



Caring Ambassadors Lung Cancer Program

Literature Review, October 2021

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SCREENING, COMPREHENSIVE BIOMARKER TESTING, DIAGNOSIS AND STAGING

[Predictive and Prognostic Biomarkers for Lung Cancer Bone Metastasis and Their Therapeutic Value](#) Xupeng Chai 1 2, Eloy Yinwang 1 2, Zenan Wang 1 2, et al. *Front Oncol.* 2021 Oct 14;11:692788. doi: 10.3389/fonc.2021.692788. eCollection 2021.

Lung cancer is the leading cause of cancer-related death worldwide. Bone metastasis, which usually accompanies severe skeletal-related events, is the most common site for tumor distant dissemination and detected in more than one-third of patients with advanced lung cancer. Biopsy and imaging play critical roles in the diagnosis of bone metastasis; however, these approaches are characterized by evident limitations. Recently, studies regarding potential biomarkers in the serum, urine, and tumor tissue, were performed to predict the bone metastases and prognosis in patients with lung cancer. In this review, we summarize the findings of recent clinical research studies on biomarkers detected in samples obtained from patients with lung cancer bone metastasis. These markers include the following: (1) bone resorption-associated markers, such as N-terminal telopeptide (NTx)/C-terminal telopeptide (CTx), C-terminal telopeptide of type I collagen (CTx-I), tartrate-resistant acid phosphatase isoform 5b (TRACP-5b), pyridinoline (PYD), and parathyroid hormone related peptide (PTHrP); (2) bone formation-associated markers, including total serum alkaline phosphatase (ALP)/bone specific alkaline phosphatase (BAP), osteopontin (OP), osteocalcin (OS), amino-terminal extension propeptide of type I procollagen/carboxy-terminal extension propeptide of type I procollagen (PICP/PINP); (3) signaling markers, including epidermal growth factor receptor/Kirsten rat sarcoma/anaplastic lymphoma kinase (EGFR/KRAS/ALK), receptor activator of nuclear factor κ B ligand/receptor activator of nuclear factor κ B/osteoprotegerin (RANKL/RANK/OPG), C-X-C motif chemokine ligand 12/C-X-C motif chemokine receptor 4 (CXCL12/CXCR4), complement component 5a receptor (C5AR); and (4) other potential markers, such as calcium sensing receptor (CASR), bone sialoprotein (BSP), bone morphogenetic protein 2 (BMP2), cytokeratin 19 fragment/carcinoembryonic antigen (CYFRA/CEA), tissue factor, cell-free DNA, long non-coding RNA, and microRNA. The prognostic value of these markers is also investigated. Furthermore, we listed some clinical trials targeting hotspot biomarkers in advanced lung cancer referring for their therapeutic effects.

[Biomarkers of response to checkpoint inhibitors beyond PD-L1 in lung cancer](#) Mod Pathol. 2021 Oct 4. doi: 10.1038/s41379-021-00932-5. Online ahead of print. Lynette M Sholl 1

Immunotherapy, including use of checkpoint inhibitors against PD-1, PD-L1, and CTLA-4, forms the backbone of oncologic management for the majority of non-small cell lung carcinoma patients. However, response to these therapies varies widely, from patients who have complete resolution of metastatic disease and long-term remission, to those who rapidly progress and succumb to their cancer despite use of the newest checkpoint inhibitors. While PD-L1 protein expression by immunohistochemistry serves as the principle predictive biomarker for immunotherapy response, neither the sensitivity nor the specificity of this approach is optimal, and clinical PD-L1 testing is plagued by concerns around result reproducibility and confusion born from the proliferation of different companion diagnostic assays. At the same time, insights into tumor and host immune-specific factors that inform both prognosis and response prediction are beginning to define better immunotherapy biomarkers. Beyond immune checkpoint expression status, common themes in analyses of immunotherapy response prediction include cancer neoantigen production, the state of the antigen presentation pathway in both tumor and antigen presenting cells, the admixture of effector and suppressor immune cells in the tumor microenvironment, and the genomic drivers and comutations that can influence the all of these variables. This review will address the state of PD-L1 testing in lung cancer, the role for tumor mutation burden as a predictive biomarker, the evolving status of human leukocyte antigen/major histocompatibility complex expression as a marker of antigen presentation, approaches to tumor immune cell quantitation including by multiplex immunofluorescence, and the importance of tumor genomic profiling to ascertain oncogenic driver (EGFR, ALK, KRAS, MET, etc.) and co-mutation (STK11, KEAP1, SMARCA4) status.

[Clinical Outcomes for Plasma-Based Comprehensive Genomic Profiling Versus Standard-of-Care Tissue Testing in Advanced Non-Small Cell Lung Cancer](#) Clin Lung Cancer. 2021 Oct 10;S1525-7304(21)00262-X. doi: 10.1016/j.clcc.2021.10.001. Online ahead of print. Ray D Page 1, Leylah M Drusbosky 2, Hiba Dada 3, et al.

BACKGROUND: Somatic genomic testing is recommended by numerous expert guidelines to inform targeted therapy treatment for patients with advanced nonsquamous non-small cell lung cancer (aNSCLC). The NILE study was a prospective observational study that demonstrated noninferiority of cell-free circulating tumor DNA (cfDNA)-based tumor genotyping compared to tissue-based genotyping to find targetable genomic alterations in patients with newly diagnosed nonsquamous aNSCLC. As the cohort has matured, clinical outcomes data can now be analyzed. **METHODS:** This prospective, multicenter North American study enrolled patients with previously untreated nonsquamous aNSCLC who had standard of care (SOC) tissue genotyping performed and concurrent comprehensive cfDNA analysis (Guardant360). Patients with targetable genomic alterations, as defined by NCCN guidelines, who were treated with physician's choice of therapy had objective response rates, disease control rate, and time to treatment collected and compared to published outcomes. **RESULTS:** Among 282 patients, 89 (31.6%) had an actionable biomarker, as defined by NCCN, detected by tissue (21.3%) and/or cfDNA (27.3%) analysis. Sixty-one (68.5%) of these were treated with an FDA-approved targeted therapy guided by somatic genotyping results (EGFR, ALK, ROS1). Thirty-three patients were eligible for clinical response evaluation and demonstrated an objective response rate of 58% and disease control rate of 94%. Twenty-five (76%) and 17 (52%) achieved a durable response > 6 months and 12 months, respectively. The time to treatment (TtT) was significantly faster for cfDNA-informed biomarker detection as compared to tissue genotyping (18 vs. 31 days, respectively; $P = .0008$). **CONCLUSIONS:** cfDNA detects guideline-recommended biomarkers at a rate similar to tissue genotyping, and therapeutic outcomes based on plasma-based comprehensive genomic profiling are comparable to published targeted therapy outcomes with tissue profiling, even in community-based centers.

[Evaluation of Population-Level Changes Associated With the 2021 US Preventive Services Task Force Lung Cancer Screening Recommendations in Community-Based Health Care Systems](#)

JAMA Netw Open. 2021 Oct 1;4(10):e2128176. doi: 10.1001/jamanetworkopen.2021.28176. Debra P Ritzwoller¹, Rafael Meza², Nikki M Carroll¹, Erica Blum-Barnett¹, Andrea N Burnett-Hartman¹, Robert T Greenlee³, Stacey A Honda⁴, Christine Neslund-Dudas⁵, Katharine A Rendle⁶, Anil Vachani⁶

IMPORTANCE: The US Preventive Services Task Force (USPSTF) released updated lung cancer screening recommendations in 2021, lowering the screening age from 55 to 50 years and smoking history from 30 to 20 pack-years. These changes are expected to expand screening access to women and racial and ethnic minority groups. **OBJECTIVE:** To estimate the population-level changes associated with the 2021 USPSTF expansion of lung cancer screening eligibility by sex, race and ethnicity, sociodemographic factors, and comorbidities in 5 community-based health care systems. **DESIGN, SETTING, AND PARTICIPANTS:** This cohort study analyzed data of patients who received care from any of 5 community-based health care systems (which are members of the Population-based Research to Optimize the Screening Process Lung Consortium, a collaboration that conducts research to better understand how to improve the cancer screening processes in community health care settings) from January 1, 2010, through September 30, 2019. Individuals who had complete smoking history and were engaged with the health care system for 12 or more continuous months were included. Those who had never smoked or who had unknown smoking history were excluded. **EXPOSURES:** Electronic health record-derived age, sex, race and ethnicity, socioeconomic status (SES), comorbidities, and smoking history. **MAIN OUTCOMES AND MEASURES: DIFFERENCES** in the proportion of the newly eligible population by age, sex, race and ethnicity, Charlson Comorbidity Index, chronic obstructive pulmonary disease diagnosis, and SES as well as lung cancer diagnoses under the 2013 recommendations vs the expected cases under the 2021 recommendations were evaluated using χ^2 tests. **RESULTS:** As of September 2019, there were 341 163 individuals aged 50 to 80 years who currently or previously smoked. Among these, 34 528 had electronic health record data that captured pack-year and quit-date information and were eligible for lung cancer screening according to the 2013 USPSTF recommendations. The 2021 USPSTF recommendations expanded screening eligibility to 18 533 individuals, representing a 53.7% increase. Compared with the 2013 cohort, the newly eligible 2021 population included 5833 individuals (31.5%) aged 50 to 54 years, a larger proportion of women (52.0% [n = 9631]), and more racial or ethnic minority groups. The relative increases in the proportion of newly eligible individuals were 60.6% for Asian, Native Hawaiian, or Pacific Islander; 67.4% for Hispanic; 69.7% for non-Hispanic Black; and 49.0% for non-Hispanic White groups. The relative increase for women was 13.8% higher than for men (61.2% vs 47.4%), and those with a lower comorbidity burden and lower SES had higher relative increases (eg, 68.7% for a Charlson Comorbidity Index score of 0; 61.1% for lowest SES). The 2021 recommendations were associated with an estimated 30% increase in incident lung cancer diagnoses compared with the 2013 recommendations. **CONCLUSIONS AND RELEVANCE:** This cohort study suggests that, in diverse health care systems, adopting the 2021 USPSTF recommendations will increase the number of women, racial and ethnic minority groups, and individuals with lower SES who are eligible for lung cancer screening, thus helping to minimize the barriers to screening access for individuals with high risk for lung cancer.

[Cost-effectiveness Evaluation of the 2021 US Preventive Services Task Force Recommendation for Lung Cancer Screening](#)

JAMA Oncol. 2021 Oct 21;e214942. doi: 10.1001/jamaoncol.2021.4942. Online ahead of print. Iakovos Toumazis¹, Koen de Nijs², Pianpian Cao³, et al.

IMPORTANCE: The US Preventive Services Task Force (USPSTF) issued its 2021 recommendation on lung cancer screening, which lowered the starting age for screening from 55 to 50 years and the minimum cumulative smoking exposure from 30 to 20 pack-years relative to its 2013 recommendation. Although costs are expected to increase because of the expanded screening eligibility criteria, it is unknown whether the new guidelines for lung cancer screening are cost-effective. **OBJECTIVE:** To evaluate the cost-effectiveness of the 2021 USPSTF recommendation for lung cancer screening compared with the 2013 recommendation and to explore the cost-effectiveness of 6 alternative screening strategies that maintained a minimum cumulative smoking exposure of 20 pack-years and an ending age for screening of 80 years but varied the starting ages for screening (50 or 55 years) and the number of years since smoking cessation (≤ 15 , ≤ 20 , or ≤ 25). **DESIGN, SETTING, AND PARTICIPANTS:** A comparative cost-effectiveness analysis using 4 independently developed microsimulation models that shared common inputs to assess the population-level health benefits and costs of the 2021 recommended screening strategy and 6 alternative screening strategies compared with the 2013 recommended screening strategy. The models simulated a 1960 US birth cohort. Simulated individuals entered the study at age 45 years and were followed up until death or age 90 years, corresponding to a study period from January 1, 2005, to December 31, 2050. **EXPOSURES:** Low-dose computed tomography in lung cancer screening programs with a minimum cumulative smoking exposure of 20 pack-years. **MAIN OUTCOMES AND MEASURES:** Incremental cost-effectiveness ratio (ICER) per quality-adjusted life-year (QALY) of the 2021 vs 2013 USPSTF lung cancer screening recommendations as well as 6 alternative screening strategies vs the 2013 USPSTF screening strategy. Strategies with a mean ICER lower than \$100 000 per QALY were deemed cost-effective. **RESULTS:** The 2021 USPSTF recommendation was estimated to be cost-effective compared with the 2013 recommendation, with a mean ICER of \$72 564 (range across 4 models, \$59 493-\$85 837) per QALY gained. The 2021 recommendation was not cost-effective compared with 6 alternative strategies that used the 20 pack-year criterion. Strategies associated with the most cost-effectiveness included those that expanded screening eligibility to include a greater number of former smokers who had not smoked for a longer duration (ie, ≤ 20 years and ≤ 25 years since smoking cessation vs ≤ 15 years since smoking cessation). In particular, the strategy that screened former smokers who quit within the past 25 years and began screening at age 55 years was associated with screening coverage closest to that of the 2021 USPSTF recommendation yet yielded greater cost-effectiveness, with a mean ICER of \$66 533 (range across 4 models, \$55 693-\$80 539). **CONCLUSIONS AND RELEVANCE:** This economic evaluation found that the 2021 USPSTF recommendation for lung cancer screening was cost-effective; however, alternative screening strategies that maintained a minimum cumulative smoking exposure of 20 pack-years but included individuals who quit smoking within the past 25 years may be more cost-effective and warrant further evaluation.

[Estimating heterogeneous survival treatment effects of lung cancer screening approaches: A causal machine learning analysis](#) Ann Epidemiol. 2021 Oct;62:36-42. doi: 10.1016/j.annepidem.2021.06.008.

Epub 2021 Jun 23. Liangyuan Hu ¹, Jung-Yi Lin (Joyce) ², Keith Sigel ³, Minal Kale ³

The National Lung Screening Trial (NLST) found that low-dose computed tomography (LDCT) screening provided lung cancer (LC) mortality benefit compared to chest radiography (CXR). Considerable research concerns identifying the differential treatment effects that may exist in certain subpopulations. We shed light on several important issues in existing research and highlight the need for further investigation of the heterogeneous comparative effect of LDCT versus CXR, using more flexible and rigorous statistical approaches. We used a high-performance Bayesian machine learning approach designed for censored survival data, accelerated failure time Bayesian additive regression trees model (AFT-BART), to flexibly capture the relationships between the failure time and predictors. We then used the counterfactual framework to draw Markov chain Monte Carlo samples of the individual treatment effect for each participant. Using these posterior samples, we explored the possible treatment effect heterogeneity via a

stepwise binary tree approach. When re-analyzed with AFT-BART, LDCT did not have a statistically significant LC or overall mortality benefit compared to CXR. The Asian and Black (particularly those with pack-year ≥ 37 years and without emphysema) NLST population were shown to have enhanced overall mortality benefit from LDCT than the population average. Although inconclusive for LC mortality benefit, Asians, Blacks and Whites with history of chronic obstructive pulmonary disease showed a small trend towards benefit from LDCT. Causal inference with flexible machine learning modeling can provide valuable knowledge for informing treatment decision and planning targeted clinical trials emphasizing personalized medicine approaches.

[Blood-based liquid biopsy: Insights into early detection and clinical management of lung cancer](#)

Cancer Lett. 2022 Jan 1;524:91-102. doi: 10.1016/j.canlet.2021.10.013. Epub 2021 Oct 14. Cuiliu Liu 1 , Xiaoqiang Xiang 2 , Shuangqing Han 1 , et al.

