Caring Ambassadors Lung Cancer Program
Literature Review, March 2021

SCREENING, COMPREHENSIVE BIOMARKER TESTING, DIAGNOSIS AND STAGING

Real-World Lung Cancer CT Screening Performance, Smoking Behavior, and Adherence to Recommendations: Lung-RADS Category and Smoking Status Predict Adherence AJR Am J Roentgenol. 2021 Feb 17;1-8. doi: 10.2214/AJR.20.23637. Online ahead of print. Eduardo J Mortani Barbosa Jr 1 , Rochelle Yang 1 , Michelle Hershman 1

BACKGROUND. Low-dose CT (LDCT) lung cancer screening (LCS) has been shown to decrease mortality in persons with a significant smoking history. However, adherence in real-world LCS programs is significantly lower than in randomized controlled trials. OBJECTIVE. The purpose of this article is to assess real-world LDCT LCS performance and factors predictive of adherence to LCS recommendations. **METHODS.** We retrospectively identified all persons who underwent at least two LCS examinations from 2014 to 2019. Patient demographics, smoking history and behavior changes, Lung-RADS category, PPV, NPV, and adherence to screening recommendations were recorded. Predictors of adherence were assessed via univariate comparisons and multivariate logistic regression. **RESULTS.** A total of 260 persons returned for follow-up LDCT (57.7% had two, 34.2% had three, 7.7% had four, and 0.4% had five LDCT examinations). A total of 43 of 260 (16.5%) had positive (Lung-RADS category 3 or above) scans, of which 27 of 260 persons (10.3%) were graded as Lung-RADS category 3, eight of 260 (3.1%) were category 4A, six of 260 (2.3%) were category 4B, and two of 260 (0.8%) were category 4X. Cancer was diagnosed in four of the 260 (three with lung cancer and one with metastatic melanoma). A total of 143 of 260 (55.0%) persons were current smokers at baseline and 121 of 260 (46.5%) were current smokers at the last round of LCS. LCS had sensitivity of 100.0%, specificity of 84.8%, PPV of 9.3%, and NPV of 100%. Overall adherence was 43.0% but increased progressively with higher Lung-RADS category (Lung-RADS 1: 33.2%; Lung-RADS 2: 46.3%; Lung-RADS 3: 53.8%; Lung-RADS 4A: 77.8%; Lung-RADS 4B: 83.3%; Lung-RADS 4X: 100%; p < .001). was also higher in former versus current smokers (50.0% vs 36.2%; p < .001). Being a former smoker and having a nodule that is Lung-RADS category 3 or greater were the only significant independent predictors of adherence. **CONCLUSION.** Our real-world LCS program showed very high sensitivity and NPV, but moderate specificity and very low PPV. Adherence to LCS recommendations increased with former versus current smokers and in those with positive (Lung-RADS categories 3, 4A, 4B, or 4X) LCS examinations. Adherence was less than 50.0% in current smokers and persons with negative (Lung-RADS categories 1 or 2) LCS examinations.

CLINICAL IMPACT. Our results offer a road map for targeted performance improvement by focusing on LCS subjects less likely to remain in the program, such as persons with negative LCS examinations and persons who continue to smoke, potentially improving LCS cost effectiveness and maximizing its societal benefits.

[Improvement of EGFR Testing over the Last Decade and Impact of Delaying TKI Initiation](#) Curr Oncol. 2021 Feb 26;28(2):1045-1055. doi: 10.3390/curroncol28020102. Félix Blanc-Durand 1 , Marie Florescu 1 , Mustapha Tehfe 1 , et al.

BACKGROUND: Epidermal growth factor receptor (EGFR) is the most common oncogenic mutation in lung adenocarcinoma and tyrosine kinase inhibitors (TKIs) have been considered standard treatment for more than a decade. However, time to initiation of TKIs (TTIT) from diagnosis is often delayed and represents a challenge for clinicians. We aimed to assess the impact of TTIT on clinical outcomes and complications. **METHOD:** TTIT was defined as the time between confirmed advanced diagnosis and the initiation of a TKI. Complications during this pre-TKI period were retrospectively collected from all patients with EGFR-mutant non small cell lung cancer (NSCLC) in our institution. **RESULTS:** 102 patients were diagnosed with EGFR mutated NSCLC between 2006 and 2019. The median PFS and OS were 12.9 and 22.5 months, respectively. TTIT was 5.7 months (95% CI 3.4-8) with a significant decrease in the latter years of this cohort. During the pre-TKI period, 23 patients received chemotherapy as first line treatment, of which 5 developed severe adverse events and 3 were not fit to receive TKI thereafter. Additionally, 29 patients had rapid clinical deterioration before initiation of first line TKI and 16 had to be hospitalized. Among the patients presenting a performance status deterioration, their prognosis was markedly affected compared to the remainder of the cohort (p = 0.01). **CONCLUSION:** Our real-world evidence study supports the concept that a delay to treat EGFR mutant NSCLC with TKIs is associated with adverse events, patient progression, hospitalization, and decreased overall survival. Rapid molecular diagnosis, including access to ctDNA technology may circumvent these deleterious delays.

[Potential Disparities by Sex and Race-ethnicity in Lung Cancer Screening Eligibility Rates](#) Chest. 2021 Feb 2;S0012-3692(21)00232-4. doi: 10.1016/j.chest.2021.01.070. Online ahead of print. Paul F Pinsky 1 , Yan Kwan Lau 2 , Chyke A Doubeni 3

BACKGROUND: Criteria for low-dose CT lung cancer screening vary across guidelines. Knowledge of the eligible pool across demographic groups can enable policy and programmatic decision-making, particularly for disproportionately affected populations. **RESEARCH QUESTION:** What are the eligibility rates for low-dose CT screening according to sex and race/ethnicity and how do these rates relate to corresponding lung cancer incidence rates? **STUDY DESIGN AND METHODS:** This was a cross-sectional study using data from the 2015 National Health Interview Survey adult and cancer control supplement files. In addition to eligibility rates, the ratio of the eligibility rate to the lung cancer incidence rate in a given population group (E-I ratio) was also determined. Guidelines assessed were: Centers for Medicare and Medicaid Services, National Comprehensive Cancer Network, and US Preventive Services Task Force (USPSTF) current or with expansion of age and smoking/quit thresholds. We also assessed a risk model (PLCOM2012). **RESULTS:** Total numbers eligible based on current guidelines ranged from 8.3-13.3 million, representing 8.3%-13.4% of the U.S. population aged 50-80, and up to 17.5 million with expanded criteria. Overall eligibility rates were on average about 10 percentage points higher for men than women. For both men and women, and both overall and among ever-smokers, non-Hispanic Whites had the highest eligibility rates across all guidelines, followed generally by non-Hispanic Blacks, and then Asians and Hispanics. Among both men and women, non-Hispanic Whites had the highest E-I ratios across all guidelines; non-Hispanic Black men had higher lung cancer incidence but 30-50% lower E-I ratios than non-Hispanic White men. **INTERPRETATION:** Screening eligibility rates vary widely across guidelines with disparities evident in eligibility-to-incidence ratios, including for among non-

Hispanic Black men despite higher lung cancer burden. Consideration of smoking duration in risk assessment criteria may address current disparities.

[Lung Cancer Screening with Low Dose Computed Tomography in Patients With and Without Prior History of Cancer in the National Lung Screening Trial](#) J Thorac Oncol. 2021 Feb 10;S1556-0864(21)01703-2. doi: 10.1016/j.jtho.2021.02.003. Online ahead of print. Louise M Henderson 1 , Danielle D Durham 2 , Martin C Tammemägi 3 , Thad Benefield 2 , Mary W Marsh 2 , M Patricia Rivera 4

INTRODUCTION: Patients with a prior history of cancer (PHC) are at increased risk of second primary malignancy, of which lung cancer is the most common. We compared the performance metrics of positive screening rates and cancer detection rates among those with versus without PHC. **METHODS:** We conducted a secondary analysis of 26,366 National Lung Screening Trial participants screened with LDCT between August 2002 and September 2007. We examined absolute rates and age-adjusted relative risks (RRs) of positive screening rates based on retrospective Lung-RADS application, invasive diagnostic procedure rate, complication rate, and cancer detection rate in those with versus without PHC using a binary logistic regression model using Firth's penalized likelihood. We also compared histology, stage, and treatment in those with versus without PHC. **RESULTS:** 4.1% (n=1,071) of patients had PHC. Age-adjusted rates of positive findings were similar in those with versus without PHC (Baseline: PHC=13.7% versus no PHC=13.3%, RR (95%CI)=1.04 (0.88-1.24); Subsequent: PHC=5.6% versus no PHC=5.5%, RR (95%CI)=1.02 (0.84-1.23)). Age-adjusted cancer detection rates were higher in those with versus without PHC on baseline (PHC=1.9% versus no PHC=0.8%, RR (95%CI)=2.51 (1.67-3.81)) but not on subsequent screenings (PHC=0.6% versus no PHC=0.4%, RR (95%CI)=1.37 (0.99-1.93)). There were no differences in cancer stage, histology, or treatment by PHC status. **CONCLUSIONS:** Patients with PHC may benefit from lung cancer screening, and with their providers, should be made aware of the possibility of higher cancer detection, invasive procedures, and complication rates on baseline lung cancer screening, but not on subsequent LDCT screening examinations.

[Detection Of Lung Cancer On Computed Tomography Using Artificial Intelligence Applications Developed By Deep Learning Methods And The Contribution Of Deep Learning To The Classification Of Lung Carcinoma](#) Curr Med Imaging. 2021 Feb 4. doi: 10.2174/1573405617666210204210500. Online ahead of print. Nevin Aydin 1 , Özer Çelik 2 , Ahmet Faruk Aslan 2 , Alper Odabaş 2 , Emine Dündar 3 , Meryem Cansu Şahin 4

BACKGROUND: In every year, lung cancer is an important cause of deaths in the world. Early detection of lung cancer is important for treatment, and non-invasive rapid methods are needed for diagnosis. **INTRODUCTION:** In this study, we aimed to detect lung cancer using deep learning methods and determine the contribution of deep learning to the classification of lung carcinoma using a convolutional neural network (CNN). **METHOD:** A total of 301 patients with diagnosed with lung carcinoma pathologies in our hospital were included in the study. In the thorax computed tomography (CT) performed for diagnostic purposes prior to treatment. After tagging the section images, tumor detection, small-non-small cell lung carcinoma differentiation, adenocarcinoma-squamous cell lung carcinoma differentiation, and adenocarcinoma-squamous cell-small cell lung carcinoma differentiation were sequentially performed using deep CNN methods. **RESULT:** In total, 301 lung carcinoma images were used to detect tumors, and the model obtained with the deep CNN system had 0.93 sensitivity, 0.82 precision, and 0.87 F1 score in detecting lung carcinoma. In the differentiation of small cell-non-small cell lung carcinoma, the sensitivity, precision and F1 score of the CNN model at the test stage were 0.92, 0.65, and 0.76, respectively. In the adenocarcinoma-squamous cancer differentiation, the sensitivity, precision, and F1 score were 0.95, 0.80, and 0.86, respectively. The patients were finally grouped as small cell lung carcinoma, adenocarcinoma, and squamous cell lung carcinoma, and the CNN model was used

to determine whether it could differentiate these groups. The sensitivity, specificity, and F1 score of this model were 0.90, 0.44, and 0.59, respectively for this differentiation. **CONCLUSION**: In this study, we successfully detected tumors and differentiated between adenocarcinoma-squamous cell carcinoma groups with the deep learning method using the CNN model. Due to their non-invasive nature and success of the deep learning methods, they should be integrated into radiology to diagnose lung carcinoma.

[False-Negative Results in Lung Cancer Screening-Evidence and Controversies](#) J Thorac Oncol. 2021 Feb 3;S1556-0864(21)01652-X. doi: 10.1016/j.jtho.2021.01.1607. Online ahead of print. Emily C Bartlett 1, Mario Silva 2 , Matthew E Callister 3 , Anand Devaraj 4

Identifying false-negative cases is an important quality metric in lung cancer screening, but it has been infrequently and variably reported in previous studies. Although as a proportion of all screening participants, false-negative cases are uncommon, such cases may constitute a substantial proportion of all lung cancers diagnosed (up to 15%) within a screening program. This article reviews the impact and causes of false-negative lung cancer screening tests, including those related to radiologic evaluation, nodule management protocols, and management decisions made by multidisciplinary teams. Following a review of data from international screening studies, this article discusses the controversies within the screening literature surrounding the definition and classification of a false-negative lung cancer screening test and how data on false-negative rates should be captured and recorded. Challenges, such as avoiding overly cautious surveillance of lung nodules while minimizing overdiagnosis and investigation of indolent or benign lesions, are considered. Finally, the advantages and disadvantages of different approaches to dealing with false-negative results in lung cancer screening are discussed.

[Using Implementation Science to Disseminate a Lung Cancer Screening Education Intervention Through Community Health Workers](#) J Community Health. 2021 Feb;46(1):165-173. doi: 10.1007/s10900-020-00864-2.

