2021.7076. Nicole A Arrato 1 , Stephen B Lo 1 , Clarence A Coker 1 , Jonathan J Covarrubias 1 , Tessa R Blevins 1 , Sarah A Reisinger 2 , Carolyn J Presley 3 , Peter G Shields 2 3 , Barbara L Andersen 1

BACKGROUND: Among all patients with cancer, those with advanced non-small cell lung cancer (NSCLC) experience the most distress. Although new therapies are improving survival, it is unknown whether receiving immunotherapy or targeted therapy during the COVID-19 pandemic increases patients' psychological vulnerability. To meet clinical needs, knowledge of patients' COVID-19 perceptions and safety behaviors is essential. Thus, this study compared patients' psychological responses at diagnosis and during COVID-19 and compared patients with similar individuals without cancer during the same period. Patients and **METHODS:** Patients with advanced NSCLC enrolled at diagnosis for cohort study participated (ClinicalTrials.gov identifier: NCT03199651). Those with follow-ups from April 28, 2020, through July 14, 2020 (n=76), were assessed again including COVID-19 measures. Simultaneously, community controls with similar sociodemographics and smoking histories were solicited (n=67). Measures were COVID-19 perceptions (Brief Illness Perception Questionnaire), social distancing, and depressive (Patient Health Questionnaire-9) and anxiety (Generalized Anxiety Disorder-7) symptoms. First, analyses evaluated differences in the psychological responses of patients with NSCLC at diagnosis and during COVID-19. Second, patients and controls were contrasted on COVID-19 perceptions, social distancing, and psychological symptoms. **RESULTS:** The depressive and anxious symptoms of patients with NSCLC were greater at diagnosis (P<.02) than during COVID-19, approximately 1 year later. Patients with NSCLC and controls did not differ in terms of sociodemographics, except those with NSCLC were more racially diverse and older, and had greater smoking history (P<.03). Groups did not differ regarding concern, understanding, or perceived control over COVID-19 (P>.406). Notably, controls anticipated the COVID threat would last longer, practiced more social distancing, were more concerned about family (P<.04), and reported worse psychological symptoms (P<.023). With less depression and anxiety, patients with NSCLC viewed COVID-19 as a shorter-term threat and had fewer COVID-19-related worries than did controls. For controls, COVID-19 was more salient, heightening worries and psychological symptoms. **CONCLUSIONS:** Despite multiple health stressors, patients with NSCLC demonstrated resilience when receiving cancer treatment during COVID-19. Nonetheless, this population remains psychologically vulnerable, requiring support at diagnosis and thereafter.

[Racial Differences in Survival Among Advanced-stage Non-small-Cell Lung Cancer Patients Who Received Immunotherapy: An Analysis of the US National Cancer Database (NCDB)](#) J Immunother. 2022 Feb-Mar 01;45(2):132-137. doi: 10.1097/CJI.0000000000000400. Anjali Gupta 1 , Dongyu Zhang 2 , Dejana Braithwaite 2 , Shama D Karanth 3 , Tina D Tailor 4 , Jeffrey M Clarke 5 , Tomi

Lung cancer is the most common cause of cancer death among men and women in the United States, with significant racial disparities in survival. It is unclear whether these disparities persist upon equal utilization of immunotherapy. The purpose of this study was to evaluate the association between race and all-cause mortality among non-small-cell lung cancer (NSCLC) patients who received immunotherapy. We obtained data from the 2016 National Cancer Database on patients diagnosed with advanced-stage (III-IV) NSCLC from 2015 to 2016. Multivariable Cox proportional hazards models were used to calculate hazard ratios (HR) and 95% confidence intervals (95% CI) by race/ethnicity. A total of 2940 patients were included. Non-Hispanic (NH)-Black patients had a lower risk of death relative to NH-White patients (HR: 0.85; 95% CI: 0.73, 0.98) after adjusting for sociodemographic, clinical, and treatment factors. Formal tests of interaction evaluating race with Charlson-Deyo comorbidity score and race with area-level median income were nonsignificant. However, in stratified analyses, NH-Black versus NH-White patients had a lower risk of death in models adjusted for sociodemographic factors among those with at least 1 comorbidity (HR: 0.75; 95% CI: 0.57, 0.97), and those living in regions within the 2 lowest quartiles of median income (HR: 0.82; 95% CI: 0.68, 0.99). Among advanced-stage NSCLC patients who received immunotherapy, NH-Black patients experienced higher survival compared with NH-White patients. We urge the implementation of policies and interventions that seek to equalize access to care as a means of addressing differences in overall NSCLC survival by race.