Currently, early detection of lung cancer relies on the characterisation of images generated from computed tomography (CT). However, lung tissue biopsy, a highly invasive surgical procedure, is required to confirm CT-derived diagnostic results with very high false-positive rates. Hence, a non-invasive or minimally invasive biomarkers is essential to complement the existing low-dose CT (LDCT) for early detection, improve responses to a certain treatment, predict cancer recurrence, and to evaluate prognosis. In the past decade, liquid biopsies (e.g., blood) have been demonstrated to be highly effective for lung cancer biomarker discovery. In this review, the roles of emerging liquid biopsy-derived biomarkers such as circulating nucleic acids, circulating tumour cells (CTCs), long non-coding RNA (lncRNA), and microRNA (miRNA), as well as exosomes, have been highlighted. The advantages and limitations of these blood-based minimally invasive biomarkers have been discussed. Furthermore, the current progress of the identified biomarkers for clinical management of lung cancer has been summarised. Finally, a potential strategy for the early detection of lung cancer, using a combination of LDCT scans and well-validated biomarkers, has been discussed.

[Lung Cancer Screening: Development and Replication of a Decentralized Program to Increase Access](#)

Clin J Oncol Nurs. 2021 Oct 1;25(5):523-529. doi: 10.1188/21.CJON.523-529.

Carolyn Austin 1

BACKGROUND: Throughout its evolution, lung cancer screening has remained an evidence-based tool to detect earlier-stage disease and improve survival. Many lung cancer screening programs are planned and developed in one central location, which limits patient access. **OBJECTIVES:** The purpose was to develop necessary and complex decentralized program components in affiliation with a large cancer care delivery system and a regional community hospital network in northeast Florida. **METHODS:** A program was pilot tested among five geographically diverse primary care offices for three years. The role of oncology nursing was crucial to achieve quality and efficacy in program development, regulatory compliance, and screening outcomes. **FINDINGS:** The program resulted in an increase in lung cancer screenings within the large healthcare network. The percentage of early-stage lung cancers identified increased, which led to improved patient outcomes and survival.

[A Cost-Effectiveness Analysis of Lung Cancer Screening With Low-Dose Computed Tomography and a Diagnostic Biomarker](#)

JNCI Cancer Spectr. 2021 Oct 6;5(6):pkab081. doi:

10.1093/jncics/pkab081. eCollection 2021 Dec. Iakovos Toumazis 1 , S Ayca Erdogan 2 , Mehrad Bastani 1 , Ann Leung 2 , Sylvia K Plevritis 1

BACKGROUND: The Lung Computed Tomography Screening Reporting and Data System (Lung-RADS) reduces the false-positive rate of lung cancer screening but introduces prolonged periods of uncertainty for indeterminate findings. We assess the cost-effectiveness of a screening program that assesses indeterminate findings earlier via a hypothetical diagnostic biomarker introduced in place of

Lung-RADS 3 and 4A guidelines. **METHODS:** We evaluated the performance of the US Preventive Services Task Force (USPSTF) recommendations on lung cancer screening with and without a hypothetical noninvasive diagnostic biomarker using a validated microsimulation model. The diagnostic biomarker assesses the malignancy of indeterminate nodules, replacing Lung-RADS 3 and 4A guidelines, and is characterized by a varying sensitivity profile that depends on nodules' size, specificity, and cost. We tested the robustness of our findings through univariate sensitivity analyses. **RESULTS:** A lung cancer screening program per the USPSTF guidelines that incorporates a diagnostic biomarker with at least medium sensitivity profile and 90% specificity, that costs \$250 or less, is cost-effective with an incremental cost-effectiveness ratio lower than \$100 000 per quality-adjusted life year, and improves lung cancer-specific mortality reduction while requiring fewer screening exams than the USPSTF guidelines with Lung-RADS. A screening program with a biomarker costing \$750 or more is not cost-effective. The health benefits accrued and costs associated with the screening program are sensitive to the disutility of indeterminate findings and specificity of the biomarker, respectively. **CONCLUSIONS:** Lung cancer screening that incorporates a diagnostic biomarker, in place of Lung-RADS 3 and 4A guidelines, could improve the cost-effectiveness of the screening program and warrants further investigation.

[Management of Lung Cancer Screening Results Based on Individual Prediction of Current and Future Lung Cancer Risks](#) J Thorac Oncol. 2021 Oct 11;S1556-0864(21)03244-5. doi:

10.1016/j.jtho.2021.10.001. Online ahead of print. 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.

[Impact of Joint Lung Cancer Screening and Cessation Interventions Under the New Recommendations of the U.S. Preventive Services Task Force](#) J Thorac Oncol. 2021 Oct 12;S1556-

0864(21)03208-1. doi: 10.1016/j.jtho.2021.09.011. Online ahead of print. Rafael Meza 1, Pianpian Cao 2, Jihyoun Jeon 2, Kathryn L Taylor 3, Jeanne S Mandelblatt 3, Eric J Feuer 4, Douglas R Lowy 5

INTRODUCTION: In 2021, the U.S. Preventive Services Task Force (USPSTF) revised its lung cancer screening recommendations expanding its eligibility. As more smokers become eligible, cessation interventions at the point of screening could enhance the benefits. Here, we evaluate the effects of joint screening and cessation interventions under the new recommendations. **METHODS:** A validated lung

cancer natural history model was used to estimate lifetime number of low-dose computed tomography screens, percentage ever screened, lung cancer deaths, lung cancer deaths averted, and life-years gained for the 1960 U.S. birth cohort aged 45 to 90 years (4.5 million individuals). Screening occurred according to the USPSTF 2013 and 2021 recommendations with varying uptake (0%, 30%, 100%), with or without a cessation intervention at the point of screening with varying effectiveness (15%, 100%).

RESULTS: Screening 30% of the eligible population according to the 2021 criteria with no cessation intervention (USPSTF 2021, 30% uptake, without cessation intervention) was estimated to result in 6845 lung cancer deaths averted and 103,725 life-years gained. These represent 28% and 34% increases, respectively, relative to screening according to the 2013 guidelines (USPSTF 2013, 30% uptake, without cessation intervention). Adding a cessation intervention at the time of the first screen with 15% effectiveness (USPSTF 2021, 30% uptake, with cessation intervention with 15% effectiveness) was estimated to result in 2422 additional lung cancer deaths averted (9267 total, ~73% increase versus USPSTF 2013, 30% uptake, without cessation intervention) and 322,785 life-years gained (~318% increase). Screening 100% of the eligible according to the 2021 guidelines with no cessation intervention (USPSTF 2021, 100% uptake, without cessation intervention) was estimated to result in 23,444 lung cancer deaths averted (~337% increase versus USPSTF 2013, 30% uptake, without cessation intervention) and 354,330 life-years gained (~359% increase). Adding a cessation intervention with 15% effectiveness (USPSTF 2021, 100% uptake, with cessation intervention with 15% effectiveness) would result in 31,998 lung cancer deaths averted (~497% increase versus USPSTF 2013, 30% uptake, without cessation intervention) and 1,086,840 life-years gained (~1309% increase). **CONCLUSIONS:** Joint screening and cessation interventions would result in considerable lung cancer deaths averted and life-years gained. Adding a one-time cessation intervention of modest effectiveness (15%) results in comparable life-years gained as increasing screening uptake from 30% to 100% because while cessation decreases mortality from many causes, screening only reduces lung cancer mortality. This simulation indicates that incorporating cessation programs into screening practice should be a priority as it can maximize overall benefits.

[The trajectory of racial/ethnic disparities in the use of cancer screening before and during the COVID-19 pandemic: A large U.S. academic center analysis](#) *Prev Med.* 2021 Oct;151:106640. doi: 10.1016/j.ypmed.2021.106640. Epub 2021 Jun 30. Felipe O Marcondes ¹, David Cheng ², Erica T Warner ³, Sophia C Kamran ⁴, Jennifer S Haas ⁵

Cancer screening rates declined sharply early in the COVID-19 pandemic. The impact of the pandemic may have exacerbated existing disparities in cancer screening due to the disproportionate burden of illness and job loss among racial/ ethnic minorities, and potentially, uneven resumption of care between different racial/ ethnic groups. Using electronic health record data from Mass General Brigham (MGB), we assessed changes in rates of breast, cervical, colorectal and lung cancer screening before and during the pandemic. Among patients who received primary care in an MGB-affiliated primary care practice, cancer screening rates were calculated as the number of individuals who received a screening test for each cancer type over the number of individuals due for each test, during each month between April 2019–November 2020. We conducted an interrupted time-series analysis to test for changes in screening rates by race/ethnicity before and during the pandemic. Prior to the pandemic, relative to White individuals, Asian women were less likely to receive breast cancer screening ($p < 0.001$), and Latinx and Black individuals were less likely to screen for lung cancer ($p < 0.001$ and $p = 0.02$). Our results did not show significant improvement or worsening of racial/ethnic disparities for any cancer screening type as screening resumed. However, as of November 2020 rates of screening for breast cancer were lower than pre-pandemic levels for Latinx individuals, and lung cancer screening rates were higher than baseline for Latinx, Black or White individuals. Further monitoring of disparities in cancer screening is warranted as the pandemic evolves.

[Community Size and Lung Cancer Resection Outcomes: Studying The Society of Thoracic Surgeons Database](#)

John Nicholas Melvan 1, Onkar Khullar 2, Sreekanth Vemulapalli 3, Andrzej S Kosinski 4, Allan Pickens 2, Seth D Force 2, Shuaiqi Zhang 4, Manu S Sancheti 2 Ann Thorac Surg. 2021 Oct;112(4):1076-1082. doi: 10.1016/j.athoracsur.2020.08.076. Epub 2020 Nov 13.

BACKGROUND: Socioeconomic factors play key roles in surgical outcomes. Socioeconomic data within The Society of Thoracic Surgeons (STS) General Thoracic Surgery Database (GTSD) are limited. Therefore, we utilized community size as a surrogate to understand socioeconomic differences in lung cancer resection outcomes. **METHODS:** We retrospectively reviewed all lung cancer resections from January 2012 to January 2017 in the STS GTSD. This captured 68,722 patients from 286 centers nationwide. We then linked patient zip codes with 2013 Rural-Urban Continuum Codes to understand the association between community size and postoperative outcomes. Demographic and clinical variables were evaluated for relationships with 30-day mortality, major morbidity, and readmission. **RESULTS:** Zip codes were included in 47.2% of patients. Zip-coded patients were older, were more comorbid, had less advanced disease, and were more commonly treated with minimally invasive approaches than were those without zip code classification. For geocoded patients, multivariable analyses demonstrated that sex, insurance payor, and hospital region were associated with all 3 major endpoints. Community size, based on Rural-Urban Continuum Codes coding, was not associated with any primary endpoint. Invasive mediastinal staging was related to morbidity, greater pathological stage predicted mortality, and worsened clinical stage was associated with readmission. More invasive surgery and greater extent of lung resection were associated with all primary endpoints. **CONCLUSIONS:** Incomplete data capture can promote selection bias within the STS GTSD and skew outcomes reporting. Moreover, community size is an insufficient surrogate, compared with sex, insurance payor, hospital region, for understanding socioeconomic differences in lung cancer resection outcomes.

[Thoracic surgery improved overall survival in patients with stage IIIB-IV epidermal growth factor receptor-mutant lung adenocarcinoma who received and responded to tyrosine kinase inhibitor treatment](#)

Lung Cancer. 2021 Oct 13;162:29-35. doi: 10.1016/j.lungcan.2021.10.003. Online ahead of print. Yu-Ning Chien 1, Yi-Chun Lin 2, Chia-Lun Chang 3, Wei-Chun Lin 4, Szu-Yuan Wu 5

PURPOSE: No large-scale, prospective, randomized study has evaluated the effect of thoracic surgery on patients with unresectable stage IIIB-IV epidermal growth factor receptor (EGFR)-mutant lung adenocarcinoma who received and responded to EGFR tyrosine kinase inhibitor (TKI) treatment. Therefore, we designed a propensity-score-matched, nationwide, population-based, cohort study to investigate the effects of thoracic surgery on patients with EGFR-mutant lung adenocarcinoma. Patients and **METHODS:** We included patients with unresectable stage IIIB-IV EGFR-mutant lung adenocarcinoma and categorized them into two groups according to their treatment modalities and compared their outcomes: the case group consisted of patients who underwent thoracic surgery for lung tumors after receiving and responding to EGFR-TKI treatment and the comparison group consisted of patients who received EGFR-TKI treatment alone until tumor progression. Patients in both groups were matched at a ratio of 1:4. **RESULTS:** The matching process yielded a final cohort of 1395 patients (279 and 1,116 in the case and comparison groups, respectively) who were eligible for further analysis. According to multivariable Cox regression analyses, the adjusted hazard ratio (aHR; 95% confidence interval [CI]) for thoracic surgery for lung tumors after EGFR-TKI use and tumor response (group 2) compared with EGFR-TKI treatment alone (group 1) was 0.445 (0.351-0.564). **CONCLUSIONS:**

Thoracic surgery prolonged overall survival in patients with unresectable stage IIIB-IV EGFR-mutant lung adenocarcinoma who received and responded to EGFR-TKI treatment.

[Surgical perspective in neoadjuvant chemoimmunotherapy for stage II-III non-small cell lung cancer](#)

Thorac Cancer. 2021 Oct;12(20):2796-2802. doi: 10.1111/1759-7714.14127. Epub 2021 Aug 30. Tao Hong ^{1 2}, Teng Sun ^{1 2}, Miao Zhang ³, Xinlong Liu ^{1 2}, Yanliang Yuan ^{1 2}, Ponnire Robertlee Dolo ⁴, Bi Chen ⁵, Hao Zhang ^{1 2}

BACKGROUND: There are many studies on neoadjuvant immunotherapy for locally advanced non-small cell lung cancer (NSCLC) patients. Expert consensus recommends neoadjuvant immunotherapy for patients with resectable stage IB-IIIa NSCLC. However, there are few clinical studies or cases to verify this. **METHODS:** Data were collected from all NSCLC patients who underwent surgical resection after neoadjuvant chemoimmunotherapy admitted to the Affiliated Hospital of Xuzhou Medical University and Xuzhou Central Hospital between September 2020 and April 2021. Data collected included patient information, relevant examination results, intraoperative parameters, postoperative complications, pathological changes, and 90-day mortality. **RESULTS:** In total, 25 patients achieved R0 resection. Eleven (44%) patients completed surgery by thoracotomy, and three (12%) procedures were changed from minimally invasive procedures due to dense adhesions of hilar lymph nodes, which rendered it difficult to dissect the blood vessels. Thirteen (52%) patients achieved a major pathological response (MPR) with eight (32%) of these patients having a pathological complete response (pCR). Twenty-two (88%) patients showed radiological regression, and three (12%) patients had stable disease. The median drainage time was 8.50 (3-27) days. Thirteen (52%) postoperative complications were observed, but none were above grade 3. **CONCLUSIONS:** In this study, neoadjuvant chemoimmunotherapy was found to reduce tumor volume, cause pathological downstaging, and raise the surgical resection rate of patients with locally advanced NSCLC, and achieve a 100% R0 resection rate. There was an acceptable rate of postoperative complications. Thus, neoadjuvant chemoimmunotherapy is safe and practical.