Lovoria B Williams 1 , Brent J Shelton 2 , Maria L Gomez 3 , Yazan D Al-Mrayat 3 , Jamie L Studts 4

National lung cancer screening with low dose computed tomography (LDCT) uptake is suboptimal. One factor contributing to slow uptake is lack of awareness. Trained Community Health Workers (CHWs) may be effective in increasing lung cancer screening awareness among disparate populations, however little is known about the processes necessary to scale an intervention for implementation by CHWs in a new area. We examined implementation processes with the RE-AIM framework and pilot tested a CHW-delivered lung cancer education intervention based on the Health Belief Model. We measured pre-post participant knowledge, attitudes and beliefs regarding cancer screening, lung cancer stigma, and intent to obtain LDCT screening. We used community-engaged strategies to collaborate with a local health system, to identify CHWs. CHWs were trained to recruit participants and deliver the one-session lung cancer education intervention. Seven CHWs and eight community sites participated. Participants (n = 77) were female (53%) primarily low income (62.9%); tobacco use was high (36.9%). Post intervention changes in lung cancer screening knowledge (p = < .0001), attitudes regarding lung cancer screening benefit (p = .034) and lung cancer stigma. (p = .024) We learned important lessons that will be useful in subsequent scaling. Collaborating with a local health system is a promising method to disseminate a lung cancer screening education intervention.

[Proposed Quality Metrics for Lung Cancer Screening Programs: A National Lung Cancer Roundtable Project](#) Chest. 2021 Feb 1;S0012-3692(21)00223-3. doi: 10.1016/j.chest.2021.01.063. Online ahead of print. Peter J Mazzone 1 , Carey C Thomson 2 , Ella A Kazerooni 3, Robert A Smith 4 , Charles S White 5

Lung cancer screening with a low radiation dose chest CT scan is the standard of care for screen eligible individuals. The net benefit of screening may be optimized by delivering high-quality care, capable of

maximizing the benefit and minimizing the harms of screening. Valid, feasible, and relevant indicators of the quality of lung cancer screening may help programs evaluate their current practice and develop quality improvement plans. The purpose of this project was to develop quality indicators related to the processes and outcomes of screening. Potential quality indicators were explored through surveys of multi-disciplinary lung cancer screening experts. Those that achieved pre-defined measures of consensus for each of the validity, feasibility, and relevance domains are proposed as quality indicators. Each of the proposed indicators is described in detail, with guidance on how to define, measure, and improve program performance within the indicator.

CLINICAL TRIALS, COHORT STUDIES, PILOT STUDIES

NSCLC - SURGERY

[Current Understanding on Perioperative Management in Lung Cancer: Implications for Anesthetic Considerations](#) Drug Des Devel Ther. 2021 Feb 25;15:835-842. doi: 10.2147/DDDT.S297200. eCollection 2021. Jian Wang 1 , Lei Liu 2 , Yuli Song 3 , Jinghua Jiao 4 , Yifan Zhong 2
Narcotic drugs are often used to treat perioperative pain for patients with lung cancer. However, anesthetic management and narcotic substance use may have significant impacts on patients with lung cancer, including anti-cancer or promoting cancer effects. In this study, we summarize the effects of anesthetic management and its related substances on lung cancer. An evidence-based review of the influence of anesthetic techniques and narcotic substances used on lung cancer was performed. The effects of perioperative pain management and the method of choosing anesthesia for patients with lung cancer were explored. Different management techniques of anesthesia have been indicated to suppress both cell-mediated immunity and humoral immunity and have effects on the recurrence and metastasis of lung cancer. Evidence suggests that the effects of narcotic substances used on lung cancer were still inconsistent. However, the mechanisms by which anesthetics and analgesics inhibit the tumor are complicated. Perioperative management leads to decreased immunity in patients with lung cancer, which to some extent contributes to recurrence and metastasis. Various narcotic substances used may modulate signal pathways, including the mitochondrial pathway, and appear to exert different effects on the recurrence and metastasis of lung cancer. The anesthesiologists should consider these effects on perioperative

[Surgical Impacts of Metastatic Non-small Cell Lung Cancer to the Thoracic and Lumbar Spine](#) J Korean Med Sci. 2021 Feb 22;36(7):e52. doi: 10.3346/jkms.2021.36.e52. Jong Myung Jung 1 , Seung Jae Hyun 2 , Ki Jeong Kim 3
BACKGROUND: Surgery for spinal metastasis is rapidly increasing in frequency with procedures ranging from laminectomy to spondylectomy combined with stabilization. This study investigated the effect of various surgical procedures for spinal metastasis of non-small cell lung cancer (NSCLC). **METHODS:** A single-center consecutive series of patients who underwent surgery for spinal metastasis of NSCLC were retrospectively reviewed. Patients' characteristics, radiographic parameters, operative data, clinical outcomes, and complications were analyzed. Surgical outcomes were assessed according to pain and performance status before and after surgery. Overall survival (OS) rate was estimated using the Kaplan-Meier method. Multivariate analysis was performed to detect factors independently associated with OS using a Cox proportional hazards model. **RESULTS:** Twenty-one patients were treated with laminectomy, 24 with corpectomy, 13 with spondylectomy (piecemeal or total en bloc fashion), and all procedures were combined with stabilization. Back pain and performance status improved significantly after surgical treatment among the three groups. Revision surgery due to tumor progression at the index level or spinal metastasis at another level were four patients (19.0%) in the laminectomy group, six

patients (25.0%) in the corpectomy group, and one patient (7.7%) in the spondylectomy group. A Charlson comorbidity index and the number of spinal metastasis negatively affected OS (hazard ratio [HR], 19.613 and 2.244). Postoperative chemotherapy, time to metastasis, spondylectomy, and corpectomy had favorable associations with OS (HR, 0.455, 0.487, 0.619, and 0.715, respectively). **CONCLUSION:** Postoperative chemotherapy was the most critical factor in OS of patients with metastatic NSCLC to the spine. An extensive surgical procedure (corpectomy/spondylectomy) with stabilization also could be beneficial for limited patients with spinal metastasis of NSCLC.

[Chemotherapy and surgical resection for N1 positive non-small cell lung cancer: Better than expected outcomes](#) Semin Thorac Cardiovasc Surg. 2021 Feb 15;S1043-0679(21)00029-0. doi: 10.1053/j.semtcvs.2021.01.012. Online ahead of print. Abby White 1 , Suden Kucukak 2 , Daniel N Lee 2 , Emanuele Mazzola 3, Daniel Dolan 2 , Raphael Bueno 2 , Michael T Jaklitsch 2 , Scott J Swanson 2 N1-positive (T1-3, N1, M0) non-small cell lung cancer (NSCLC) represents a minority distribution (∼8%) of the approximately 234,000 diagnosed cases per year. As such, there is a paucity of modern high-quality data regarding outcomes following surgically-resected, stage N1-positive NSCLC. Randomized controlled trials from more than a decade ago have demonstrated a modest 5.4% survival benefit with adjuvant chemotherapy but have included heterogenous patient populations and stage distributions. Large database analyses have questioned the role of perioperative chemotherapy in resected patients with N1 disease, but without much granular detail regarding staging, quality of surgery, and chemotherapy. This single-institution study sought to evaluate the role of perioperative chemotherapy, specifically in N1-positive NSCLC patients. Data for all patients with surgically-resected N1-positive NSCLC (T1-3, N1, M0) between 2006 and 2016 were collected for this study. Patients who underwent pneumonectomy were excluded from analysis. A retrospective chart review was conducted, and comprehensive clinicopathologic data were collected relative to staging, surgery, pathologic review, and perioperative oncology treatment. After exclusion criteria were applied, 148 patients with surgically-resected, N1-positive disease (T1-3, N1, M0) remained for analysis. The majority of patients underwent lobectomy (75.0%), of which 55.4% underwent minimally-invasive resection. There were no differences in postoperative complications, length of stay, number of lymph nodes sampled, or mortality associated with the surgery only and surgery with adjuvant therapy subgroups. 107 patients (72.3%) received adjuvant therapy, and this was associated with higher 5-year overall survival (62.8%) and disease-free survival (45.1%) than patients who underwent surgery only (33.9% overall survival at 5 years, p=0.01; 22.4% disease-free survival at 5 years, p=0.04). The presence of multi-station N1 nodal metastases in patients was associated with lower 5-year overall survival (22.7%) and disease-free survival (5.6%) than patients with single-station N1 nodal metastasis (60.4% overall survival at 5 years, p=0.003; 46.0% disease-free survival at 5 years, p<0.001). On multivariable analysis, receiving any adjuvant chemotherapy was associated with improved overall survival and disease-free survival (Overall Survival HR 0.47, p<0.01 | Disease-Free Survival HR 0.46, p<0.01). Multi-station N1 disease was associated with significantly worse disease-free survival (HR 2.11, p= 0.04). Perioperative chemotherapy was associated with improved survival in N1-positive NSCLC, and the potential magnitude of benefit exceeded 25% in this study. Patients with single-station N1 lymph node metastasis were observed to have better disease-free survival.

[Symptom Assessment Following Surgery for Lung Cancer: A Canadian Population-Based Retrospective Cohort Study](#) Ann Surg. 2021 Feb 10. doi: 10.1097/SLA.0000000000004802. Online ahead of print. Dhruvin H Hirpara 1 , Natalie Coburn, Gail Darling, Biniam Kidane, Mathieu Rousseau, Vaibhav Gupta, Mark Doherty, Victoria Zuk, Victoria Delibasic, Wing Chan, Julie Hallet **OBJECTIVE:** To conduct a population-level analysis of temporal trends and risk factors for high symptom burden in patients receiving surgery for non-small-cell lung cancer (NSCLC). **SUMMARY**

BACKGROUND DATA: A population-level overview of symptoms after curative intent surgery is necessary to inform decision making and supportive care for patients with lung cancer. **METHODS:** Retrospective cohort study of patients receiving surgery for stage I-III NSCLC between January 2007-September 2018. Prospectively collection Edmonton Symptom Assessment System (ESAS) scores, linked to provincial administrative data, were used to describe the prevalence, trajectory and predictors of moderate-to-severe symptoms in the year following surgery. **RESULTS:** A total of 5,350 patients, with 28,490 unique ESAS assessments, were included in the analysis. Moderate-to-severe tiredness (68%), poor wellbeing (63%) and shortness of breath (60%) were the most common symptoms reported. The rise and fall in the proportion of patients experiencing moderate-to-severe symptoms after surgery coincided with the median time to first (58 days, IQR: 47-72) and last cycle of chemotherapy (140 days, IQR: 118-168), respectively. There was eventual stabilization, albeit above the pre-operative baseline, within 6-7 months after surgery. Female sex (RR 1.09-1.26), lower income (RR 1.08-1.23), stage III disease (RR 1.15-1.43), adjuvant therapy (RR 1.09-1.42), chemotherapy within two weeks of an ESAS assessment (RR 1.14-1.73), and pneumonectomy (RR 1.05-1.15) were associated with moderate-to-severe symptoms following surgery. **CONCLUSIONS:** Knowledge of population-level prevalence, trajectory and predictors of moderate-to-severe symptoms after surgery for NSCLC can be used to facilitate shared decision making and improve symptom management throughout the course of illness.

[Predicting post-discharge cancer surgery complications via telemonitoring of patient-reported outcomes and patient-generated health data](#) J Surg Oncol. 2021 Feb 23. doi: 10.1002/jso.26413. Online ahead of print. Lorenzo A Rossi 1 , Laleh G Melstrom 2 , Yuman Fong 2 , Virginia Sun 2 3
BACKGROUND AND OBJECTIVES: Post-discharge oncologic surgical complications are costly for patients, families, and healthcare systems. The capacity to predict complications and early intervention can improve postoperative outcomes. In this proof-of-concept study, we used a machine learning approach to explore the potential added value of patient-reported outcomes (PROs) and patient-generated health data (PGHD) in predicting post-discharge complications for gastrointestinal (GI) and lung cancer surgery patients. **METHODS:** We formulated post-discharge complication prediction as a binary classification task. Features were extracted from clinical variables, PROs (MD Anderson Symptom Inventory [MDASI]), and PGHD (VivoFit) from a cohort of 52 patients with 134 temporal observation points pre- and post-discharge that were collected from two pilot studies. We trained and evaluated supervised learning classifiers via nested cross-validation. **RESULTS:** A logistic regression model with L2 regularization trained with clinical data, PROs and PGHD from wearable pedometers achieved an area under the receiver operating characteristic of 0.74. **CONCLUSIONS:** PROs and PGHDs captured through remote patient telemonitoring approaches have the potential to improve prediction performance for postoperative complications.

