



Caring Ambassadors Lung Cancer Program

Literature Review, May 2022

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SCREENING, COMPREHENSIVE BIOMARKER TESTING, DIAGNOSIS AND STAGING

[Lung Cancer: Diagnosis, Treatment Principles, and Screening](#) Am Fam Physician. 2022 May 1;105(5):487-494. Jeffrey Kim 1 , Hobart Lee 1 , Brian W Huang 1

Lung cancer is the second most common cancer in men and women in the United States; however, it remains the leading cause of cancer-related death in the United States and worldwide. The most common but nonspecific symptom of lung cancer is cough. Associated symptoms, including hemoptysis or shortness of breath, or systemic symptoms, including anorexia or weight loss, greatly increase the likelihood of having lung cancer. Referral to a multidisciplinary lung cancer team, imaging, and confirmation through sputum cytology, thoracentesis, fine-needle aspiration, or mediastinoscopy are recommended. If lung cancer is confirmed, treatment options vary based on staging, histology, immunotherapy biomarker testing, and patient health status. Treatments include surgical resection, immunotherapy, chemotherapy, and/or radiotherapy. Family physicians should focus on primary prevention of lung cancer by encouraging tobacco cessation and early recognition by screening at-risk individuals and following guidelines for pulmonary nodules. As of 2021, the U.S. Preventive Services Task Force recommends annual lung cancer screening using low-dose computed tomography starting at 50 years of age in patients with a 20 pack-year history.

[Examining Tobacco Treatment Perceptions and Barriers among Black versus Non-Black Adults Attending Lung Cancer Screening](#) Cancer Prev Res (Phila). 2022 May 3;15(5):327-333. doi:

10.1158/1940-6207.CAPR-21-0398. Krysten W Bold 1 , Sydney Cannon 1 , Bennie B Ford 1 , Susan Neveu 1 , Polly Sather 2 , Benjamin A Toll 1 3 , Lisa M Fucito 1 4 5

The US Preventive Services Task Force recommends annual lung cancer screening for patients at high risk based on age and smoking history. Understanding the characteristics of patients attending lung cancer screening, including potential barriers to quitting smoking, may inform ways to engage these high-risk patients in tobacco treatment and address health disparities. Patients attending lung cancer screening who currently smoke cigarettes completed a survey at Smilow Cancer Hospital at Yale-New Haven (N = 74) and the Medical University of South Carolina (N = 73) at the time of their appointment. The survey assessed demographics, smoking history, and perceptions and concerns about quitting smoking.

Patients were 55 to 76 years old (mean = 63.3, SD = 5.3), N = 64 (43.5%) female, and N = 31 (21.1%) non-Hispanic Black. Patients smoked 16.3 cigarettes per day on average (SD = 9.2) and rated interest in quitting smoking in the next month as moderate (mean = 5.6, SD = 3.1, measured from 0 = "very definitely no" to 10 = "very definitely yes"). The most frequently endorsed concerns about quitting smoking were missing smoking (70.7%), worry about having strong urges to smoke (63.9%), and concerns about withdrawal symptoms (59.9%). In comparison with other races/ethnicities, Black patients were less likely to report concerns about withdrawal symptoms and more likely to report smoking less now and perceiving no need to quit. Findings identified specific barriers for tobacco treatment and differences by race/ethnicity among patients attending lung cancer screening, including concerns about withdrawal symptoms and perceived need to quit. Identifying ways to promote tobacco treatment is important for reducing morbidity and mortality among this high-risk population. Prevention relevance: The current study examines patient characteristics and tobacco treatment perceptions and barriers among patients attending lung cancer screening who continue to smoke cigarettes that may help inform ways to increase treatment engagement and address tobacco-related health disparities to reduce morbidity and mortality from smoking.

Patient Identification of Lung Cancer Screening Follow-Up Recommendations and the Association with Adherence Ann Am Thorac Soc. 2022 May;19(5):799-806. doi: 10.1513/AnnalsATS.202107-887OC. Matthew Triplette^{1 2}, David S Wenger¹, Shahida Shahrir¹, Erin K Kross^{1 3}, Christine Kava⁴, Amanda Phipps⁴, Stephen E Hawes⁴, Allison Cole⁵, Madison Snidarich², Kristina Crothers^{1 6}

RATIONALE: Adherence to follow-up lung cancer screening (LCS) in real-world settings is suboptimal. Patient understanding of screening results and anticipated follow-up may be crucial to adherence.

OBJECTIVES: To determine patient factors associated with identification of follow-up recommendations as a measure of patient understanding of screening results after LCS, and to determine whether misidentification of follow-up is associated with lower adherence to recommendations.

METHODS: We performed a prospective study of patients in the University of Washington/Seattle Cancer Care Alliance LCS registry who underwent an initial LCS examination between June 2017 and September 2019. We mailed potential participants a survey after the initial LCS examination, with additional data abstracted from the electronic health record and LCS registry. Participants were asked to identify the timing and next step for their follow-up, with answers corresponding to the lung imaging reporting and data system (Lung-RADS) recommendations. We examined associations between incorrect identification of recommended follow-up and patient-level characteristics, self-perceived benefit/harm of LCS, LCS knowledge, Lung-RADS score, and patient-reported method of LCS results communication (letter, telephone, or in-person). We used multivariable logistic regression to evaluate associations with incorrect identification of recommendations and assessed incorrect identification of recommendations as a potential mechanism for poor adherence in a separate regression model. **RESULTS:** One hundred eighty-eight participants completed the survey (response rate 44%); 47% misidentified their follow-up recommendation. Those with Lung-RADS scores ≥ 3 had higher odds of incorrectly identifying follow-up recommendations than those with scores < 3 , as did those with lower educational attainment. However, there was no significant association between incorrect identification of follow-up and ultimate adherence to follow-up. **CONCLUSIONS:** Understanding of LCS follow-up appears to be poor, especially among those with lower education levels and positive findings. Among survey responders, incorrect identification of follow-up was not associated with poor adherence, suggesting that other factors, such as provider interventions, may be driving adherence behavior. These results can inform efforts to target improved patient education regarding follow-up for LCS.

[Segmentectomy versus wedge resection for radiological solid predominant and low metabolic non-small cell lung cancer](#) Interact Cardiovasc Thorac Surg. 2022 May 2;34(5):814-821. doi:

10.1093/icvts/ivac028. Atsushi Kagimoto 1 , Yasuhiro Tsutani 1 , Takahiro Mimae 1 , Yoshihiro Miyata 1 , Morihito Okada 1

OBJECTIVES: The prognosis of segmentectomy and wedge resection for solid predominant early-stage non-small cell lung cancer with low metabolic activity is unclear. **METHODS:** This study aimed to assess patients who underwent segmentectomy or wedge resection with curative intent for clinically node-negative non-small cell lung cancer presenting as a solid predominant tumour (consolidation tumour ratio >50%) with a whole size ≤ 3 cm and [18F]-fluoro-2-deoxy-D-glucose accumulation weaker than that of the mediastinum tissue (Deauville score, 1 or 2) on positron emission tomography/computed tomography. The cumulative incidence of recurrence (CIR) was compared using the Gray method, and the predictive factor of CIR was analysed using the Fine and Gray method. **RESULTS:** Of 140 patients included in this study, 93 (66.4%) underwent segmentectomy and 47 (33.6%) underwent wedge resection. No significant difference in the clinical stage was found between the 2 groups. The CIR was higher with wedge resection than with segmentectomy ($P = 0.004$). Recurrence after wedge resection was noted in 4 (8.5%) patients, 2 of whom had a recurrent site containing lung parenchyma of the preserved lobe and hilum lymph node, which would have been resected if segmentectomy had been performed. In the multivariable analysis for CIR using inverse probability of treatment weighting and the procedure, wedge resection was a significantly worse predictive factor (hazard ratio, 12.280; $P = 0.025$). **CONCLUSIONS:** Segmentectomy rather than wedge resection should be considered for solid predominant, small-size non-small cell lung cancer even if [18F]-fluoro-2-deoxy-D-glucose accumulation is low.

[Is surgery worthwhile in locally-advanced NSCLC patients with persistent N2-disease after neoadjuvant therapy?](#) Rev Recent Clin Trials. 2022 May 18. doi:

10.2174/1574887117666220518102321. Online ahead of print. Filippo Lococo 1 2 , Marco Chiappetta 2 , Carolina Sassorossi 2 , et al.

AIMS: To explore the long-term survivals in lung cancer patients with persistent mediastinal lymph nodal disease after neoadjuvant followed by surgical resection and to analyse prognostic factor in this specific subset of patients **BACKGROUND:** Surgery in non-small-cell lung cancer (NSCLC) patients with N2-disease after neoadjuvant therapy (NAD) has been debated and, with the advent of immunotherapy, has been even more questioned. Objective: Describe long-term results of multimodal approach in locally-advanced NSCLC patients with persistence of N2-disease and identify prognostic factors to target the strategy of care Method: We retrospectively reviewed data of 121 consecutive Stage IIIA-N2 NSCLC patients who underwent NAD (chemoradiotherapy or chemotherapy) from 01/00 to 12/19, focusing our analysis on 37 patients with persistent N2s status after surgery. The associations between mortality and potential risk factors were explored with Kaplan-Meier and Cox regression analysis. **RESULT:** The 5-year survival was 29.8%. Cox regression analysis suggested that young age (HR=0.98, C.I.95%: 0.97- 1.00; $p=0.062$), male sex (HR=3.8,C.I.95%:1.06-13.73; $p=0.04$), and adjuvant therapy (HR=6.81,C.I.95%:0.96-53.94; $p=0.06$) influenced long-term outcomes in these patients. **CONCLUSION:** We herein observed suboptimal long-term results in this NSCLC patient subset and, considering emerging results adopting immunotherapy following chemoradiotherapy, surgery should be carefully considered in very selected cases (young and clinically fit patients) and combined with adjuvant therapy after surgery.

[Early discharge on postoperative day 1 following lobectomy for stage I non-small-cell lung cancer is safe in high-volume surgical centres: a national cancer database analysis](#) Eur J Cardiothorac Surg. 2022 May 2;61(5):1022-1029. doi: 10.1093/ejcts/ezab490. Hans E Drawbert 1 , Matthew T Hey 1 , Francisco Tarrazzi 1 , Mark Block 1 , Syed S Razi 1 2

OBJECTIVES: Shortening hospital length of stay after lobectomy for stage I non-small-cell lung cancer (NSCLC) remains a challenge, and the literature regarding factors associated with safe early discharge is limited. We sought to evaluate the safety of postoperative day (POD) 1 discharge after lobectomy and its correlation with institutional caseload using the National Cancer Database, jointly sponsored by the American College of Surgeons and the American Cancer Society. **METHODS:** We identified patients with stage I NSCLC (tumour ≤ 4 cm, clinical N0, M0) in the National Cancer Database who underwent lobectomy from 2010 to 2015. Hospital surgical volume was assigned based on total surgical volume for lung cancer. The cohort was divided into 2 groups: POD 1 discharge [length of stay (LOS) ≤ 1] and the standard discharge (LOS > 1). Outcome variables were compared in propensity matched cohorts, and the multivariable regression model was created to assess factors associated with LOS ≤ 1 and the occurrence of adverse events (unplanned readmissions, 30- and 90-day deaths). **RESULTS:** A total of 52 830 patients underwent lobectomy for stage I NSCLC across 1231 treating facilities; 3879 (7.3%) patients were discharged on day 1 (LOS ≤ 1), whereas 48 951 (92.7%) were discharged after day 1 (LOS > 1). Factors associated with LOS ≤ 1 included male sex, higher socioeconomic status, right middle lobectomy, minimally invasive surgery and high-volume centres. The risk of adverse events was higher for LOS ≤ 1 in low [odds ratio (OR): 1.913, 95% confidence interval (CI) 1.448-2.527; $P < 0.001$] and median quartiles (OR: 2.258; 95% CI 1.881-2.711; $P < 0.001$), but equivalent in high-volume centres (OR: 0.871, 95% CI 0.556-1.364; $P = 0.54$). **CONCLUSIONS:** The safety and efficacy of early discharge on POD 1 following lobectomy are associated with lung cancer surgical volume. Implementation of 'enhanced recovery' protocols is likely related to safe early discharges from high-volume centres.

[Lobectomy versus segmentectomy in patients with stage T \(\$> 2\$ cm and \$\leq 3\$ cm\) N0M0 non-small cell lung cancer: a propensity score matching study](#) J Cardiothorac Surg. 2022 May 11;17(1):110. doi: 10.1186/s13019-022-01867-x. Linlin Wang # 1 , Lihui Ge # 2 , Sibou You 1 , Yongyu Liu 1 , Yi Ren 3

BACKGROUND: The safety and effectiveness of lung segmentectomy in patients with early non-small cell lung cancer (NSCLC) remains controversial. We have therefore reviewed the clinicopathologic characteristics and survival outcomes of patients treated with lobectomy or segmentectomy for early T (> 2 and ≤ 3 cm) N0M0 NSCLC. **METHODS:** We obtained data from the Surveillance, Epidemiology, and End Results database for patients who underwent lobectomy or segmentectomy between 2004 and 2015. To reduce bias and imbalances between the treatment groups, propensity score matching analysis was performed. We used Kaplan-Meier curves to estimate overall survival (OS) and lung cancer-specific survival (LCSS). We conducted univariate and multivariate Cox proportional hazards regression analyses to identify independent prognostic factors for OS and cancer-specific survival, and applied the Cox proportional hazards model to create forest plots. **RESULTS:** Before matching, both univariate and multivariate Cox regression analyses revealed that patients who underwent lobectomy exhibited better OS ($P < 0.001$) and LCSS ($P = 0.001$) than patients who underwent segmentectomy. However, after matching, survival differences between the groups were not significant; OS ($P = 0.434$) and LCSS ($P = 0.593$). Regression analyses revealed that age and tumor grade were independent predictors of OS and LCSS ($P < 0.05$). **CONCLUSIONS:** Patients with stage T (> 2 and ≤ 3 cm) N0M0 NSCLC undergoing segmentectomy can obtain OS and LCSS similar to those obtained with lobectomy. Further studies are required considering the solid component effects and pathologic tumor types regarding segmentectomies. Additional long-term survival and outcome analyses should be conducted with larger cohorts.