[Upfront Brain Treatments Followed by Lung Surgery Improves Survival for Stage IV Non-small Cell Lung Cancer Patients With Brain Metastases: A Large Cohort Analysis](#)

Front Surg. 2021 Oct 13;8:649531. doi: 10.3389/fsurg.2021.649531. eCollection 2021 Xiaopeng He ^{1 2}, Shen Yin ^{2 3}, Hongyu Liu ², Rong Lu ², Kemp Kernstine ⁴, David E Gerber ^{5 6 7}, Yang Xie ^{2 7 8}, Donghan M Yang ²

BACKGROUND: Current treatment guidelines for stage IV non-small cell lung cancer (NSCLC) with brain metastases recommend brain treatments, including surgical resection and radiotherapy (RT), in addition to resection of the primary lung tumor. Here, we investigate the less-studied impact of treatment sequence on the overall survival. **METHODS:** The National Cancer Database was queried for NSCLC patients with brain metastases who underwent surgical resection of the primary lung tumor (n = 776). Kaplan-Meier survival curves with log-rank test and propensity score stratified Cox regression with Wald test were used to evaluate the associations between various treatment plans and overall survival (OS). **RESULTS:** Compared to patients who did not receive any brain treatment (median OS = 6.05 months), significantly better survival was observed for those who received brain surgery plus RT (median OS = 26.25 months, p < 0.0001) and for those who received brain RT alone (median OS = 14.49 months, p < 0.001). Patients who received one upfront brain treatment (surgery or RT) before lung surgery were associated with better survival than those who received lung surgery first (p < 0.05). The best survival outcome (median OS 27.1 months) was associated with the sequence of brain surgery plus postoperative brain RT followed by lung surgery. **CONCLUSIONS:** This study shows the value of performing upfront brain treatments followed by primary lung tumor resection for NSCLC patients with brain metastases, especially the procedure of brain surgery plus postoperative brain RT followed by lung surgery.

[Quality of life after VATS lung resection and SABR for early-stage non-small cell lung cancer: A longitudinal study](#) Lung Cancer. 2021 Oct 23;162:71-78. doi: 10.1016/j.lungcan.2021.10.004. Online ahead of print. Cecilia Pompili 1, Zoe Rogers 2, Kate Absolom 3, et al. .

INTRODUCTION: Video-assisted thoracoscopic (VATS) lung resection is the recommended curative treatment for early-stage non-small cell lung cancer (NSCLC). Patients considered at high surgical risk, are treated with stereotactic ablative body radiotherapy (SABR) as a lower morbidity alternative. This study aims to investigate the impact of SABR and VATS resection on patients' quality of life (QoL) over the first year after treatment. **METHODS:** A prospective longitudinal observational study recruiting early-stage NSCLC patients from a single UK centre. QoL was assessed with EORTC QLQ-C30 and Lung Cancer Module LC13 at baseline, 6 weeks and 3, 6 and 12 months post-treatment. **RESULTS:** From 01.03.2017 till 01.03.2018, 244/281 patients (87%) consented to participate, 225 (95 SABR and 130 VATS) were included in the analysis. SABR patients had significantly worse baseline QoL scores than VATS patients, even after adjusting for preoperative clinical factors (C-30 Global Health mean: SABR = 53.8, VATS = 71.2; Physical Functioning mean: SABR = 57, VATS = 82.2; Fatigue mean: SABR = 43.5, VATS = 23.7; C30 Dyspnea mean: SABR = 49.5, VATS = 26.2). During the 12 months post SABR treatment patients' QoL scores remained stable. In the VATS group, there was a deterioration 6-weeks after treatment in Role, Physical, Social Functions, Global Health, Fatigue, C30/LC13 Dyspnoea, Pain, Appetite loss, Constipation, LC13 Pain in Chest and Arms. The scores improved by 12 months without reaching the preoperative values. **CONCLUSIONS:** Although QoL outcomes for SABR and VATS are not comparable due to different medical selection criteria, the QoL impact of the two treatments during the first year showed different trends which will inform patients and clinicians during decision-making discussions.

[\[Surgery for small-cell lung cancer\]](#) Rev Mal Respir. 2021 Oct;38(8):840-847. doi: 10.1016/j.rmr.2021.05.008. Epub 2021 Jun 5. [Article in French] C Al Zreibi 1, L Gibault 2, E Fabre 3, F Le Pimpec-Barthes 4

Small-cell lung cancer (SCLC) is a high-grade neuroendocrine carcinoma, metastatic at the time of initial diagnosis in 70% of cases. Within the 30% of localised tumours only 5% of patients are eligible for surgical treatment according to the recommendations of learned societies. These recommendations are mainly based on old phase II and III randomised prospective trials and more recent registry studies. Surgical care is only possible within a multimodal treatment and essentially concerns small-sized tumours without involvement of hilar or mediastinal lymph nodes. As with non-small cell lung cancer (NSCLC), lobectomy with radical lymph node removal is the recommended procedure to achieve complete tumour resection. Patient selection for surgery includes age, performance status and comorbidity factors. Adjuvant chemotherapy combining Platinum salts and Etoposide for resected stage I tumours is recommended by ASCO, ACCP and NCCN. The precise sequence of neo-adjuvant or adjuvant treatments remains controversial because of the large heterogeneity in clinical practice reported in the studies and the context at the time of SCLC discovery. The 5-year survival rate of patients with early stage disease (pT1-2N0M0) treated by lobectomy and adjuvant chemotherapy is between 30% and 58%, which validates the primary place that surgery must have in these early forms. There is certainly little or even no place for such a therapeutic sequence in locally advanced stages (T3-T4 or N2). However, the stage heterogeneity, as in NSCLC, makes final conclusions difficult. In fact, some registry studies with pairing scores reported a median survival of more than 20 months in N2 SCLC. So, all files of SCLC must be evaluated in a multidisciplinary meeting in order to find the optimal solution for patients with rare and heterogeneous tumours.

[Propensity score matched analysis for the role of surgery in stage III small cell lung cancer based on the eighth edition of the TNM classification: a population study of the US SEER database and a](#)

[Chinese hospital](#) Lung Cancer. 2021 Oct 25;162:54-60. doi: 10.1016/j.lungcan.2021.10.009. Online ahead of print. Lin Gao 1, Lan Shen 1, Kaixuan Wang 1, Shun Lu 2

OBJECTIVE: Patients with very early stage small cell lung cancer (SCLC) can benefit from surgery. However, the role of surgery in local advanced SCLC patients remains controversial. We designed this study to investigate the role of surgery on survival of this subset population. **METHODS:** The included patients were identified from the Surveillance, Epidemiology, and End Results SEER database from 1998 to 2016 and Shanghai Chest Hospital of China from 2009 to 2016. Propensity score matching (PSM) was used to balance clinical bias. The overall survival (OS) and lung cancer-specific survival (LCSS) were compared by the Kaplan-Meier analysis. Cox proportional hazards regression was used to identify factors associated with survival. **RESULTS:** Among the 3005 stage III patients, 570 (18.97%) patients underwent surgery. Compared with non-surgical group, patients undergoing surgery were more likely to be male, had smaller tumor size, mediastinal lymph node involvement and lower pathologic stage. The Kaplan-Meier analysis showed that surgical patients had a better OS and LCSS before and after PSM. 418 surgical patients were well matched with non-surgical patients. In matched surgical group, there were 224 (53.59%) patients who underwent lobectomy (LB), 147 (35.17%) patients who received sublobectomy (SLB), 31 (7.41%) patients who underwent pneumonectomy and 16 (3.83%) patients with unknown surgery type. The 5-year OS of the 4 subgroups were 28.80%, 12.50%, 8.70% and 13.50%, respectively ($P = 0.002$). In a multivariable Cox model, SLB (hazard ratio, 1.53; 95% CI, 1.20-1.96; $P = 0.001$) and pneumonectomy (hazard ratio, 1.72; 95% CI, 1.12-2.65; $P = 0.013$) were associated with worse OS compared with LB. **CONCLUSION:** Surgical resection significantly improved OS and LCSS of stage III SCLC patients in our study. Furthermore, LB had advantage over other surgery type but further exploration in larger prospective clinical trials is needed.

[Video-assisted thoracic surgery sleeve resection and bronchoplasty using 3D imaging system: its safety and efficacy](#) J Cardiothorac Surg. 2021 Oct 16;16(1):302. doi: 10.1186/s13019-021-01685-7.

Yong Won Seong 1, Jae Hyun Jeon 2, Hyo-Jun Jang 3, Sukki Cho 2, Sanghoon Jheon 2, Kwhanmien Kim 4

BACKGROUND: Video-assisted thoracic surgery sleeve resection with bronchial anastomosis or bronchoplasty is a technically demanding procedure. Three-dimensional endoscopic surgery has been reported to be helpful in decreasing operation time and improving spatial perception with less surgical errors, but there have been rare reports about relatively difficult thoracoscopic procedures utilizing 3D thoracoscope. We performed this study to evaluate early clinical outcomes of thoracoscopic sleeve resection and bronchoplasty utilizing 3D thoracoscope. **METHODS:** Data from a total of 36 patients who underwent thoracoscopic sleeve lobectomy or bronchoplasty at our institution from December 2015 to October 2017 were retrospectively reviewed. Three-port approach with one utility incision was used with a 10 mm, 30° three-dimensional thoracoscope. Twenty-three patients (81%) were male, and mean age was 65.9 ± 9.4 years. Fourteen patients (38.9%) underwent sleeve resection with bronchial anastomosis, 22 (61.1%) underwent wedge or simple bronchoplasty, and one patient received concomitant PA procedure. Bronchial anastomosis sites were not covered with viable tissue flaps. **RESULTS:** There was no (0%) suture needle injury from spatial misperception during bronchoplasty or sleeve anastomosis. There was no (0%) operative mortality. The pathologic report revealed squamous cell carcinoma (63.9%), adenocarcinoma (19.4%), carcinoid (6.9%), adenosquamous carcinoma (3.4%), and sarcomatoid carcinoma (2.8%). One (2.8%) late mortality was due to systemic recurrence of sarcomatoid carcinoma. There was no (0.0%) anastomotic failure. The mean number of dissected lymph nodes were 27.4 ± 13.2 , and mean operation time was 216.8 ± 60.0 min. Median postoperative 24-h drain amount was 315 mL. Median chest tube days and hospital days were 4 and 6, respectively. Two patients (5.6%) had complications greater than Clavien-Dindo grade II-one case of ARDS, and the other case of a delayed bronchopleural fistula. **CONCLUSIONS:** Thoracoscopic sleeve resection and bronchoplasty utilizing

HD 3D thoracoscope is a safe and effective procedure with excellent early clinical outcomes. Further investigation for long-term outcomes will be needed.

What Should Thoracic Surgeons Consider during Surgery for Ground-Glass Nodules?: Lymph

Node Dissection J Chest Surg. 2021 Oct 5;54(5):342-347. doi: 10.5090/jcs.21.030. Hong Kwan Kim 1
Thoracic surgeons need to be aware of several important points regarding intraoperative lymph node dissection during surgery for non-small cell lung cancer with ground-glass opacities. The first point relates to the need for lymph node dissection during sublobar resection. Since even patients undergoing sublobar resection may benefit from lymph node dissection, it should be selectively performed according to adequate indications, which require further study. Second, there seems to be no difference in postoperative morbidity between systematic sampling and systematic dissection, but the survival benefit from systematic dissection remains unclear. The results of randomized controlled trials on this topic are conflicting, and their evidence is jeopardized by a high risk of bias in terms of the study design. Therefore, further randomized controlled trials with a sound design should investigate this issue. Third, more favorable survival outcomes tend to be positively associated with the number of examined lymph nodes. Minimum requirements for the number of examined lymph nodes in non-small cell lung cancer should be defined in the future. Finally, lobe-specific lymph node dissection does not have a negative prognostic impact. It should not be routinely performed, but it can be recommended in selected patients with smaller, less invasive tumors. Results from an ongoing randomized controlled trial on this topic should be awaited.

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

Non-small cell lung cancer: Emerging molecular targeted and immunotherapeutic agents Biochim Biophys Acta Rev Cancer. 2021 Dec;1876(2):188636. doi: 10.1016/j.bbcan.2021.188636. Epub 2021 Oct 14. Takshveer Singh 1 , Mortaza Fatehi Hassanabad 1 , Ali Fatehi Hassanabad 2

Abstract

Non-small cell lung cancer (NSCLC) represents the most common and fatal type of primary lung malignancies. NSCLC is often diagnosed at later stages and requires systemic therapies. Despite recent advances in surgery, chemotherapy, and targeted molecular therapies the outcomes of NSCLC remain disproportionately poor. Immunotherapy is a rapidly developing area in NSCLC management and presents opportunities for potential improvements in clinical outcomes. Indeed, different immunotherapeutics have been approved for clinical use in various settings for NSCLC. Their promise is especially poignant in light of improved survival and quality of life outcomes. Herein, we comprehensively review emerging NSCLC therapeutics. We discuss the limitations of such strategies and summarize the present status of various immunotherapeutic agents in key patient populations. We also examine the data from ongoing studies in immunotherapy and consider future areas of study, including novel inhibition targets, therapeutic vaccination, tumor genome modification, and improvements to drug delivery systems.

Aneuploid Circulating Tumor Cells as a Predictor of Response to Neoadjuvant Chemotherapy in Non-Small Cell Lung Cancer Int J Gen Med. 2021 Oct 11;14:6609-6620. doi: 10.2147/IJGM.S330361.

eCollection 2021. Miao Huang # 1 , Yuanyuan Ma # 1 , Chao Lv 1 , Shaolei Li 1 , Fangliang Lu 1 , Shanyuan Zhang 1 , Daisy Dandan Wang 2 , Peter Ping Lin 2 , Yue Yang 1

PURPOSE: This study aimed to explore the potential application of circulating tumor cells (CTCs) in predicting the therapeutic effect of neoadjuvant chemotherapy (NAC) in non-small-cell lung cancer (NSCLC). **METHODS:** Using integrated subtraction enrichment and immunostaining-fluorescence in situ hybridization, the serial CTCs of patients with NSCLC were detected in 7.5 mL of blood at baseline

and after two cycles of cisplatin-based NAC, and all aneuploidies of chromosome 8 were examined in the enriched CTCs. Tumor responses were evaluated radiologically with serial chest computed tomography (CT) using the response evaluation criteria in solid tumors and microscopically using the tumor cell necrosis rate (TCNR) of the resected specimen after NAC. **RESULTS:** After two cycles of cisplatin-based NAC, 89% (8/9) of the patients with radiological partial response to NAC had reduced CTC numbers, while 73% (8/11) of the patients with stable disease exhibited increased CTC numbers ($P = 0.0098$). On pathological examination, 90% (9/10) of patients with a TCNR lower than 30% had >1 CTC post-NAC, while 80% (4/5) of patients with a TCNR higher than 30% had ≤ 1 CTC post-NAC ($P = 0.017$). In aneuploidy analysis, the positive rate (CTC > 0) of triploid CTCs was found to have increased after NAC, in contrast with the tetraploid and multiploid CTCs. Furthermore, tetraploid and multiploid CTCs were found to be significantly downregulated in the patients with partial response to NAC. **CONCLUSION:** The correlations of aneuploid CTCs with both radiological and pathological responses in patients with NSCLC who received NAC were summarized, and the findings indicate that enumerating and karyotyping aneuploid CTCs can serve as a surrogate marker for disease monitoring in NSCLC..

[Treating disease progression with osimertinib in EGFR-mutated non-small-cell lung cancer: novel targeted agents and combination strategies](#) ESMO Open. 2021 Oct 8;6(6):100280. doi:

10.1016/j.esmoop.2021.100280. Online ahead of print. V Di Noia 1, A D'Aveni 2, E D'Argento 3, S Rossi 4, P Ghirardelli 2, L Bortolotti 2, V Vavassori 2, E Bria 5, G L Ceresoli 2

A precision medicine approach has been successfully applied in medical oncology for the treatment of non-small-cell lung cancer (NSCLC) through the identification of targetable driver molecular aberrations; activating mutations of epidermal growth factor receptor (EGFR) are the most common. Osimertinib, a third-generation, wild-type sparing, irreversible EGFR tyrosine kinase inhibitor (TKI), originally showed a striking activity after progression to first- and second-generation EGFR-TKIs when T790M resistance mutation was identified. Thereafter, upfront use of osimertinib became the standard of care based on overall survival benefit over first-generation TKIs erlotinib and gefitinib as reported in the FLAURA trial. For patients progressing on osimertinib, identification of resistance mechanisms is crucial to develop novel targeted therapeutic approaches. Moreover, innovative drugs or combination therapies are being developed for cases in which a specific resistance mechanism is not identifiable. In this review, the post-osimertinib treatment options for EGFR-mutated NSCLC are analyzed, with an outlook to ongoing clinical trials. An algorithm to guide clinicians in managing progression on osimertinib is proposed.