[**Disparities in clinical and demographic characteristics among Asian/Pacific Islander and Non-Hispanic White newly diagnosed lung cancer patients**](#) Cancer Causes Control. 2022 Jan 19. doi: 10.1007/s10552-021-01548-5. Online ahead of print. Parth B Patel 1 , Naomi Alpert 2 , Emanuela Taioli 1 2 , Raja Flores 3

PURPOSE: Racial disparities persist among lung cancer patients but have not been adequately studied among Asian/Pacific Islander (API) subgroups, which are heterogeneous. This study compared clinical and demographic characteristics at diagnosis of API subgroups and NHW patients. **METHODS:** NHW and API adults diagnosed with lung cancer were identified from the Surveillance, Epidemiology, and End Results database (1990-2015). API was divided into eight subgroups: Chinese, Japanese, Filipino, Hawaiian/Pacific Islander, Korean, Vietnamese, Asian Indian/Pakistani, and Other. Multivariable multinomial logistic regression models were used to assess adjusted associations of clinical and demographic factors with API/subgroups. **RESULTS:** There were 522,702 (92.6%) NHW and 41,479 (7.4%) API lung cancer patients. API were less likely to be diagnosed at the age of ≥ 80 years (ORadj 0.53, 95% CI 0.48-0.58 for ≥ 80 vs. ≤ 39 years) than NHW. However, Japanese patients were more often diagnosed at ≥ 80 years compared to other ethnic subgroups. API were less often female (ORadj 0.85, 95% CI 0.83-0.86), and unmarried (ORadj 0.71, 95% CI 0.68-0.74); however, among API, Japanese, Hawaiian/Pacific Islander, Korean, and Vietnamese were more often unmarried, compared to Chinese patients. API were more frequently diagnosed at stage IV, compared to stage I (ORadj 1.31, 95% CI 1.27-1.35). API had significantly less squamous cell carcinoma (ORadj 0.54, 95% CI 0.52-0.56, compared to adenocarcinoma); among API, Japanese, Filipino, Hawaiian/Pacific Islander, Korean, Asian Indian/Pakistani, and Other were more likely than Chinese patients to present with squamous cell histology (range: ORadj[Other] 1.24, 95% CI 1.09-1.41; ORadj[Hawaiian/Pacific Islander] 2.47, 95% CI 2.22-2.75). **CONCLUSION:** At diagnosis, there are significant differences in demographic and clinical characteristics between NHW, API, and API subgroups. Treating API patients as a single population may overlook biological, environmental, and behavioral differences that might be beneficial in designing prevention strategies and treatment.

[**Indoor Air Pollution Increases the Risk of Lung Cancer**](#) Int J Environ Res Public Health. 2022 Jan 21;19(3):1164. doi: 10.3390/ijerph19031164 Ke-Cheng Chen 1 2 , Shih-Wei Tsai 3 4 , Ruei-Hao Shie 5 , Chian Zeng 6 , Hsiao-Yu Yang 3 4 7

BACKGROUND: Cooking and burning incense are important sources of indoor air pollutants. No studies have provided biological evidence of air pollutants in the lungs to support this association. Analysis of pleural fluid may be used to measure the internal exposure dose of air pollutants in the lung. The objective of this study was to provide biological evidence of indoor air pollutants and estimate their risk of lung cancer. **METHODS:** We analyzed 14 common air pollutants in the pleural fluid of 39 cases of lung adenocarcinoma and 40 nonmalignant controls by gas chromatography-mass spectrometry. **RESULTS:** When we excluded the current smokers and adjusted for age, the adjusted odds ratios (ORs) were 2.22 (95% confidence interval CI = 0.77-6.44) for habitual cooking at home and 3.05 (95% CI = 1.06-8.84) for indoor incense burning. In females, the adjusted ORs were 5.39 (95% CI = 1.11-26.20) for habitual cooking at home and 6.01 (95% CI = 1.14-31.66) for indoor incense burning. In pleural fluid, the most important exposure biomarkers for lung cancer were naphthalene, ethylbenzene, and o-xylene. **CONCLUSIONS:** Habitual cooking and indoor incense burning increased the risk of lung adenocarcinoma.