[The impact of segmentectomy versus lobectomy on pulmonary function in patients with non-small-cell lung cancer: a meta-analysis](#) J Cardiothorac Surg. 2022 May 7;17(1):107. doi: 10.1186/s13019-022-01853-3. Yuan Xu # 1 , Yingzhi Qin # 1 , Dongjie Ma 1 , Hongsheng Liu 2

OBJECTIVE: Segmentectomy has been reported as an alternative to lobectomy for small-sized NSCLC without detriment to survival. The long-term benefits of segmentectomy over lobectomy on pulmonary function have not been firmly established. This meta-analysis aims to compare postoperative changes in pulmonary function in NSCLC patients undergoing segmentectomy or lobectomy. **METHODS:** Medline, Embase, Web of Science and Scopus were searched through March 2021. Statistical comparisons were made when appropriate. **RESULTS:** Fourteen studies (2412 participants) out of 324 citations were included in this study. All selected studies were high quality, as indicated by the Newcastle-Ottawa scale for assessing the risk of bias. Clinical outcomes were compared between segmentectomy and lobectomy. Δ FEV1 [10 studies, $P < 0.01$, WMD = 0.40 (0.29, 0.51)], Δ FVC [4 studies, $P < 0.01$, WMD = 0.16 (0.07, 0.24)], Δ FVC% [4 studies, $P < 0.01$, WMD = 4.05 (2.32, 5.79)], Δ FEV1/FVC [2 studies, $P < 0.01$, WMD = 1.99 (0.90, 3.08)], and Δ DLCO [3 studies, $P < 0.01$, WMD = 1.30 (0.69, 1.90)] were significantly lower in the segmentectomy group than in the lobectomy group. Subgroup analysis showed that in stage IA patients, the Δ FEV1% [3 studies, $P < 0.01$, WMD = 0.26 (0.07, 0.46)] was significantly lower in the segmentectomy group. The Δ DLCO% and Δ MVV% were incomparable. **CONCLUSION:** Segmentectomy preserves more lung function than lobectomy. There were significantly smaller decreases in FEV1, FVC, FVC%, FEV1/FVC and DLCO in the segmentectomy group than in the lobectomy group.

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

[Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer](#) N Engl J Med. 2022 May 26;386(21):1973-1985. doi: 10.1056/NEJMoa2202170. Epub 2022 Apr 11. Patrick M Forde 1 , Jonathan Spicer 1 , Shun Lu 1 , et al.

BACKGROUND: Neoadjuvant or adjuvant chemotherapy confers a modest benefit over surgery alone for resectable non-small-cell lung cancer (NSCLC). In early-phase trials, nivolumab-based neoadjuvant regimens have shown promising clinical activity; however, data from phase 3 trials are needed to confirm these findings. **METHODS:** In this open-label, phase 3 trial, we randomly assigned patients with stage IB to IIIA resectable NSCLC to receive nivolumab plus platinum-based chemotherapy or platinum-based chemotherapy alone, followed by resection. The primary end points were event-free survival and pathological complete response (0% viable tumor in resected lung and lymph nodes), both evaluated by blinded independent review. Overall survival was a key secondary end point. Safety was assessed in all treated patients. **RESULTS:** The median event-free survival was 31.6 months (95% confidence interval [CI], 30.2 to not reached) with nivolumab plus chemotherapy and 20.8 months (95% CI, 14.0 to 26.7) with chemotherapy alone (hazard ratio for disease progression, disease recurrence, or death, 0.63; 97.38% CI, 0.43 to 0.91; $P = 0.005$). The percentage of patients with a pathological complete response was 24.0% (95% CI, 18.0 to 31.0) and 2.2% (95% CI, 0.6 to 5.6), respectively (odds ratio, 13.94; 99% CI, 3.49 to 55.75; $P < 0.001$). Results for event-free survival and pathological complete response across most subgroups favored nivolumab plus chemotherapy over chemotherapy alone. At the first prespecified interim analysis, the hazard ratio for death was 0.57 (99.67% CI, 0.30 to 1.07) and did not meet the criterion for significance. Of the patients who underwent randomization, 83.2% of those in the nivolumab-plus-chemotherapy group and 75.4% of those in the chemotherapy-alone group underwent surgery. Grade 3 or 4 treatment-related adverse events occurred in 33.5% of the patients in the nivolumab-plus-chemotherapy group and in 36.9% of those in the chemotherapy-alone group. **CONCLUSIONS:** In patients with resectable NSCLC, neoadjuvant nivolumab plus chemotherapy resulted in significantly longer event-free survival and a higher percentage of patients with a pathological complete response than chemotherapy alone. The addition of nivolumab to neoadjuvant chemotherapy did not increase the

incidence of adverse events or impede the feasibility of surgery. (Funded by Bristol Myers Squibb; CheckMate 816 ClinicalTrials.gov number, NCT02998528.).

Lorlatinib Versus Pemetrexed-Based Chemotherapy in Patients With ALK-rearranged NSCLC Previously Treated With Alectinib JTO Clin Res Rep. 2022 Mar 17;3(5):100311. doi:

10.1016/j.jtocrr.2022.100311. eCollection 2022 May. Yuki Takeyasu 1 2 , Tatsuya Yoshida 1 , Ken Masuda 1 , Yuji Matsumoto 1 , Yuki Shinno 1 , Yusuke Okuma 1 , Yasushi Goto 1 , Hidehito Horinouchi 1 , Noboru Yamamoto 1 , Yuichiro Ohe 1

INTRODUCTION: Lorlatinib (LOR) or pemetrexed-based chemotherapy (PEM) is the standard treatment after failure of a second-generation ALK tyrosine kinase inhibitor, such as alectinib, in patients with ALK-positive NSCLC. Nevertheless, there have been few data on the clinical outcomes of these treatments after alectinib failure. **METHODS:** We retrospectively analyzed patients with ALK-rearranged NSCLC who received LOR (LOR group) or PEM (PEM group) as post-treatment after alectinib failure between December 2012 and August 2020. **RESULTS:** Among 90 patients who experienced disease progression during alectinib treatment, 38 of them received either PEM (n = 22) or LOR (n = 16) as subsequent treatment. The objective response rate and the median progression-free survival were similar in the PEM and LOR groups (objective response rate: 45% versus 44%, p = 0.92; median progression-free survival: 6.9 mo versus 6.2 mo, p = 0.83, respectively). Disease progression during treatment occurred in 22 patients with PEM and 14 patients with LOR. The central nervous system (CNS) was the most common site of progression in both groups. In patients without CNS metastasis at baseline, the cumulative incidence rate of CNS progression was lower over time in the LOR group compared with the PEM group (p = 0.045), whereas in patients with CNS metastasis at baseline, there were no significant differences in cumulative incidence rate of CNS progression between both groups (p = 0.43). **CONCLUSIONS:** Clinical outcomes of PEM and LOR after failure of alectinib were similar in patients with ALK-positive NSCLC.

Real-World longitudinal practice patterns in the use of PD-1 and PD-L1 inhibitors as First-Line therapy in patients with Non-Small cell lung cancer in the United States Cancer Med. 2022 May 2.

doi: 10.1002/cam4.4785. Online ahead of print. Rajwanth Veluswamy 1 2 3 , Fred R Hirsch 2 , Emanuela Taioli 1 3 , Juan Wisnivesky 1 4 5 , Ross Strauss 6 , Douglas Harrouh 6 , Boxiong Tang 6 , Gisoo Barnes 6

BACKGROUND: Immune checkpoint inhibitors targeting the programmed cell death protein-1 (PD-1) and programmed death ligand-1 (PD-L1) axis (collectively referred to as PD[L]1i) have demonstrated clinical benefits in non-small cell lung cancer (NSCLC) patients. The purpose of this United States-based real-world study is to examine changes in the landscape of first-line therapies for NSCLC since the introduction of PD(L)1i. **METHODS:** Patients with NSCLC initiating first-line treatment between May 1, 2017, and October 31, 2020, were identified in the IBM MarketScan® database. Patients were assigned groups based on first-line therapy: PD(L)1i monotherapy, chemotherapy alone, PD(L)1i with chemotherapy, or targeted therapy for patients with actionable driver mutations. **RESULTS:** A total of 5431 patients with NSCLC starting first-line treatment were identified: chemotherapy alone 2568 (47%), PD(L)1i with chemotherapy 1364 (25%), PD(L)1i monotherapy 790 (15%), and targeted therapy 709 (13%). The use of PD(L)1i monotherapy and targeted therapy remained consistent, while the percentage of patients receiving PD(L)1i with chemotherapy more than doubled. Over a third of patients in 2019 and 2020 received chemotherapy alone. Patients aged ≥ 65 years (odds ratio [OR]: 0.80; 95% confidence interval [CI]: 0.68-0.95), females (OR: 0.86; 95% CI: 0.74-0.98), and those with respiratory (OR: 0.82; 95% CI: 0.71-0.94) or kidney (OR: 0.56; 95% CI: 0.40-0.77) disease were less likely to have received PD(L)1i with chemotherapy than patients that received chemotherapy alone. **CONCLUSIONS:** Since the approval of PD(L)1i for NSCLC, their use has significantly increased for first-line treatment, especially

when used in combination with chemotherapy. A significant proportion of patients received chemotherapy alone.

Chemoradiation followed by adjuvant durvalumab in stage III non-small cell lung cancer: Real-world comparison of treatment outcomes to historical controls treated with chemoradiation alone

Thorac Cancer. 2022 May 11. doi: 10.1111/1759-7714.14452. Online ahead of print. Akram Saad 1 2 , Jeffrey Goldstein 3 , Sarit Appel 1 2 , Sameh Daher 1 2 , Damien Urban 1 2 , Amir Onn 1 2 , Hadas Gantz-Sorotsky 1 2 , Anastasiya Lobachov 1 , Teodor Gottfried 1 , Benjamin Spieler 4 , Jair Bar 1 2

OBJECTIVE: Compare outcomes in patients with stage III non-small cell lung cancer (NSCLC) treated with chemoradiation and adjuvant durvalumab to historical controls treated with chemoradiation alone.

METHODS: The records of patients with stage III NSCLC treated with definitive chemoradiation ± adjuvant durvalumab were reviewed retrospectively. Primary endpoints were progression free survival (PFS), overall survival (OS), and adverse events (AE). **RESULTS:** Between September 2009 and September 2020, 215 patients were treated with concurrent chemoradiation (n = 144) or concurrent chemoradiation followed by adjuvant durvalumab (n = 71). Compared to historical controls, durvalumab use was associated with improved PFS: median (27 months vs. 10 months, $p < 0.0001$), 1-year (83.1% vs. 43.8, $p < 0.0001$); and improved OS; median (not reached vs. 24 months, $p < 0.0001$), 1-year (85.9% vs. 81.9%, $p < 0.0001$). Multivariate analysis showed adjuvant durvalumab was associated with increased OS ($p = 0.005$) and PFS ($p = 0.001$). Within the durvalumab group, only clinical stage IIIA versus IIIB/C was associated with improved OS ($p = 0.049$), but not PFS. There was no association between PFS or OS and Eastern Cooperative Oncology Group (ECOG) score, prior history of immune disease, programmed death-ligand 1 (PD-L1) receptor status, delay in starting durvalumab beyond 42 days, or development of an AE. During durvalumab treatment, 63 AE were reported in 52 patients with treatment discontinuation in 11. Pneumonitis was the most common AE reported (n = 35, 49%). Most AE were grade 1-2 (n = 57). Grade 3-4 AE were uncommon (n = 6) and none were grade 5. **CONCLUSION:** Treatment with adjuvant durvalumab following chemoradiation was associated with improved PFS and OS compared to chemoradiation alone.

Modeling the Cost-Effectiveness of Adjuvant Osimertinib for Patients with Resected EGFR-mutant Non-Small Cell Lung Cancer

Oncologist. 2022 May 6;27(5):407-413. doi: 10.1093/oncolo/oyac021.

Christopher A Lemmon 1 , Emily C Zabor 2 , Nathan A Pennell 1

INTRODUCTION: The epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor osimertinib was recently approved for resected EGFR-mutant stages IB-III A non-small cell lung cancer due to improved disease-free survival (DFS) in this population compared with placebo. This study aimed to evaluate the cost-effectiveness (CE) of this strategy. **METHODS:** We constructed a Markov model using post-resection health state transitions with digitized DFS data from the ADAURA trial to compare cost and quality-adjusted life years (QALYs) of 3 years of adjuvant osimertinib versus placebo over a 10-year time horizon. An overall survival (OS) benefit of 5% was assumed. Costs and utility values were derived from Medicare reimbursement data and literature. A CE threshold of 3 times the gross domestic product per capita was used. Sensitivity analyses were performed. **RESULTS:** The incremental cost-effectiveness ratio for adjuvant osimertinib was \$317 119 per QALY-gained versus placebo. Initial costs of osimertinib are higher in years 1-3. Costs due to progressive disease (PD) are higher in the placebo group through the first 6.5 years. Average pre-PD, post-PD, and total costs were \$2388, \$379 047, and \$502 937, respectively, in the placebo group, and \$505 775, \$255 638, and \$800 697, respectively, in the osimertinib group. Sensitivity analysis of OS gains reaches CE with a hazard ratio (HR) of 0.70-0.75 benefit of osimertinib over placebo. A 50% discount to osimertinib drug cost yielded an ICER of \$115 419. **CONCLUSIONS:** Three-years of adjuvant osimertinib is CE if one is

willing to pay \$317 119 more per QALY-gained. Considerable OS benefit over placebo or other economic interventions will be needed to reach CE.

[MYC Promotes Tyrosine Kinase Inhibitor Resistance in ROS1-Fusion-Positive Lung Cancer](#) Mol Cancer Res. 2022 May 4;20(5):722-734. doi: 10.1158/1541-7786.MCR-22-0025. Sudarshan R Iyer¹, Igor Odintsov^{2,3}, Adam J Schoenfeld⁴, et al.