[Immunotherapy in the frontline management of advanced and metastatic NSCLC](#) Am J Manag Care. 2021 Oct;27(18 Suppl):S323-S332. doi: 10.37765/ajmc.2021.88769. Eve M Segal 1

The frontline treatment paradigm for patients with advanced or metastatic non-small cell lung cancer (NSCLC) has changed dramatically in the past decade amid efforts to tackle this leading cause of cancer-related mortality. Immune checkpoint inhibitors (ICIs) targeting the programmed cell death protein 1 (PD-1) receptor and its ligand PD-L1 are an important therapeutic option for patients whose tumors lack genetic alterations that dictate response to molecularly targeted therapies. With a growing number of FDA-approved ICI monotherapy and combination therapy options for first-line therapy, the use of biomarkers such as PD-L1 expression has become increasingly important in guiding therapeutic decision making. Presently, PD-L1 expression remains a key biomarker in this setting, in spite of its limitations. This article will evaluate the current and evolving clinical trends in the use of ICIs in the frontline management of metastatic NSCLC, as well as the challenges associated with PD-L1 expression analysis and biomarker implementation.

[Factors affecting the efficacy and safety of docetaxel combined with platinum in the treatment of advanced non-small cell lung cancer](#) Expert Rev Clin Pharmacol. 2021 Oct;14(10):1295-1303. doi:

10.1080/17512433.2021.1976638. Epub 2021 Sep 24. FengLi Wang 1 , ChenYang Zhao 1 , Xin Wen 2 , Qingshan Zheng 1 , Lujin Li 1

BACKGROUND: This study aimed to quantitatively evaluate factors influencing the efficacy and safety of the docetaxel-platinum regimen to provide reliable information for optimizing chemotherapy regimens. Research design and **METHODS:** A parametric survival function model was used to describe the time course of overall survival (OS) of patients with advanced non-small cell lung cancer (NSCLC) receiving a docetaxel-platinum regimen. A random-effects model in a single-arm meta-analysis was used to analyze the objective response rate and grade 3-4 adverse event rates based on various docetaxel-platinum regimens. **RESULTS:** The model revealed that the risk of death in East Asians was approximately 1.5-fold higher than that in non-East Asians, with a median OS of 13.7 (95% confidence interval [CI]: 12.8-14.7) months and 9.3 (95% CI: 7.7-11.1) months, respectively. No significant impact of different administration regimens on OS was found. However, when drug exposure increased, the incidence of grade 3-4 anemia or neutropenia significantly increased. **CONCLUSIONS:** The docetaxel-platinum regimen has different efficacies in the treatment of advanced NSCLC between East Asian and non-East Asian populations. A better benefit-risk ratio can be obtained with a lower exposure regimen of docetaxel combined with platinum.

[Major breakthroughs in lung cancer adjuvant treatment: Looking beyond the horizon](#) Cancer Treat Rev. 2021 Dec;101:102308. doi: 10.1016/j.ctrv.2021.102308. Epub 2021 Oct 18.

Francesco Passiglia 1 , Valentina Bertaglia 2 , Maria Lucia Reale 3 , Marco Donatello Delcuratolo 2 , Fabrizio Tabbò 2 , Emanuela Olmetto 2 , Enrica Capelletto 4 , Paolo Bironzo 5 , Silvia Novello 6
We are witnessing a silent revolution in the treatment of early stage non-small cell lung cancer (NSCLC), with a series of practice-changing clinical trials enriching the therapeutic perspectives of lung cancer patients with potentially curable disease. The ADAURA study marked the advent of precision medicine and biomarker testing to the early stages setting. The IMPower-010 trial interrupted the negative trend of adjuvant lung cancer immunotherapy, paving the way to the application of immune-checkpoint inhibition in the resected disease. The ITACA trial definitively established no role for tailored adjuvant chemotherapy in NSCLC, while the Lung Art data questioned the efficacy of post-operative radiotherapy for pN2 resected disease. Growing evidence is supporting MRD as effective adjuvant prognostic biomarker to stratify disease's recurrence risk after radical interventions and select best candidates to the adjuvant strategies. This work summarizes the recent major breakthroughs in lung cancer adjuvant treatment, and provides a snapshot of the current real-world scenario, discussing the upcoming challenges and opportunities featuring the clinical management of early stage NSCLC patients.

[Prognostic factors of patients with advanced lung cancer treated with anlotinib: a retrospective cohort study](#) J Int Med Res. 2021 Oct;49(10):3000605211046173. doi: 10.1177/03000605211046173.

Bijun Fan 1 , Xiaoming Tan 1 , Yueyan Lou 1 , Yu Zheng 1 , Liyan Zhang 1 , Xuelling Wu 1
OBJECTIVE: Our study aimed to evaluate the main factors affecting the efficacy of anlotinib to determine the therapeutically dominant populations. **METHODS:** The medical records of patients with lung cancer who were treated with anlotinib from July 2018 to February 2020 at Renji Hospital, School of Medicine, Shanghai Jiaotong University were retrospectively reviewed. The optimal cutoff prognostic nutritional index (PNI) value for predicting efficacy was determined according to receiver operating characteristic curves. Progression-free survival (PFS) and overall survival (OS) were calculated and compared using the Kaplan-Meier method and log-rank test. The prognostic values of each variable were evaluated with univariate and multivariate Cox proportional hazard regression analyses. **RESULTS:** The overall disease control rate of 44 patients with lung cancer was 93.2% (41/44). The median PFS was 5.0 months (95% [confidence interval] CI: 2.2-7.8), and the median OS was 6.5 months (95% CI: 3.6-9.3). The multivariate analysis results indicated that hand-foot syndrome and high PNI values were

independent protective factors of PFS and OS. **CONCLUSIONS:** Anlotinib was effective in treating locally advanced or advanced lung cancer. High pretreatment PNI scores and the presence of hand-foot syndrome after treatment were independent prognostic markers for favorable OS and PFS.

[Dynamic functional network connectivity reveals the brain functional alterations in lung cancer patients after chemotherapy](#) Brain Imaging Behav. 2021 Oct 31. doi: 10.1007/s11682-021-00575-9.

Online ahead of print. Lanyue Hu # 1, Shaohua Ding # 2, Yujie Zhang 1, et al.

This study aimed to investigate alterations of brain functional network connectivity (FNC) in lung cancer patients after chemotherapy and explore links between these FNC differences and cognitive impairment. Twenty-two lung cancer patients receiving chemotherapy and 26 healthy controls (HCs) underwent resting-state functional MRI (rs-fMRI) and neuropsychological testing. Group independent component analysis (GICA) was applied to rs-fMRI data to extract whole-brain resting state networks (RSNs). Static and dynamic FNC (dFNC) were constructed to reveal RSNs connectivity alterations between lung cancer patients and HCs group, and the correlations between the group differences in RSNs and cognitive performance were analyzed. Our findings revealed that chemotherapeutics can produce widespread connectivity abnormalities in RSNs, mainly focused on default mode network (DMN) and executive control network. Furthermore, the dFNC analysis help identify network configurations of each state and capture more chemotherapy-induced disorders of interactions between and within RSNs, which mainly includes sensorimotor network, attentional network and auditory network. In addition, after chemotherapy, the lung cancer patients spend shorter mean dwell time (MDT) in state 2. The decreased dFNC between DMN [independent component 5 (IC5)] and DMN (IC6) in the lung cancer patients after chemotherapy in state 4 was negatively correlated with Montreal Cognitive Assessment (MoCA) scores ($r=-0.447$, $p=0.042$). The dFNC analysis enrich our understanding of the neural mechanisms underlying the chemobrain, and suggested that the temporal dynamics of FNC could be a potential effective method to detect cognitive changes in lung cancer patients receiving chemotherapy.

[The impact of immune checkpoint inhibitors on cost and quality of life in the initial treatment of patients with advanced or metastatic NSCLC](#) Am J Manag Care. 2021 Oct;27(18 Suppl):S333-S339.

doi: 10.37765/ajmc.2021.88770. Kelly Procailo 1

Immune checkpoint inhibitors (ICIs) represent a significant benefit for the initial treatment of patients with advanced or metastatic non-small cell lung cancer (NSCLC). Beyond clinical benefit of increased overall survival, it represents a class of medications with a favorable adverse effect profile compared with chemotherapy. Drugs that target programmed cell death protein 1 (PD-1) receptor and its ligand PD-L1 are ICIs that work by taking the brakes off the immune system and promote T-cell-mediated cancer cell destruction. Current NCCN guidelines recommend that all patients with advanced or metastatic NSCLC have their PD-L1 status (amount of PD-L1 on cancer cells) assessed to guide treatment selection. However, this recommendation is not always followed and may lead to inappropriate treatment selection and potential increased cost. Through appropriate biomarker testing, subsequent appropriate utilization of ICIs may help to drive down other costs and improve health-related quality of life. Managed care pharmacists should continue to focus on promotion of guideline concordant care that includes appropriate biomarker testing and selection of an evidence-based preferred treatment option.

[Long-Term Favorable Outcome With Nivolumab in a Case of Advanced Non-Small Cell Lung Cancer: A Case Report](#) Cureus. 2021 Oct 6;13(10):e18526. doi: 10.7759/cureus.18526. eCollection

2021 Oct. Vijay Ketan Reddy 1, Dhan B Shrestha 1, Suman Gaire 2, Wasey Ali Yadullahi Mir 1, Mohammed Kassem 3

Non-small cell lung cancer (NSCLC) constitutes around 85% of lung cancer cases. Advanced non-small cell lung cancer has a poor prognosis. Immunotherapy plays a pivotal role in managing advanced non-

small cell lung cancer not positive for driver mutations. Nivolumab is a monoclonal antibody against programmed death-ligand 1 (PDL1). It is approved as a second-line treatment for patients with advanced non-small cell lung cancer who progress on or after chemotherapy. We present a case of a 71-year-old female with advanced non-small cell lung cancer without any driver mutations diagnosed four years ago. Her disease progressed while on conventional chemotherapy, and she was started on nivolumab three and a half years ago. Her lung nodules resolved, she did not show signs of progression, and her performance status improved while on nivolumab. This case report highlights the current role of nivolumab in the management of NSCLC. Patients whose condition worsens while on conventional chemotherapy can respond very well to modern targeted immunotherapy.

NSCLC - RADIOTHERAPY

[Development and validation of a prognostic model for non-lung cancer death in elderly patients treated with stereotactic body radiotherapy for non-small cell lung cancer](#) J Radiat Res. 2021 Oct 6;rrab093. doi: 10.1093/jrr/rrab093. Online ahead of print. Hideki Hanazawa 1 , Yukinori Matsuo 1 , Atsuya Takeda 2 , Yuichiro Tsurugai 2 , Yusuke Iizuka 1 , Noriko Kishi 1 , Keiichi Takehana 1 , Takashi Mizowaki 1

This study sought to develop and validate a prognostic model for non-lung cancer death (NLCD) in elderly patients with non-small cell lung cancer (NSCLC) treated with stereotactic body radiotherapy (SBRT). Patients aged ≥ 65 diagnosed with NSCLC (Tis-4N0M0), tumor diameter ≤ 5 cm and SBRT between 1998 and 2015 were retrospectively registered from two independent institutions. One institution was used for model development (arm D, 353 patients) and the other for validation (arm V, 401 patients). To identify risk factors for NLCD, multiple regression analysis on age, sex, performance status (PS), body mass index (BMI), Charlson comorbidity index (CCI), tumor diameter, histology and T-stage was performed on arm D. A score calculated using the regression coefficient was assigned to each factor and three risk groups were defined based on total score. Scores of 1.0 (BMI ≤ 18.4), 1.5 (age ≥ 5), 1.5 (PS ≥ 2), 2.5 (CCI 1 or 2) and 3 (CCI ≥ 3) were assigned, and risk groups were designated as low (total ≤ 3), intermediate (3.5 or 4) and high (≥ 4.5). The cumulative incidences of NLCD at 5 years in the low, intermediate and high-risk groups were 6.8, 23 and 40% in arm D, and 23, 19 and 44% in arm V, respectively. The AUC index at 5 years was 0.705 (arm D) and 0.632 (arm V). The proposed scoring system showed usefulness in predicting a high risk of NLCD in elderly patients treated with SBRT for NSCLC.

[Stereotactic body radiotherapy to the primary lung lesion improves the survival of the selected patients with non-oligometastatic NSCLC harboring EGFR activating mutation with first-line EGFR-TKIs: a real-world study](#) J Cancer Res Clin Oncol. 2021 Oct 20. doi: 10.1007/s00432-021-03831-z. Online ahead of print. Hao Wei # 1 , Xiaojuan Zhou # 1 , Hui Yang 1 2 , et al.

PURPOSE: This study aimed to explore the clinical value of SBRT for primary lung lesions of EGFR-mutant NSCLC patients with non-oligometastatic disease during first-line EGFR-TKI treatment.

METHODS: We identified patients with stage IV EGFR-mutant non-oligometastatic NSCLC who were suitable to receive SBRT for the primary tumors after EGFR-TKI treatment. All selected patients were treated with first-line EGFR-TKIs and SBRT for their primary lesions. The primary endpoints were the progression-free survival 1 (PFS1, time of first TKI dose relative to disease progression based on RECIST) and PFS2 (time of first TKI dose relative to disease progression after SBRT). The secondary endpoints were overall survival (OS) and safety. **RESULTS:** Seventy-nine patients were enrolled, including 45 patients who received SBRT for their primary tumor at the maximal response of EGFR-TKI (the preemptive RT group) and 34 patients who received SBRT for their primary tumor after the occurrence of oligoprogression (the delayed RT group). The preemptive RT group had a significantly

better median PFS1 than the delayed RT group (22.3 months vs. 12.9 months, $P = 0.0031$). The median PFS2 in the preemptive RT and delayed RT groups were 22.3 and 28.9 months, respectively ($P = 0.17$). The median OS did not differ significantly between the preemptive RT group and the delayed RT group (46.6 versus 51.3 months, $P = 0.54$). No severe toxicities (\geq grade 3) were recorded. **CONCLUSION:** This real-world study showed that preemptive RT to primary lung tumors is a feasible option for selected patients with EGFR-mutant non-oligometastatic NSCLC who had stable disease during first-line EGFR-TKI treatment, and that it significantly improved PFS.

Combined treatment of non-small cell lung cancer using radiotherapy and immunotherapy: challenges and updates

Cancer Commun (Lond). 2021 Oct 17. doi: 10.1002/cac2.12226. Online ahead of print. Shijie Shang ¹, Jie Liu ², Vivek Verma ³, Meng Wu ², James Welsh ³, Jinming Yu ^{1 2}, Dawei Chen ^{1 2}

The efficacy of immunotherapy for advanced non-small cell lung cancer (NSCLC) remains unsatisfactory, as the majority of patients either do not experience an objective response or acquire secondary resistance. As a result, several methods to enhance the systemic efficacy of immunotherapy have been investigated, including a large area of active research by combining immunotherapy with radiation therapy (RT). Given the rapidly burgeoning concept of combining immunotherapy and RT for increasing therapeutic benefit, we review the progress in this field thus far and explore further avenues for enhancing this combination. This review commences with a discussion of the only two existing randomized trials (and a pooled analysis) showing that the addition of RT to immunotherapy improves the abscopal response rate, progression-free survival, and overall survival in metastatic NSCLC patients. We then discussed factors and biomarkers that may be associated with a proportionally greater benefit to additional RT, such as low programmed cell death protein ligand 1 (PD-L1) status, tumor mutational burden (TMB), and patient's immune function. Next, the implementation of RT to overcome immunotherapy resistance is discussed, including a mechanistic discussion and methods with which these mechanisms could be exploited. Lastly, the emerging role of low-dose RT is discussed, which may help to overcome inhibitory signals in the tumor stroma that limit T-cell infiltration. Taken together, given the current state of this rapidly expanding realm, these futuristic strategies may be reflected upon to further enhance the efficacy of immunotherapy for a wider group of patients.