[Subsegmental resection preserves regional pulmonary function: A focus on thoracoscopy](#) Thorac Cancer. 2021 Feb 14. doi: 10.1111/1759-7714.13841. Online ahead of print. Hiroaki Kuroda 1 , Shozo Sakata 1 , Yusuke Takahashi 1 2 , et al.
BACKGROUND: The aim of this study was to evaluate regional postoperative preserved pulmonary function (PPPF) and three-dimensional (3D) volumetric changes according to the number of resected subsegments and investigate the factors that most affected pre-/post PPPF. **METHODS:** Patients who underwent thoracoscopic lobectomy (n = 73), and segmentectomy (n = 87) were eligible for inclusion in the study. They were classified according to the number of resected subsegments which ranged from 1 to 10. The percentage of pre-/postoperative forced expiratory volume in 1 s (FEV1) was used for comparison. Furthermore, lung volumetric changes were calculated using 3D computed tomography (CT) volumetry. **RESULTS:** The percentage of pre-/postoperative EFV1 between 4 and 5-7 and between 5-7 and 10 were significant (p = 0.03 and p < 0.01, respectively), but not between 1-2 to 4 (p = 0.99). The

difference between volumetric changes in the left lower lobe of patients with a number of resected subsegments was significant (p < 0.01). On univariate and multivariate analyses, chronic inflammation was significant for decrease in recovery percentages. When the PPPF was compared among resected subsegments, it gradually decreased with an increase in the number of patients without a postoperative procrastination of inflammation (p < 0.01). **CONCLUSIONS:** Segmentectomy is feasible and useful for PPPF. Even a relatively large-volume resection procedure where 5-7 subsegments are resected can preserve pulmonary function. Chronic inflammation was statistically identified as a risk factor for postoperative preserved pulmonary function.

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

[Efficacy of epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) combined with bevacizumab for advanced non-squamous non-small-cell lung cancer patients with gradual progression on EGFR-TKI treatment: A cohort study](#) Medicine (Baltimore). 2021 Feb 5;100(5):e23712. doi: 10.1097/MD.000000000023712. Yuman Yu 1 , Yuehong Wang, Linying Wu, Xuanli Xu, Hua Zhou, Qing Wang, Jianying Zhou
Epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) significantly improve outcomes of patients with EGFR-mutated non-small-cell lung cancer (NSCLC). However, acquired resistance inevitably emerges and remains a major challenge. The present study aimed to evaluate the efficacy of EGFR-TKIs plus bevacizumab in advanced non-squamous NSCLC patients with gradual progression on EGFR-TKIs.Advanced non-squamous EGFR-mutated NSCLC patients with gradual progression on EGFR-TKIs were administered bevacizumab while EGFR-TKIs were continued until disease progression occurred. Tumor lesions were assessed, and blood samples were collected at the start of the combination treatment and every 6 weeks until disease progression.Among the 15 included patients, there were no grade 3 or higher adverse events (AEs). Partial response (PR) and stable disease (SD) were achieved in 1 and 13 patients, respectively, with an objective response rate (ORR) of 6.7% and a disease control rate (DCR) of 93.3%. The median progression-free survival 2 (PFS2), defined as the time from the initiation of combination treatment to disease progression, was 5.0 (95% confidence interval [CI]: 4.0-6.0) months. Additionally, Spearman correlation analysis revealed that PFS2 was positively correlated with the serum vascular endothelial growth factor (VEGF) level at baseline (r = 0.7212, P = .0234). Patients with high baseline serum VEGF levels showed a better median PFS2 than those with low baseline serum VEGF levels (5.5 months vs 3.6 months, P = .0333).EGFR-TKIs plus bevacizumab led to a durable prolongation of PFS in non-squamous NSCLC patients with gradual progression on EGFR-TKIs. This therapeutic regimen was well tolerated and could be a promising strategy for these patients. Serum VEGF could be a potential biomarker to predict a subset of patients who are likely to benefit from EGFR-TKIs combined with bevacizumab.

[Neoadjuvant nivolumab or nivolumab plus ipilimumab in operable non-small cell lung cancer: the phase 2 randomized NEOSTAR trial](#) Nat Med. 2021 Feb 18. doi: 10.1038/s41591-020-01224-2. Online ahead of print. Tina Cascone 1 , William N William Jr 2 3 , Annikka Weissferdt 4 5 , et al.
Ipilimumab improves clinical outcomes when combined with nivolumab in metastatic non-small cell lung cancer (NSCLC), but its efficacy and impact on the immune microenvironment in operable NSCLC remain unclear. We report the results of the phase 2 randomized NEOSTAR trial (NCT03158129) of neoadjuvant nivolumab or nivolumab + ipilimumab followed by surgery in 44 patients with operable NSCLC, using major pathologic response (MPR) as the primary endpoint. The MPR rate for each treatment arm was tested against historical controls of neoadjuvant chemotherapy. The nivolumab + ipilimumab arm met the prespecified primary endpoint threshold of 6 MPRs in 21 patients, achieving a 38% MPR rate (8/21). We observed a 22% MPR rate (5/23) in the nivolumab arm. In 37 patients resected

on trial, nivolumab and nivolumab + ipilimumab produced MPR rates of 24% (5/21) and 50% (8/16), respectively. Compared with nivolumab, nivolumab + ipilimumab resulted in higher pathologic complete response rates (10% versus 38%), less viable tumor (median 50% versus 9%), and greater frequencies of effector, tissue-resident memory and effector memory T cells. Increased abundance of gut Ruminococcus and Akkermansia spp. was associated with MPR to dual therapy. Our data indicate that neoadjuvant nivolumab + ipilimumab-based therapy enhances pathologic responses, tumor immune infiltrates and immunologic memory, and merits further investigation in operable NSCLC.

[Activity and Safety of Mobocertinib (TAK-788) in Previously Treated Non-Small Cell Lung Cancer With EGFR Exon 20 Insertion Mutations From a Phase 1/2 Trial](#) Cancer Discov. 2021 Feb 25;candisc.1598.2020. doi: 10.1158/2159-8290.CD-20-1598. Online ahead of print. Gregory J Riely 1 , Joel W Neal 2 , D Ross Camidge 3 , et al.

Mobocertinib, an oral epidermal growth factor receptor (EGFR) inhibitor targeting EGFR gene mutations including exon 20 insertions (EGFRex20ins) in non-small cell lung cancer, was evaluated in a phase 1/2 dose-escalation/expansion trial (ClinicalTrials.gov NCT02716116). Dose escalation identified 160 mg daily as the recommended phase 2 dose and maximum tolerated dose. Among 136 patients treated with 160 mg daily, the most common any grade treatment-related adverse events (TRAEs; >25%) were diarrhea (83%), nausea (43%), rash (33%), and vomiting (26%), with diarrhea (21%) the only grade {greater than or equal to}3 TRAE >5%. Among 28 EGFRex20ins patients treated at 160 mg daily, the investigator-assessed confirmed response rate was 43% (12/28; 95% confidence interval (CI): 24-63%) with median duration of response of 14 months (5.0-not reached), and median progression-free survival of 7.3 months (4.4-15.6). Mobocertinib demonstrated antitumor activity in patients with diverse EGFRex20ins variants with a safety profile consistent with other EGFR inhibitors.

[nab-Paclitaxel Plus Durvalumab in Patients With Previously Treated Advanced Stage Non-small Cell Lung Cancer (ABOUND.2L+)](#) Front Oncol. 2021 Feb 11;10:569715. doi: 10.3389/fonc.2020.569715. eCollection 2020. Daniel Morgensztern 1 , Manuel Cobo Dols 2 , Santiago Ponce Aix 3 , et al.

BACKGROUND: The standard therapy for advanced stage non-small cell lung cancer (NSCLC) with no actionable gene alterations is a platinum-based chemotherapy doublet and immune checkpoint blocker (ICB), either concurrently or sequentially, followed by docetaxel at the time of tumor progression. However, more effective treatments are needed. We evaluated the nab-paclitaxel and durvalumab combination in patients with previously treated advanced stage NSCLC. **METHODS:** Patients with advanced stage NSCLC previously treated with one line of platinum-based doublet with or without an ICB and no activating EGFR mutations or ALK translocations received nab-paclitaxel 100 mg/m2 (days 1 and 8) plus durvalumab 1,125 mg (day 15) every 21 days. The primary endpoint was progression-free survival (PFS). Key secondary endpoints included overall survival (OS) and safety. **RESULTS:** Between February 2016 and December 2016, 79 patients were enrolled. The median age was 63 years. Most patients were males (68.4%), had non-squamous histology (69.6%), and had no prior ICB treatment (88.6%). The median PFS was 4.5 months; median OS was 10.1 months. A post hoc analysis of survival by prior ICB treatment revealed a median PFS and OS of 4.4 and 9.9 months, respectively, in ICB-naive patients and 6.9 months and not estimable, respectively, in patients previously treated with ICB. The most common treatment-emergent adverse events were asthenia (46.2%) and diarrhea (34.6%); four treatment-related deaths (5.1%) occurred. **CONCLUSIONS:** The nab-paclitaxel and durvalumab combination is feasible and demonstrated antitumor activity without new safety signals. Additional studies using taxanes and ICB in patients with previously treated NSCLC are warranted.

[Dramatic intracranial response to tepotinib in a patient with lung adenocarcinoma harboring MET exon 14 skipping mutation](#) Thorac Cancer. 2021 Feb 3. doi: 10.1111/1759-7714.13871. Online ahead of print. Shinkichi Takamori 1, Taichi Matsubara 1, Takatoshi Fujishita 1, Kensaku Ito 1, Ryo Toyozawa 1, Takashi Seto 1, Masafumi Yamaguchi 1, Tatsuro Okamoto 1

Mesenchymal-epithelial transition (MET) pathway activation is associated with the mechanisms that influence properties affecting cancer cell survival and invasiveness. The MET exon 14 skipping mutation (METex14del) is found in 2%-3% of patients with non-small cell lung cancer (NSCLC). Previous studies reported that NSCLC patients harboring a METex14del responded well to MET-tyrosine kinase inhibitors (TKIs), including tepotinib. Tepotinib is a highly selective, once-daily oral MET inhibitor that has shown promising clinical activity in patients with NSCLC with METex14del. The Food and Drug Administration accepted a new drug application for tepotinib as a treatment for patients with metastatic NSCLC harboring METex14del in September 2019. However, in the previous clinical trials involving MET-TKIs, only patients with stable central nervous system metastases were eligible, and those with untreated symptomatic brain metastases (BMs) were excluded. Therefore, the efficacy and safety of MET-TKIs in that population remains unknown. We herein report a case of dramatic intracranial response to tepotinib in a patient with symptomatic BMs from lung adenocarcinoma harboring METex14del. In the current report, the symptoms derived from multiple BMs (headache and loss of appetite) rapidly disappeared, and brain magnetic resonance imaging (MRI) examination showed that all the lesions were too small to measure only 23 days after the commencement of tepotinib. For NSCLC patients with multiple BMs, whole-brain irradiation is a standard-of-care therapy, but its adverse effects on neurocognition are concerning. Tepotinib might therefore be a therapeutic option for NSCLC patients with symptomatic multiple BMs harboring METex14del.

[Dacomitinib induces objective responses in metastatic brain lesions of patients with EGFR-mutant non-small-cell lung cancer: A brief report](#) Lung Cancer. 2021 Feb;152:66-70. doi: 10.1016/j.lungcan.2020.12.008. Epub 2020 Dec 9.Wenying Peng 1, Xingxiang Pu 1, Meilin Jiang 1, Jingyi Wang 1, Jia Li 1, Kang Li 1, et al.

OBJECTIVE: Dacomitinib is a potent, irreversible and pan-HER tyrosine kinase inhibitor (TKI) of epidermal growth factor receptor (EGFR) mutant non-small cell lung cancer (NSCLC). Currently, evidence of its activity on brain metastasis is lacking. **MATERIALS AND METHODS:** NSCLC patients diagnosed at Hunan Cancer Hospital between July, 2019 and July, 2020 with enhanced MRI-detected brain metastasis prior to treatment and laboratory-confirmed EGFR mutations were reviewed. In total, 14 EGFR-mutant NSCLC patients with brain metastasis were treated with first-line dacomitinib. The first radiographic review of chest CT and brain MRI was after one month and thereafter every 2 months. The objective response rate (ORR) and the depth of the brain metastasis response were determined via RECIST 1.1 and RANO-LM criteria. **RESULTS:** In total, 14 of 59 EGFR-mutant advanced NSCLC patients who received first-line dacomitinib therapy had brain metastasis before treatment. Among these patients, 5 were given a dacomitinib starting dose of 45 mg once daily, while 9 received 30 mg daily until disease progression or unbearable toxicity. Eight patients harbored EGFR 19del, 5 had EGFR L858R, and one patient had EGFR G719A and I706 T co-mutations. The median duration of follow-up was 4.5 months. All patients received at least one review. The ORR was 92.9 % (13/14) and the disease control rate (DCR) was 100 %. A measurable response of the intracranial metastases was observed in 12 of 14 patients (85.7 %), including 12 of 13 (92.3 %) with brain parenchymal metastasis, but the one patient with meningeal metastasis did not respond well. All patients (100 %) had grade 1-2 adverse effects, but none discontinued treatment or required a dosage adjustment. **CONCLUSIONS:** This case series study of 14 patients has shown that dacomitinib has potent efficacy for central nervous system (CNS) metastasis in EGFR-positive NSCLC. More data are required to confirm its advantages and optimize its clinical application.