Targeted therapy of ROS1-fusion-driven non-small cell lung cancer (NSCLC) has achieved notable clinical success. Despite this, resistance to therapy inevitably poses a significant challenge. MYC amplification was present in ~19% of lorlatinib-resistant ROS1-driven NSCLC. We hypothesized that MYC overexpression drives ROS1-TKI resistance. Using complementary approaches in multiple models, including a MYC-amplified patient-derived cell line and xenograft (LUAD-0006), we established that MYC overexpression induces broad ROS1-TKI resistance. Pharmacologic inhibition of ROS1 combined with MYC knockdown were essential to completely suppress LUAD-0006 cell proliferation compared with either treatment alone. We interrogated cellular signaling in ROS1-TKI-resistant LUAD-0006 and discovered significant differential regulation of targets associated with cell cycle, apoptosis, and mitochondrial function. Combinatorial treatment of mitochondrial inhibitors with crizotinib revealed inhibitory synergism, suggesting increased reliance on glutamine metabolism and fatty-acid synthesis in chronic ROS1-TKI treated LUAD-0006 cells. In vitro experiments further revealed that CDK4/6 and BET bromodomain inhibitors effectively mitigate ROS1-TKI resistance in MYC-overexpressing cells. Notably, in vivo studies demonstrate that tumor control may be regained by combining ROS1-TKI and CDK4/6 inhibition. Our results contribute to the broader understanding of ROS1-TKI resistance in NSCLC. **IMPLICATIONS:** This study functionally characterizes MYC overexpression as a novel form of therapeutic resistance to ROS1 tyrosine kinase inhibitors in non-small cell lung cancer and proposes rational combination treatment strategies.

[Efficacy and safety of anlotinib with and without EGFR-TKIs or immunotherapy in the treatment of elder patients with non-small-cell lung cancer: a retrospective study](#) BMC Pulm Med. 2022 May 6;22(1):179. doi: 10.1186/s12890-022-01981-5. Wenxian Wang^{1,2}, Lan Shao^{2,3}, Yibing Xu², Zhengbo Song^{2,3}, Guangyuan Lou^{2,3}, Yiping Zhang^{2,3}, Ming Chen⁴

BACKGROUND: Anlotinib is a multitarget tyrosine kinase inhibitor for treating patients with advanced non-small cell lung cancer (NSCLC). We aimed to assess the efficacy and safety of anlotinib in elder patients with advanced NSCLC. **METHODS:** Elder patients with advanced NSCLC who received anlotinib were enrolled. They were all age ≥ 65 years and with demonstrated records of EGFR gene status. All patients had received treatment with anlotinib or immune checkpoint inhibitors (ICIs)/EGFR-TKIs. The efficacy was evaluated according to the efficacy evaluation criteria for solid tumors (RECIST 1.1). Common Adverse Events Evaluation Criteria (CTCAE 4.03) were used to evaluate adverse drug reactions. **RESULTS:** A total of 91 patients were included in this study. We divided the patients into two groups (EGFR wild type: 60 patients; EGFR mutation: 31 patients). Among EGFR negative patients, the progression-free survival (PFS) for anlotinib monotherapy and anlotinib combination ICI therapy was 3.2 months and 5.0 months, respectively ($P = 0.012$). The difference in overall survival (OS) between monotherapy and combination therapy was also significant (9.5 vs. 18.4 months, respectively $P = 0.010$). Interestingly, we further analyzed differences between patients with hypertension and without hypertension, and found that hypertension was associated with better prognosis (5.7 vs. 1.4 months, $P < 0.0001$). In the EGFR mutation group, the PFS for anlotinib and EGFR-TKI combination treatment indicated better efficacy than that of anlotinib monotherapy (1.83 months vs. 7.03 months, respectively, $P = 0.001$). The median OS for monotherapy and combination therapy in the EGFR mutation group showed no statistical difference (28.34 months vs. 31.37 months, $P = 0.223$). The most common adverse reactions were hypertension, fatigue, and hand-foot syndrome, mainly of grade 1 or 2. No significant increase in

adverse reactions was observed in patients ≥ 70 years of age. **CONCLUSIONS:** Anlotinib treatment and combination regimens resulted in good efficacy and controllable adverse reactions in elder patients with advanced NSCLC.

Phase II Study of Lorlatinib in Patients With Anaplastic Lymphoma Kinase-Positive Lung Cancer and CNS-Specific Relapse JCO Precis Oncol. 2022 May;6:e2100522. doi: 10.1200/PO.21.00522. Ibiayi

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PURPOSE: The CNS is a recurrent site of progression in anaplastic lymphoma kinase (ALK)-rearranged (ALK+) lung cancer. Lorlatinib is a third-generation ALK inhibitor developed to penetrate the CNS and overcome ALK resistance mutations. We conducted a phase II study to evaluate the intracranial activity of lorlatinib in patients with CNS-only progression on second-generation ALK inhibitors. **METHODS:** Patients with ALK+ lung cancer who had intracranial progression on ≥ 1 ALK inhibitor without measurable extracranial disease received lorlatinib 100 mg once daily. The primary end point was intracranial disease control rate at 12 weeks per modified RECIST v1.1. Secondary end points included intracranial progression-free survival, intracranial objective response rate, and safety/tolerability.

RESULTS: Twenty-three patients were enrolled between November 2016 and January 2019. Fifteen (65%) patients had irradiated CNS metastases, with a median of 20.2 months between radiation and lorlatinib. Control of intracranial disease was observed in 21 (95%) evaluable patients at 12 weeks. The intracranial objective response rate was 59% with six complete and seven partial responses. The median intracranial progression-free survival was 24.6 months (95% CI, 20.2 to not reached). With a median follow-up of 16.8 months, nine patients developed disease progression, including four patients with CNS progression. The most common treatment-related adverse events were hypercholesterolemia (96%), hypertriglyceridemia (87%), edema (65%), cognitive effects (52%), and mood effects (43%). Three patients discontinued treatment because of toxicity, including two patients with fatal respiratory events.

CONCLUSION: Lorlatinib induced durable intracranial disease control in patients with CNS-only relapse on second-generation ALK inhibitors, suggesting that tumors with CNS-limited progression on brain-penetrant ALK tyrosine kinase inhibitors remain ALK-dependent.

Pralsetinib: A Review in Advanced RET Fusion-Positive NSCLC Drugs. 2022 May;82(7):811-816. doi: 10.1007/s40265-022-01720-4. Epub 2022 May 19. Yahiya Y Syed 1

Activating mutations in the proto-oncogene RET have been identified as an oncogenic driver of non-small cell lung cancer (NSCLC) in a small subset of patients. Pralsetinib (Gavreto®) is an orally-administered, next-generation, small-molecule selective RET inhibitor that is approved for the treatment of RET fusion-positive metastatic NSCLC. In the pivotal phase I/II ARROW trial, pralsetinib demonstrated rapid and durable anti-tumour activity in patients with advanced RET fusion-positive NSCLC who were previously treated with platinum-based chemotherapy or were treatment-naïve. Pralsetinib also showed clinical activity against intracranial metastases arising from NSCLC. Pralsetinib had a manageable tolerability profile, with the most common grade 3 treatment-related adverse events being neutropenia, hypertension, anaemia and decreased white blood cell count. Currently available data indicate that pralsetinib is a promising new targeted treatment option for patients with advanced RET fusion-positive NSCLC. **PLAIN LANGUAGE SUMMARY:** RET fusions are known to drive non-small cell lung cancer (NSCLC) in a small subset of patients. Non-RET-specific multikinase inhibitors have been evaluated as targeted therapy for these patients in clinical trials, with limited success. Pralsetinib (Gavreto®) is an oral drug that directly and selectively inhibits the RET tyrosine kinase activity and is recently approved for the treatment of RET-driven NSCLC. In the pivotal ARROW trial, pralsetinib as first- or subsequent-line therapy showed rapid and durable clinical activity in patients with advanced RET fusion-positive NSCLC. The drug was also active against brain metastases from NSCLC. Pralsetinib had a manageable tolerability

profile. Therefore, pralsetinib is a promising new targeted therapy option for patients with advanced RET fusion-positive NSCLC.

[Treatment Sequencing Strategies in Lung Cancer](#) Zhongguo Fei Ai Za Zhi. 2022 May 20;25(5):323-336. doi: 10.3779/j.issn.1009-3419.2022.104.01. Daniel Humberto Pozza 1 , Ramon Bezerra Andrade de Mello 2

BACKGROUND: The advances in the lung cancer screening methods and therapeutics, together with awareness towards deleterious habits, such as smoking, is increasing the overall survival with better quality of life for the patients. However, lung cancer is still one of the most common and fatal neoplasm with a high incidence and consequently burden to public health worldwide. Thus, based on guidelines and recent phases II and III clinical trials studies, this manuscript summarizes the current treatment sequencing strategies in lung cancer. **METHODS:** A comprehensive search of related articles was performed focused on phases II and III clinical trials studies. **RESULTS:** The lung cancer management should take into consideration the tumor characteristics, histology, molecular pathology and be discussed in a multidisciplinary team. Lung cancer treatment options comprises surgery whenever possible, radiotherapy associate with/or chemotherapy and immunotherapy as monotherapy, or combined with chemotherapy and best palliative care. **CONCLUSIONS:** The screening predictability in more patients, smoking reduction, early diagnosis, better disease understanding and individualized, more effective and tolerable therapeutics are related to an increasing in overall survival and quality of life. In the near future improvement of personalized therapy in precision medicine is expected, enhancing new predictive biomarkers, optimal doses and optimal treatment sequencing as well as anti-cancer vaccines development.

[Association Between Smoking History and Overall Survival in Patients Receiving Pembrolizumab for First-Line Treatment of Advanced Non-Small Cell Lung Cancer](#) JAMA Netw Open. 2022 May 2;5(5):e2214046. doi: 10.1001/jamanetworkopen.2022.14046. Sanjay Popat 1 , Stephen V Liu 2 , Nicolas Scheuer 3 , Alind Gupta 4 , Grace G Hsu 4 , Sreeram V Ramagopalan 5 , Frank Griesinger 6 , Vivek Subbiah 7

IMPORTANCE: There is a need to tailor treatments to patients who are most likely to derive the greatest benefit from them to improve patient outcomes and enhance cost-effectiveness of cancer therapies. **Objective:** To compare overall survival (OS) between patients with a current or former history of smoking with patients who never smoked and initiated pembrolizumab monotherapy as first-line (1L) treatment for advanced non-small lung cancer (NSCLC). **DESIGN, SETTING, AND PARTICIPANTS:** This retrospective cohort study compared patients diagnosed with advanced NSCLC aged 18 or higher selected from a nationwide real-world database originating from more than 280 US cancer clinics. The study inclusion period was from January 1, 2011, to October 1, 2019. **EXPOSURES:** Smoking status at the time of NSCLC diagnosis. **MAIN OUTCOMES AND MEASURES:** OS measured from initiation of 1L pembrolizumab monotherapy. **RESULTS:** In this retrospective cohort study, a total of 1166 patients (median [IQR] age, 72.9 [15.3] years; 581 [49.8%] men and 585 [50.2%] women) were assessed in the primary analysis, including 91 patients [7.8%] with no history of smoking (ie, never-smokers) and 1075 patients [92.2%] who currently or formerly smoked (ie, ever-smokers). Compared with ever-smokers, never-smokers were older (median age [IQR] of 78.2 [12.0] vs 72.7 [15.5] years), more likely to be female (61 [67.0%] vs 524 [48.7%]) and to have been diagnosed with nonsquamous tumor histology (70 [76.9%] vs 738 [68.7%]). After adjustment for baseline covariates, ever-smokers who initiated 1L pembrolizumab had significantly prolonged OS compared to never-smokers (median OS: 12.8 [10.9-14.6] vs 6.5 [3.3-13.8] months; hazard ratio (HR): 0.69 [95% CI, 0.50-0.95]). This trend was observed across all sensitivity analyses for the 1L pembrolizumab cohort, but not for initiators of 1L platinum chemotherapy, for which ever-smokers showed significantly shorter OS compared with never-smokers (HR, 1.2 [95% CI, 1.07-1.33]). **CONCLUSIONS AND RELEVANCE:** In patients with advanced

NSCLC who received 1L pembrolizumab monotherapy in routine clinical practices in the US, patients who reported a current or former history of smoking at the time of diagnosis had consistently longer OS than never-smokers. This finding suggests that in never-smoking advanced NSCLC, 1L pembrolizumab monotherapy may not be the optimal therapy selection, and genomic testing for potential genomically matched therapies should be prioritized over pembrolizumab in never-smokers.

[Efficacy of first-line treatments in the elderly and non-elderly patients with advanced epidermal growth factor receptor mutated, non-small cell lung cancer: a network meta-analysis](#) BMC Cancer. 2022 May 7;22(1):514. doi: 10.1186/s12885-022-09592-3. Ziyi Xu # 1 , Chengcheng Liu # 2 , Yixiang Zhu # 1 , Zihua Zou 1 , Tongji Xie 1 , Puyuan Xing 1 , Le Wang 3 , Junling Li 4

OBJECTIVE: Epidermal growth factor receptor (EGFR)-tyrosine kinase inhibitors (TKIs) are the current standard of care for advanced or metastatic non-small cell lung cancer (NSCLC) patients harboring EGFR activating mutations. However, the optimal strategy for elderly NSCLC patients is still under debate. This study was designed to explore the optimal first-line regimens by comparing diverse strategies for elderly and non-elderly EGFR-mutated NSCLC patients. **METHODS:** A systematic review was conducted to summarize all available randomized controlled trials (RCTs) from PubMed, EMBASE, Cochrane Central Register of Controlled Trials databases, and international conferences before September 30, 2020. The primary outcome was progression free survival (PFS), and the secondary outcome was overall survival (OS). A network meta-analysis (NMA) was constructed using the Bayesian statistical model to synthesize the survival outcomes of all the treatments. **RESULTS:** In total, 12 RCTs were deemed eligible for inclusion with 3779 patients who have received 10 diverse treatments including EGFR-TKIs. Results from the Bayesian ranking suggested that osimertinib was most likely to rank the first in overall population and in elderly patients in PFS, with the cumulative probabilities of 42.20% and 31.46%, respectively. In non-elderly group (younger than 65 years old), standard of care (SoC, representing first-generation EGFR-TKIs in this NMA) + chemotherapy ranked the first (31.66%). As for OS, SoC + chemotherapy ranked first in all patients (64.33%), patients younger than 65 years old (61.98%), or older than 65 years old (34.45%). **CONCLUSION:** The regimen of osimertinib is associated with the most favorable PFS in elderly advanced EGFR-mutated NSCLC patients, while SoC + chemotherapy is the optimal strategy in PFS for non-elderly NSCLC patients harboring EGFR activating mutations, and in OS for both elderly and non-elderly EGFR-mutated advanced NSCLC patients.