Split course palliative radiotherapy for advanced lung cancer with 3D planning based analysis of outcome: a retrospective review

Ann Palliat Med. 2021 Oct 22;apm-21-1589. doi: 10.21037/apm-21-1589. Online ahead of print. Andrew R Bruggeman ¹, Reith R Sarkar ¹, Grace Sora Ahn ¹, Emily I Fuster ¹, Anna Dornisch ¹, Andrew B Sharabi ¹, James D Murphy ¹, Ajay P Sandhu ¹

BACKGROUND: Durable palliation of advanced lung cancer is a common objective for radiation oncologists. However, there is no consensus on how to deliver the radiation course. Herein we report our experience of using split course radiotherapy and our assessment of outcomes based on planning from three-dimensional (3D) simulation before each treatment course. **METHODS:** All lung cancer patients from 2006-2020 were identified. Of these, 52 patients received a split course treatment of 50-60 Gy in 18-25 fractions intended to provide durable palliation for disease not amenable to curative therapy. Treatment involved 3D planning with repeat computed tomography (CT) simulation prior to the second course. Survival and symptomatic response were analyzed via chart review. We categorized rapid responders versus non-rapid responders from the initial radiation course based on $\geq 30\%$ gross tumor volume (GTV) reduction at the second CT simulation. We evaluated the impact of response on overall survival and palliative response. **RESULTS:** Among our cohort treated with split course palliative radiotherapy, 33 (63%) had a rapid response to initial treatment. There was no difference in survival between groups [hazard ratio (HR) =1.30, $P=0.47$]. There was no significant difference in palliative response rates between rapid and non-rapid responders. On multivariable analysis, only female sex (HR =0.26, $P<0.01$)

and receipt of systemic therapy following radiotherapy (HR =0.19, P<0.01) were associated with improved survival. **CONCLUSIONS:** There is currently significant practice pattern variability for palliative lung radiotherapy. Split course palliative radiation of 50-60 Gy in 18-25 fractions represents an option to consider for patients with advanced lung cancer who do not undergo definitive therapy and may benefit from a higher dose regimen. Our retrospective review suggests that rapid tumor response in a split course model does not predict survival or symptomatic response. Prospective studies are needed to further define which lung cancer patients may benefit from higher dose regimens.

Immunotherapy in association with stereotactic radiotherapy for non-small cell lung cancer brain metastases: results from a multicentric retrospective study on behalf of AIRO Neuro Oncol. 2021 Oct 1;23(10):1750-1764. doi: 10.1093/neuonc/noab129. Silvia Scoccianti 1, Emanuela Olmetto 2, Valentina Pinzi 3, et al.

BACKGROUND: To define efficacy and toxicity of Immunotherapy (IT) with stereotactic radiotherapy (SRT) including radiosurgery (RS) or hypofractionated SRT (HFSRT) for brain metastases (BM) from non-small cell lung cancer (NSCLC) in a multicentric retrospective study from AIRO (Italian Association of Radiotherapy and Clinical Oncology). **METHODS:** NSCLC patients with BM receiving SRT + IT and treated in 19 Italian centers were analyzed and compared with a control group of patients treated with exclusive SRT. **RESULTS:** One hundred patients treated with SRT + IT and 50 patients treated with SRT-alone were included. Patients receiving SRT + IT had a longer intracranial Local Progression-Free Survival (iLPFS) (propensity score-adjusted P = .007). Among patients who, at the diagnosis of BM, received IT and had also extracranial progression (n = 24), IT administration after SRT was shown to be related to a better overall survival (OS) (P = .037). A multivariate analysis, non-adenocarcinoma histology, KPS = 70 and use of HFSRT were associated with a significantly worse survival (P = .019, P = .017 and P = .007 respectively). Time interval between SRT and IT ≤7 days (n = 90) was shown to be related to a longer OS if compared to SRT-IT interval >7 days (n = 10) (propensity score-adjusted P = .008). The combined treatment was well tolerated. No significant difference in terms of radionecrosis between SRT + IT patients and SRT-alone patients was observed. The time interval between SRT and IT had no impact on the toxicity rate. **CONCLUSIONS:** Combined SRT + IT was a safe approach, associated with a better iLPFS if compared to exclusive SRT.

Safety of thoracic radiotherapy after PD-(L)1 inhibitor treatment in patients with lung cancer Cancer Med. 2021 Oct 19. doi: 10.1002/cam4.4363. Online ahead of print. Yu Chen 1 2, Xinchao Liu 1 2, Zhaoqin Huang 3, Kaikai Zhao 4, Yao Wang 2, Fei Ren 2, Jinming Yu 1 2, Xiangjiao Meng 1 2

BACKGROUND: The safety of thoracic radiotherapy (TRT) after programmed death 1/programmed death ligand 1 (PD-(L)1) inhibitor treatment in patients with lung cancer was scarcely reported. This retrospective study was conducted to evaluate the incidence, severity, and risk factors of symptomatic treatment-related pneumonitis in patients with lung cancer who received this sequential combination. **METHODS:** We conducted a retrospective study of a cohort of patients with lung cancer who received TRT after at least two cycles of PD-(L)1 inhibitor treatment between January 2018 and August 2020. Treatment-related pneumonitis was evaluated and analyzed to illustrate the safety profile of this sequential combination. Potential risk factors were explored by univariate and multivariate logistic regression analyses. **RESULTS:** Among the 828 patients with prior PD-(L)1 inhibitor treatment, 96 patients receiving subsequent TRT were included in the analysis. Of these, 49 patients (51%) received radical TRT while 47 patients (49%) received palliative TRT. The median total dose was 52 Gy (IQR 50-60 Gy). The median time from the initiation of PD-(L)1 inhibitor treatment to TRT was 4.8 months (1.6-14.1 months) with most of the patients (74%) administering no less than four cycles of PD-(L)1 inhibitor. During follow-up, 47 patients (48.96%) developed symptomatic treatment-related pneumonitis (grade 2 n = 28, grade ≥3 n = 19) while six patients (6.25%) suffered from fatal toxicity. The median time of

pneumonitis onset after completion of TRT was 35 days (0-177 days) with six patients developing during TRT. Pulmonary emphysema and lung V20 were demonstrated to be independent risk factors of symptomatic pneumonitis (OR: 5.67, 95% CI: 1.66-19.37, $p = 0.006$; OR: 3.49, 95% CI: 1.41-8.66, $p = 0.007$, respectively). **CONCLUSION:** TRT after PD-(L)1 inhibitor treatment resulted in significantly increased incidence and severity of treatment-related pneumonitis in patients with lung cancer. Intensive attention should be emphasized to the safety of this sequential combination in clinical practice.

[Surgical complications and clinical outcomes after dose-escalated trimodality therapy for non-small cell lung cancer in the era of intensity-modulated radiotherapy](#) Radiother Oncol. 2021 Oct 22;165:44-51. doi: 10.1016/j.radonc.2021.10.012. Online ahead of print. Kevin X Liu ¹, Kailan Sierra-Davidson ², Kevin Tyan ³, Lawrence T Orlina ⁴, J Paul Marcoux ⁵, Benjamin H Kann ⁴, David E Kozono ⁴, Raymond H Mak ⁴, Abby White ⁶, Lisa Singer ⁷

BACKGROUND: Trimodality therapy (TMT) with preoperative chemoradiation followed by surgical resection is used for locally-advanced non-small-cell lung cancer (LA-NSCLC). Traditionally, preoperative radiation doses ≤ 54 Gy are used due to concerns regarding excess morbidity, but little is known about outcomes and toxicities after TMT with intensity-modulated radiotherapy (IMRT) to higher doses. **METHODS:** A retrospective analysis of patients who received planned TMT with IMRT for LA-NSCLC at Brigham and Women's Hospital/Dana-Farber Cancer Institute between 2008 and 2017 was performed. Clinical and treatment characteristics, pathologic response, and surgical toxicity were assessed. Kaplan-Meier method and log-rank test was used for survival outcomes. Cox proportional-hazards regression was used for multivariable analysis. **RESULTS:** Forty-six patients received less than definitive doses of < 60 Gy and 30 patients received definitive doses ≥ 60 Gy. Surgical outcomes, pathologic complete response, and postoperative toxicity did not differ significantly between the groups. With median follow-up of 3.6 years (range: 0.4-11.4), three-year locoregional recurrence-free survival (78.0% vs. 68.3%, $p = 0.51$) and overall survival (OS) (61.0% vs. 69.4%, $p = 0.32$) was not significantly different between patients receiving < 60 Gy and ≥ 60 Gy, respectively. On multivariable analysis, older age, clinical stage, and length of hospital stay (LOS) > 7 days were associated with OS.

CONCLUSIONS: With IMRT, there was no increased rate of surgical complications in patients receiving higher doses of radiation. Survival outcomes or LOS did not differ based on radiation dose, but increased LOS was associated with worse OS. Larger prospective studies are needed to further examine outcomes after IMRT in patients with LA-NSCLC receiving TMT.

SMALL CELL LUNG CANCER - SCLC

[Diagnostic and prognostic nomograms for bone metastasis in small cell lung cancer](#) J Int Med Res. 2021 Oct;49(10):3000605211050735. doi: 10.1177/03000605211050735. Chenan Liu ¹ ², Jiahong Yi ¹, Junmei Jia ²

OBJECTIVE: Patients with bone metastasis (BM) of small cell lung cancer (SCLC) have a poor prognosis. We aimed to identify predictors and prognostic factors in patients with BM of SCLC and construct nomograms to predict BM. **METHODS:** We retrospectively analyzed 18,187 cases from the Surveillance, Epidemiology, and End Results database reported between 2010 and 2016. Differences in overall survival (OS) and cancer-specific survival (CSS) were evaluated after propensity score matching. Independent predictors for BM and prognostic factors for patients with BM of SCLC were determined using univariate and multivariate regression analyses. Two nomograms were constructed and evaluated using C-statistics. **RESULTS:** BM was observed in 4014 (22.07%) patients. Kaplan-Meier survival analysis revealed significant differences between BM and non-BM groups. The median OS for patients with and without BM was 6 and 7 months, respectively. The median CSS for patients with and without BM was 9 and 13 months, respectively. Age, sex, tumor size, N stage, chemotherapy, surgery,

radiotherapy, and liver/brain/lung metastases were related to BM and independent prognostic factors for OS and CSS. Diagnostic and prognostic nomograms were generated. **CONCLUSION:** Our nomograms predicted the incidence of BM and the 5-month survival rate of patients with SCLC and BM.

[Chronic Pleuritis and Recurrent Pleural Effusion After Atezolizumab for Small Cell Lung Cancer](#)

Am J Case Rep. 2021 Oct 4;22:e933396. doi: 10.12659/AJCR.933396. Julie Lin 1 , Bruce Fernando Sabath 1

BACKGROUND: As use of immune checkpoint inhibitors consistently grows, so does knowledge of immune-related adverse events. Pleural complications from PD-L1 inhibitors such as atezolizumab have never been reported. We describe the first reported case of biopsy-proven pleuritis manifesting as recurrent pleural effusion in a patient treated with atezolizumab. **CASE REPORT:** A 66-year-old woman with history of extensive-stage small cell lung cancer presented with a new pleural effusion. She was previously treated with carboplatin, etoposide, and atezolizumab followed by atezolizumab maintenance, but this later was stopped due to pneumonitis. She had been on no systemic therapy for 6 months prior; radiation to the chest was completed 1 year earlier. Thoracentesis revealed an exudate with eosinophilia but no malignancy. She underwent medical thoracoscopy, which showed normal pleura with no evidence of radiation changes. Random pleural biopsies revealed only chronic pleuritis. Given normal-appearing pleura, radiation pleuritis was ruled out. It was felt that the chemotherapy had occurred too long ago to be a present cause of her pleuritis. As such, after extensive workup, the eosinophilic pleural effusion was felt to be due to pleuritis from atezolizumab. The effusion has ultimately recurred 5 times over 1 year, and cytology remains negative for malignancy. **CONCLUSIONS:** Patients with prior cancer presenting with a new pleural effusion should undergo an extensive workup to evaluate for recurrence. When other causes have been ruled out, ongoing immune-related effects of immunotherapy should be considered. Pleural complications from PD-L1 inhibitors have not been reported; we present a possible case of chronic pleuritis and recurrent effusion due to atezolizumab.

[Immunotherapy for small cell lung cancer: established applications and novel approaches](#)

Clin Adv Hematol Oncol. 2021 Oct;19(10):654-663. Susan C Scott 1 , Christine L Hann 1

Small cell lung cancer (SCLC) is a devastating disease that has a case fatality rate of more than 90% despite best available treatments. As a result, patients with SCLC are in critical need of improved therapeutic approaches. Immunotherapies, in particular immune checkpoint inhibitors (ICIs), have transformed the treatment of many cancers and are of great interest in SCLC. In recent years, the addition of anti-programmed death ligand 1 (PD-L1) inhibitors to frontline platinum-based chemotherapy in extensive-stage SCLC has improved survival, and combination chemoimmunotherapy is now approved as the standard of care. ICIs are also under investigation in other settings, including as consolidation therapy in limited-stage SCLC following chemoradiation and in combination with chemoradiation. PD-L1 expression and tumor mutational burden are not reliably associated with ICI benefit in SCLC, and predictive biomarkers of ICI response in SCLC are actively sought. Novel immunotherapeutic approaches are under investigation in SCLC. Rational targets and combinations, which stem from investigations of SCLC biology and the immune tumor microenvironment, include combinations with inhibitors of TIGIT or LAG3; targeting alternative signaling pathways, such as DNA damage repair; and co-targeting SCLC-specific tumor antigens, such as fucosyl-GM1 and DLL3. This review summarizes approaches to immunotherapy in SCLC, including current evidence and approvals, as well as key questions and future directions.

[Immunotherapy in Extensive-Stage Small Cell Lung Cancer](#)

Curr Oncol. 2021 Oct 12;28(5):4093-4108. doi: 10.3390/currenol28050347. Rola El Sayed 1 , Normand Blais 1

Small cell lung cancer (SCLC) remains a poorly understood disease with aggressive features, high relapse rates, and significant morbidity as well as mortality, yet persistently limited treatment options. For three decades, the treatment algorithm of SCLC has been stagnant despite multiple attempts to find alternative therapeutic options that could improve responses and increase survival rates. On the other hand, immunotherapy has been a thriving concept that revolutionized treatment options in multiple malignancies, rendering previously untreatable diseases potentially curable. In extensive stage SCLC, immunotherapy significantly altered the course of disease and is now part of the treatment algorithm in the first-line setting. Nevertheless, the important questions that arise are how best to implement immunotherapy, who would benefit the most, and finally, how to enhance responses.

[Current state of the art and future perspectives with immunotherapy in the management of small cell lung cancer](#) Expert Rev Respir Med. 2021 Nov;15(11):1427-1435. doi: 10.1080/

17476348.2021.1987887. Epub 2021 Oct 15. Erika Rijavec ¹, Carlo Genova ², Federica Biello ³, Giovanni Rossi ⁴ ⁵, Alice Indini ¹, Francesco Grossi ⁶

INTRODUCTION: Small cell lung cancer (SCLC) is an aggressive tumor with a severe prognosis. At the time of diagnosis, most patients present with extensive-stage (ES) disease. For decades, platinum-based chemotherapy has been the only pillar of SCLC treatment, but now, the clinical management of this disease is rapidly evolving thanks to the introduction of immune checkpoint inhibitors (ICIs). **AREAS COVERED:** In this review, we describe the most recent advances in the treatment of SCLC and discuss the emerging challenges associated with ICI treatments. Meaningful data were collected from the currently available literature on PubMed and in international oncology meetings. Expert opinion: Recently, meaningful improvements in outcomes of SCLC patients have been achieved with anti-PD-L1 atezolizumab or durvalumab combined with chemotherapy in first line. **Results of studies** evaluating the role of ICIs in limited-stage (LS) SCLC patients are awaited. Further efforts are required to better understand the role of immunotherapy in the treatment of SCLC and to identify patients most likely to benefit from this treatment strategy.