KRAS G12C-mutated advanced non-small cell lung cancer: A real-world cohort from the German prospective, observational, nation-wide CRISP Registry (AIO-TRK-0315) Lung Cancer. 2021 Feb 13;154:51-61. doi: 10.1016/j.lungcan.2021.02.005. Online ahead of print. Martin Sebastian 1 , Wilfried E E Eberhardt 2 , Petra Hoffknecht 3 , et al.

OBJECTIVES: After decades of unsuccessful efforts in inhibiting KRAS, promising clinical data targeting the mutation subtype G12C emerge. Since little is known about outcome with standard treatment of patients with G12C mutated non-small cell lung cancer (NSCLC), we analyzed a large, representative, real-world cohort from Germany. **PATIENTS AND METHODS:** A total of 1039 patients with advanced KRAS-mutant or -wildtype NSCLC without druggable alterations have been recruited in the prospective, observational registry CRISP from 12/2015 to 06/2019 by 98 centers in Germany. Details on treatment, best response, and outcome were analyzed for patients with KRAS wildtype, G12C, and non-G12C mutations. **RESULTS:** Within the study population, 160 (15.4 %) patients presented with KRAS G12C, 251 (24.2 %) with non-G12C mutations, 628 (60.4 %) with KRAS wildtype. High PD-L1 expression (Tumor Proportion Score, TPS > 50 %) was documented for 28.0 %, 43.5 %, and 28.9 % (wildtype, G12C, non-G12C) of the tested patients; 68.8 %, 89.3 %, and 87.7 % of the patients received first-line treatment combined with an immune checkpoint-inhibitor in 2019. TPS > 50 % vs. TPS < 1 % was associated with a significantly decreased risk of mortality in a multivariate Cox model (HR 0.39, 95 % CI 0.26-0.60, p=<0.001). There were no differences in clinical outcome between KRAS wildtype, G12C or non-G12C mutations and KRAS mutational status was not prognostic in the model. **CONCLUSION:** Here we describe the so far largest prospectively recruited cohort of patients with advanced NSCLC and KRAS mutations, with special focus on the G12C mutation. These data constitute an extremely valuable historical control for upcoming clinical studies that employ KRAS inhibitors.

Pembrolizumab as First-Line Palliative Therapy in PD-L1 Overexpressing (≥ 50%) NSCLC: Real-world Results with Special Focus on PS ≥ 2, Brain Metastases, and Steroids Clin Lung Cancer. 2021 Feb 6;S1525-7304(21)00024-3. doi: 10.1016/j.cllc.2021.02.001. Online ahead of print. Nikolaj Frost 1 , Jens Kollmeier 2 , Daniel Misch 2 , et al.

INTRODUCTION: Pembrolizumab is a highly effective standard of care in PD-L1 overexpressing (≥ 50%) non-small-cell lung cancer. However, a substantial share of patients from everyday clinical practice is treated without clear evidence from clinical trials. **PATIENTS AND METHODS:** We performed a retrospective multicentric study including all consecutive patients from 6 certified lung cancer centers in Berlin, Germany, having received pembrolizumab as first-line palliative therapy from January 1 until December 31, 2017. Aims were to validate published clinical trials with a special focus on efficacy and outcome in patients with reduced performance status (PS), brain metastases, and steroids. **RESULTS:** A total of 153 patients were included (median age 69 years, 58% men, 69% adenocarcinoma). Rates for PS ≥ 2, brain metastases, and steroids were 24.8%, 20.9%, and 24.2%, respectively. Median objective response rate, progression-free and overall survival were 48.5%, 8.2 and 22.0 months for all patients and 52.4%, 8.8 and 29.2 months in patients fulfilling the inclusion criteria for the KEYNOTE-024 trial. Patients with a comorbidity-defined PS ≥ 2, symptomatic brain metastases requiring upfront radiotherapy, or baseline steroids had significantly reduced survival. In contrast, durable responses occurred with a tumor-related PS ≥ 2 or asymptomatic brain metastases. Grade 3/4 and 5 immune-related adverse events affected 13.7% and 2.0% of patients. **CONCLUSION:** Real-world and clinical trial efficacy with upfront pembrolizumab correspond well. Pembrolizumab may sufficiently control asymptomatic brain metastases and may improve a cancer-related reduced PS. However, the frail share of patients with a comorbidity-defined PS ≥ 2, symptomatic brain metastases, or baseline steroids derives no relevant benefit.

[Survival benefit from immunocheckpoint inhibitors in stage IV non-small cell lung cancer patients with brain metastases: A National Cancer Database propensity-matched analysis](#) Cancer Med. 2021 Feb;10(3):923-932. doi: 10.1002/cam4.3675. Epub 2020 Dec 19. Shinkichi Takamori 1 , Takefumi Komiya 2 , Emily Powell 3   4

Immunocheckpoint inhibitors (ICIs) have become a standard pharmacological therapy in non-small cell lung cancer (NSCLC). Because brain metastases (BMs) have historically been listed as exclusion criteria in previous clinical trials involving ICIs in advanced NSCLC, the survival benefit from ICI in NSCLC patients with BMs remains unclear. The National Cancer Database was queried for stage IV NSCLC patients with or without BMs between 2014 and 2015. Overall survival (OS) of stage IV NSCLC patients who received immunotherapy and that of stage IV NSCLC patients who did not receive immunotherapy were compared according to the presence or absence of BMs. Multivariable logistic analyses identified the clinical characteristics predictive of overall survival. A propensity score analysis was conducted with the aim of adjusting the potential biases arising from the clinical characteristics. This study included 42,512 patients with stage IV NSCLC; 11,810 patients with BMs and 30,702 patients without BMs. In univariate analysis, stage IV NSCLC patients with BMs treated with immunotherapy had a significantly longer OS than those without immunotherapy after propensity score matching (median OS: 12.8 vs 10.1 months, hazard ratio [HR]: 0.80, 95% confidence interval [CI]: 0.72-0.89, p < 0.0001). Multivariable Cox modeling after propensity score matching confirmed the survival benefit from ICI for stage IV NSCLC patients with BMs (HR: 0.75, 95% CI: 0.67-0.83, p < 0.0001). The HR in NSCLC patients without BMs treated with ICI compared with those without ICI was 0.77 (95% CI: 0.73-0.82, p < 0.0001). Survival in stage IV NSCLC patients with BMs was significantly improved by ICI treatment at levels comparable to those without BMs using a retrospective database. ICI may be one of the promising treatment options for stage IV NSCLC patients with BMs. These findings should be validated in future prospective studies.

[Entinostat plus Pembrolizumab in Patients with Metastatic NSCLC Previously Treated with Anti-PD-(L)1 Therapy](#) Clin Cancer Res. 2021 Feb 15;27(4):1019-1028. doi: 10.1158/1078-0432.CCR-20-3305. Epub 2020 Nov 17. Matthew D Hellmann 1 , Pasi A Jänne 2 , Mateusz Opyrchal 3 , et al.

PURPOSE: New therapies are needed to treat immune checkpoint inhibitor-resistant non-small cell lung cancer (NSCLC) and identify biomarkers to personalize treatment. Epigenetic therapies, including histone deacetylase inhibitors, may synergize with programmed cell death-1 (PD-1) blockade to overcome resistance. We report outcomes in patients with anti-programmed cell death ligand-1 [PD-(L)1]-resistant/refractory NSCLC treated with pembrolizumab plus entinostat in ENCORE 601. **PATIENTS AND METHODS:** The expansion cohort of ENCORE 601 included patients with NSCLC who previously experienced disease progression with immune checkpoint inhibitors. The primary endpoint for the phase II expansion cohort is overall response rate (ORR); safety, tolerability, and exploratory endpoints are described. **RESULTS:** Of 76 treated patients, 71 were evaluable for efficacy. immune-regulated RECIST-assessed ORR was 9.2% [95% confidence interval (CI): 3.8-18.1], which did not meet the prespecified threshold for positivity. Median duration of response was 10.1 months (95% CI: 3.9-not estimable), progression-free survival (PFS) at 6 months was 22%, median PFS was 2.8 months (95% CI: 1.5-4.1), and median overall survival was 11.7 months (95% CI: 7.6-13.4). Benefit was enriched among patients with high levels of circulating classical monocytes at baseline. Baseline tumor PD-L1 expression and IFNγ gene expression were not associated with benefit. Treatment-related grade ≥3 adverse events occurred in 41% of patients. **CONCLUSIONS:** In anti-PD-(L)1-experienced patients with NSCLC, entinostat plus pembrolizumab did not achieve the primary response rate endpoint but provided a clinically meaningful benefit, with objective response in 9% of patients. No new toxicities, including immune-related adverse events, were seen for either drug. Future studies will continue to evaluate the association of monocyte levels and response.

[Predictors of In-Hospital Death in Patients with Lung Cancer Admitted for Acute Radiation Pneumonitis: A Healthcare Cost and Utilization Project (HCUP) Analysis](#) Clin Lung Cancer. 2021 Feb 3;S1525-7304(21)00019-X. doi: 10.1016/j.cllc.2021.01.016. Online ahead of print. R Spencer Kirkland 1 , Adam J Kole 2 , Hitesh Batra 3 , et al.

BACKGROUND: Radiation pneumonitis (RP) is a dose-limiting and potentially fatal toxicity of thoracic radiotherapy most often seen in patients treated for primary lung cancer. The purpose of this study was to identify predictors of in-hospital death among lung cancer patients admitted for acute RP in the Healthcare Cost and Utilization Project (HCUP) database. **MATERIALS AND METHODS:** The HCUP National Inpatient Sample database was queried from 2012 through 2016 to capture adult lung cancer patients admitted to the hospital with a principal diagnosis of acute RP. Multivariate logistic regression modeling and $\chi2$ tests were used to determine predictors of in-hospital death. **RESULTS:** Of the 882 patients with lung cancer admitted for RP, 67 patients (7.6%) died during the hospitalization and 90 patients (10.2%) required mechanical ventilation. Of those requiring mechanical ventilation, 38 patients (42.2%) died. The average age at hospitalization was 70.4 years (range, 35-90). Of those factors associated with death on univariate analysis, interstitial lung disease (odds ratio [OR] = 6.14; 95% confidence interval [CI], 1.9-19.4; P = .002), pulmonary hypertension (OR = 3.1; 95% CI, 1.6-6.2; P = .001), diabetes mellitus (OR = 2.0; 95% CI, 1.1-3.3; P = .013), and more affluent Zip Code (OR = 1.9; 95% CI, 1.1-3.2; P = .021) remained statistically significant on multivariate logistic regression. **CONCLUSION:** In the largest reported cohort of patients with lung cancer hospitalized with a principal diagnosis of acute RP, the presence of interstitial lung disease, pulmonary hypertension, diabetes mellitus, and more affluent Zip Code were associated with in-hospital death. Comorbid diagnoses may be useful for risk-stratified management of inpatients with RP.

[Association of HIF1-α gene polymorphisms with advanced non-small cell lung cancer prognosis in patients receiving radiation therapy](#) Aging (Albany NY). 2021 Feb 17;13. doi: 10.18632/aging.202542. Online ahead of print. Yan Zhang 1 , Jian Wang 2 , Zhanzhan Li 3

We investigated the association between single nucleotide polymorphisms (SNPs) in the HIF1A gene and the prognosis of advanced non-small cell lung cancer (NSCLC) patients undergoing radiation therapy. Patient overall survival (OS) and progression-free survival (PFS) were analyzed. The rs11549465 TT genotype was associated with poor PFS (P<0.001) and OS (P=0.001). The rs2057482 TT genotype was also associated with poor PFS (P=0.002) and OS (P=0.007). Stratified analyses revealed that these associations occurred in patients with a smoking history, squamous cell carcinoma, and stage IIIA disease, as well as those receiving radiation therapy a radiation dose of ≥70 Gy. We found associations between SNPs and PFS but not OS in patients without a smoking history, other histological types, and stage IIIB disease, as well as those undergoing chemoradiotherapy with a radiation dose of <70 Gy. No associations were observed between rs11549467 or rs110873142 and NSCLC prognosis. These results suggest that HIF1A polymorphisms can be used as independent prognostic biomarkers for NSCLC patients receiving radiation therapy.