[Mubritinib enhanced the inhibiting function of cisplatin in lung cancer by interfering with mitochondrial function](#) Thorac Cancer. 2022 May;13(10):1513-1524. doi: 10.1111/1759-7714.14425. Epub 2022 Apr 16. Jingyao Dong 1 , Dongshan Zhu 1 , Mengmeng Chen 1 , Taiwei Wang 1 , Yan Gao 1 , Wei Liu 1

BACKGROUND: Lung cancer is one of the most lethal cancers worldwide. Cisplatin, a widely used anti-lung cancer drug, has been limited in clinical application due to its drug resistance. Medicines targeting mitochondrial electron transport chain (ETC) complexes may be effective candidates for cisplatin-based chemotherapy. **METHODS:** In this study, the small molecule drug library from Food and Drug Administration FDA was used to screen for medicines targeting ETC. MTT and colony formation assays were used to investigate cell proliferation. Flow cytometry was employed to analyze cell cycle, apoptosis, reactive oxygen species (ROS), and mitochondrial membrane potential. Wound scratch and transwell assays were used to detect migration and invasion abilities. The activities of the ETC complex were tested using kits. Western blot analysis was used to investigate the expressions of related proteins. A mouse xenograft model was constructed to verify the antitumor effect in vivo. **RESULTS:** The results showed that mubritinib can reduce the activation of the PI3K/mTOR signal pathway, disrupt mitochondrial function, significantly increase ROS levels and induce oxidative stress, and ultimately exert its antitumor effect against non-small cell lung cancer (NSCLC) both in vivo and in vitro. In addition, the

combination of cisplatin and mubritinib can improve the tumor-suppressive effect of cisplatin.

CONCLUSION: Mubritinib can upregulate intracellular ROS concentration and cell apoptosis, inhibit the PI3K signaling pathway and interfere with the function of mitochondria, thus reducing cell proliferation and increasing ROS induced apoptosis by reducing the activation of Nrf2 by PI3K.

[Combination of Bevacizumab and Osimertinib in Patients with EGFR T790M-Mutated Non-small Cell Lung Cancer](#)

Clin Drug Investig. 2022 May;42(5):459-464. doi: 10.1007/s40261-022-01145-7. Epub 2022 May 5. Sha Liu # 1 , Tao Pan # 1 , Ming-Kun Wang 1 , Jie Wang 2 , Shuang Zhang 1 , Ping Zhou 3

BACKGROUND: Osimertinib may improve the prognosis of patients with epidermal growth factor receptor (EGFR) T790M-mutated non-small cell lung cancer (NSCLC); however, to date, the efficacy and safety of osimertinib plus bevacizumab have not been elucidated. Objective: We aimed to investigate the additional effect of bevacizumab plus osimertinib compared with osimertinib alone in NSCLC patients with EGFR T790M mutation. **METHODS:** In this study, 32 patients received osimertinib alone, while 20 patients received osimertinib plus bevacizumab. The median follow-up was 12 months. Overall survival (OS) and progression-free survival (PFS) were estimated and adverse events (AEs) were compared.

RESULTS: The overall response rate (ORR) was higher in the combination group than in the osimertinib-alone group (70.0% vs. 43.8%), and the OS ($12.8\% \pm 7.7\%$ vs. $45.4\% \pm 12.0\%$; $p = 0.038$) and PFS ($37.3\% \pm 11.9\%$ vs. $55.3\% \pm 14.3\%$; $p = 0.045$) were also significantly improved in patients who underwent osimertinib plus bevacizumab. Furthermore, the incidence of hypertension was significantly higher in the combination arm when compared with osimertinib alone ($p = 0.003$), and the number of other AEs were not significantly increased by adding bevacizumab (all $p > 0.05$). **CONCLUSION:** Concomitant use of bevacizumab and osimertinib in NSCLC patients with EGFR T790M mutation may have potential therapeutic effect than osimertinib alone. Further studies with a larger number of patients are warranted to confirm results of this study.

[Comparison of 2-Weekly Versus 4-Weekly Durvalumab Consolidation for Locally Advanced NSCLC Treated With Chemoradiotherapy: A Brief Report](#)

JTO Clin Res Rep. 2022 Mar 30;3(5):100316. doi: 10.1016/j.jtocrr.2022.100316. eCollection 2022 May. Marie-Hélène Denault 1 2 , Shelley Kuang 1 , Aria Shokoochi 1 , Bonnie Leung 1 , Mitchell Liu 3 , Eric Berthelet 3 , Janessa Laskin 1 , Sophie Sun 1 , Tina Zhang 3 , Barbara Melosky 1 , Cheryl Ho 1

INTRODUCTION: Durvalumab 10 mg/kg every 2 weeks for 1 year after chemoradiation has improved overall survival (OS) in unresectable stage III NSCLC. Subsequently, a 20 mg/kg 4-weekly regimen was approved. The study goal was to compare the efficacy and toxicity of the two regimens. **METHODS:** All patients with NSCLC treated with curative-intent chemoradiation followed by durvalumab from March 1, 2018 to December 31, 2020 at BC Cancer, British Columbia, Canada were included in this retrospective review. Durvalumab dosing schedule, toxicity, progression, and OS were collected. Comparisons between treatment groups were made using chi-square and independent t tests. Kaplan-Meier curves and log-rank test were used to analyze OS. **RESULTS:** A total of 152 patients were included in the 2-weekly group and 53 patients in the 4-weekly group. The median follow-up was 19.7 months and 12.0 months, respectively. The median OS was not reached, but 12-month survival rates were 88.4% versus 85.2% ($p = 0.55$). Toxicity profiles were similar in terms of sites and severity. **CONCLUSIONS:** There was no significant difference in efficacy or toxicity between the 2-weekly and 4-weekly durvalumab in this cohort of patients with advanced NSCLC previously treated with curative-intent chemoradiation.

[Indirect comparisons of brigatinib and alectinib for front-line ALK-positive non-small-cell lung cancer](#)

Future Oncol. 2022 May 24. doi: 10.2217/fon-2022-0194. Online ahead of print. Karen L Reckamp 1 , Huamao M Lin 2 , Holly Cranmer 3 , Yanyu Wu 2 , Pingkuan Zhang 2 , Laura J Walton

4 , Stephen Kay 5 , Allie Cichewicz 6 , Binod Neupane 6 , Kyle Fahrbach 6 , Sanjay Popat 7 , D Ross Camidge 8

AIM: To conduct an indirect treatment comparison (ITC) of the relative efficacy of brigatinib and alectinib for progression-free survival in people with tyrosine kinase inhibitor (TKI)-naive ALK-positive non-small-cell lung cancer (NSCLC). **METHODS:** Final aggregate and patient-level data from the ALTA-1L trial comparing brigatinib to crizotinib and published aggregate data from ALEX (comparing alectinib to crizotinib) were contrasted using Bucher ITC and matching-adjusted indirect comparisons (MAICs). **RESULTS:** No statistically significant differences were identified between brigatinib and alectinib in reducing the risk of disease progression overall and in patients with baseline central nervous system metastases. **CONCLUSION:** Brigatinib appeared similar to alectinib in reducing risk of disease progression for people with TKI-naive ALK-positive NSCLC. **PLAIN LANGUAGE SUMMARY:** Patients with advanced non-small-cell lung cancer (NSCLC) who have a genetic marker called rearrangement in the anaplastic lymphoma kinase, or ALK-positive disease, are treated with targeted medications taken by mouth. Two medications, alectinib and brigatinib, are both considered first-line treatment for these patients but have not been compared head-to-head. Recently, updated clinical trial results were published for these medications. The present study utilized these updated results and advanced statistical tests to indirectly compare the effectiveness of the two treatments to help guide clinical treatment choices. Results showed brigatinib and alectinib have a similar magnitude of effect in decreasing the risk of a patient with ALK-positive NSCLC developing worsening disease.

[Trimodality therapy for patients with stage III non-small-cell lung cancer: A comprehensive surveillance, epidemiology, and end results analysis](#)

Cancer Treat Res Commun. 2022 May 2;32:100571. doi: 10.1016/j.ctarc.2022.100571. Online ahead of print. Vincent P Grzywacz 1 , Thomas J Quinn 2 , Muayad F Almahariq 2 , Zaid A Siddiqui 3 , Sang W Kim 4 , Thomas M Guerrero 2 , Craig W Stevens 2 , Inga S Grills 2

PURPOSE: Debate exists regarding the optimal management for patients with stage III non-small-cell lung cancer (NSCLC). Recent inclusion of chemotherapeutic data in the Surveillance, Epidemiology, and End Results (SEER) database has made it possible to identify patients with NSCLC who received chemotherapy. We hypothesized that patients with stage III NSCLC experience improved overall survival from trimodality therapy (TMT) versus definitive chemoradiation therapy (CRT) alone. **MATERIALS AND METHODS:** We analyzed the overall survival of stage III NSCLC patients based on the receipt of TMT versus CRT alone. This included crude and adjusted univariate models as well as crude and doubly robust adjusted multivariable analyses, both utilizing propensity score matching and inverse probability of treatment weighting. Factors included in the multivariable analyses included: age, sex, marital status, income, date of diagnosis, primary site, histology, grade, T stage, N stage, and intended treatment. Planned subset analyses were performed for stage III(N2) patients. **RESULTS:** Adult patients with stage III NSCLC (N = 9008) from the SEER database were included in our analyses. In our univariate analyses, an overall survival benefit was observed for TMT versus CRT (CrudeHR = 0.58, 95% CI = 0.55-0.61, p < 0.001; AdjHR = 0.58, 95% CI = 0.54-0.61, p < 0.001). This persisted in both crude and doubly robust multivariable analyses (CrudeHR = 0.57, 95% CI = 0.53-0.61, p < 0.001; AdjHR = 0.56, 95% CI = 0.53-0.59, p < 0.001). Patients with stage III(N2) disease also demonstrated a significant benefit to OS with TMT versus CRT alone. **CONCLUSION:** The significant difference in overall survival seen with TMT suggests this may be an effective treatment approach for select patients.

[Camrelizumab Plus Apatinib in Treatment-Naive Patients With Advanced Nonsquamous NSCLC: A Multicenter, Open-Label, Single-Arm, Phase 2 Trial](#)

JTO Clin Res Rep. 2022 Mar 30;3(5):100312. doi: 10.1016/j.jtocrr.2022.100312. eCollection 2022 May. Shengxiang Ren 1 , Jianxing He 2 , Yong

Fang 3 , Gongyan Chen 4 , Zhiyong Ma 5 , Jianhua Chen 6 , Renhua Guo 7 , Xiaoyan Lin 8 , Yu Yao 9 , Gang Wu 10 , Quanren Wang 11 , Caicun Zhou 1

INTRODUCTION: Our preclinical work suggests that low-dose angiogenesis inhibition could potentiate programmed cell death protein 1 and programmed death-ligand 1 (PD-L1) blockade. In a cohort of our multicenter phase 1b and 2 study (NCT03083041), promising antitumor activity was observed with camrelizumab plus low-dose apatinib in chemotherapy-pretreated patients with advanced nonsquamous NSCLC. We hereby reported the results in treatment-naïve patients (cohort 4) from the same study.

METHODS: Eligible patients had untreated advanced nonsquamous NSCLC with a high tumor mutational burden (TMB) (tissue TMB >10 mutations per megabase or blood TMB \geq 1.54 mutations per megabase) and without sensitizing EGFR or ALK alterations. Patients received camrelizumab 200 mg intravenously every 2 weeks plus apatinib 250 mg orally once daily. The primary end point was the objective response rate (ORR) per investigator. **RESULTS:** A total of 25 patients were enrolled and treated. A total of 10 (40.0%) confirmed partial responses and 13 (52.0%) stable diseases were observed. The ORR was 40.0% (95% confidence interval [CI]: 21.1-61.3) and disease control rate was 92.0% (95% CI: 74.0-99.0). With a median follow-up of 19.5 months, the median progression-free survival was 9.6 months (95% CI: 5.5-not reached), whereas the overall survival was not reached; the median duration of response was 15.6 months (95% CI: 3.8-not reached). Similar ORR and progression-free survival were observed regardless of PD-L1 tumor proportion score (\geq 1% versus <1%). The most common treatment-related grade 3 or higher adverse events were increased gamma-glutamyltransferase (24.0%), increased alanine aminotransferase (16.0%), and abnormal hepatic function (16.0%). **CONCLUSIONS:** Frontline camrelizumab plus low-dose apatinib exhibited promising clinical activity with acceptable safety in patients with advanced nonsquamous NSCLC regardless of PD-L1 expression.