[Treatment of small cell lung cancer: recent advances](#) Curr Opin Oncol. 2021 Oct 25. doi:

10.1097/CCO.0000000000000804. Online ahead of print. Xiangling Chu ¹, Chaonan Han, Chunxia Su

PURPOSE OF REVIEW: In this article, we aimed to summarize the recent progress being made in treatment of small cell lung cancer (SCLC). **RECENT FINDINGS:** SCLC is characterized by strong invasiveness, easy recurrence and early metastasis. In recent years, the emergence of immune checkpoint inhibitors (ICIs) therapy has broken the deadlock in the treatment field of SCLC. Combination strategies, such as the addition of ICIs to chemotherapy and radiotherapy, are actively underway. Some of these strategies have yielded significant survival benefits and tolerable adverse events, whereas several of them have failed with no significant improvement. In addition, the new classification of SCLC based on genomic analysis has deepened the understanding of SCLC and suggested new therapeutic directions. Similarly, the discovery of some new therapeutic targets, such as DDL3, CDK7 and PARP, also brings new hope for improving the survival of patients with SCLC. **SUMMARY:** In this article, we will review the recent advances of therapeutic regimen for patients with SCLC. Following the revolutionary success of adding ICIs to chemotherapy, more varieties of combination strategies have been explored in recent trials. In addition, therapeutic drug research and efficacy evaluation against for new targets are under investigation. Altogether, progress on genomic analysis, investigation of biological pathways and treatment regimen combination are providing renewed hope for patients with SCLC.

[The benefits and risks of pembrolizumab in combination with chemotherapy as first-line therapy in small-cell lung cancer: a single-arm meta-analysis of noncomparative clinical studies and randomized control trials](#) World J Surg Oncol. 2021 Oct 14;19(1):298. doi: 10.1186/s12957-021-02410-

3. Qiangyun Liu ^{1 2}, Yixuan Zhang ^{1 2}, Miaowen Liu ^{2 3}, Ruoxin Xu ^{2 3}, Fengming Yi ³, Yiping Wei ¹, Shuqiang Zhu ⁴, Wenxiong Zhang ⁵

BACKGROUND: Although pembrolizumab has shown clinical benefit in patients with small-cell lung cancer (SCLC), its actual efficacy in combination with a conventional chemotherapy drug has not been determined. We performed this study to discern the efficacy and risk of pembrolizumab in combination with chemotherapy as first-line therapy in SCLC patients. **METHODS:** We systematically searched the PubMed, ScienceDirect, Cochrane Library, Scopus, Ovid MEDLINE, Embase, Web of Science, and Google Scholar databases for relevant studies. The main outcomes were overall survival (OS) and progression-free survival (PFS). **RESULTS:** We identified 2980 articles and included 6 studies (5 were noncomparative open-label studies and 1 was a randomized controlled trial [RCT]) involving 396 patients in our meta-analysis. The pooled median OS (mOS) was 9.6 months (95% CI, 8.0-11.2), and the pooled median PFS (mPFS) was 4.2 months (95% CI, 2.2-6.1). The 1-year overall survival rate (OSR-1y) and 6-month progression-free survival rate (PFSR-6m) were 45.1% (95% CI, 33-57.2%) and 41.6% (95% CI, 24.3-59%), respectively. The objective response rate (ORR) was 38.8% (95% CI, 11.9-65.67%), disease control rate (DCR) was 69.30% (95% CI, 51.6-87.0%), complete response (CR) was 2.20% (95% CI, 0.8-3.7%), partial response (PR) was 34.70% (95% CI, 7.8-61.5%), and stable disease (SD) was 20.90% (95% CI, 9.1-32.6%). The grade 3-4 adverse effect (AE) rate was 20.88% (95% CI, 1.22-54.85%). The most common AEs were neutropenia (90.16%), anemia (53.21%), dysphagia (41.96%), platelet count decrease (34.87%), and esophagitis (32.89%); severe AEs included neutropenia, respiratory failure, pneumonitis, acute coronary syndrome, and colitis/intestinal ischemia. **CONCLUSIONS:** The combination of pembrolizumab with conventional chemotherapy is an effective therapeutic schedule with acceptable and manageable efficacy and toxicity in patients with SCLC. More high-quality and well-designed RCTs with large sample sizes are warranted to further validate our findings.

[Optimizing Whole Brain Radiotherapy Treatment and Dose for Patients With Brain Metastases From Small Cell Lung Cancer](#)

Front Oncol. 2021 Oct 25;11:726613. doi: 10.3389/fonc.2021.726613. eCollection 2021. Hanming Li ¹, Wang Li ², Chao Qi ¹, Lu Zhou ², Fengyun Wen ², Yanli Qu ², Hong Yu ²

PURPOSE: This study aimed to evaluate the survival outcomes of whole brain radiotherapy (WBRT) compared to whole brain radiotherapy plus local radiation boost (WBRT + boost), and further identify whether higher biologically effective dose (BED) of WBRT + boost translates into a survival benefit in small cell lung cancer (SCLC) patients with brain metastasis (BM). **METHODS:** SCLC patients with BM from January 1, 2012, to December 31, 2019, were retrospectively analyzed. Overall survival (OS) and intracranial progression-free survival (iPFS) were evaluated by the Kaplan-Meier method and compared by the log-rank test. Univariate and multivariate regression analyses of prognostic factors for OS were performed using Cox proportional hazards regression models. The cutoff value of BED was determined by the receiver operating characteristic (ROC) curve analysis. **RESULTS:** Among the 180 eligible patients, 82 received WBRT + boost and 98 received WBRT. Both OS and iPFS in the WBRT + boost group were significantly superior to those in the WBRT group (median OS: 20 vs. 14 months, $p = 0.011$; median iPFS: 16 vs. 10 months, $p = 0.003$). At a cutoff value of 58.35 Gy in the WBRT + boost group, 52 for the high-BED (>58.35 Gy) group, 30 for the low-BED (≤ 58.35 Gy) group. High BED was significantly associated with improved OS and iPFS compared with low BED in the WBRT + boost group (median OS: 23 vs. 17 months, $p = 0.002$; median iPFS: 17 vs. 10 months, $p = 0.002$). **CONCLUSIONS:** Compared with WBRT alone, WBRT + boost improved OS and iPFS in SCLC patients with BM. High BED (>58.35 Gy) for WBRT + boost may be a reasonable consideration for SCLC patients with BM.

[The Feasibility of Using Biomarkers Derived from Circulating Tumor DNA Sequencing as Predictive Classifiers in Patients with Small-Cell Lung Cancer](#) Cancer Res Treat. 2021 Oct 5. doi: 10.4143/crt.2021.905. Online ahead of print. Yu Feng 1 , Yutao Liu 1 , Mingming Yuan 2 , et al.

PURPOSE: To investigate the feasibility of biomarkers based on dynamic circulating tumor DNA (ctDNA) to classify small cell lung cancer (SCLC) into different subtypes. **Materials and METHODS:** Tumor and longitudinal plasma ctDNA samples were analyzed by next-generation sequencing of 1,021 genes. PyClone was used to infer the molecular tumor burden index (mTBI). Pre-treatment tumor tissues [T1] and serial plasma samples were collected (pre-treatment [B1], after two [B2], six [B3] cycles of chemotherapy and at progression [B4]). **RESULTS:** Overall concordance between T1 and B1 sequencing (n=30) was 66.5%, and 89.5% in the gene of RB1. A classification method was designed according to the changes of RB1 mutation, named as subtype I (both positive at B1 and B2), subtype II (positive at B1 but negative at B2), and subtype III (both negative at B1 and B2). The median progressive-free survival for subtype I patients (4.5 months [95%CI: 2.6-5.8]) was inferior to subtype II (not reached, p<0.0001) and subtype III (10.8 months [95%CI: 6.0-14.4], p=0.002). The median overall survival for subtype I patients (16.3 months [95%CI: 5.3-22.9]) was inferior to subtype II (not reached, p=0.01) and subtype III (not reached, p=0.02). Patients with a mTBI dropped to zero at B2 had longer median overall survival (not reached vs. 19.5 months, p=0.01). The changes of mTBI from B4 to B1 were sensitive to predict new metastases, with a sensitivity of 100% and a specificity of 85.7%. **CONCLUSION:** Monitoring ctDNA based RB1 mutation and mTBI provided a feasible tool to predict the prognosis of SCLC.

[Treatment and Prevention of Brain Metastases in Small Cell Lung Cancer](#) Am J Clin Oncol. 2021 Oct 11. doi: 10.1097/COC.0000000000000867. Online ahead of print. Rebekah Rittberg 1 , Shantanu Banerji, Julian O Kim, Shrinivas Rathod, David E Dawe

Central nervous system (CNS) metastasis will develop in 50% of small cell lung cancer (SCLC) patients throughout disease course. Development of CNS metastasis poses a particular treatment dilemma due to the accompanied cognitive changes, poor permeability of the blood-brain barrier to systemic therapy and relatively advanced state of disease. Survival of patients with untreated SCLC brain metastases is generally <3 months with whole brain radiotherapy used as first-line management in most SCLC patients. To prevent development of CNS metastasis prophylactic cranial irradiation (PCI) is recommended in limited stage disease, after response to chemotherapy and radiation, while PCI may be considered in extensive stage disease after favorable response to upfront treatment. Neurocognitive toxicity with whole brain radiotherapy and PCI is a concern and remains difficult to predict. The mechanism of toxicity is likely multifactorial, but a potential mechanism of injury to the hippocampus has led to hippocampal sparing radiation techniques. Treatment of established non-small cell lung cancer CNS metastases has increasingly focused on using stereotactic radiotherapy (SRS) and it is tempting to extrapolate these results to SCLC. In this review, we explore the evidence surrounding the prediction, prevention, detection, and treatment of CNS metastases in SCLC. We further review whether existing evidence supports extrapolating less toxic treatments to SCLC patients with CNS metastases and discuss trials that may shed more light on this question.

PALLIATIVE AND SUPPORTIVE CARE

[Engaging Patients with Late-Stage Non-Small Cell Lung Cancer in Shared Decision Making about Treatment](#) J Pers Med. 2021 Oct 1;11(10):998. doi: 10.3390/jpm11100998. Ronald E Myers 1 , Shailesh M Advani 2 , Pamela Myers 1 , et al.

Few treatment decision support interventions (DSIs) are available to engage patients diagnosed with late-stage non-small cell lung cancer (NSCLC) in treatment shared decision making (SDM). We designed a novel DSI that includes care plan cards and a companion patient preference clarification tool to assist in

shared decision making. The cards answer common patient questions about treatment options (chemotherapy, chemotherapy plus immunotherapy, targeted therapy, immunotherapy, clinical trial participation, and supportive care). The form elicits patient treatment preference. We then conducted interviews with clinicians and patients to obtain feedback on the DSI. We also trained oncology nurse educators to implement the prototype. Finally, we pilot tested the DSI among five patients with NSCLC at the beginning of an office visit scheduled to discuss treatment with an oncologist. Analyses of pilot study baseline and exit survey data showed that DSI use was associated with increased patient awareness of the alternatives' treatment options and benefits/risks. In contrast, patient concern about treatment costs and uncertainty in treatment decision making decreased. All patients expressed a treatment preference. Future randomized controlled trials are needed to assess DSI implementation feasibility and efficacy in clinical care.

[Psychological Symptom Trajectories and Non-Small Cell Lung Cancer Survival: A Joint Model](#)

[Analysis](#) Psychosom Med. 2021 Oct 9. doi: 10.1097/PSY.0000000000001027. Online ahead of print. 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 following 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; PHQ9) and anxiety symptoms (Generalized Anxiety Disorder-7; GAD7). Patients were reassessed every 1-to 2-months thru 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 two-year trajectory of depressive symptoms was significantly associated with cancer survival after adjustment for covariates [Hazard ratio = 1.09 per unit increase in PHQ9, 95% CI 1.03-1.15, p = 0.002]. Anxiety was marginally significant in the unadjusted (p = 0.053) but not the adjusted (p = 0.39) model. **CONCLUSIONS:** For the first time, joint model analyses test the interaction of a longitudinal trajectory of psychological symptoms, assessed from diagnosis through 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.

[Usefulness of Pulmonary Rehabilitation in Non-small Cell Lung Cancer Patients Based on Pulmonary Function Tests and Muscle Analysis Using Computed Tomography Images](#)

Cancer Res Treat. 2021 Oct 20. doi: 10.4143/crt.2021.769. Online ahead of print. Juwhan Choi ¹, Zepa Yang ², Jinhwan Lee ³, Jun Hee Lee ⁴, Hyun Koo Kim ⁴, Hwan Seok Yong ², Sung Yong Lee ¹

PURPOSE: The usefulness of rehabilitation in patients with reduced lung function before lung surgery remains unclear, and there is no adequate method for evaluating the effect of rehabilitation. We aimed to evaluate the usefulness of rehabilitation in patients with non-small cell lung cancer (NSCLC) undergoing lung cancer surgery. **MATERIALS AND METHODS:** We retrospectively analyzed the medical records of NSCLC patients at Korea University Guro Hospital between 2018 and 2020. Patients were divided into two groups depending on whether they underwent rehabilitation. Pulmonary function test (PFT) data and muscle determined using chest computed tomography (CT) images were analyzed. Because the baseline

characteristics were different between the two groups, propensity score matching was performed.

RESULTS: Of 325 patients, 75 (23.1%) and 250 (76.9%) were included in the rehabilitation and non-rehabilitation (control) groups, respectively. The rehabilitation group had a worse general condition at baseline. After propensity score matching, 45 patients remained in each group. Pulmonary function (forced expiratory volume in 1 s, %) ($p=0.001$) and the Hounsfield unit of erector spinae muscle ($p=0.001$) were better preserved in the rehabilitation group. Muscle loss of 3.4% and 0.6% was observed in the control and rehabilitation groups, respectively ($p=0.003$). In addition, the incidence of embolic events was lower in the rehabilitation group ($p=0.044$). **CONCLUSION:** Pulmonary rehabilitation is useful in patients with NSCLC undergoing lung surgery. Pulmonary rehabilitation preserves lung function, muscle and reduces embolic events after surgery. Pulmonary rehabilitation is recommended for patients with NSCLC undergoing surgery.

[A case series of morbid COPD exacerbations during immune checkpoint inhibitor therapy in cancer patients](#) Respir Med Case Rep. 2021 Oct 23;34:101541. doi: 10.1016/j.rmcr.2021.101541.

eCollection 2021. Viswam S Nair 1 2 , Keith Eaton 3 4 , A McGarry Houghton 1 2

BACKGROUND: Immune checkpoint inhibitor therapy is rapidly becoming front line adjuvant or primary therapy in a number of solid cancer types. Since many of these cancers are a result of tobacco smoking, a large number of these patients will have underlying comorbid conditions attributed to smoking such as Chronic Obstructive Pulmonary Disease (COPD). The effect of immune checkpoint inhibitor therapy on COPD is not well documented, and COPD exacerbations are not currently considered a pulmonary associated immune checkpoint inhibitor toxicity in current guidelines. Case presentation: We describe and summarize here a series of patients with prolonged and severe COPD exacerbations upon the initiation of immune checkpoint inhibitor therapy for cancers of the skin and lung without radiographic evidence of pneumonitis. **CONCLUSIONS:** COPD exacerbation from immune checkpoint inhibitor is not reported in the literature and is associated with prolonged and severe episodes without radiographic evidence of pneumonitis. Awareness of this potential morbid toxicity and research efforts to understand its etiology are required.