[Computer Tomography Radiomics-Based Nomogram in the Survival Prediction for Brain Metastases From Non-Small Cell Lung Cancer Underwent Whole Brain Radiotherapy](#) Front Oncol. 2021 Feb 11;10:610691. doi: 10.3389/fonc.2020.610691. eCollection 2020. Ji Zhang 1 , Juebin Jin 1 , Yao Ai 1 , Kecheng Zhu 1 , Chengjian Xiao 1 , Congying Xie 1 2 , Xiance Jin 1

Prognostic parameters and models were believed to be helpful in improving the treatment outcome for patients with brain metastasis (BM). The purpose of this study was to investigate the feasibility of computer tomography (CT) radiomics based nomogram to predict the survival of patients with BM from

non-small cell lung cancer (NSCLC) treated with whole brain radiotherapy (WBRT). A total of 195 patients with BM from NSCLC who underwent WBRT from January 2012 to December 2016 were retrospectively reviewed. Radiomics features were extracted and selected from pretherapeutic CT images with least absolute shrinkage and selection operator (LASSO) regression. A nomogram was developed and evaluated by integrating radiomics features and clinical factors to predict the survival of individual patient. Five radiomics features were screened out from 105 radiomics features according to the LASSO Cox regression. According to the optimal cutoff value of radiomics score (Rad-score), patients were stratified into low-risk (Rad-score <= -0.14) and high-risk (Rad-score > -0.14) groups. Multivariable analysis indicated that sex, karnofsky performance score (KPS) and Rad-score were independent predictors for overall survival (OS). The concordance index (C-index) of the nomogram in the training cohort and validation cohort was 0.726 and 0.660, respectively. An area under curve (AUC) of 0.786 and 0.788 was achieved for the short-term and long-term survival prediction, respectively. In conclusion, the nomogram based on radiomics features from CT images and clinical factors was feasible to predict the OS of BM patients from NSCLC who underwent WBRT.

[Stereotactic body radiotherapy for synchronous early stage non-small cell lung cancer](#) Acta Oncol. 2021 Feb 27;1-12. doi: 10.1080/0284186X.2021.1892182. Online ahead of print. Cole R Steber 1 , Ryan T Hughes 1 , Michael H Soike 2 , et al.
INTRODUCTION: In patients with non-small cell lung cancer (NSCLC) who present with multiple pulmonary nodules, it is often difficult to distinguish metastatic disease from synchronous primary lung cancers (SPLC). We sought to evaluate clinical outcomes after stereotactic body radiotherapy (SBRT) alone to synchronous primary lesions. **MATERIAL AND METHODS:** Patients with synchronous AJCC 8th Edition Stage IA-IIA NSCLC and treated with stereotactic body radiation therapy (SBRT) to all lesions between 2009-2018 were reviewed. SPLC was defined as patients having received two courses of SBRT within 180 days for treatment of separate early stage tumors. In total, 36 patients with 73 lesions were included. Overall survival (OS), progression-free survival (PFS), cumulative incidence of local failure (LF), and regional/distant failure (R/DF) were estimated and compared with a control cohort of solitary early stage NSCLC patients. **RESULTS:** Median PFS was 38.8 months (95% CI 14.3-not reached [NR]); 3-year PFS rates were 50.6% (35.6-72.1). Median OS was 45.9 months (95% CI: 35.9-NR); 3-year OS was 63.0% (47.4-83.8). Three-year cumulative incidence of LF and R/DF was 6.6% (3.7-13.9) and 35.7% (19.3-52.1), respectively. Patients with SPLC were compared to a control group (n = 272) of patients treated for a solitary early stage NSCLC. There was no statistically significant difference in PFS (p = .91) or OS (p = .43). Evaluation of the patterns of failure showed a trend for worse cumulative incidence of R/DF in SPLC patients as compared to solitary early stage NSCLC (p = .06). **CONCLUSION:** SBRT alone to multiple lung tumors with SPLC results in comparable PFS, OS, and LF rates to a cohort of patients treated for solitary early stage NSCLC. Those with SPLC had non-significantly higher R/DF. Patients with SPLC should be followed closely for failure and possible salvage therapy.

[Lung stereotactic body radiation therapy for elderly patients aged ≥ 80 years with pathologically proven early-stage non-small cell lung cancer: a retrospective cohort study](#) Radiat Oncol. 2021 Feb 23;16(1):39. doi: 10.1186/s13014-021-01769-7. Kenta Watanabe 1 , Kuniaki Katsui 2 , Soichiro Sugiyama 1 , et al.
BACKGROUND: Stereotactic body radiation therapy (SBRT) is an established therapy for medically inoperable early-stage non-small cell lung cancer (NSCLC). Many elderly patients are medically inoperable owing to comorbidities. Therefore, SBRT may be a useful therapy for elderly patients. However, the application of SBRT for patients aged ≥ 80 years has not been completely elucidated. Therefore, this study aimed to assess the clinical utility of SBRT for elderly patients aged ≥ 80 years with

pathologically proven early-stage NSCLC. **METHODS:** We retrospectively evaluated the data of patients aged ≥ 80 years with pathologically proven primary NSCLC who underwent SBRT at our institution between January 2009 and March 2020. Treatment outcomes and toxicities were analyzed. We used the Kaplan-Meier method to estimate survival curves and the log-rank test to compare the survival curves. We performed univariate and multivariate Cox regression analyses. p-values < 0.05 were regarded significant. **RESULTS:** Sixty-four patients (65 lesions) were included, and the median follow-up period was 38.7 (range 3.5-95.7) months. The median age was 82.9 (range 80.0-94.8) years. Sixteen patients were medically operable, and 48 patients were medically inoperable. The prescribed dose of SBRT was either 48 Gy in four fractions or 60 Gy in 10 fractions. The median survival time was 60.0 months (95% confidence interval, 43.5-71.1). The 1-, 3-, and 5-year local control, cancer-specific survival, progression-free survival, and overall survival rates were 98.4%, 98.4%, 81.0%, and 88.9%; 90.1%, 93.7%, 58.9%, and 68.3%; and 87.4%, 83.5%, 38.2%, and 47.5%, respectively. Multivariate analysis revealed that inoperability and solid nodules were the predictors of poor overall survival after SBRT in elderly patients. Two patients (3.1%) had grade 3 radiation pneumonitis, and one patient (1.6%) had grade 5 radiation pneumonitis. **CONCLUSIONS:** SBRT was feasible in patients aged ≥ 80 years with NSCLC. It achieved good local control with minimal toxicity. SBRT may be beneficial in elderly patients with early-stage NSCLC.

[Survival after palliative radiation therapy for cancer: the METSSS model](link) Radiother Oncol. 2021 Feb 18;S0167-8140(21)06071-0. doi: 10.1016/j.radonc.2021.02.011. Online ahead of print.
Nicholas G Zaorsky 1 , Menglu Liang 2 , Rutu Patel 3 , Christine Lin 3 , Leila T Tchelebi 3 , Kristina B Newport 4 , Edward J Fox 5 , Ming Wang 2
BACKGROUND: We propose a predictive model that identifies patients at greatest risk of death after palliative radiotherapy, which can help medical professionals choose treatments that better align with patient choice and prognosis. **METHODS:** The National Cancer Database was queried for recipients of palliative radiotherapy during first course of treatment. Cox regression models and adjusted hazard ratios with 95% confidence intervals were used to evaluate survival predictors. The mortality risk index was calculated using predictors from the estimated Cox regression model, with higher values indicating higher mortality risk. Based on tertile cutpoints, patients were divided into low, medium, and high risk groups. **RESULTS:** A total of 68,505 patients were included from 2010-2014 (median age 65.7 years, standard deviation 11.8 years, IQR 16, median 66). Upon univariable and multivariable analyses, several risk factors were found to predict survival: (1) location of metastases (liver, bone, lung, and brain); (2) age >65 years; (3) tumor primary (prostate, breast, and lung); (4) male; (5) Charlson-Deyo comorbidity score of 3+; and (6) radiotherapy site, including bone, brain and eye, thorax, and stomach, liver, pancreas, kidney, and abdomen. The median survival times were 11.66 months, 5.09 months, and 3.28 months in the low (n=22,621), medium (n=22,638), and high risk groups (n=22,611), respectively. A nomogram was created and validated to predict survival, available online, https://tinyurl.com/METSSSmodel. **CONCLUSION:** We created a predictive nomogram for survival of patients receiving palliative radiotherapy during their first course of treatment (named METSSS), based on Metastases location, Elderly (>65 years), Tumor primary, Sex, Sickness/comorbidity, and Site of radiotherapy.

SMALL CELL LUNG CANCER - SCLC

[[The role of prophylactic cranial irradiation in small cell lung cancer]](link) Rev Mal Respir. 2021 Feb 2;S0761-8425(21)00004-8. doi: 10.1016/j.rmr.2021.01.003. Online ahead of print. [Article in French] L Fievet 1 , J-P Sculier 1 , A-P Meert 1 , T Berghmans 2
INTRODUCTION: Prophylactic cranial irradiation (PCI) is considered standard therapeutic management in small cell lung cancer (SCLC). This is based on old randomised trials with

methodological limitations, namely the absence of magnetic resonance imaging (MRI) of the brain. The aim of this study is to assess the risk not administering PCI when systematic brain imaging is applied. **METHODS:** Retrospective study including untreated SCLC, without PCI and receiving brain imaging at the time of diagnosis. Kaplan-Meier and log-rank statistics were used for survival analyses. **RESULTS:** Among 150 patients, 75 were possibly eligible for PCI. Thirteen patients presented with an isolated brain recurrence as the first site of progression with no other metastatic sites apparent, and in 6 patients, the brain was the only recurrent site during the whole follow-up. In the group of patients eligible for PCI, there was no statistically significant survival difference according to the brain progression status (P=0.11). **CONCLUSIONS:** The expected impact of PCI seems limited in terms of overall survival and prevention of isolated brain metastases in patients having systematic brain imaging during SCLC work-up.

[**Video-Assisted Thoracoscopic Segmentectomy for Deep and Peripheral Small Lung Cancer**](#) Thorac Cardiovasc Surg. 2021 Feb 4. doi: 10.1055/s-0040-1722172. Online ahead of print.
Satoshi Takamori 1 , Hiroyuki Oizumi 1 , Jun Suzuki 1 , Katsuyuki Suzuki 1 , Takanobu Kabasawa 2
BACKGROUND: We aimed to retrospectively compare the long-term prognosis and recurrence after segmentectomy between nonsmall cell lung cancer (NSCLC) patients with deep and peripheral lesions. **METHODS:** Data were extracted for 85 lobectomy-tolerable NSCLC patients with tumors measuring ≤2 cm, who underwent video-assisted thoracoscopic segmentectomy with curative intent during January 2006 to December 2014. Tumor location was determined by the surgeon using thin-slice (1 mm) and three-dimensional computed tomography. Overall and recurrence-free survival was compared between patients with peripheral and deep lesions using univariate and multivariate Cox proportional hazard models. The indications for segmentectomy included NSCLC measuring ≤2 cm and consolidation/tumor ratio ≤20%, solid NSCLC ≤1 cm, and indeterminate nodule ≤1.5 cm. **RESULTS:** No recurrence of peripheral and deep lesions was noted. The 5-year overall survival was 96.4% for all patients, and 100 and 95.3% for patients with deep and peripheral lesions, respectively. There was no significant difference between the overall survival rates associated with the deep and peripheral lesions (95% confidence interval [CI], 89.5-98.8, nonsignificant, 86.4-98.4, respectively; p = 0.189). In a multivariate analysis, the American Society of Anesthesiologists score (hazard ratio [HR], 13.30; 95% CI, 1.31-210.36; p = 0.028) and histology (HR, 0.03; 95% CI, 0.00-0.32; p = 0.037) were independent prognostic factors for overall survival; tumor location was not a prognostic factor. **CONCLUSIONS:** When video-assisted thoracoscopic segmentectomy with curative intent was performed with sufficient surgical margins, the location of small NSCLC did not affect recurrence risk and prognosis. Video-assisted thoracoscopic segmentectomy for small NSCLC is acceptable, regardless of the tumor location.

[**Second-Line Nivolumab in Relapsed Small-Cell Lung Cancer: CheckMate 331**](#) Ann Oncol. 2021 Feb 1;S0923-7534(21)00099-5. doi: 10.1016/j.annonc.2021.01.071. Online ahead of print. D R Spigel 1 , D Vicente 2 , T E Ciuleanu 3 , et al.
S Gettinger 4 , S Peters 5 , L Horn 6 , C Audigier-Valette 7 , N Pardo Aranda 8 , O Juan-Vidal 9 , Y
BACKGROUND: Patients with relapsed small-cell lung cancer (SCLC) have few treatment options and dismal survival. Phase 1/2 data show activity of nivolumab in previously treated SCLC. **PATIENTS AND METHODS:** CheckMate 331 is a randomized, open-label, phase 3 trial of nivolumab versus standard chemotherapy in relapsed SCLC. Patients with relapse after first-line platinum-based chemotherapy were randomized 1:1 to nivolumab 240 mg every 2 weeks or chemotherapy (topotecan or amrubicin) until progression or unacceptable toxicity. Primary endpoint was overall survival (OS). **RESULTS:** Overall, 284 patients were randomized to nivolumab and 285 to chemotherapy. Minimum follow-up was 15.8 months. No significant improvement in OS was seen with nivolumab versus chemotherapy (median OS, 7.5 vs 8.4 months; hazard ratio [HR], 0.86; 95% confidence interval [CI], 0.72-1.04; P = 0.11). A survival benefit with nivolumab was suggested in patients with baseline lactate

dehydrogenase ≤ upper limit of normal and in those without baseline liver metastases. OS (nivolumab vs chemotherapy) was similar in patients with programmed death ligand 1 combined positive score ≥ 1% versus < 1%. Median progression-free survival was 1.4 versus 3.8 months (HR, 1.41; 95% CI, 1.18-1.69). Objective response rate was 13.7% versus 16.5% (odds ratio, 0.80; 95% CI, 0.50-1.27); median duration of response was 8.3 versus 4.5 months. Rates of grade 3 or 4 treatment-related adverse events were 13.8% versus 73.2%. **CONCLUSION:** Nivolumab did not improve survival versus chemotherapy in relapsed SCLC. No new safety signals were seen. In exploratory analyses, select baseline characteristics were associated with improved OS for nivolumab.