NSCLC - RADIOTHERAPY

[Prognostic Factors of Survival After Radiotherapy for Lung Cancer-The Impact of Smoking Pack Years](#) In Vivo. May-Jun 2022;36(3):1297-1301. doi: 10.21873/invivo.12830. Elisa M Werner 1 , Esther Glatzel 1 , Sabine Bohnet 2 , Steven E Schild 3 , Dirk Rades 1

BACKGROUND/AIM: The prognostic role of smoking pack years after thoracic irradiation for lung cancer needs further clarification, since previous studies showed conflicting results. Therefore, this study investigated potential prognostic factors for survival including pack years in 170 lung cancer patients receiving local radiotherapy. **PATIENTS AND METHODS:** Twelve factors were retrospectively evaluated for survival including age, sex, tumor site, histology, primary tumor stage, nodal stage, distant metastasis, radiation dose, upfront surgery or systemic treatment, pulmonary function, and number of pack years. **RESULTS:** On univariate analyses, absence of distant metastasis ($p=0.049$), radiation dose >56 Gy ($p=0.019$), and \leq 40 pack years ($p=0.005$) were significantly associated with better survival. In the multivariate analysis, number of pack years (hazard ratio 2.18, 95% confidence interval 1.25-3.82, $p=0.006$) maintained significance; distant metastasis ($p=0.34$) and radiation dose ($p=0.16$) were not significant. **CONCLUSION:** Number of pack years was an independent predictor of survival after thoracic irradiation for lung cancer.

[Surgical Evaluation in Patients Undergoing Radiation Therapy for Early-stage Lung Cancer](#) Ann Thorac Surg. 2022 May 21;S0003-4975(22)00720-2. doi: 10.1016/j.athoracsur.2022.04.055. Online ahead of print. Marcelo Cerullo, Hui-Jie Lee, Christopher Kelsey, Norma E Farrow, Charles D Scales, Betty C Tong

BACKGROUND: Stereotactic body radiation therapy (SBRT) is used to treat stage I non-small cell lung cancer (NSCLC) in non-surgical candidates, though guidelines specify that inoperability be determined in multidisciplinary fashion. We characterized NSCLC patients treated with SBRT undergoing thoracic

surgical evaluation (TSUe) and quantified TSUe's impact on time-to-treatment, receipt of diagnostic staging procedures, and healthcare costs. **METHODS:** Adults with newly diagnosed NSCLC undergoing SBRT were identified in the MarketScan all-payer claims database (2014-2018). TSUe was defined as an outpatient encounter with a thoracic surgeon or multispecialty group. Time-to-treatment and total costs in the six months preceding treatment were examined using multivariable regression by receipt of TSUe, adjusting for demographic and clinical factors. **RESULTS:** Of 1894 patients, 36.3% (n=687) underwent TSUe. Compared to patients without TSUe, these patients were younger (mean age 73.6 versus 76.3 years) and more likely to undergo invasive biopsy/staging procedures (90% versus 82%) or pulmonary function testing (80.6% versus 69.5%). Patients undergoing TSUe had a median time-to-treatment of 64 days (IQR: 43-98d), compared to 44 days (IQR: 29-70d) for no TSUe. Adjusted time-to-treatment was 43% longer (incident rate ratio: 1.43, 95% CI: 1.32-1.54, p<0.001) with TSUe. Patients undergoing TSUe also incurred 30% higher costs (adjusted cost ratio: 1.30, 95% CI: 1.20-1.41, p<0.001).

CONCLUSIONS: Among patients with early-stage NSCLC undergoing SBRT as primary treatment, a minority are evaluated by a thoracic surgeon. Because they have a longer time-to-treatment, more invasive diagnostic procedures, and higher costs, this represents a targetable gap to make workup protocols more efficient.

[Repeated Stereotactic Body Radiotherapy for Lung Malignancies: Toxicity Can Be Reduced by Sparing Lung Irradiation](#) Anticancer Res. 2022 May;42(5):2701-2709. doi: 10.21873/anticancer.15748. Shou Watanabe 1, Hideya Yamazaki 2 3, Takyua Kimoto 2 3, Gen Suzuki 2 3, Kei Yamada 2

BACKGROUND/AIM: Evidence on the use of repeated stereotactic body radiotherapy (SBRT) is limited. We investigated the efficacy of repeated SBRT and predictors of lung toxicity. **PATIENTS AND METHODS:** We reviewed 20 patients (27 lesions) with primary or metastatic lung cancer who underwent repeated SBRT with CyberKnife®. We generated a composite plan for dosimetric analysis based on equivalent doses in 2.0-Gy fractions ($\alpha/\beta=3$). Predictors of Grade 2+ radiation pneumonitis (RP) were examined. **RESULTS:** The median follow-up duration was 18.0 months. The 1-year and 2-year local control were both 95.2%. Five patients (25%) developed Grade 2+ RP, including a Grade 5 RP. The Grade 2+ RP group showed higher composite mean lung dose (MLD) and lower lung volumes spared from 5-20 Gy (VS5-VS20). **CONCLUSION:** Repeated SBRT with CyberKnife® showed favorable local control, but a high rate of Grade 2+ RP. Accumulated MLD and VS5-VS20 may predict RP.

[Magnetic resonance guided adaptive stereotactic body radiotherapy for lung tumors in ultracentral location: the MAGELLAN trial \(ARO 2021-3\)](#) Radiat Oncol. 2022 May 25;17(1):102. doi: 10.1186/s13014-022-02070-x. Sebastian Regnery 1 2 3 4 5, Jonas Ristau 1 2 3 4, Fabian Weykamp 1 2 3 4 5, et al.

BACKGROUND: Stereotactic Body Radiotherapy (SBRT) is a standard treatment for inoperable primary and secondary lung tumors. In case of ultracentral tumor location, defined as tumor contact with vulnerable mediastinal structures such as the proximal bronchial tree (PBT) or esophagus, SBRT is associated with an increased risk for severe complications. Magnetic resonance (MR)-guided SBRT can mitigate this risk based on gated dose delivery and daily plan adaptation. The MAGELLAN trial aims to find the maximum tolerated dose (MTD) of MR-guided SBRT of ultracentral lung tumors (ULT). Patients and **METHODS:** MAGELLAN is a prospective phase I dose escalation trial. A maximum of 38 patients with primary and secondary ULT with a tumor size ≤ 5 cm will be enrolled. Ultracentral location is defined as an overlap of the planning target volume (PTV) with the PBT or esophagus. Patients are treated at a 0.35 Tesla MR-linac (MRIdian® Linac, ViewRay Inc.) employing a gating strategy and daily plan adaptation. Dose escalation starts at 10×5.5 Gy (biologically effective dose BED3/10: 155.83 Gy/85.25 Gy), may proceed up to 10×6.5 Gy (BED3/10: 205.83 Gy/107.25 Gy) and is guided by a customized time-to-event continual reassessment method (TITE CRM) with backup element, which alternately

assigns patients to dose escalation and backup cohorts. **DISCUSSION:** The results of the MAGELLAN trial will guide further research and clinical implementation of MR-guided SBRT as ablative treatment of ULT. Moreover, the combination of MR-guided radiotherapy with TITE-CRM including a backup element may serve as blueprint for future radiation dose escalation studies in critical locations.

Multi-institutional phase II study on the safety and efficacy of dynamic tumor tracking-stereotactic body radiotherapy for lung tumors Radiother Oncol. 2022 May 2;172:18-22. doi:

10.1016/j.radonc.2022.04.028. Online ahead of print. Yukinori Matsuo 1 , Masahiro Hiraoka 2 , Katsuyuki Karasawa 3 , et al.

BACKGROUND AND PURPOSE: This study aimed to evaluate the safety and efficacy of dynamic tumor tracking-stereotactic body radiotherapy (DTT-SBRT) for lung tumors. **Materials and METHODS:** Patients with cStage I primary lung cancer or metastatic lung cancer with an expected range of respiratory motion of ≥ 10 mm were eligible for the study. The prescribed dose was 50 Gy in four fractions. A gimbal-mounted linac was used for DTT-SBRT delivery. The primary endpoint was local control at 2 years. **RESULTS:** Forty-eight patients from four institutions were enrolled in this study. Forty-two patients had primary non-small-cell lung cancer, and six had metastatic lung tumors. DTT-SBRT was delivered for 47 lesions in 47 patients with a median treatment time of 28 min per fraction. The median respiratory motion during the treatment was 13.7 mm (range: 4.5-28.1 mm). The motion-encompassing method was applied for the one remaining patient due to the poor correlation between the abdominal wall and tumor movement. The median follow-up period was 32.3 months, and the local control at 2 years was 95.2% (lower limit of the one-sided 85% confidence interval [CI]: 90.3%). The overall survival and progression-free survival at 2 years were 79.2% (95% CI: 64.7%-88.2%) and 75.0% (95% CI: 60.2%-85.0%), respectively. Grade 3 toxicity was observed in one patient (2.1%) with radiation pneumonitis. Grade 4 or 5 toxicity was not observed. **CONCLUSION:** DTT-SBRT achieved excellent local control with low incidences of severe toxicities in lung tumors with respiratory motion.

Causal relation between heart irradiation and survival of lung cancer patients after radiotherapy

Radiother Oncol. 2022 May 8;172:126-133. doi: 10.1016/j.radonc.2022.05.002. Online ahead of print. Carsten Brink 1 , Uffe Bernchou 2 , Anders Bertelsen 3 , et al.

INTRODUCTION: In a recent study, setup uncertainties in the direction of the heart were shown to impact the overall survival of non-small cell lung cancer (NSCLC) patients after radiotherapy, indicating the causal effect between heart irradiation and survival. The current study aims to externally evaluate this observation within a patient cohort treated using daily IGRT. **METHOD:** NSCLC patients with locally-advanced disease and daily CBCT were included. For all treatment fractions, the distance between the isocenter and the heart was evaluated based on the clinical setup registrations. The variation in heart position between planning and treatment (DeltaDistance) was estimated from these registrations. The possible impact of DeltaDistance on survival was analysed by a multivariable Cox model of overall survival, allowing for a time-dependent impact of DeltaDistance to allow for toxicity latency. **RESULTS:** Daily CBCT information was available for 489 patients at Odense University Hospital. The primary Cox model contained GTV volume, patient age, performance status, and DeltaDistance. DeltaDistance significantly impacted overall survival approximately 50 months after radiotherapy. Subanalyses indicated that the observed effect is mainly present among the patients with the least clinical risk factors. **CONCLUSION:** Our results confirm the impact of setup variations in the direction of the heart on the survival of NSCLC patients, even within a cohort using daily CBCT setup guidance. This result indicates a causal effect between heart irradiation and survival. It will be challenging to reduce the setup uncertainty even further; thus, increased focus on dose constraints on the heart seems warranted.

[The incidences of adverse events in small-cell lung cancer patients after radiotherapy and immunotherapy treatment: a systematic review and meta-analysis](#) Eur Rev Med Pharmacol Sci. 2022 May;26(9):3062-3073. doi: 10.26355/eurrev_202205_28723.

Q Wang ¹, A-H Liu, H-J Fan, A-B He, D-D Cao, W Hu, H-L Xu

Immunotherapy is important in treating small-cell lung cancer (SCLC), and its anti-tumor effects are better when combined with radiotherapy. However, the toxicity of this combination is little known. This study assessed the incidences of adverse events when adding radiotherapy to ICIs in patients with SCLC. We searched the online databases to identify eligible studies and included nine references. For extensive-stage SCLC patients, the median PFS ranged from 4.5 to 12.5 months, and median OS ranged from 8.4 to NR months, respectively. The incidences of grade 3 or higher pneumonitis, lung infection, diarrhea, and fatal adverse events were 8.7% (95% CI: 5%-14.7%), 6.7% (95% CI: 2.5%-16.5%), 12.6% (95% CI: 7.6%-20%), and 5.1% (95% CI: 2.1%-11.6%), respectively. Our findings suggest that radiotherapy plus ICIs may provide acceptable safety and favorable efficacy for SCLC patients.

[Small cell lung cancer patients treated with immune checkpoint inhibitor: a systematic literature review of treatment efficacy, safety, and quality of life](#) Curr Med Res Opin. 2022 May 14;1-13. doi:

10.1080/03007995.2022.2078101. Online ahead of print. Rasika Korde ¹, Rajwanth Veluswamy ² ³ ⁴, Gisoo Barnes ⁵

BACKGROUND: This systematic literature review examines the current immune checkpoint inhibitors treatment paradigms, treatment gaps, and unmet needs for treating SCLC with respect to efficacy, safety, health-related quality of life (HRQoL), and cost-effectiveness. **METHODS:** A search strategy was developed and executed using the National Library of Medicine bibliographic database (PubMed), Cochrane Library, Embase, and Google Scholar. Data regarding efficacy, safety, cost-effectiveness, and HRQoL were extracted and entered in a data extraction sheet created a priori. **RESULTS:** A total of 4,961 patients were comprised in all the 12 studies combined. All the studies focus on extensive stage SCLC (ES-SCLC) and not limited stage SCLC (LS-SCLC). All studies used an ICI as the intervention arm and chemotherapy as the control arm. A statistically significant increase in overall survival (OS) and progression free survival (PFS) was observed when ICIs were added to chemotherapy, especially atezolizumab and durvalumab. ICIs in SCLC resulted in immune-related toxicities that have been well-documented in prior immunotherapy trials; their addition to cytotoxic chemotherapy did not worsen chemotherapy-related toxicities. Out of 12 studies, only 3 (25%) included measures to assess the impact of immunotherapy on SCLC patients' HRQoL. Although domain level scores were limited, the addition of ICIs did not seem to worsen symptoms. Two studies conducted a cost-effectiveness analysis of the combination of atezolizumab plus chemotherapy versus chemotherapy. The addition of atezolizumab to chemotherapy was not found to be cost-effective in either study. **CONCLUSION:** Combining ICIs with chemotherapy enhanced OS and PFS as well as not worsening HRQoL. Among all ICIs, PDL1 inhibitors showed better effectiveness. Future studies should focus on real world settings and more clinical trials using ICIs for not only ES-SCLC but also LS-SCLC.

[Targeting the Ubiquitin-Proteasome System Using the UBA1 Inhibitor TAK-243 is a Potential Therapeutic Strategy for Small-Cell Lung Cancer](#) Clin Cancer Res. 2022 May 2;28(9):1966-1978. doi:

10.1158/1078-0432.CCR-21-0344. Safa Majeed ¹, Mansi K Aparnathi ², Kevin C J Nixon ², et al.