[Social support and outcomes in older adults with lung cancer](#) J Geriatr Oncol. 2021 Oct 7;S1879-4068(21)00210-1. doi: 10.1016/j.jgo.2021.09.009. Online ahead of print. Andrew Chambers 1 , Emily Damone 2 , Yi Tang Chen 3 , Kirsten Nyrop 4 , Allison Deal 5 , Hyman Muss 6 , Marjory Charlot 7

BACKGROUND: Insufficient social support is associated with increased mortality among older adults. Lung cancer is primarily a disease of older adults and is the leading cause of all cancer deaths. We assessed the association of social support with outcomes among older adults with lung cancer. Materials and **METHODS:** Adults age 65 and older with lung cancer with a completed geriatric assessment (GA) were assessed. Emotional social support (ES) and tangible (material, instrumental) support (TS) measures and patient characteristics were obtained from the GA. The electronic health record was used to extract clinical variables. Simple linear regression models evaluated the association between social support scales with patient and clinical factors. **RESULTS:** 79 adults were assessed. White race was positively associated with ES score ($p=.04$), while higher BMI ($p=.03$), depression ($p=.03$) and anxiety ($p=.02$) were associated with worse ES. Higher BMI was associated with higher/better TS score ($p=.02$) while living alone was associated with lower/worse TS score ($p=.03$). Completion of platinum-based doublet chemotherapy with immunotherapy as planned was associated with higher ES scores ($p=.02$) and higher TS scores ($p=.02$). Disease progression was associated with lower ES scores ($p=.03$). **CONCLUSION:** Social support may influence clinical outcomes in older adults with lung cancer. As lung cancer often portends to poor prognosis, social support may be an important prognostic indicator.

[The effect of progressive relaxation exercises on treatment-related symptoms and self-efficacy in patients with lung cancer receiving chemotherapy](#) Complement Ther Clin Pract. 2021 Nov;45:101488. doi: 10.1016/j.ctcp.2021.101488. Epub 2021 Oct 2. Kamile Kirca 1 , Sevinç Kutlutürk 2

BACKGROUND: Patients with lung cancer receiving chemotherapy experience many symptoms, simultaneously or separately, that limit their daily living activities. This study aimed to determine the effect of progressive relaxation exercises on treatment-related symptoms and self-efficacy in patients with lung cancer receiving chemotherapy. **MATERIALS AND METHODS:** This randomized controlled experimental study was conducted in a university hospital chemotherapy outpatient clinic in Turkey. The study sample consisted of 84 patients, randomly allocated to an experimental group (n = 42) and a control group (n = 42). The experimental group received applied training in progressive relaxation exercises using an MP3 player. The control group received only standard nursing interventions in the chemotherapy unit. Data were collected from patients using a personal information form, a telephone counseling follow-up form, the Memorial Symptom Assessment Scale and the Strategies Used by People to Promote Health Scale. Data collection tools were administered at four different times (at first interview and three times on the seventh day of the end of the chemotherapy cycle) and weekly telephone follow-ups were performed. **RESULTS:** The symptom scores (frequency, severity and level of distress) significantly decreased in the experimental group, compared with the control group (p = 0.0001). Similarly, self-efficacy scores significantly improved in the experimental group (p = 0.001). **CONCLUSION:** Progressive relaxation exercises were potentially effective in promoting symptom management and improving the level of self-efficacy. immunotherapy as planned was associated with higher ES scores (p=.02) and higher TS scores (p=.02). Disease progression was associated with lower ES scores (p=.03).

[Exercise training-induced adaptations in lung cancer patients who have undergone a lobectomy](#)

Exp Gerontol. 2021 Nov;155:111587. doi: 10.1016/j.exger.2021.111587. Epub 2021 Oct 9. Nicholas Harman 1 , Michael Lazio 2 , Reid Hayward 3

PURPOSE: To determine the safety and effectiveness of a prescribed, individualized, 12-week exercise intervention on cardiorespiratory function, muscular strength, and quality of life in lung cancer patients who have undergone a lobectomy. In addition, we sought to compare the exercise training response of lung cancer patients who have undergone a lobectomy to a population of cancer patients with all other cancers in order to examine the specific effects of a lobectomy when compared to cancer patients at large. **METHODS:** Participants were referred by a physician, and upon entry, completed an exercise-based assessment and surveys to assess various quality of life measures. Participants were divided into two groups: lung cancer patients having undergone a lobectomy (LOB, n = 9) or those diagnosed with all other cancers (AOC, n = 201). Participants underwent 12 weeks of supervised exercise based on an individualized exercise prescription. Measures of cardiorespiratory function, muscular strength, and quality of life were collected prior to the intervention and after 12 weeks of exercise training. **RESULTS:** Significant improvements to VO₂peak (p < 0.05) were seen in both groups. Significant improvements to muscular strength (p < 0.05) were seen in both groups for all measures aside from shoulder press in the LOB group. Both groups showed significant improvements to aspects of fatigue and quality of life (p < 0.05), but only the AOC group significantly improved in measures of depression (p < 0.05). **CONCLUSION:** Exercise-based rehabilitation is a safe and effective intervention for lung cancer survivors who have undergone a lobectomy. These individuals saw significant improvements in cardiorespiratory fitness, muscular strength, and quality of life. Although there were similarities in the pattern of these training-induced improvements for these groups, lung cancer patients undergoing a lobectomy consistently demonstrated lower absolute values when compared to patients with all other cancer diagnoses.

[Combined effects of acupuncture and auricular acupressure for relieving cancer-related fatigue in patients during lung cancer chemotherapy: A protocol for systematic review and meta-analysis](#)

Medicine (Baltimore). 2021 Oct 22;100(42):e27502. doi: 10.1097/MD.00000000000027502.

Han Li ¹, Huan Liu ²

BACKGROUND: Increasing attention has been paid to acupuncture and auricular acupressure as alternative strategies for cancer related fatigue (CRF) management. Therefore, we design this systematic review and meta-analysis to explore the efficacy and safety of acupuncture and auricular acupressure for relieving CRF in patients during lung cancer chemotherapy. **METHODS:** From the inception to August 2021, the Web of Science, EMBASE, PubMed, and Cochrane Library electronic databases were searched using the key phrases "acupuncture", "auricular acupressure", and "lung cancer" for all relevant trials. Trials that compared acupuncture (including electroacupuncture) and auricular acupressure with acupuncture alone were included. The primary outcome was the measurement of the CRF symptoms. Secondary outcome measures were physical activity, quality of life, and adverse events. A P value of <.05 was considered to be statistically significant. **RESULTS:** It will be the first such study and will obtain evidence for utilizing acupuncture and auricular acupressure for lung cancer patients. **CONCLUSION:** Combined acupuncture and auricular acupressure may be effective for relieving CRF in patients during lung cancer chemotherapy.

[He-Chan Pian inhibits the metastasis of non-small cell lung cancer via the miR-205-5p-mediated regulation of the GREM1/Rap1 signaling pathway](#)

Phytomedicine. 2021 Oct 24;94:153821. doi: 10.1016/j.phymed.2021.153821. Online ahead of print.

Jun Kan ¹, Biqian Fu ², Ruisheng Zhou ³, et al.

BACKGROUND: He-Chan Pian (HCP), a traditional Chinese medicinal formula, shows promising efficacy for the treatment of lung cancer. **PURPOSE:** Gremlin (GREM1) plays an important role in gastrointestinal tumor metastasis; however, little is known about its role in lung cancer. We determined the mechanism underlying the protective effect of HCP against metastasis in a mouse model of non-small cell lung cancer (NSCLC) and demonstrated the role of GREM1. **METHODS:** Ultra-high performance liquid chromatography-mass spectrometry (UPLC-MS) was used to analyze the herbal components and metabolites from the serum of HCP-treated mice. The tumor, liver, and kidney were examined histologically, and the antitumor effects and toxicity of HCP were evaluated. Levels of epithelial-mesenchymal transition (EMT)-associated transcription factors were measured using western blotting in tumors from five groups (i.e., model, HCP [L], HCP [M], HCP [H], and positive control [cisplatin, DDP]). Differentially expressed proteins and genes were identified using protein chip and sequencing analyzes, respectively. Short hairpin RNAs and overexpression plasmids were introduced into cells to evaluate the effects of GREM1. To evaluate proliferation, migration, and invasion, the expression levels of proteins involved in the Rap1 pathway and EMT were measured in vitro. Xenograft tumors with overexpression-GREM1 (OE-GREM1) in A549 cells were examined for cell proliferation. A dual-luciferase assay was performed to verify the direct interaction of GREM1 with miR-205-5p in lung cancer. **RESULTS:** Thirty-six ingredients and bioactive constituents detected in the serum of HCP-treated mice were identified as the key compounds involved in the inhibition of tumor growth. Animal experiments revealed that HCP significantly decreased tumor volumes and had no adverse effects on the liver or kidney or side effects. GREM1 upregulation was closely related to tumor metastasis and was regulated by miR-205-5p, as confirmed using a dual-luciferase reporter assay. OE-GREM1 promoted A549 cell migration and invasion, promoted EMT, and increased the expression of Rap1 pathway intermediaries, whereas shGREM1 had the opposite effects. Furthermore, the effects of OE-GREM1 on proliferation in the A549 xenograft mouse model were attenuated, although HCP has an inhibitory effect

on tumors. **CONCLUSION:** Our results suggest that HCP contributes to the inhibition of NSCLC metastasis via the Gremlin/Rap1 signaling pathway regulated by miR-205-5p.

Screening for Selective Anticancer Activity of 65 Extracts of Plants Collected in Western Andalusia, Spain Plants (Basel). 2021 Oct 15;10(10):2193. doi: 10.3390/plants10102193. José Manuel Calderón-

Montaño 1 , Sara María Martínez-Sánchez 2 3 , Víctor Jiménez-González 1 , Estefanía Burgos-Morón 1 , Emilio Guillén-Mancina 1 , Julio José Jiménez-Alonso 1 , Patricia Díaz-Ortega 1 , Felipe García 2 , Abelardo Aparicio 2 , Miguel López-Lázaro 1

Finding cytotoxic drugs with a high selectivity towards cancer cells is crucial to improve the low survival rates of patients diagnosed with metastatic cancers. Since plants are an important source of anticancer drugs, we have screened 65 extracts from 45 plants collected in several areas of Western Andalusia (Spain) for cytotoxic activity on lung cancer cells versus lung normal cells. An extract from the leaves of *Tetraclinis articulata* (Vahl) Mast. (Cupressaceae) showed a marked cytotoxicity ($IC_{50} = 0.37 \pm 0.03$ μ g/mL) and selectivity (selectivity index = 378.3) against the lung cancer cells; cisplatin, 5-fluorouracil, and an extract from the leaves of *Taxus baccata* L. (Taxaceae) were less cytotoxic and selective. Extracts from *Cascabela thevetia* (L.) Lippold (Apocynaceae), *Frangula alnus* Mill. (Rhamnaceae), *Iberis ciliata* subsp. *contracta* (Pers.) Moreno (Brassicaceae), *Juniperus macrocarpa* Sm (Cupressaceae), and *Pancreaticum maritimum* L. (Amaryllidaceae) also showed selective cytotoxicity (selectivity index > 10). Active extracts were also tested against a panel of cancer cell lines from a variety tissues. The plants identified in this work are potential sources of natural compounds with selective toxicity towards cancer cells.

Acupuncture against chronic postsurgical pain in non-small cell lung cancer patients: A protocol of randomized controlled trial Medicine (Baltimore). 2021 Oct 8;100(40):e27461. doi:

10.1097/MD.00000000000027461. Gang Li 1 , Changxi Zhang, Congyi Wang, Ling Xiao

INTRODUCTION: Video-assisted thoracoscopic lobectomy is the prior recommended treatment for non-small cell lung cancer (NSCLC), with the advantages of small trauma, less postoperative pain, and quick recovery. However, a large number of patients may suffer chronic postsurgical pain (CPSP), which makes the patients unwilling to practice pulmonary exercises, and it would directly affect patient's cough, sputum expectoration, and mobility. Opioids could greatly improve the quality of postoperative analgesia and the quality of life after surgery, but it is accompanied with obvious side effects. A number of clinical studies have proved that acupuncture could improve postoperative pain and reduce opioid use. In this study, we try to conduct a randomized controlled study to evaluate the efficacy and safety of plum-blossom needle acupuncture combined with Tramadol in improving CPSP after lobectomy in NSCLC patients. **METHODS:** Patients will be randomly divided into treatment group (acupuncture plus Tramadol) and control group (sham acupuncture plus Tramadol) with a random number table in 1:1 ratio. The patients, outcome assessor, and statistician will be blinded. The outcomes are changes of numerical rating scale, Karnofsky performance score, brief pain inventory, blood routine, liver and kidney function. The data will be analyzed by SPSS 22.0. **CONCLUSIONS:** The results will help to evaluate the efficacy and safety of plum-blossom needle acupuncture in improving CPSP after lobectomy in NSCLC patients.

Lung cancer patient who had declined conventional cancer treatment: could the self-administration of 'CBD oil' be contributing to the observed tumour regression? BMJ Case Rep. 2021 Oct

14;14(10):e244195. doi: 10.1136/bcr-2021-244195. Kah Ling Liew 1 , Ermanno Capuano 2 , Bernard Yung 3

Conventional lung cancer treatments include surgery, chemotherapy and radiotherapy; however, these treatments are often poorly tolerated by patients. Cannabinoids have been studied for use as a primary cancer treatment. Cannabinoids, which are chemically similar to our own body's endocannabinoids, can

interact with signalling pathways to control the fate of cells, including cancer cells. We present a patient who declined conventional lung cancer treatment. Without the knowledge of her clinicians, she chose to self-administer 'cannabidiol (CBD) oil' orally 2-3 times daily. Serial imaging shows that her cancer reduced in size progressively from 41 mm to 10 mm over a period of 2.5 years. Previous studies have failed to agree on the usefulness of cannabinoids as a cancer treatment. This case appears to demonstrate a possible benefit of 'CBD oil' intake that may have resulted in the observed tumour regression. The use of cannabinoids as a potential cancer treatment justifies further research.

MISCELLANEOUS WORKS

[Lung Cancer and SARS-CoV-2 infection: Identifying important knowledge gaps for investigation](#)

J Thorac Oncol. 2021 Nov 10;S1556-0864(21)03309-8. doi: 10.1016/j.jtho.2021.11.001. Online ahead of print. Christian Rolfo 1, Noy Meshulami 1, Alessandro Russo 2, et al.

Patients with lung cancer are especially vulnerable to COVID-19 with a >7-fold higher rate of becoming infected with SARS-CoV-2 COVID-19, a >3-fold higher hospitalization rate with high complication rates, and an estimated case fatality rate of over 30%. The reasons for the increased vulnerability are not known. In addition, beyond the pandemic's direct impact on morbidity and mortality among patients with lung cancer, COVID-19, with its disruption of patient care, has also resulted in substantial impact on lung cancer screening and treatment/management. COVID-19 vaccines are safe and effective in people with lung cancer. Based on the available data, patients with lung cancer should continue their course of cancer treatment and get vaccinated against the SARS-CoV-2 virus. For unknown reasons, some patients with lung cancer mount poor antibody responses to vaccination. Thus, boost vaccination seems urgently indicated in this subgroup of vulnerable lung cancer patients. However, many unanswered questions regarding vaccination in this population remain, including the magnitude, quality, and duration of antibody response, and the role of innate and acquired cellular immunity for clinical protection. Additional important knowledge gaps also remain including: how can we best protect patients with lung cancer from developing COVID-19 including managing lung cancer patient care and the home environment of lung cancer patients; are there clinical/treatment demographics and tumor molecular demographics that impact severity of COVID-19 disease in lung cancer patients; does anticancer treatment impact antibody production and protection; does SARS-CoV-2 infection impact the development/progression of lung cancer; and are special measures and vaccine strategies need for patients with lung cancer as viral variants of concern emerge.