[**Small-cell lung cancer in never-smokers**](#) ESMO Open. 2021 Feb 25;6(2):100059. doi: 10.1016/j.esmoop.2021.100059. Online ahead of print. M Torres-Durán 1 , M T Curiel-García 2 , A Ruano-Ravina 3 , M Provencio 4 , I Parente-Lamelas 5 , J Hernández-Hernández 6 , A Fernández-Villar 1 , J M Barros-Dios 7 , M Pérez-Ríos 7

BACKGROUND: Lung cancer is a public health problem worldwide. Small-cell lung cancer (SCLC) is the most aggressive histologic type, with a 5-year survival <10%. SCLC is closely associated with tobacco consumption and infrequent in never-smokers. We aim to describe SCLC characteristics in never-smokers recruited in a radon-prone area. **PATIENTS AND METHODS:** We designed a multicentric case series where SCLC cases were recruited consecutively following histologic confirmation. Detailed information was obtained for indoor radon exposure, occupation and environmental tobacco smoke. We also collected different clinical characteristics such as extended or limited disease at diagnosis. **RESULTS:** We recruited 32 never-smoking SCLC cases. Median age was 75 years and 87.5% were women; 47% had extended disease. Median radon concentration was 182 Bq/m3. There were no statistically significant differences in residential radon concentration neither regarding age at diagnosis nor regarding sex. The most frequent symptoms were constitutional syndrome (23.1%) and coughing (23.1%). As much as 63% of cases had an Eastern Cooperative Oncology Group Study (ECOG) status of 0-2. The 1- and 2-year survival rates were 34.4% and 21.9%, respectively. The 2-year survival rate with a localized tumor was 26.7%, compared with 18.8% for extended disease. **CONCLUSIONS:** These results show, for the first time, that indoor radon might not be associated with SCLC characteristics at diagnosis in never-smokers, and also confirms the low survival of this aggressive type of lung cancer also for never-smokers.

[**Fragmentation of Small-cell Lung Cancer Regulatory States in Heterotypic Microenvironments**](#)
Cancer Res. 2021 Feb 2;canres.1036.2020. doi: 10.1158/0008-5472.CAN-20-1036. Online ahead of print. Dylan L Schaff 1 , Shambhavi Singh 1 , Kee-Beom Kim 2 , Matthew D Sutcliffe 1 , Kwon-Sik Park 3 , Kevin A Janes 4

Small-cell lung cancers derive from pulmonary neuroendocrine cells, which have stem-like properties to reprogram into other cell types upon lung injury. It is difficult to uncouple transcriptional plasticity of these transformed cells from genetic changes that evolve in primary tumors or secondary metastases. Profiling of single cells is also problematic if the required sample dissociation activates injury-like signaling and reprogramming. Here we defined cell state heterogeneities in situ through laser capture microdissection-based 10-cell transcriptomics coupled with stochastic-profiling fluctuation analysis. In labeled cells from a small-cell lung cancer mouse model initiated by neuroendocrine deletion of Rb1-Trp53, variations in transcript abundance revealed cell-to-cell differences in regulatory state in vitro and in vivo. Fluctuating transcripts in spheroid culture were partly shared among Rb1-Trp53-null models, and heterogeneities increased considerably when cells were delivered intravenously to colonize the liver. Colonization of immunocompromised animals drove a fractional appearance of alveolar type II-like markers and poised cells for paracrine stimulation from immune cells and hepatocytes. Immunocompetency further exaggerated the fragmentation of tumor states in the liver, yielding mixed

stromal signatures evident in bulk sequencing from autochthonous tumors and metastases. Dozens of transcript heterogeneities recurred irrespective of biological context; their mapped orthologs brought together observations of murine and human small-cell lung cancer. Candidate heterogeneities recurrent in the liver also stratified primary human tumors into discrete groups not readily explained by molecular subtype but with prognostic relevance. These data suggest that heterotypic interactions in the liver and lung are an accelerant for intratumor heterogeneity in small-cell lung cancer.

PALLIATIVE AND SUPPORTIVE CARE

[Nutritional status and symptom burden in advanced non-small cell lung cancer: results of the dietetic assessment and intervention in lung cancer (DAIL) trial](#) BMJ Support Palliat Care. 2021 Feb 9;bmjspcare-2020-002838. doi: 10.1136/bmjspcare-2020-002838. Online ahead of print.

Iain Phillips 1   2 , Lindsey Allan 3 , Adele Hug 3 , Naomi Westran 3 , Claudia Heinemann 4 , Madeleine Hewish 5 , Ajay Mehta 5 , Helen Saxby 5 , Veni Ezhil 5

INTRODUCTION: European Society for Clinical Nutrition and Metabolism guidelines recommend that patients with cancer should be screened for malnutrition at diagnosis. The dietetic assessment and intervention in lung cancer study investigated the nutritional status of patients with non-small cell lung cancer (NSCLC) and the need for dietetic intervention. **METHODS:** In this observational cohort pilot study, patients with stage 3b and 4 NSCLC were assessed prior to starting first line systemic anticancer therapy (SACT) with a range of measurements and questionnaires. We report the outcomes related to the Patient Generated Subjective Global Assessment tool (PG-SGA), RESULTS: 96 patients were consented between April 2017 and August 2019. The PG-SGA identified that 78% of patients required specialist nutritional advice; with 52% patients having a critical need for dietetic input and symptom management. Results were dominated by symptom scores. As a screening test, one or more symptoms or recent weight loss history had a sensitivity of 88% (95% CI 78.44% to 94.36%) and specificity of 95.24% (95% CI 76.18% to 99.88%) for need for dietetic intervention. **CONCLUSION:** A large proportion of patients with NSCLC have a high symptom burden and are at risk of malnutrition prior to starting SACT and would benefit from dietetic review. It is imperative that oncologists and healthcare professionals discuss weight loss history and symptoms with lung cancer patients to correct nutritional deficiencies and resolve symptoms prior to starting treatment.

[Management of Dyspnea in Advanced Cancer: ASCO Guideline](#) J Clin Oncol. 2021 Feb 22;JCO2003465. doi: 10.1200/JCO.20.03465. Online ahead of print. David Hui 1 , Kari Bohlke 2 , Ting Bao 3 , et al.

PURPOSE: To provide guidance on the clinical management of dyspnea in adult patients with advanced cancer. **METHODS:** ASCO convened an Expert Panel to review the evidence and formulate recommendations. An Agency for Healthcare Research and Quality (AHRQ) systematic review provided the evidence base for nonpharmacologic and pharmacologic interventions to alleviate dyspnea. The review included randomized controlled trials (RCTs) and observational studies with a concurrent comparison group published through early May 2020. The ASCO Expert Panel also wished to address dyspnea assessment, management of underlying conditions, and palliative care referrals, and for these questions, an additional systematic review identified RCTs, systematic reviews, and guidelines published through July 2020. **RESULTS:** The AHRQ systematic review included 48 RCTs and two retrospective cohort studies. Lung cancer and mesothelioma were the most commonly addressed types of cancer. Nonpharmacologic interventions such as fans provided some relief from breathlessness. Support for pharmacologic interventions was limited. A meta-analysis of specialty breathlessness services reported improvements in distress because of dyspnea. **RECOMMENDATIONS:** A hierarchical approach to dyspnea management is recommended, beginning with dyspnea assessment, ascertainment and

management of potentially reversible causes, and referral to an interdisciplinary palliative care team. Nonpharmacologic interventions that may be offered to relieve dyspnea include airflow interventions (eg, a fan directed at the cheek), standard supplemental oxygen for patients with hypoxemia, and other psychoeducational, self-management, or complementary approaches. For patients who derive inadequate relief from nonpharmacologic interventions, systemic opioids should be offered. Other pharmacologic interventions, such as corticosteroids and benzodiazepines, are also discussed.Additional information is available at www.asco.org/supportive-care-guidelines.

[Improved survival without increased toxicity with influenza vaccination in cancer patients treated with checkpoint inhibitors](#) Oncoimmunology. 2021 Feb 17;10(1):1886725. doi: 10.1080/2162402X.2021.1886725. Antonios Valachis 1 , Camilla Rosén 2 , Anthoula Koliadi 3   4 , Evangelos Digkas 5 , Alice Gustavsson 2 , Andreas Nearchou 5 , Gustav J Ullenhag 3   4
In international guidelines, influenza vaccination is recommended to cancer patients receiving antitumor treatment. Whether this recommendation should include patients treated with the recently introduced and now widely used checkpoint inhibitors (CPIs) is unclear. The immune hyperactivation after vaccination in a patient on CPI treatment may strengthen the antitumor immunity and improve patients´ prognosis. On the other hand, the hyperactivation might increase the risk for immune-related adverse events (IRAEs). Furthermore, there is a risk for decreased antitumor effect by the phenomenon of antigenic competition. Only results from few studies addressing survival have been reported and the results from studies on IRAEs are contradictory. We performed a multi-center retrospective cohort study at three Swedish centers in patients with metastatic cancer. All patients previously not treated with CPIs and who received monotherapy with a PD-1 or PD-L1 blocker between January 1st, 2016 until May 31st, 2019 were included. The most common type of malignancy was melanoma (47.8%) followed by non-small cell lung cancer (31.0%). Statistically significant longer PFS and OS were observed in multivariate analyses at 6-month landmark time in the vaccinated compared to the non-vaccinated group after adjustment for age, gender, comorbidity, performance status, CNS metastasis and line of treatment (p = .041 and 0.028, respectively). Furthermore, the incidence of any IRAE grade was comparable between vaccinated and non-vaccinated group (p = .85). In conclusion, the current study indicates that survival improves with influenza vaccination while not increasing the risk for side effects in cancer patients treated with checkpoint inhibitors. Hence, our results strongly support influenza vaccination in cancer patients receiving checkpoint inhibitors.

[Patient-Reported and End-of-Life Outcomes Among Adults with Lung Cancer Receiving Targeted Therapy in a Clinical Trial of Early Integrated Palliative Care: A Secondary Analysis](#) J Pain Symptom Manage. 2021 Feb 19;S0885-3924(21)00173-1. doi: 10.1016/j.jpainsymman.2021.02.010. Online ahead of print. Laura A Petrillo 1 , Areej El-Jawahri 2 , Emily R Gallagher 2 , Vicki A Jackson 3 , Jennifer S Temel 2 , Joseph A Greer 4
CONTEXT: Targeted therapy has revolutionized lung cancer treatment and markedly increased survival, though data are lacking on patient-reported and end-of-life (EOL) outcomes among patients receiving targeted therapy. **OBJECTIVES:** This study aimed to compare quality of life (QOL), symptoms, prognostic communication, and EOL care between patients receiving targeted therapy and patients with lung cancer without targetable mutations. **METHODS:** In this secondary analysis of a randomized trial of early palliative care in advanced lung cancer (n=154), we compared change in QOL and symptoms (per the Functional Assessment of Cancer Treatment [FACT]-Lung scale) over 24 weeks among patients with lung cancer receiving targeted therapy versus those without targetable mutations using linear mixed effects models, adjusted for receipt of palliative care, age and gender. We also compared prognostic communication and decedents' EOL health care utilization using logistic regression, adjusted for palliative care. **RESULTS:** Compared to individuals without targetable mutations, patients receiving targeted

therapy (n=35) reported greater improvements in QOL (FACT-General B=0.46; 95% CI=0.19, 0.73) and symptoms (FACT-Lung Cancer Subscale B=0.12; 95% CI=0.03, 0.20) over time, independent of palliative care. Patients receiving targeted therapy were also more likely to report they rarely discussed prognosis with their clinicians (OR=2.59, 95% CI=1.01, 6.63) and were more likely to receive cancer-directed therapy in their last 14 days of life (OR=14.98, 95% CI=4.08, 54.96). **CONCLUSIONS:** Relative to patients without targetable mutations, patients with lung cancer who receive targeted therapy experience improved QOL and symptoms, are less likely to discuss prognosis early in their illness course, and more likely to continue treatment until death and die in the hospital.