PURPOSE: Small cell lung cancer (SCLC) is an aggressive disease with an overall 5-year survival rate of less than 10%. Treatment for SCLC with cisplatin/etoposide chemotherapy (C/E) ± radiotherapy has changed modestly over several decades. The ubiquitin-proteasome system is an underexplored therapeutic target for SCLC. We preclinically evaluated TAK-243, a first-in-class small molecule E1 inhibitor against

UBA1. EXPERIMENTAL DESIGN: We assessed TAK-243 in 26 SCLC cell-lines as monotherapy and combined with C/E, the PARP-inhibitor, olaparib, and with radiation using cell viability assays. We interrogated TAK-243 response with gene expression to identify candidate biomarkers. We evaluated TAK-243 alone and in combination with olaparib or radiotherapy with SCLC patient-derived xenografts (PDX). **RESULTS:** Most SCLC cell lines were sensitive to TAK-243 monotherapy (EC50 median 15.8 nmol/L; range 10.2 nmol/L-367.3 nmol/L). TAK-243 sensitivity was associated with gene-sets involving the cell cycle, DNA and chromatin organization, and DNA damage repair, while resistance associated with cellular respiration, translation, and neurodevelopment. These associations were also observed in SCLC PDXs. TAK-243 synergized with C/E and olaparib in vitro across sensitive and resistant SCLC cell lines. Considerable TAK-243-olaparib synergy was observed in an SCLC PDX resistant to both drugs individually. TAK-243 radiosensitization was also observed in an SCLC PDX. **CONCLUSIONS:** TAK-243 displays efficacy in SCLC preclinical models. Enrichment of gene sets is associated with TAK-243 sensitivity and resistance. TAK-243 exhibits synergy when combined with genotoxic therapies in cell lines and PDXs. TAK-243 is a potential therapeutic strategy to improve SCLC patient outcomes, both as a single agent and in combination with existing therapies.

Small Cell Lung Cancer Staging: Prospective Comparison of Conventional Staging Tests, FDG PET/CT, Whole-Body MRI, and Coregistered FDG PET/MRI AJR Am J Roentgenol. 2022

May;218(5):899-908. doi: 10.2214/AJR.21.26868. Epub 2021 Dec 8. Yoshiharu Ohno 1 2 3 , Takeshi Yoshikawa 3 4 , Daisuke Takenaka 4 5 , et al.

BACKGROUND: Whole-body MRI and FDG PET/MRI have shown encouraging results for staging of thoracic malignancy but are poorly studied for staging of small cell lung cancer (SCLC). **OBJECTIVE:** The purpose of our study was to compare the performance of conventional staging tests, FDG PET/CT, whole-body MRI, and FDG PET/MRI for staging of SCLC. **METHODS:** This prospective study included 98 patients (64 men, 34 women; median age, 74 years) with SCLC who underwent conventional staging tests (brain MRI; neck, chest, and abdominopelvic CT; and bone scintigraphy), FDG PET/CT, and whole-body MRI within 2 weeks before treatment; coregistered FDG PET/MRI was generated. Two nuclear medicine physicians independently reviewed conventional tests and FDG PET/CT examinations in separate sessions, and two chest radiologists independently reviewed whole-body MRI and FDG PET/MRI examinations in separate sessions. Readers assessed T, N, and M categories; TNM stage; and Veterans Administration Lung Cancer Study Group (VALSG) stage. Reader pairs subsequently reached consensus. Stages determined clinically during tumor board sessions served as the reference standard. **RESULTS:** Accuracy for T category was higher ($p < .05$) for whole-body MRI (94.9%) and FDG PET/MRI (94.9%) than for FDG PET/CT (85.7%). Accuracy for N category was higher ($p < .05$) for whole-body MRI (84.7%), FDG PET/MRI (83.7%), and FDG PET/CT (81.6%) than for conventional staging tests (75.5%). Accuracy for M category was higher ($p < .05$) for whole-body MRI (94.9%), FDG PET/MRI (94.9%), and FDG PET/CT (94.9%) than for conventional staging tests (84.7%). Accuracy for TNM stage was higher ($p < .05$) for whole-body MRI (88.8%) and FDG PET/MRI (86.7%) than for FDG PET/CT (77.6%) and conventional staging tests (72.4%). Accuracy for VALSG stage was higher ($p < .05$) for whole-body MRI (95.9%), FDG PET/MRI (95.9%), and FDG PET/CT (98.0%) than for conventional staging tests (82.7%). Interobserver agreement, expressed as kappa coefficients, ranged from 0.81 to 0.94 across imaging tests and staging endpoints. **CONCLUSION:** FDG PET/CT, whole-body MRI, and coregistered FDG PET/MRI outperformed conventional tests for various staging endpoints in patients with SCLC. Whole-body MRI and FDG PET/MRI outperformed FDG PET/CT for T category and thus TNM stage, indicating the utility of MRI for assessing extent of local invasion in SCLC. **CLINICAL IMPACT:** Incorporation of either MRI approach may improve initial staging evaluation in SCLC.

[Radiation therapy for extensive-stage small-cell lung cancer in the era of immunotherapy](#) Cancer Lett. 2022 May 18;541:215719. doi: 10.1016/j.canlet.2022.215719. Online ahead of print. Yaru Tian 1 , Ji Ma 2 , Xuquan Jing 1 , Xiaoyang Zhai 1 , Yuying Li 1 , Zhijun Guo 3 , Jinming Yu 4 , Hui Zhu 5 Unlike non-small-cell lung cancer (NSCLC), the progression of small-cell lung cancer (SCLC) is slow. Extensive-stage SCLC (ES-SCLC) is a serious threat to human health, with a 5-year survival rate of <7%. Chemotherapy has been the first-line treatment for the past 30 years. The anti-PD-L1 checkpoint blockades durvalumab and atezolizumab have greatly prolonged overall survival and have become the standard first-line therapy for ES-SCLC since the CASPIAN and IMpower133 trials. In the era of chemotherapy, radiation therapy (RT), including thoracic radiation therapy (TRT) and brain radiation therapy (BRT), has shown clinical effects in randomized and retrospective studies on ES-SCLC. RT-immunotherapy has shown exciting synergistic effects in NSCLC. For ES-SCLC, the clinical effects of combining TRT/BRT with immunotherapy have not yet been systematically explored. In this review, we found that studies on RT-immunotherapy in ES-SCLC are relatively few and limited to early phase studies focusing on toxicity. The efficacy and safety profiles of early phase studies encourage prospective clinical trials. In this review, we discuss the best population, optimum TRT dose, proper TRT time, and strategies for reducing radiation-induced neurotoxicity. Furthermore, we suggest that biomarkers and patient performance status should be fully assessed before RT-immunotherapy treatment. Prospective trials are needed to provide more evidence for RT-immunotherapy applications in ES-SCLC.

PALLIATIVE AND SUPPORTIVE CARE

[Exercise, Diet, and Weight Management During Cancer Treatment: ASCO Guideline](#) J Clin Oncol. 2022 May 16;JCO2200687. doi: 10.1200/JCO.22.00687. Online ahead of print. Jennifer A Ligibel 1 , Kari Bohlke 2 , Anne M May 3 , Steven K Clinton 4 , Wendy Demark-Wahnefried 5 , Susan C Gilchrist 6 , Melinda L Irwin 7 , Michele Late 8 , Sami Mansfield 9 , Timothy F Marshall 10 , Jeffrey A Meyerhardt 1 , Cynthia A Thomson 11 , William A Wood 12 , Catherine M Alfano 13

PURPOSE: To provide guidance on exercise, diet, and weight management during active cancer treatment in adults. **METHODS:** A systematic review of the literature identified systematic reviews and randomized controlled trials evaluating the impact of aerobic and resistance exercise, specific diets and foods, and intentional weight loss and avoidance of weight gain in adults during cancer treatment, on quality of life, treatment toxicity, and cancer control. PubMed and the Cochrane Library were searched from January 2000 to May 2021. ASCO convened an Expert Panel to review the evidence and formulate recommendations. **RESULTS:** The evidence base consisted of 52 systematic reviews (42 for exercise, nine for diet, and one for weight management), and an additional 23 randomized controlled trials. The most commonly studied types of cancer were breast, prostate, lung, and colorectal. Exercise during cancer treatment led to improvements in cardiorespiratory fitness, strength, fatigue, and other patient-reported outcomes. Preoperative exercise in patients with lung cancer led to a reduction in postoperative length of hospital stay and complications. Neutropenic diets did not decrease risk of infection during cancer treatment. Recommendations: Oncology providers should recommend regular aerobic and resistance exercise during active treatment with curative intent and may recommend preoperative exercise for patients undergoing surgery for lung cancer. Neutropenic diets are not recommended to prevent infection in patients with cancer during active treatment. Evidence for other dietary and weight loss interventions during cancer treatment was very limited. The guideline discusses special considerations, such as exercise in individuals with advanced cancer, and highlights the critical need for more research in this area, particularly regarding diet and weight loss interventions during cancer treatment. Additional information is available at www.asco.org/supportive-care-guidelines.

Prolonged administration of aprepitant improves cisplatin-based chemotherapy-induced nausea and vomiting

Future Oncol. 2022 May 19. doi: 10.2217/fon-2021-1523. Online ahead of print. Yanying Li 1 , Yu Sun 2 , Bin Liu 3 , Yi Sun 4 , Ping Chen 5 , Ke Xie 6 , Yan Wang 7 , Jiang Zhu 1

AIMS: To determine the antiemetic efficacy of a 6-day aprepitant schedule in patients receiving multiple-day cisplatin. Patients & **METHODS:** Patients diagnosed with lung cancer and who were chemotherapy naive were screened. The patients willing to use aprepitant were randomly divided into two groups: prolonged use of aprepitant (PA; 6-day aprepitant) and standard use of aprepitant (SA; 3-day aprepitant); the patients who rejected aprepitant were recruited into the control group (group C). Primary end points included the safety and the number of days without chemotherapy-induced nausea and vomiting.

RESULTS: There was no statistical difference in adverse events among the three groups. The average days without chemotherapy-induced nausea and vomiting of group PA (18.28 ± 3.35) was significantly longer than in groups SA and C. Furthermore, better life function scores were achieved in group PA according to the Functional Living Index - Emesis questionnaire. **CONCLUSION:** In this study 6-day aprepitant was safe and more effective than standard 3-day aprepitant in controlling chemotherapy-induced nausea and vomiting due to 3-day cisplatin regimens. **PLAIN LANGUAGE SUMMARY:** The aim of this study was to determine the effectiveness of a 6-day aprepitant schedule in patients receiving a multiple-day highly emetogenic chemotherapy drug (cisplatin). Aprepitant is an important medication used to prevent chemotherapy-induced nausea and vomiting (CINV). The patients willing to use aprepitant were randomly divided into two groups: prolonged use of aprepitant (PA; 6-day aprepitant) and standard use of aprepitant (SA; 3-day aprepitant). The patients who rejected aprepitant were recruited into the control group. The results showed that cases of CINV in group PA ended more quickly. Group PA also had more days with no vomiting and no nausea than the other two groups. The results of this study propose 6-day aprepitant use as more effective to prevent CINV in patients receiving 3-day cisplatin-based chemotherapy. Clinical trial registration: ChiCTR-IPR-15005933 (<http://www.chictr.org.cn>).

Long-term assessment of efficacy with a novel Thoracic Survivorship Program for patients with lung cancer

J Thorac Cardiovasc Surg. 2022 May;163(5):1645-1653.e4. doi:

10.1016/j.jtcvs.2021.11.026. Epub 2021 Nov 20 Hari B Keshava 1 , Kay See Tan 2 , Joe Dycoco 1, et al.

OBJECTIVE: We developed a novel, nurse practitioner-run Thoracic Survivorship Program to aid in long-term follow-up. Patients with non-small cell lung cancer who were disease-free at least 1 year after resection could be referred to the Thoracic Survivorship Program by their surgeon. Our objectives were to summarize follow-up compliance and assess long-term outcomes between Thoracic Survivorship Program enrollment and non-Thoracic Survivorship Program. **METHODS:** Patients who underwent R0 resection for stages I to IIIA between 2006 and 2016 were stratified by enrollment in Thoracic Survivorship Program versus surgeon only follow-up (non-Thoracic Survivorship Program). Follow-up included 6-month chest computed tomography scans for 2 years and then annually. Lack of follow-up compliance was defined by 2 or more consecutive delayed annual computed tomography scans/visits ± 90 days.

Relationships between Thoracic Survivorship Program and second primary non--small cell lung cancers, extrathoracic cancers, and survival were quantified using multivariable Cox proportional hazards regression with time-varying covariate reflecting timing of enrollment. **RESULTS:** A total of 1162 of 3940 patients (29.5%) were enrolled in the Thoracic Survivorship Program. The median time to enrollment was 2.3 years; 3279 of 3940 (83%) had complete computed tomography scan data, and 60 of 3279 (1.8%) had 2 or more delayed scans; 323 of 9082 (3.6%) non-Thoracic Survivorship Program visits were noncompliant versus 132 of 4823 (2.7%) of Thoracic Survivorship Program visits ($P = .009$); 136 of 1146 Thoracic Survivorship Program patients developed second primary non-small cell lung cancer, and 69 of 1123 developed extrathoracic cancer, whereas 322 of 2794 of non-Thoracic Survivorship Program patients developed second primary non-small cell lung cancer and 225 of 2817 patients developed extrathoracic cancer. In multivariable analyses, Thoracic Survivorship Program enrollment was associated

with improved disease-free survival (hazard ratio, 0.57; 95% confidence interval, 0.48-0.67; $P < .001$).

CONCLUSIONS: Our novel nurse practitioner-run Thoracic Survivorship Program is associated with high patient compliance and outcomes not different from those seen with physician-based follow-up. These results have important implications for health care resource allocation and costs.