[**International Association for the Study of Lung Cancer (IASLC) Study of the Impact of COVID-19 on International Lung Cancer Clinical Trials**](#) J Thorac Oncol. 2022 Feb 15;S1556-0864(22)00086-7.

INTRODUCTION: To determine the effects of the global COVID-19 pandemic on lung cancer trials, we surveyed investigators and collected aggregate enrollment data for lung cancer trials across the world before and during the pandemic. **METHODS:** A Data Collection Survey collected aggregate monthly enrollment numbers from 294 global lung cancer trials for 2019-2020. A 64-question Action Survey assessed the impact of COVID-19 on clinical trials and identified mitigation strategies implemented. **RESULTS:** Clinical trial enrollment declined from 2019 to 2020 by 14% globally. Most reductions in enrollment occurred in April-June where we found significant decreases in individual site enrollment (p=0.0309). Enrollment was not significantly different in October-December of 2019 versus 2020 (p=0.25). The most frequent challenges identified by the Action Survey (N=173) were fewer eligible patients (63%), decrease in protocol compliance (56%), and suspension of trials (54%). Patient-specific challenges included access to trial site (49%), ability to travel (54%), and willingness to visit site (59%). The most frequent mitigation strategies included modified monitoring requirements (47%), telehealth visits (45%), modified required visits (25%), mail-order medications (25%), and laboratory (27%) and radiology (21%) tests at non-study facilities. Sites felt the most effective mitigation strategies were telehealth visits (85%), remote patient reported symptom collection (85%), off-site procedures (85%), and remote consenting (89%). **CONCLUSION:** The COVID-19 pandemic created many challenges for lung cancer clinical trials conduct and enrollment. Mitigation strategies were employed and, although the pandemic worsened, trial enrollment improved. A more flexible approach may improve enrollment and access to clinical trials, even beyond the pandemic.

[Disparities in Lung Cancer Treatment](#) Curr Oncol Rep. 2022 Feb;24(2):241-248. doi: 10.1007/s11912-022-01193-4. Epub 2022 Jan 26. Sharon Harrison 1 2, Julia Judd 3, Sheray Chin 2 4 , Camille Ragin 5 6

PURPOSE OF REVIEW: Despite an overall reduction in lung cancer incidence and mortality rates worldwide, Blacks still have higher mortality rates compared to Whites. There are many factors that contribute to this difference. This review seeks to highlight racial disparities in treatment and the possible reasons for these disparities. **RECENT FINDINGS:** Factors attributing to racial disparities in lung cancer treatment include social determinants of health, differences in the administration of guideline-concordant therapy as well as molecular testing that is essential for most NSCLC patients. One way to circumvent disparities in lung cancer survivorship is to ensure equal representation of race in research at all levels that will provide insight on interventions that will address social determinants of health, differences in treatment patterns, molecular testing, and clinical trial involvement.

[Social Disparities in Lung Cancer](#) Thorac Surg Clin. 2022 Feb;32(1):33-42. doi: 10.1016/j.thorsurg.2021.09.009. Irmina Elliott 1 , Cayo Gonzalez 1 , Leah Backhus 1 , Natalie Lui 2

Social disparities in lung cancer diagnosis, treatment, and survival have been studied using national databases, statewide registries, and institution-level data. Some disparities emerge consistently, such as lower adherence to treatment guidelines and worse survival by race and socioeconomic status, whereas other disparities are less well studied. A critical appraisal of current data is essential to increasing equity in lung cancer care.