[Lung cancer stigma is a predictor for psychological distress: A longitudinal study.: Lung cancer stigma is a predictor for psychological distress](#) Psychooncology. 2021 Feb 23. doi: 10.1002/pon.5665. Online ahead of print. Shiho Rose 1   2 , Allison Boyes 1   2 , Brian Kelly 2   3 , Martine Cox 1   2 , BNutDiet Kerrin Palazzi 4 , Christine Paul 1   2   5
OBJECTIVES: To examine if baseline stigma predicts psychological distress at 3 months and 6 months follow-up among patients newly diagnosed with lung cancer. **METHODS:** This longitudinal study was nested within a larger randomised controlled trial. Eligible participants were recruited via respiratory and oncology out-patient clinics in Australia (n=194). Consenting participants were asked to complete surveys at baseline, 3 months and 6 months post-recruitment. Measures included lung cancer stigma (Cataldo Lung Cancer Stigma Scale) and psychological distress (General Health Questionnaire 12). **RESULTS:** One-hundred and ninety-four participants were included for analysis. Most were male (57.7%) with a mean age of 68 years (SD=8.8). A significant relationship between baseline lung cancer stigma and psychological distress at six months was found, where a one unit increase in lung cancer stigma increases psychological distress by 0.044 when adjusting for age, gender, smoking status, baseline GHQ-12 scores and intervention allocation (as part of the larger trial; p=0.001; β=0.044, 95% CI=0.010, 0.079). **CONCLUSION:** Temporal links between lung cancer stigma and psychological distress was found at 6 months, suggesting stigma-related experiences may have a delayed impact. Development of routine lung cancer stigma assessments is recommended to identify those at risk of psychological distress. This article is protected by copyright. All rights reserved.

[Dietary quality using four dietary indices and lung cancer risk: the Golestan Cohort Study (GCS) Cancer Causes Control.](#) 2021 Feb 21. doi: 10.1007/s10552-021-01400-w. Online ahead of print. Qian Wang 1 , Maryam Hashemian 2   3 , Sadaf G Sepanlou 2   4 , et al.
PURPOSE: The lung cancer incidence in Iran has increased almost ten times over the past three decades. In addition to the known causes such as smoking and certain occupational exposure, dietary quality has been suggested to play a role in lung cancer. We aim to explore the association between dietary pattern and lung cancer risk among a Middle East population. **METHODS:** Data came from Golestan Cohort Study which included 48,421 participants with 136 lung cancer cases diagnosed during a median follow-up of 12 years. Multivariable Cox proportional hazards regression models were used to calculate the HRs and 95% CI of lung cancer risk by tertile of the four dietary index scores-the Health Eating Index (HEI)-2015, the Alternative Health Eating Index (AHEI)-2010, the Alternative Mediterranean Diet (AMED), and the Dietary Approach to Stop Hypertension (DASH)-Fung. **RESULTS:** A higher DASH-Fung score was inversely associated with risk of lung cancer after adjusting for potential confounders (tertile three vs. tertile one: HR = 0.59 (0.38-0.93); p for trend = 0.07), and pinteraction with smoking was 0.46. Similar findings were observed among current smokers with the HEI-2015 score (tertile three vs. tertile one: HR = 0.22 (0.08-0.60): p for trend < 0.01), and pinteraction between smoking and the HEI-2015 score was 0.03. **CONCLUSION:** In the GCS, consuming a diet more closely aligned with the DASH diet was associated with a reduced risk of lung cancer, which appeared to be independent of smoking status. There was also an inverse link between the HEI-2015 score and lung cancer risk among current smokers. Our

finding is particularly important for the Middle East population, as diet may play an important role in cancer prevention and overall health.

COMPLEMENTARY & ALTERNATIVE THERAPY

[Traditional Chinese medicine and lung cancer--From theory to practice](#) Biomed Pharmacother. 2021 Feb 15;137:111381. doi: 10.1016/j.biopha.2021.111381. Online ahead of print. Zhang Li 1 , Zhang Feiyue 1 , Li Gaofeng 2

With the continuous breakthroughs in molecular biology and biochemistry, we have constantly made great progress in the treatment of lung cancer. There is no doubt that standard treatment (such as surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy) has greatly improved the prognosis of lung cancer populations. In particular, the immunotherapy has brought more and more good news to countless lung cancer patients. In contrast to these standard treatments, traditional Chinese medicine (TCM) rarely has a profound and comprehensive overview in the field of lung cancer. This article will summarize the latest progress of TCM in lung cancer which is mainly non-small cell lung cancer (NSCLC) from theory to clinical practice, which would carry forward the sophisticated TCM and promote the development of modern medicine.

[Randomized Efficacy Trial of Conventional, TCM Herb, and TEAS on Bone Marrow Suppression in Patients with Small Cell Lung Cancer after Initial Chemotherapy](#) Evid Based Complement Alternat Med. 2021 Feb 2;2021:2693472. doi: 10.1155/2021/2693472. eCollection 2021. Fangchao Zhao 1 , Zengying Wang 2 , Yanlin Gao 3 , Yusi Wu 4 , Jianming Liu 1 , Shuangliang He 5

OBJECTIVE: To compare the efficiency of transcutaneous electrical acupoint stimulation (TEAS) with those of conventional and TCM herb on bone marrow suppression in small cell lung cancer (SCLC) patients after initial chemotherapy. **METHODS:** We recruited 139 participants with pathologically confirmed SCLC who had not received chemotherapy. The conventional group (n = 37) received gemcitabine and cisplatin chemotherapy and routine care. The TCM herb group (n = 35) received 3 Diyushengbai tablets thrice a day for one day prior to chemotherapy and maintained during the trial. The TEAS group (n = 42) received TEAS at a frequency of 65-100 Hz with a pulse width of 100-200 μsec. Acupoints were selected from Dazhui (DU14), Geshu (BL17), Zusanli (ST36), Sanyinjiao (SP6), and Hegu (LI4) and were treated on days 1, 2, 3, 5, 8, 14, 21, and 28 of chemotherapy for 30 min each day. All three groups underwent a 28-day treatment for a total of one treatment course. Changes in the white blood cell, neutrophil, platelet, and hemoglobin indices on day 1 before chemotherapy and days 5, 8, 11, 14, 21, and 28 days after chemotherapy were compared among the groups. Comfort levels of patients on day 1 before chemotherapy and days 5, 11, and 21 after chemotherapy were observed. **RESULTS:** Compared with the conventional group, the white blood cell counts in the TEAS group on days 8 (7.07 ± 2.11 vs. 5.97 ± 2.10 × 109/L) and 14 (6.14 ± 1.51 vs. 5.07 ± 2.41 × 109/L) of chemotherapy and that in the TCM herb group on day 14 (6.63 ± 3.44 vs. 5.07 ± 2.41 × 109/L) of chemotherapy were increased (P < 0.05). Compared with the conventional group, the neutrophil count in the TEAS group on days 5 (4.28 ± 1.54 vs. 3.01 ± 1.41 × 109/L), 8 (3.75 ± 1.21 vs. 2.77 ± 1.17 × 109/L), 11 (3.46 ± 1.31 vs. 2.31 ± 1.24 × 109/L), 14 (3.18 ± 1.29 vs. 2.07 ± 1.14 × 109/L), and 21 (4.67 ± 1.31 vs. 3.58 ± 1.23 × 109/L) of chemotherapy and that in the TCM herb group on day 5 (3.88 ± 1.05 vs. 3.01 ± 1.41 × 109/L) of chemotherapy were increased (P < 0.05). Compared with the conventional group, the platelet count of patients in the TEAS group increased on days 5 (264.7 ± 64.1 vs. 201.0 ± 55.7 × 109/L), 8 (251.3 ± 74.9 vs. 188.2 ± 65.8 × 109/L), 11 (236.7 ± 74.9 vs. 181.3 ± 84.3 × 109/L), and 14 (238.3 ± 75.9 vs. 192.8 ± 95.8 × 109/L) of chemotherapy (P < 0.05). Compared with the TCM herb group, the platelet count in the TEAS group increased on days 5 (264.7 ± 64.1 vs. 216.3 ± 57.9 × 109/L), 8 (251.3 ± 74.9 vs. 213.7 ± 70.3 × 109/L), 11 (236.7 ± 74.9 vs. 181.3 ± 84.3 × 109/L), and 21 (254.8 ± 81.8 vs. 213.9 ± 82.6 × 109/L)

of chemotherapy (P < 0.05). Compared with the conventional group, the hemoglobin level in the TCM herb group increased on day 14 (135.03 ± 28.06 vs. 122.09 ± 12.63 g/L) of chemotherapy (P < 0.05). Compared with the conventional group, the comfort score of the TEAS group increased on days 5 (78.31 ± 10.21 vs. 70.18 ± 9.34 score) and 11 (80.07 ± 10.44 vs. 72.11 ± 9.47 score) of chemotherapy (P < 0.05). **CONCLUSION:** TEAS is an effective and safe treatment modality for improving bone marrow suppression in SCLC patients after initial chemotherapy. TEAS improved comfort levels more effectively than did conventional and TCM herb

[Efficacy of ginseng and its ingredients as adjuvants to chemotherapy in non-small cell lung cancer](#)

Food Funct. 2021 Feb 17. doi: 10.1039/d0fo03341c. Online ahead of print. He Zhu 1 , Hui Liu 2 , Jin-Hao Zhu 2 , Si-Yu Wang 2 , Shan-Shan Zhou 3 , Ming Kong 3 , Qian Mao 3 , Fang Long 3 , Zhi-Jun Fang 4 , Song-Lin Li 1

Chemotherapy is applied to treat non-small cell lung cancer (NSCLC), but often limited due to its unstable therapeutic effects and adverse reactions (ADRs). Ginseng and its main ingredients (ginsenosides and polysaccharides) have been clinically used as adjuvants to chemotherapy. However, their efficacies were based on individual trials with relatively small sample sizes, and it is difficult to draw a valid conclusion. In this study, eligible randomized controlled trials (RCTs) were searched in six international and Chinese databases (PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure, Chinese VIP Information and Wanfang). The outcomes of the objective response rate (ORR), disease control rate (DCR), ADRs, quality of life (QOL), survival rates and immunity were extracted using standard data extraction forms. The efficacies of ginseng and its ingredients as adjuvants to chemotherapy in NSCLC were investigated and compared by meta-analysis and subgroup meta-analysis, respectively. A total of 28 RCTs including 2503 subjects were enrolled, and most of the eligible studies were of low-to-moderate quality. For the evaluation of ginseng and its ingredients as adjuvants to chemotherapy, the risk ratio (RR) or standardized mean difference (SMD) and 95% confidence intervals (CI) of the ORR, DCR, leucopenia, thrombocytopenia, myelosuppression, hepatotoxicity, nausea and vomiting, diarrhea, CD4+/CD8+ and one- and two-year survival rates, and QOL were 1.35 (1.21,1.50), 1.20 (1.14,1.28), 0.59 (0.50, 0.70), 0.53 (0.37, 0.76), 0.30 (0.17, 0.53), 0.67 (0.52, 0.87), 0.67 (0.53, 0.86), 0.42 (0.19, 0.96), 1.39 (0.63, 2.16), 1.35 (1.13, 1.60), 3.21 (1.51, 6.81) and 1.31 (1.22, 1.41) with significant differences. Subgroup analysis showed that ginseng enhanced nausea and vomiting and QOL, ginsenosides increased ORR, DCR, QOL, leucopenia, thrombocytopenia, myelosuppression, hepatotoxicity, diarrhea, CD4+/CD8+, and one- and two-year survival rates, while polysaccharides improved ORR, DCR, leucopenia, thrombocytopenia, myelosuppression, hepatotoxicity and nausea and vomiting during chemotherapy. In conclusion, ginseng and its ingredients facilitated the therapeutic effects of chemotherapy on NSCLC patients. Ginseng had beneficial effects on alleviating ADRs and enhancing QOL, ginsenosides demonstrated beneficial effects on enhancing therapeutic effects, reducing ADRs, improving immunity, prolonging survival rates and promoting QOL, while polysaccharides showed beneficial effects on promoting therapeutic effects and reducing ADRs.