Feasibility of Rehabilitation during Chemoradiotherapy among Patients with Stage III Non-Small Cell Lung Cancer: A Proof-of-Concept Study *Cancers (Basel)*. 2022 May 12;14(10):2387. doi:

10.3390/cancers14102387. Melissa J J Voorn ^{1 2 3}, Bart C Bongers ^{4 5}, Vivian E M van Kampen-van den Boogaart ⁶, Elisabeth J M Driessen ¹, Maryska L G Janssen-Heijnen ^{1 3}

Rehabilitation during chemoradiotherapy (CHRT) might (partly) prevent reduction in physical fitness and nutritional status and could improve treatment tolerance in patients with stage III non-small cell lung cancer (NSCLC). The aim of this proof-of-concept study was to investigate the feasibility of a multimodal program for rehabilitation during CHRT. A home-based multimodal rehabilitation program (partly supervised moderate-intensity physical exercise training and nutritional support) during CHRT was developed in collaboration with patients with stage III NSCLC and specialized healthcare professionals. A predetermined number of six patients with stage III NSCLC (aged ≥ 50 years) who underwent CHRT and participated in this program were monitored in detail to assess its feasibility for further development and optimization of the program. The patient's level of physical functioning (e.g., cardiopulmonary exercise test, six-minute walking test, handgrip strength, body mass index, fat free mass index, energy and protein intake) was evaluated in order to provide personalized advice regarding physical exercise training and nutrition. The program appeared feasible and well-tolerated. All six included patients managed to perform the assessments. Exercise session adherence was high in five patients and low in one patient. The performed exercise intensity was lower than prescribed for all patients. Patients were motivated to complete the home-based rehabilitation program during CHRT. Preliminary effects on physical and nutritional parameters revealed relatively stable values throughout CHRT, with inter-individual variation. Supervised and personalized rehabilitation in patients with stage III NSCLC undergoing CHRT seems feasible when the intensity of the physical exercise training was adjusted to the possibilities and preferences of the patients. Future research should investigate the feasibility of a supervised and personalized rehabilitation program during CHRT with a low-to-moderate exercise intensity with the aim to prevent physical decline during CHRT.

Incidence, Clinical Characteristics, and Predictors of Cardiovascular Immune-Related Adverse Events Associated with Immune Checkpoint Inhibitors *Oncologist*. 2022 May 6;27(5):e410-e419. doi:

10.1093/oncolo/oyac056. Tsuyoshi Isawa ¹, Yukihiro Toi ², Shunichi Sugawara ², Masataka Taguri ³, Shigeru Toyoda ⁴

BACKGROUND: Cardiovascular immune-related adverse events (CV-irAEs) associated with immune checkpoint inhibitors (ICIs) may have been underreported given that most previous reports were retrospective. We aimed to evaluate the incidence, clinical characteristics, and predictors of CV-irAEs and determine the feasibility of serial cardiac monitoring using a combination of B-type natriuretic peptide, cardiac troponin T, and electrocardiogram for the prediction of future symptomatic (grade ≥ 2) CV-irAEs.

Materials and METHODS: This was a prospective observational study that included 129 consecutive patients with non-small-cell lung cancer who received ICI monotherapy at a single center. Serial cardiac monitoring was performed during ICI monotherapy. **RESULTS:** A total of 35 (27%) patients developed any grade ≥ 1 CV-irAEs with a median time of onset of 72 (interquartile range 44-216) days after ICI treatment initiation. Multivariate Fine-Gray regression analysis showed that prior acute coronary syndrome (adjusted hazard ratio [HR] 3.15 [95% [CI], 2.03-4.91), prior heart failure hospitalization (adjusted HR 1.65 [95% CI, 1.17-2.33]), and achievement of disease control (adjusted HR 1.91, [95% CI, 1.16-3.14]) were significantly associated with grade ≥ 1 CV-irAEs. Serial cardiac monitoring revealed that

patients with preceding grade 1 CV-irAEs were associated with a significantly higher risk of onset of grade ≥ 2 CV-irAEs compared with those without preceding grade 1 CV-irAEs (HR: 6.17 [95% CI, 2.97-12.83]). **CONCLUSION:** CV-irAEs were more common than previously recognized and have several predictors. Moreover, serial cardiac monitoring may be feasible for the prediction of future grade ≥ 2 CV-irAEs.

COMPLEMENTARY & ALTERNATIVE THERAPY

Cytotoxic screening and antibacterial activity of Withaferin A J Toxicol Environ Health A. 2022 May 17;1-14. doi: 10.1080/15287394.2022.2071787. Online ahead of print. Altevira Rossato Viana 1 , B Godoy Noro 2 , J C Lenz 2 , M Luiza Machado Teixeira 1 , M Bolson Serafin 3 , R Hörner 3 , C Franco 4 , L Maria Fontanari Krause 5 , B Stefanello Vizzotto 1 , B Jalfim Maraschin 6
Cancer and bacterial infections are among the leading causes of death worldwide. Plant-derived bioactive compounds constitute promising alternatives for development of new therapeutics. This study aimed at evaluating the biological activity of Withaferin A using 6 tumor cell lines: A549 (lung cancer), U87MG (glioblastoma), SH-SY5Y (neuroblastoma), B16-F10 (mouse melanoma), HeLa (uterine colon cancer) and K562 (chronic myeloid leukemia). In addition, 17 other standard bacterial strains and several multidrug resistant bacteria (MDR) clinical isolates were examined. Cell viability was assessed using the following assays: MTT, neutral red, and dsDNA PicoGreen®. Further, oxidative stress was measured by quantification of reactive oxygen species (ROS) production. The activity against bacteria was determined by the minimum inhibitory concentration (MIC), minimum bacterial concentration (CBM) and antibiofilm activity in the production of strains. Withaferin A was effective, as evidenced by its cytotoxic activity in tumor cell lines, enhanced ROS production in tumor cells and bactericidal and antibiofilm activity. Data demonstrated that Withaferin A may be therapeutically considered as an antitumor and antibacterial agent.

MISCELLANEOUS WORKS

Lung Cancer Stem Cells and Their Clinical Implications Cold Spring Harb Perspect Med. 2022 May 17;12(4):a041270. doi: 10.1101/cshperspect.a041270. Samuel P Rowbotham 1 2 , Mounika U L Goruganthu 3 , et al.

It is now widely accepted that stem cells exist in various cancers, including lung cancer, which are referred to as cancer stem cells (CSCs). CSCs are defined in this context as the subset of tumor cells with the ability to form tumors in serial transplantation and cloning assays and form tumors at metastatic sites. Mouse models of lung cancer have shown that lung CSCs reside in niches that are essential for the maintenance of stemness, plasticity, enable antitumor immune evasion, and provide metastatic potential. Similar to normal lung stem cells, Notch, Wnt, and the Hedgehog signaling cascades have been recruited by the CSCs to regulate stemness and also provide therapy-driven resistance in lung cancer. Compounds targeting β -catenin and Sonic hedgehog (Shh) activity have shown promising anti-CSC activity in preclinical murine models of lung cancer. Understanding CSCs and their niches in lung cancer can answer fundamental questions pertaining to tumor maintenance and associated immune regulation and escape that appear important in the quest to develop novel lung cancer therapies and enhance sensitivity to currently approved chemo-, targeted-, and immune therapeutics.

Impact of clinical pathways on treatment patterns and outcomes for patients with non-small-cell lung cancer: real-world evidence from a community oncology practice J Comp Eff Res. 2022 Jun;11(8):609-619. doi: 10.2217/ce-2021-0290. Epub 2022 May 12. Natalie R Dickson 1 , Karen D

Beauchamp 2 , Toni S Perry 3 , Ashley Roush 1 , Deborah Goldschmidt 4 , Marie Louise Edwards 4 , Laura J Blakely 1

INTRODUCTION: The evolving treatment landscape for non-small-cell lung cancer (NSCLC) and complexities of regulations and reimbursement present challenges to community oncologists. Clinical pathways are tools to optimize care, but information on their value in the real world is limited. This retrospective study assessed treatment patterns and clinical outcomes in patients with stage I-III NSCLC pre- and post-pathways implementation at Tennessee Oncology, a large, community-based oncology practice in the USA. **METHODS & MATERIALS:** Chart data were abstracted for adults diagnosed with stage I-III NSCLC who received systemic treatment. Patients were divided into pre-pathways (treatment initiation 2014-2015) and post-pathways (treatment initiation 2016-2018) cohorts. Patient characteristics, treatment patterns and outcomes were summarized descriptively. Kaplan-Meier curves were used to assess time-dependent outcomes, and log-rank test was used to compare the cohorts. **RESULTS:** 291 patients were included (stage I-II: 38 pre-pathways, 55 post-pathways; stage III: 105 pre-pathways, 93 post-pathways). Duration on first-line (1L) therapy was similar for stage I-II patients pre- and post-pathways (median 1.9 months vs 2.1 months; $p = 0.75$), but increased for stage III patients post-pathways (2.1 months vs 1.4 months pre-pathways; $p < 0.01$). Achievement of a complete or partial response with 1L therapy was similar post-pathways among stage I-stage -III patients (60.0% vs 55.2% pre-pathways), but increased for stage III patients (56.0% vs 35.2% pre-pathways). **CONCLUSION:** Given that improvements in rates of treatment response post-pathways occurred only for patients diagnosed with stage III NSCLC, among whom immunotherapy uptake increased post-pathways, such improvements may be attributable to evolving practices in cancer care, including advances in treatment and care delivery, rather than clinical pathways implementation. Further research is warranted to assess the impact of clinical pathways in the current treatment era, given that immunotherapy has now become the standard of care in NSCLC.

[Associations Between Medicaid Insurance, Biomarker Testing, and Outcomes in Patients With Advanced NSCLC](#) Natl Compr Canc Netw. 2022 May;20(5):479-487.e2. doi: 10.6004/jnccn.2021.7083.

Cary P Gross 1 2 , Craig S Meyer 3 , Sarika Ogale 3 , Matthew Kent 4 , William B Wong 3

BACKGROUND: Evidence suggests that patients with Medicaid experience lower-quality cancer care than those with commercial insurance. Whether this trend persists in the era of personalized medicine is unclear. This study examined the associations between Medicaid (vs commercial) insurance and receipt of biomarker testing, targeted therapy, and overall survival in patients with advanced non-small cell lung cancer (aNSCLC). **METHODS:** We conducted a retrospective study of patients who received an aNSCLC diagnosis from January 2011 to September 2019 using a nationwide US healthcare database. Eligible patients were aged 18 to 64 years with Medicaid or commercial insurance at diagnosis. Receipt of biomarker testing (ALK, EGFR, ROS1, BRAF, and PD-L1) was assessed. The likelihood of testing, biomarker-driven therapy (cancer immunotherapy or tyrosine kinase inhibitor treatment), and mortality were compared by insurance type using adjusted Cox regression. **RESULTS:** Our sample included 6,145 commercially insured and 865 Medicaid beneficiaries. Medicaid beneficiaries were more likely to be Black or African American (20% vs 9.3%; $P < .001$) and were less likely to have undergone biomarker testing (57% vs 71%; $P < .001$). In the adjusted analysis, Medicaid beneficiaries were less likely to have evidence of testing (hazard ratio [HR], 0.81; $P < .001$), any first-line treatment (HR, 0.72; $P < .001$), and first-line biomarker-driven therapy (HR, 0.70; $P < .001$). Medicaid beneficiaries with evidence of biomarker testing had a lower risk of death compared with those without evidence of biomarker testing (HR, 1.27 [95% CI, 1.06-1.52]; $P = .010$). Higher risk of death was observed in patients with Medicaid versus commercially insured patients (HR, 1.23; $P < .001$); this result remained unchanged after adjusting for biomarker testing (HR, 1.22; $P < .001$) but was partially ameliorated after adjustment for testing and treatment type (HR, 1.12; $P = .010$). **CONCLUSIONS:** Medicaid beneficiaries with aNSCLC were less

likely to receive biomarker testing and biomarker-driven therapies, which may in part contribute to a higher observed risk of mortality compared with commercially insured patients.

Identifying Determinants of Disparities in Lung Cancer Survival Rates from Electronic Health Record Data Stud Health Technol Inform. 2022 May 25;294:715-716. doi: 10.3233/SHTI220567.

Wanting Cui 1 , Joseph Finkelstein 1

The goal of this pilot study was to identify significant factors that affect disparities in lung cancer survival. A de-identified dataset was generated by querying electronic health records (EHR) from an academic medical center in New York City between January 2003 and November 2020. Socio-demographic characteristics, cancer stage, and genetic profile were analyzed using logistic regression. Two subsets of adult patients were identified: patients who were deceased less than 1 year after diagnosis and patients who survived over 5 years after diagnosis. Male, Black and Hispanic patients and those who were diagnosed in later stages were the people most susceptible to a shorter length of survival after cancer diagnoses. In addition, we identified three genetic oncodrivers (KRAS, EGFR and TP53) which were highly correlated with the length of survival after lung cancer diagnoses and their distribution was associated with race. We concluded that EHR data provide important insights on cancer survival disparities.

Long-term exposure to wildfires and cancer incidence in Canada: a population-based observational cohort study Lancet Planet Health. 2022 May;6(5):e400-e409. doi: 10.1016/S2542-5196(22)00067-5. Jill

Korsiak 1 , Lauren Pinault 2 , Tanya Christidis 2 , Richard T Burnett 3 , Michal Abrahamowicz 1 , Scott Weichenthal 4

BACKGROUND: Wildfires emit many carcinogenic pollutants that contaminate air, water, terrestrial, and indoor environments. However, little is known about the relationship between exposure to wildfires and cancer risk. We aimed to assess the associations between residential exposure to wildfires and the incidence of several cancer outcomes (lung cancer, brain cancer, non-Hodgkin lymphoma, multiple myeloma, and leukaemia) in Canada. **METHODS:** We did a population-based observational cohort study of participants in the 1996 Canadian Census Health and Environment Cohort. The 1996 Canadian Census Health and Environment Cohort is a nationally representative sample of Canadian adults, followed up for cancer incidence and mortality from 1996 to 2015. For this analysis, we excluded participants who lived in major Canadian cities (with a population size greater than 1.5 million people), recent immigrants, and individuals younger than 25 years or 90 years of age or older at baseline. Exposures to wildfires were assigned on the basis of area burned within a 20 km or 50 km radius of residential locations and updated for annual residential mobility. Multivariable Cox proportional hazards models were used to estimate associations between exposure to wildfires and specific cancers associated with carcinogenic compounds released by wildfires, including lung and brain cancer, non-Hodgkin lymphoma, multiple myeloma, and leukaemia, adjusted for many personal and neighbourhood-level covariates. **FINDINGS:** Our analyses included more than 2 million people followed up for a median of 20 years, for a total of 34 million person-years. Wildfire exposure was associated with slightly increased incidence of lung cancer and brain tumours. For example, cohort members exposed to a wildfire within 50 km of residential locations in the past 10 years had a 4.9% relatively higher incidence (adjusted hazard ratio [HR] 1.049, 95% CI 1.028-1.071) of lung cancer than unexposed populations, and a 10% relatively higher incidence (adjusted HR 1.100, 1.026-1.179) of brain tumours. Similar associations were observed for the 20 km buffer size. Wildfires were not associated with haematological cancers in this study, and concentration-response trends were not readily apparent when area burned was modelled as a continuous variable.