[Patients' Perceptions at Diagnosis: Lung Cancer Discovery and Provider Relationships](#) Cancer Nurs. 2022 Jan 19. doi: 10.1097/NCC.0000000000001050. Online ahead of print.Darryl Somayaji 1 , Heba Mohedat, Grace E Dean, Suzanne S Dickerson

BACKGROUND: In the United States, most lung cancer cases are diagnosed at advanced stages, limiting treatment options and impacting survival. This study presents patients' perspectives on the complexity of factors influencing a lung cancer diagnosis. Lung cancer awareness regarding risks,

symptoms, smoking behaviors, family history, and environmental factors can lead to preventative and early detection measures. **OBJECTIVE:** The aim of this study was to explore lung cancer patient perspectives on lung cancer awareness within the context of an earlier study to understand sleep-wake disturbances in adults with non-small cell lung cancer. **METHODS:** A content analysis was used to analyze the original deidentified longitudinal interview data collected from 26 patients diagnosed with lung cancer. **RESULTS:** Of the original 26 participants, 16 were included in this secondary data analysis. The participants were primarily females (n = 10) and Whites (n = 13), with ages ranging between 49 and 83 years. Half of the sample was diagnosed with stage IV lung cancer and most of the sample was on chemotherapy (n = 10). Two key themes were identified: the lung cancer discovery and the patient-physician relationship. **CONCLUSIONS:** Unspecific initial symptoms, lack of knowledge and screening, as well as fear of the diagnosis delayed seeking medical care. Patient-physician relationships were hindered by smoking-associated stigma, inadequate sharing of information, and lack of coordinated, holistic care. Positive communication strategies are critical between patients and providers to meet patients' specific needs. **IMPLICATIONS FOR PRACTICE:** Educational interventions that enhance lung cancer awareness may improve prevention and screening actions, improve timely healthcare intervention, and reduce incidence and mortality.

[**Incidence of Lung Cancer Among Never-Smoking Asian American, Native Hawaiian, and Pacific Islander Females**](#) J Natl Cancer Inst. 2022 Jan 11;114(1):78-86. doi: 10.1093/jnci/djab143. Mindy C DeRouen 1   2 , Alison J Canchola 1   3 , Caroline A Thompson 4   5   6 , et al.
BACKGROUND: Although lung cancer incidence rates according to smoking status, sex, and detailed race/ethnicity have not been available, it is estimated that more than half of Asian American, Native Hawaiian, and Pacific Islander (AANHPI) females with lung cancer have never smoked. **METHODS:** We calculated age-adjusted incidence rates for lung cancer according to smoking status and detailed race/ethnicity among females, focusing on AANHPI ethnic groups, and assessed relative incidence across racial/ethnic groups. We used a large-scale dataset that integrates data from electronic health records from 2 large health-care systems-Sutter Health in Northern California and Kaiser Permanente Hawai'i-linked to state cancer registries for incident lung cancer diagnoses between 2000 and 2013. The study population included 1 222 694 females (n = 244 147 AANHPI), 3297 of which were diagnosed with lung cancer (n = 535 AANHPI). **RESULTS:** Incidence of lung cancer among never-smoking AANHPI as an aggregate group was 17.1 per 100 000 (95% confidence interval [CI] = 14.9 to 19.4) but varied widely across ethnic groups. Never-smoking Chinese American females had the highest rate (22.8 per 100 000, 95% CI = 17.3 to 29.1). Except for Japanese American females, incidence among every never-smoking AANHPI female ethnic group was higher than that of never-smoking non-Hispanic White females, from 66% greater among Native Hawaiian females (incidence rate ratio = 1.66, 95% CI = 1.03 to 2.56) to more than 100% greater among Chinese American females (incidence rate ratio = 2.26, 95% CI = 1.67 to 3.02). **CONCLUSIONS:** Our study revealed high rates of lung cancer among most never-smoking AANHPI female ethnic groups. Our approach illustrates the use of innovative data integration to dispel the myth that AANHPI females are at overall reduced risk of lung cancer and demonstrates the need to disaggregate this highly diverse population.