MISCELLANEOUS WORKS

[Analyses of Risk, Racial Disparity, and Outcomes Among US Patients With Cancer and COVID-19 Infection](#)

JAMA Oncol. 2021 Feb 1;7(2):220-227. doi: 10.1001/jamaoncol.2020.6178. QuanQiu Wang 1 , Nathan A Berger 2 3 , Rong Xu 1 3

IMPORTANCE: Patients with specific cancers may be at higher risk than those without cancer for coronavirus disease 2019 (COVID-19) and its severe outcomes. At present, limited data are available on the risk, racial disparity, and outcomes for COVID-19 illness in patients with cancer. **OBJECTIVES:** To investigate how patients with specific types of cancer are at risk for COVID-19 infection and its adverse

outcomes and whether there are cancer-specific race disparities for COVID-19 infection. **DESIGN, SETTING, AND PARTICIPANTS:** This retrospective case-control analysis of patient electronic health records included 73.4 million patients from 360 hospitals and 317 000 clinicians across 50 US states to August 14, 2020. The odds of COVID-19 infections for 13 common cancer types and adverse outcomes were assessed. **EXPOSURES:** The exposure groups were patients diagnosed with a specific cancer, whereas the unexposed groups were patients without the specific cancer. **MAIN OUTCOMES AND MEASURES:** The adjusted odds ratio (aOR) and 95% CI were estimated using the Cochran-Mantel-Haenszel test for the risk of COVID-19 infection. **RESULTS:** Among the 73.4 million patients included in the analysis (53.6% female), 2 523 920 had at least 1 of the 13 common cancers diagnosed (all cancer diagnosed within or before the last year), and 273 140 had recent cancer (cancer diagnosed within the last year). Among 16 570 patients diagnosed with COVID-19, 1200 had a cancer diagnosis and 690 had a recent cancer diagnosis of at least 1 of the 13 common cancers. Those with recent cancer diagnosis were at significantly increased risk for COVID-19 infection (aOR, 7.14 [95% CI, 6.91-7.39]; P < .001), with the strongest association for recently diagnosed leukemia (aOR, 12.16 [95% CI, 11.03-13.40]; P < .001), non-Hodgkin lymphoma (aOR, 8.54 [95% CI, 7.80-9.36]; P < .001), and lung cancer (aOR, 7.66 [95% CI, 7.07-8.29]; P < .001) and weakest for thyroid cancer (aOR, 3.10 [95% CI, 2.47-3.87]; P < .001). Among patients with recent cancer diagnosis, African Americans had a significantly higher risk for COVID-19 infection than White patients; this racial disparity was largest for breast cancer (aOR, 5.44 [95% CI, 4.69-6.31]; P < .001), followed by prostate cancer (aOR, 5.10 [95% CI, 4.34-5.98]; P < .001), colorectal cancer (aOR, 3.30 [95% CI, 2.55-4.26]; P < .001), and lung cancer (aOR, 2.53 [95% CI, 2.10-3.06]; P < .001). Patients with cancer and COVID-19 had significantly worse outcomes (hospitalization, 47.46%; death, 14.93%) than patients with COVID-19 without cancer (hospitalization, 24.26%; death, 5.26%) (P < .001) and patients with cancer without COVID-19 (hospitalization, 12.39%; death, 4.03%) (P < .001). **CONCLUSIONS AND RELEVANCE**: In this case-control study, patients with cancer were at significantly increased risk for COVID-19 infection and worse outcomes, which was further exacerbated among African Americans. These findings highlight the need to protect and monitor patients with cancer as part of the strategy to control the pandemic.

[**The characteristics of patients who quit smoking in the year following a cancer diagnosis**](#) J Cancer Surviv. 2021 Feb 27. doi: 10.1007/s11764-021-01009-7. Online ahead of print.
Scott P Gummerson 1 , Jeremiah T Lowe 2 , Kathryn L Taylor 3 , Tania Lobo 3 , Roxanne E Jensen 4
PURPOSE: Continued tobacco smoking following a cancer diagnosis is associated with adverse outcomes. Our study aims to identify the demographic and clinical characteristics of survivors who quit smoking within a year of diagnosis. **METHODS:** We conducted a secondary analysis of the Measuring Your Health (MY-Health) study, a community-based survey cohort of 5506 cancer patients registered across four Surveillance, Epidemiology, and End Results (SEER) cancer registries. Using surveys completed 6-13 months after diagnosis, we identified 868 participants who reported smoking around the time of cancer diagnosis and compared their current smoking status. We employed logistic regression models to predict current smoking status, adjusting for clinical and demographic variables. **RESULTS:** The overall smoking cessation rate was 35% (n = 306). Survivors with non-small cell lung cancer were three times more likely to quit smoking compared to patients with non-smoking-related cancers (aOR = 3.23, 95% CI = 2.20-4.74). Participants with advanced stage cancer reported higher odds of quitting compared to those with localized cancer (aOR = 1.42, 95% CI = 1.02-1.96). Other characteristics that predicted quitting included being married, higher education level, and female sex (aOR = 2.01, 95% CI = 1.46-2.77; aOR = 1.74, 95% CI = 1.27-2.39; aOR = 1.54, 95% CI = 1.11-2.13, respectively). **CONCLUSIONS:** This is one of the first studies to examine smoking cessation trends in a community-based, US cancer cohort during the year after diagnosis. Survivors with lung cancer and advanced cancer were significantly more likely to quit smoking. **IMPLICATIONS FOR CANCER SURVIVORS**:

Practitioners may use this knowledge to target interventions and address substantial disparities in cessation rates among survivors with early stage and non-lung cancers.

[Smoking Behavior in Patients With Early-Stage NSCLC: A Report From ECOG-ACRIN 1505 Trial](#) J Thorac Oncol. 2021 Feb 1;S1556-0864(21)00026-5. doi: 10.1016/j.jtho.2020.12.017. Online ahead of print. Conor E Steuer 1 , Opeyemi A Jegede 2 , Suzanne E Dahlberg 3 , et al.
INTRODUCTION: Smoking cessation has been reported to benefit patients even after a diagnosis of lung cancer. We studied the smoking behavior of patients who participated in a phase 3 trial of adjuvant therapy following resection of stages IB-IIIA NSCLC. **METHODS:** The ECOG-ACRIN 1505 was conducted to determine whether the addition of bevacizumab to adjuvant chemotherapy would improve overall survival (OS) for patients with early-stage NSCLC. Studying the association between smoking status and OS was a secondary end point. Patients completed a questionnaire on their smoking habits at baseline, 3, 6, 9, and 12 months. **RESULTS:** A total of 1501 patients were enrolled, and 99.8%, 95%, 94%, 93%, and 93% responded to the questionnaire at baseline, 3, 6, 9, and 12 months, respectively. A total of 90% reported a current or previous history of cigarette smoking. In addition, 60% of nonsmokers at enrollment reported smoking after diagnosis (before randomization); however, 1% of them reported smoking at 12 months. Furthermore, 94% of the respondents smoked none/fewer cigarettes daily at 12 months. The incidence of grades 3-5 toxicity on treatment was 68%, 76%, and 72% in never, former, and current smokers, respectively (p = 0.05). The disease-free survival for never-smokers relative to current and former smokers was (hazard ratio [HR] 0.93, p = 0.64 and HR 1.05, p = 0.72), and OS was (adjusted HR for death 0.54, p = 0.005 and adjusted HR for death 0.68, p = 0.03), respectively. **CONCLUSIONS:** This is the first comprehensive, prospective report of smoking habits in patients with NSCLC patients from a phase III early-stage trial. There was a high rate of smoking reduction and cessation following study entry. The disease-free survival did not differ significantly between smokers and never smokers, though there were less grade 3-5 toxicities and more favorable OS in never-smokers.

[Impact of Broadening Trial Eligibility Criteria for Patients with Advanced Non-Small Cell Lung Cancer: Real-World Analysis of Select ASCO- Friends Recommendations](#) Clin Cancer Res. 2021 Feb 9. doi: 10.1158/1078-0432.CCR-20-3857. Online ahead of print. R Donald Harvey # 1 , Suanna S Bruinooge # 2 , Li Chen 3 , et al.
PURPOSE: Cancer clinical trials often accrue slowly or miss enrollment targets. Strict eligibility criteria are a major reason. Restrictive criteria also limit opportunities for patient participation while compromising external validity of trial results. We examined the impact of broadening select eligibility criteria on characteristics and number of patients eligible for trials, using recommendations of the American Society of Clinical Oncology (ASCO) and Friends of Cancer Research. **EXPERIMENTAL DESIGN:** A retrospective, observational analysis used electronic health record data from ASCO's CancerLinQ Discovery database. Study cohort included patients with advanced non-small cell lung cancer treated from 2011 to 2018. Patients were grouped by traditional criteria [no brain metastases, no other malignancies, and creatinine clearance (CrCl) ≥ 60 mL/minute] and broadened criteria (including brain metastases, other malignancies, and CrCl ≥ 30 mL/minute). **RESULTS:** The analysis cohort included 10,500 patients. Median age was 68 years, and 73% of patients were White. Most patients had stage IV disease (65%). A total of 5,005 patients (48%) would be excluded from trial participation using the traditional criteria. The broadened criteria, however, would allow 98% of patients (10,346) to be potential participants. Examination of patients included by traditional criteria (5,495) versus those added (4,851) by broadened criteria showed that the number of women, patients aged 75+ years, and those with stage IV cancer was significantly greater using broadened criteria. **CONCLUSIONS:** This analysis of real-world data demonstrated that broadening three common eligibility criteria has the potential to double the eligible

patient population and include trial participants who are more representative of those encountered in practice.

[Assessment of Outcomes Associated With the Use of Newly Approved Oncology Drugs in Medicare Beneficiaries](#)

Angela K Green 1   2 , Michael Curry 2 , Niti Trivedi 2 , Peter B Bach 2 , Sham Mailankody 2   3

IMPORTANCE: A lack of generalizability of pivotal cancer clinical trial data to treatment of older adults with Medicare could affect therapeutic decision-making in clinical practice. **OBJECTIVE:** To evaluate the differences in survival, duration of therapy, and treatment patterns between clinical trial patients and older adults with Medicare receiving cancer drugs for metastatic solid cancers in usual practice. **DESIGN, SETTING, AND PARTICIPANTS:** This retrospective cohort study, performed from May 1, 2018, to August 30, 2020, used the linked Surveillance, Epidemiology, and End Results (SEER) program and Medicare database to examine sequential US Food and Drug Administration (FDA)-approved cancer drug indications (2008-2013) for locally advanced or metastatic solid tumors to assess whether pivotal trials reflect the outcomes of Medicare patients with cancer treated in usual practice. **EXPOSURES:** Treatment with FDA-approved cancer drugs for metastatic solid cancers in pivotal clinical trials and in the SEER-Medicare database. **MAIN OUTCOMES AND MEASURES:** Overall survival, duration of treatment, and dose reductions among trial participants and treated Medicare patients. **RESULTS:** A total of 11 828 trial participants (mean age, 61.8 years; 6718 [56.8%] male; and 7605 [64.3%] White) and 9178 SEER-Medicare patients (mean age, 72.7 years; 4800 [52.3%] male; and 7437 [81.0% White]) were compared. Twenty-nine indications for 22 cancer drugs were included. Median overall survival among Medicare patients was shorter than among patients in the clinical trial intervention arm for 28 of 29 indications (median difference, -6.3 months; range, -28.7 to 2.7 months). Median duration of therapy among Medicare patients was shorter for 23 of the 27 indications with data available (median difference, -1.9 months; range, -12.4 to 1.4 months). For 9 indications, there was information available regarding dose reductions in the package insert or trial publication. In all but 1 instance, dose reductions or single prescriptions were more common in the Medicare population compared with dose reductions among the clinical trial patients; for example, in the Medicare patients, 600 of 1032 (58.1%) received dose reduction or a single prescription and 172 of 1032 (16.7%) received a single prescription vs 734 of 3416 (21.5%) in the trial intervention arm. The exception was afatinib for non-small cell lung cancer: 34 of 71 (47.9%) received dose reduction or a single prescription and 15 of 71 (21.1%) received a single prescription among the Medicare patients vs 120 of 230 (52.2%) receiving dose reductions among the trial intervention group. **CONCLUSIONS AND RELEVANCE:** In this cohort study, patients receiving Medicare who were treated with FDA-approved cancer drugs did not live as long as treated clinical trial participants and commonly received treatment modifications. This study suggests that cancer clinical data relevant to newly approved drugs lack generalizability to Medicare beneficiaries with cancer; therefore, these agents should be used with caution.

[Distinct effects of asthma and COPD comorbidity on disease expression and outcome in patients with COVID-19](#)

Jia Song 1 , Ming Zeng 1 , Hai Wang 1 , et al.

BACKGROUND: The impacts of chronic airway diseases on coronavirus disease 2019 (COVID-19) are far from understood. **OBJECTIVE:** To explore the influence of asthma and chronic obstructive pulmonary disease (COPD) comorbidity on disease expression and outcomes, and the potential underlying mechanisms in COVID-19 patients. **METHODS:** A total of 961 hospitalized COVID-19 patients with a definite clinical outcome (death or discharge) were retrospectively enrolled. Demographic and clinical information were extracted from the medical records. Lung tissue sections from patients suffering from lung cancer were used for immunohistochemistry study of angiotensin-converting enzyme

II (ACE2) expression. BEAS-2B cell line was stimulated with various cytokines. **RESULTS**: In this cohort, 21 subjects (2.2%) had COPD and 22 (2.3%) had asthma. After adjusting for confounding factors, COPD patients had higher risk of developing severe illness (OR: 23.433; 95% CI 1.525-360.135; P < .01) and acute respiratory distress syndrome (OR: 19.762; 95% CI 1.461-267.369; P = .025) than asthmatics. COPD patients, particularly those with severe COVID-19, had lower counts of CD4+ T and CD8+ T cells and B cells and higher levels of TNF-α, IL-2 receptor, IL-10, IL-8, and IL-6 than asthmatics. COPD patients had increased, whereas asthmatics had decreased ACE2 protein expression in lower airways, compared with that in control subjects without asthma and COPD. IL-4 and IL-13 downregulated, but TNF-α, IL-12, and IL-17A upregulated ACE2 expression in BEAS-2B cells. **CONCLUSION:** Patients with asthma and COPD likely have different risk of severe COVID-19, which may be associated with different ACE2 expression.