INTERPRETATION: Long-term exposure to wildfires might increase the risk of lung cancer and brain tumours. Further work is needed to develop long-term estimates of wildfire exposures that capture the complex mixture of environmental pollutants released during these events.

[Clinical features of patients with second primary lung cancer following head and neck cancer](#)

Ann Thorac Surg. 2022 May 17;S0003-4975(22)00705-6. doi: 10.1016/j.athoracsur.2022.04.052. Online ahead of print. Fumiaki Takatsu 1 , Ken Suzawa 2 , Mikio Okazaki 1 , et al. .

BACKGROUND: Survivors of head and neck cancer (HNC) often develop second primary lung cancer (SPLC), due to a common risk factor, that is, smoking. Our multicenter experience has been reviewed to evaluate how the history of diagnosis of HNC affects the outcomes of patients undergoing pulmonary resection for SPLC. **METHODS:** A multicenter retrospective analysis of patients hospitalized between January 2012 and December 2018 has been performed. From a cohort of 4,521 patients undergoing therapeutic pulmonary resection for primary non-small cell lung cancer, 100 patients with previous history of HNC (HNC group) have been identified. They were compared with a control group consisting of 200 patients without HNC history from the same cohort pair-matched with operating facility, age, sex, and pathological stage of lung cancer. **RESULTS:** At the time of surgery for SPLC, the HNC group showed malnutrition with lower prognostic nutritional index (PNI) compared with the control group ($p < 0.001$). The HNC group were determined to have postoperative complications more frequently ($p = 0.02$). The 5-year overall survival rates in the HNC and control groups were 59.0% and 83.2%, respectively ($p < 0.001$). Statistically, HNC history, lower PNI, squamous cell lung cancer, and TNM stage were identified to be independently associated with poor survival. **CONCLUSIONS:** Patients with SPLC following primary HNC often present with malnutrition and are predisposed to have postoperative complications and poor survival after pulmonary resection.

[Effect of sponsor on enrollment criteria in non-small cell lung cancer clinical trials](#) J Cancer Policy.

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BACKGROUND: Inclusion and exclusion criteria in clinical trials are used to mitigate the effects of confounding variables on study outcomes. In 2017 and 2021, ASCO and the Friends of Cancer Research published recommendations to loosen enrollment criteria in cancer clinical trials to improve generalizability. The purpose of this study is to determine if the source of funding influences the degree of transparency and selection of inclusion and exclusion criteria. **METHODS:** Phase 2 and 3 non-small cell lung cancer (NSCLC) drug trials on clinicaltrials.gov were grouped into one of three sponsor categories: industry, government/cooperative group, and academic. Strictness of specific criteria and the level of transparency in listing organ function requirements were analyzed using Fisher Exact tests. Independent sample t tests were used to assess the variability in total number of criteria. **RESULTS:** Organ function requirements listed on clinicaltrials.gov are more often vague or incomplete in industry sponsored trials compared to government/cooperative group ($p = 2.3 \times 10^{-10}$, $\alpha = 0.01$) and academic ($p = 1.8 \times 10^{-4}$, $\alpha = 0.01$) sponsored trials. Industry sponsored trials more often excluded patients with worse performance status scores compared to government/cooperative group sponsored trials ($p = 5.7 \times 10^{-6}$, $\alpha = 0.01$). **CONCLUSION:** Industry sponsored NSCLC drug trials are more likely to exclude patients with worse performance status and are less transparent in listing complete study requirements on clinicaltrials.gov. **POLICY SUMMARY:** Unnecessarily strict enrollment criteria are increasingly seen in clinical trials sponsored by industry. Regulators responsible for drug approvals should note when studies deviate from ASCO and Friends of Cancer Research framework and question the external validity of study findings with overly narrow enrollment criteria when making decisions on drug approvals.

[Prospective Comparative Effectiveness Trial of Multidisciplinary Lung Cancer Care Within a Community-Based Health Care System](#) JCO Oncol Pract. 2022 May 24;OP2100815. doi:

10.1200/OP.21.00815. Online ahead of print. Matthew P Smeltzer 1 , Meredith A Ray 1 , Nicholas R Faris 2 , et al.

PURPOSE: Multidisciplinary lung cancer care is assumed to improve care delivery by increasing transparency, objectivity, and shared decision making; however, there is a lack of high-level evidence demonstrating its benefits, especially in community-based health care systems. We used implementation and team science principles to establish a colocated multidisciplinary lung cancer clinic in a large community-based health care system and evaluated patient experience and outcomes within and outside this clinic. **METHODS:** We conducted a prospective frequency-matched comparative effectiveness study (ClinicalTrials.gov identifier: NCT02123797) evaluating the thoroughness of lung cancer staging, receipt of stage-appropriate treatment, and survival between patients receiving care in the multidisciplinary clinic and those receiving usual serial care. Target enrollment was 150 patients on the multidisciplinary arm and 300 on the serial care arm. We frequency-matched patients by clinical stage, performance status, insurance type, race, and age. **RESULTS:** A total of 526 patients were enrolled: 178 on the multidisciplinary arm and 348 on the serial care arm. After adjusting for other factors, multidisciplinary patients had significantly higher odds (odds ratio [OR]: 2.3 [95% CI, 1.5 to 3.4]) of trimodality staging compared with serial care. Patients on the multidisciplinary arm also had higher odds of receiving invasive stage confirmation (OR: 2.0 [95% CI, 1.4 to 3.1]) and mediastinal stage confirmation (OR: 1.9 [95% CI, 1.3 to 2.8]). Additionally, patients receiving multidisciplinary care were significantly more likely to receive stage-appropriate treatment (OR: 1.8 [95% CI, 1.1 to 3.0]). We found no significant difference in overall or progression-free survival between study arms. **CONCLUSION:** The multidisciplinary clinic delivered significant improvements in evidence-based quality care on multiple levels. Even in the absence of a demonstrable survival benefit, these findings provide a strong rationale for recommending this model of care.

[Cancer Epidemiology in Hispanic Populations: What Have We Learned and Where Do We Need to Make Progress?](#) *Cancer Epidemiol Biomarkers Prev.* 2022 May 4;31(5):932-941. doi: 10.1158/1055-9965.EPI-21-1303. Laura Fejerman ¹, Amelie G Ramirez ², Anna María Nápoles ³, Scarlett Lin Gomez ⁴, Mariana C Stern ⁵

The Hispanic/Latino(x) population (H/L) in the United States of America is heterogeneous and fast growing. Cancer is the number one cause of death among H/Ls, accounting for 21% of deaths. Whereas for the most common cancers, incidence rates are lower in H/Ls compared with non-H/L White (NHW) individuals, H/Ls have a higher incidence of liver, stomach, cervical, penile, and gallbladder cancers. H/L patients tend to be diagnosed at more advanced stages for breast, colorectal, prostate, and lung cancers, and melanoma compared with NHW individuals. Etiologic and cancer outcomes research among H/Ls lags other populations. In this review, we provide a summary of challenges, opportunities, and research priorities related to cancer etiology, cancer outcomes, and survivorship to make progress in addressing scientific gaps. Briefly, we prioritize the need for more research on determinants of obesity, nonalcoholic fatty liver disease and its progression to liver cancer, stomach and gallbladder cancers, and pediatric acute lymphoblastic leukemia. We emphasize the need to improve cancer screening, early detection of cancer, and survivorship care. We highlight critical resources needed to make progress in cancer epidemiologic studies among H/L populations, including the importance of training the next generation of cancer epidemiologists conducting research in H/Ls.

[Improving Sexual and Gender Minority Cancer Care: Patient and Caregiver Perspectives From a Multi-Methods Pilot Study](#) *Front Oncol.* 2022 May 6;12:833195. doi: 10.3389/fonc.2022.833195. eCollection 2022. Miria Kano ^{1 2}, Shoshana Adler Jaffe ², Stephanie Rieder ^{2 3}, et al.

PURPOSE: Up to 1 million lesbian, gay, bisexual, and transgender (i.e., sexual and gender minority, SGM) individuals in the United States have histories of cancer. This medically underserved population is diverse, with complex sexualities and gender identities, and distinct health concerns. SGM persons experience disproportionate risks for, and rates of, anal, breast, cervical, colorectal, endometrial, lung, and

prostate cancers, in addition to cancers affecting transgender persons who have undergone sex-reassignment. SGM individuals are linked by shared experiences of stigmatization as a minority population for which little cancer research has been conducted. SGM cancer patients frequently report reluctance to seek healthcare, have poorer outcomes following diagnosis, engage in elevated risk behaviors (i.e. smoking and alcohol use) even after cancer diagnosis, have difficulty making emotional adjustment to illness, and experience higher rates of psychological distress. They report less satisfaction with cancer care, deficiencies in patient-centeredness and shared decision-making, gaps in care, and social isolation. Minority stress resulting from experiences of anti-SGM sentiment and discrimination affects cancer patients and their informal cancer caregivers. Our paper presents findings from a pilot study to identify gaps and opportunities to improve cancer care for SGM patients and caregivers at the University of New Mexico Comprehensive Cancer Center. **METHODS:** Between June 2020 and July 2021, we used a multi-methods research design informed by ecological theory to collect qualitative and quantitative data regarding cancer patient and caregiver quality of life (QoL) and experiences of cancer and survivorship care. We used PROMIS measures distributed via REDCap to assess QoL (i.e., fatigue, pain interference, pain intensity, anxiety, depression, emotional support, social isolation, and companionship), and conducted in-depth semi-structured interviews. We recruited 10 SGM cancer patients and 8 heterosexual, cisgender (H/C) patient matches, and their self-identified informal cancer caregivers (n=36, dyad total n=18). Interviews ranged from 1 to 2 hours, were audio-recorded and transcribed for analysis. The study was approved by the University of New Mexico Human Research Protections Office Institutional Review Board. **RESULTS:** Results of the PROMIS QoL assessments indicated that SGM patients reported greater anxiety [mean (SD) = 54.5 (8.8)] and depression [mean (SD) = 49.3 (4.8)] than H/C patients [mean (SD)=51.6 (7.5) and 45.4 (6.8) respectively], while heterosexual, cisgender (H/C) patients reported higher fatigue [mean (SD) =52.04 (8.18)] and stronger pain intensity than SGM patients [mean (SD)=48.3 (9.1) and 37.8 (9.1) respectively]. SGM patients reported higher levels of social isolation [mean (SD) = 48.3 (7.3) vs. 42.1 (7.4) for H/C patients, whereas H/C patients reported more emotional support (mean (SD) =57.5 (9.3) vs. 53.0 (6.9)] and companionship [mean (SD) = 55.2 (8.6) vs. 51.5 (11.0)]. SGM and H/C differences in caregiver QoL were most notable with regards to higher levels of fatigue [mean (SD) = 47.1 (6.0) for SGM, and 42.4 (11.5) for H/C] and companionship [mean (SD) = 55.3 (6.0) for SGM, and 50.9 (5.5) for H/C]. Qualitative interviews supported our quantitative results. SGM patients and caregivers articulated experiences of anti-SGM stigma and discrimination contributing to minority stress that influenced their initial cancer care encounters. SGM dyads had more trepidation and/or medical mistrust during initial cancer care encounters when compared to H/C patients and caregivers. SGM patients questioned care that was not culturally responsive to SGM preferences, while H/C patients were more apt to identify gaps in communication and perceived lack of clarity regarding cancer care delivery. Although SGM patients experienced high satisfaction with their cancer care once they developed trust with their providers, they discussed desires to have more direct conversations with their oncologists about their sexual orientation and gender identities and sexual health. All patients and providers in the study (SGM and H/C) appreciated their oncology care teams. All patients and caregivers relied on social networks comprised of friends and family, although SGM patients and caregivers had smaller social networks and relied less on biological family, and single SGM individuals experienced challenges accessing cancer care and struggled with social isolation. We discovered too, that all caregivers, regardless of Sexual Orientation and Gender Identity (SOGI), perceived a lack of support and information pertaining to their loved one's treatment, side effects and best way to provide care. **CONCLUSIONS:** This study demonstrates that prior stigmatizing experiences contribute to minority stress and medical mistrust for SGM cancer patients and their informal caregivers across the cancer care experience. Findings point to specific gaps in SGM cancer patient care, including lack of conversation about patient SOGI, inadequate staff and oncology provider SGM specific knowledge and cultural competence/cultural humility training, and insufficient patient supports for those who lack social support during cancer care

treatment. Further, this study reveals inadequacies in SGM specific support, and overall support services for informal cancer caregivers. Additional research is required to develop targeted interventions to address minority stress and clinic environment concerns to improve cancer care for SGM patients. Importantly, while there were differences between SGM and H/C experiences of cancer treatment, significant similarities also emerged. Caregiver expressed consensus about the current lack of support and guidance for informal caregivers of cancer patients. Future work should focus on providing caregiver-specific resources in the clinic setting and facilitating support groups for caregivers to network with one another, as well as for tailoring SGM specific caregiver support services. Our findings highlight areas for improving cancer care for the SGM community, as well as a broader population of patients and caregivers.