[COVID and Lung Cancer](#) Curr Oncol Rep. 2021 Oct 22;23(11):134. doi: 10.1007/s11912-021-01125-8.

Luana Calabrò 1 2 , Giulia Rossi 3 , Alessia Covre 3 4 5 , Aldo Morra 6 , Michele Maio 3 4 5 7

PURPOSE OF REVIEW: Since the past year, the fast spread of coronavirus disease 2019 (COVID-19) has represented a global health threat, especially for cancer patients, that has required an urgent reorganization of clinical activities. Here, we will critically revise the profound impact that the pandemic has generated in lung cancer patients, as well the most significant challenges that oncologists have to face to maintain the highest possible standards in the management of lung cancer patients in the pandemic era. **RECENT FINDINGS:** Evidences suggested a higher susceptibility and mortality of lung cancer patients due to COVID-19. The hard management of this patient population has been also due to the potential cross interference of anti-tumor drugs on SARS-Cov-2 infection and to the differential diagnosis between COVID-19 pneumonitis and drug-related pneumonitis. COVID-19 pandemic has generated a profound reshaping of oncological activities and the development of recommendations by the oncology scientific community to prioritize anti-tumor treatments for lung cancer patients.

[Care disruptions among patients with lung cancer: A COVID-19 and cancer outcomes study](#)

Lung Cancer. 2021 Oct;160:78-83. doi: 10.1016/j.lungcan.2021.07.002. Epub 2021 Jul 16. Sheena Bhalla 1 , Ziad Bakouny 2 , Andrew L Schmidt 2 , et al.

INTRODUCTION: Patients with lung cancer (LC) are susceptible to severe outcomes from COVID-19. This study evaluated disruption to care of patients with LC during the COVID-19 pandemic.

METHODS: The COVID-19 and Cancer Outcomes Study (CCOS) is a prospective cohort study comprised of patients with a current or past history of hematological or solid malignancies with outpatient visits between March 2 and March 6, 2020, at two academic cancer centers in the Northeastern United States (US). Data was collected for the three months prior to the index week (baseline period) and the following three months (pandemic period). **RESULTS:** 313 of 2365 patients had LC, 1578 had other solid tumors, and 474 had hematological malignancies. Patients with LC were not at increased risk of COVID-19 diagnosis compared to patients with other solid or hematological malignancies. When comparing data from the pandemic period to the baseline period, patients with LC were more likely to have a decrease in in-person visits compared to patients with other solid tumors (aOR 1.94; 95% CI, 1.46-2.58), but without an increase in telehealth visits (aOR 1.13; 95% CI 0.85-1.50). Patients with LC were more likely to experience pandemic-related treatment delays than patients with other solid tumors (aOR 1.80; 95% CI 1.13-2.80) and were more likely to experience imaging/diagnostic procedure delays than patients with other solid tumors (aOR 2.59; 95% CI, 1.46-4.47) and hematological malignancies (aOR 2.01; 95% CI, 1.02-3.93). Among patients on systemic therapy, patients with LC were also at increased risk for decreased in-person visits and increased treatment delays compared to those with other solid tumors. **DISCUSSION:** Patients with LC experienced increased cancer care disruption compared to patients with other malignancies during the early phase of the COVID-19 pandemic. Focused efforts to ensure continuity of care for this patient population are warranted.

[Cancer care in a time of COVID: lung cancer patient's experience of telehealth and connectedness](#)

Support Care Cancer. 2021 Oct 4;1-8. doi: 10.1007/s00520-021-06528-8. Online ahead of print. Anne Fraser 1 2 , Rob McNeill 3 , Jackie Robinson 4 5

OBJECTIVE: To explore lung cancer patient's experiences of telehealth during COVID-19 restrictions.

METHODS: Thirty patients with lung cancer were recruited. Data was collected using a qualitative exploratory design with semi-structured interviews. Transcripts were thematically coded using NVivo software. **RESULTS:** Five key themes were identified: maintaining resilience, participants acknowledged that they were self-reliant prior to their diagnosis and that the sense of their own internal capabilities was a source of comfort for them; importance of pre-established relationships with healthcare professionals, the sense of connection established prior to the telehealth consultation supported participants to engage with healthcare professionals where the need for connectedness was amplified by a sense of isolation; seeking help, participants sought help from services that they perceived as being "expert"; convenience, factors such as costs and saving time were highlighted; and preferences for consultation type, majority of participants identified physical and emotional comfort being in their own space. For a small number of patients, continuing a face-to-face assessment was important due to expectation based on previous experience. **CONCLUSION:** The use of telehealth was supported during the management of COVID-19. Connectedness and convenience were key to the level of comfort and confidence for patients with lung cancer using telehealth during "lockdown."

[Total and Out-of-Pocket Costs of Procedures After Lung Cancer Screening in a National Commercially Insured Population: Estimating an Episode of Care](#)

J Am Coll Radiol. 2021 Oct 1;S1546-1440(21)00754-7. doi: 10.1016/j.jacr.2021.09.015. Online ahead of print. Tina D Taylor 1 , Sarah Bell 2 , A Mark Fendrick 3 , Ruth C Carlos 4

OBJECTIVE: Consequences of lung cancer screening (LCS) with low-dose chest CT in clinical settings, including procedures, costs, and complications, are incompletely understood. We evaluated downstream

invasive procedures after LCS, total and out-of-pocket (OOP) costs of these procedures, and correlates of procedural rates and costs. **METHODS:** Using the Clinformatics Data Mart, we retrospectively included patients between ages 55 and 79 years receiving LCS between 2015 and 2017. The types and frequency of downstream invasive procedures (including needle biopsy, bronchoscopy, surgery, and cytology) were described. Treating the LCS examination and downstream procedures as a single LCS episode, we described the per-episode total costs (insurance reimbursement + OOP costs of LCS and downstream procedures) and OOP costs. Correlates of costs were determined using linear and logistic regression. **RESULTS:** A total of 6,268 patients received at least one low-dose chest CT; 462 patients (7.4%) received at least one procedure within 12 months after LCS (needle biopsy 69.0%, cytology 23.6%, bronchoscopy 18.6%, surgery 23.8%). Women and patients ≥ 65 years were more likely to receive a downstream procedure. Ninety-three patients (20.1%) were diagnosed with lung cancer after LCS. The total cost of managing this population of lung screeners was \$5,060,511.04, with an average per-episode total cost of \$740.06. The aggregate OOP costs to this population of lung screeners was \$427,069.74, with an average per-episode OOP cost of \$62.46. **CONCLUSIONS:** Rates of invasive procedures after LCS in a commercially insured population exceeded those of clinical trials. Considering LCS and associated downstream procedures as an episode of care results in modest OOP cost.

[The Importance of Disease-Free Survival as a Clinical Trial Endpoint: A Qualitative Study Among Canadian Survivors of Lung Cancer](#) Patient. 2021 Oct 13. doi: 10.1007/s40271-021-00552-w. Online ahead of print. Andrea Bever 1 , Jackie Manthorne 2 , Tissa Rahim 1 , Layla Moumin 2 , Shelagh M Szabo 3

BACKGROUND: In lung cancer trials, overall survival is a well-validated and widely used endpoint; yet, in the context of adjuvant or curative intent treatments, disease-free survival (DFS) may be a better indicator of transformative patient outcomes. Although use of DFS is growing, patient perceptions of its relevance have not been established. Objective: We aimed to understand the importance of DFS as a trial endpoint, from the perspective of survivors of lung cancer. **METHODS:** Web-based qualitative interviews were conducted with Canadian survivors of stage Ib-IIIa lung cancer. Participants described their experiences of cancer diagnosis and treatment, including their treatment goals and priorities. Participants then provided their perspectives on DFS and overall survival, and how well each aligned with their treatment priorities. Thematic analysis was used to explore patterns in responses. **RESULTS:** Among the 18 participants (mean age, 64 years), 83% were female, most (89%) had received surgery, and 56% received chemotherapy. Most participants viewed DFS as an intrinsically meaningful treatment outcome, for reasons such as alignment with treatment goals, and the perception that DFS would help maintain a high quality of life. One individual was interested in DFS only as a potential surrogate for overall survival. Participants desired access to new treatments that improve DFS and emphasized this within the context of promoting patient agency in treatment decision making. **CONCLUSIONS:** These findings suggest DFS is a meaningful endpoint from the perspective of survivors of lung cancer; and may help inform decisions regarding regulatory approval and reimbursement of new treatments based on DFS data.

[The impact of social determinants of health on management of stage I non-small cell lung cancer](#) Am J Surg. 2021 Oct 15;S0002-9610(21)00614-0. doi: 10.1016/j.amjsurg.2021.10.022. Online ahead of print. Niharika Namburi 1 , Lava Timsina 1 , Nehal Ninad 1 , DuyKhanh Ceppa 1 , Thomas Birdas 2 **BACKGROUND:** Social Determinants of Health (SDOH) can be important contributors in health care outcomes. We hypothesized that certain SDOH independently impact the management and outcomes of stage I Non-Small Cell Lung Cancer (NSCLC). **STUDY DESIGN:** Patients with clinical stage I NSCLC were identified from the National Cancer Database. The impact of SDOH factors on utilization of surgery, perioperative outcomes and overall survival were examined, both in bivariate and multivariable analyses.

RESULTS: A total of 236,140 patients were identified. In multivariate analysis, SDOH marginalization were associated with less frequent use of surgery, lower 5-year survival and, in surgical patients, more frequent use of open surgery and lower 90-day postoperative survival. **CONCLUSION:** SDOH disparities have a significant impact in the management and outcomes of stage I NSCLC. We identified SDOH patient groups particularly impacted by such disparities, in which higher utilization of surgery and minimally invasive approaches may lead to improved outcomes.

[Ethnic Differences in Survival Among Lung Cancer Patients: A Systematic Review](#) JNCI Cancer Spectr. 2021 Jul 7;5(5):pkab062. doi: 10.1093/jncics/pkab062. eCollection 2021 Oct. Sarah N Price 1, Melissa Flores 1 2, Heidi A Hamann 1 3, John M Ruiz 1

BACKGROUND: Despite a substantially worse risk factor profile, Hispanics in the United States experience lower incidence of many diseases and longer survival than non-Hispanic Whites (NHWs), an epidemiological phenomenon known as the Hispanic Health Paradox (HHP). This systematic review evaluated the published longitudinal literature to address whether this pattern extends to lung cancer survival. **METHODS:** Searches of Medline, PubMed, Embase, Web of Science, and the Cochrane Library were conducted for publications dated from January 1, 2000, to July 18, 2018. Records were restricted to articles written in English, employing a longitudinal design, and reporting a direct survival comparison (overall survival [OS], cancer-specific survival [CSS]) between NHW and Hispanic lung cancer patients. **RESULTS:** A final sample of 29 full-text articles were included, with 28 fully adjusted models of OS and 21 of CSS included. Overall, 26 (92.9%) OS models and 20 (95.2%) CSS models documented either no difference (OS = 16, CSS = 11) or a Hispanic survival advantage (OS = 10, CSS = 9). Both larger studies and those including foreign-born Hispanics were more likely to show a Hispanic survival advantage, and 2 studies of exclusively no-smokers showed a survival disadvantage. A number of reporting gaps were identified including Hispanic background and sociodemographic characteristics. **CONCLUSIONS:** Hispanics exhibit similar or better survival in the context of lung cancer relative to NHWs despite a considerably worse risk factor profile. These findings support the HHP in the context of lung cancer. Further research is needed to understand the potential mechanisms of the HHP as it relates to lung cancer.

[Smoking Cessation After Lung Cancer Diagnosis and the Risk of Second Primary Lung Cancer: The Multiethnic Cohort Study](#) JNCI Cancer Spectr. 2021 Aug 23;5(5):pkab076. doi:

10.1093/jncics/pkab076. eCollection 2021 Oct. Sophia J Luo 1, Eunji Choi 1, Jacqueline V Aredo 2, et al.

BACKGROUND: Smoking cessation reduces lung cancer mortality. However, little is known about whether diagnosis of lung cancer impacts changes in smoking behaviors. Furthermore, the effects of smoking cessation on the risk of second primary lung cancer (SPLC) have not been established yet. This study aims to examine smoking behavior changes after initial primary lung cancer (IPLC) diagnosis and estimate the effect of smoking cessation on SPLC risk following IPLC diagnosis. **METHODS:** The study cohort consisted of 986 participants in the Multiethnic Cohort Study who were free of lung cancer and active smokers at baseline (1993-1996), provided 10-year follow-up smoking data (2003-2008), and were diagnosed with IPLC in 1993-2017. The primary outcome was a change in smoking status from "current" at baseline to "former" at 10-year follow-up (ie, smoking cessation), analyzed using logistic regression. The second outcome was SPLC incidence after smoking cessation, estimated using cause-specific Cox regression. All statistical tests were 2-sided. **RESULTS:** Among 986 current smokers at baseline, 51.1% reported smoking cessation at 10-year follow-up. The smoking cessation rate was statistically significantly higher (80.6%) for those diagnosed with IPLC between baseline and 10-year follow-up vs those without IPLC diagnosis (45.4%) during the 10-year period (adjusted odds ratio = 5.12, 95% confidence interval [CI] = 3.38 to 7.98; P <.001). Incidence of SPLC was statistically significantly lower

among the 504 participants who reported smoking cessation at follow-up compared with those without smoking cessation (adjusted hazard ratio = 0.31, 95% CI = 0.14 to 0.67; P = .003). **CONCLUSION:** Lung cancer diagnosis has a statistically significant impact on smoking cessation. Quitting smoking after IPLC diagnosis may reduce the risk of developing a subsequent malignancy in the lungs.

[Medicare Advantage Networks and Access to High-volume Cancer Surgery Hospitals](#)

Ann Surg. 2021 Oct 1;274(4):e315-e319. doi: 10.1097/SLA.0000000000005098. Mustafa Raouf 1 2 , Gretchen Jacobson 1 2 , Yuman Fong 1 2

Objective: To determine how Medicare Advantage (MA) health plan networks impact access to high-volume hospitals for cancer surgery. **BACKGROUND:** Cancer surgery at high-volume hospitals is associated with better short- and long-term outcomes. In the United States, health insurance is a major detriment to seeking care at high-volume hospitals. A third of older (>65 years) Americans are enrolled in privatized MA health plans. The impact of MA plan networks on access to high-volume surgery hospitals is unknown. **METHODS:** We analyzed in-network hospitals for MA plans offered in Los Angeles county during open enrollment of 2015. For the purposes of this analysis, MA network data from provider directories were linked to hospital volume data from California Office of Statewide Health Planning and Development. Volume thresholds were based on published literature. **RESULTS:** A total of 34 MA plans enrolled 554,754 beneficiaries in Los Angeles county during 2014 open enrollment for coverage starting in 2015 (MA penetration ~43%). The proportion of MA plans that included high-volume cancer surgery hospital varied by the type of cancer surgery. While most plans (>71%) included at least one high-volume hospital for colon, rectum, lung, and stomach; 59% to 82% of MA plans did not include any high-volume hospitals for liver, esophagus, or pancreatic surgery. A significant proportion of beneficiaries in MA plans did not have access to high-volume hospitals for esophagus (93%), stomach (44%), liver (39%), or pancreas (70%) surgery. In contrast, nearly all MA beneficiaries had access to at least one high-volume hospital for lung (93%), colon (100%), or rectal (100%) surgery. Overall, Centers for Medicare & Medicaid Services plan rating or plan popularity were not correlated with access to high-volume hospital (P > 0.05). **CONCLUSIONS:** The study identifies lack of high-volume hospital coverage in MA health plans as a major detriment in regionalization of cancer surgery impacting at least a third of older Americans.