



Caring Ambassadors Lung Cancer Program

Literature Review, January 2021

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SCREENING, COMPREHENSIVE BIOMARKER TESTING, DIAGNOSIS AND STAGING

[Impact of the COVID-19 Pandemic on Lung Cancer Screening Program and Subsequent Lung](#)

[Cancer](#) J Am Coll Surg. 2020 Dec 12;S1072-7515(20)32525-4. doi: 10.1016/j.jamcollsurg.2020.12.002. Online ahead of print. Robert M Van Haren 1 , Aaron M Delman 2 , Kevin M Turner 2 , Brandy Waits 3 , Mona Hemingway 3 , Shimul A Shah 2 , Sandra L Starnes 4

BACKGROUND: Low-dose computed tomography (LDCT) screening reduces lung cancer mortality by at least 20%. The COVID-19 pandemic required an unprecedented shutdown in our institutional LDCT program. The purpose of this study was to examine the impact of COVID-19 on lung cancer screening and subsequent cancer diagnosis. **STUDY DESIGN:** We analyzed our prospective institutional LDCT screening database, which began in 2012; 2,153 patients have participated. Monthly average LDCT were compared between baseline (January 2017-February 2020) and COVID-19 periods (March 2020-July 2020). **RESULTS:** LDCT was suspended on March 13, 2020 and 818 screening visits were cancelled. Phased reopening began on May 5th and full opening on June 1st. Total monthly LDCT (146±31 vs. 39±40, p<0.01) and new patient monthly LDCT (56±14 vs. 15±17, p<0.01) were significantly decreased during COVID-19 period. New patient monthly LDCT has remained low despite resuming full operations. Three and 6-month interval follow up LDCTs were prioritized and were significantly increased compared to baseline (11±4 vs. 30±4, p<0.01). The "no-show" rate was significantly increased from baseline (15% vs 40%, p<0.04). Most concerning, the percentage of patients with lung nodules suspicious for malignancy (Lung RADS 4) were significantly increased after operations resumed (8% vs. 29%, p<0.01). **CONCLUSION:** COVID-19 caused significant disruption in lung cancer screening, leading to a decrease in new patients screened and an increased proportion of nodules suspicious for malignancy once screening resumed. Using lung cancer and the LDCT screening program as a model, this early analysis shows the unrecognized consequences related to the pandemic for screening programs and cancer care.

[Successes and challenges of implementing a lung cancer screening program in federally qualified health centers: a qualitative analysis using the Consolidated Framework for Implementation](#)

[Research](#) Transl Behav Med. 2020 Dec 8;ibaa121. doi: 10.1093/tbm/ibaa121. Online ahead of print. Caitlin G Allen 1 , Megan M Cotter 2 , Robert A Smith 3 , Lesley Watson 4

In recent years, studies have shown that low-dose computed tomography (LDCT) is a safe and effective way to screen high-risk adults for lung cancer. Despite this, uptake remains low, especially in limited-resource settings. The American Cancer Society (ACS) partnered with two federally qualified health centers and accredited screening facilities on a 2 year pilot project to implement an LDCT screening program. Both sites attempted to develop a referral program and care coordination practices to move patients through the screening continuum and identify critical facilitators and barriers to implementation. Evaluators conducted key informant interviews (N = 46) with clinical and administrative staff, as well as regional ACS staff during annual site visits. The Consolidated Framework for Implementation Research guided our analysis of factors associated with effective implementation and improved screening outcomes. One study site established a sustainable lung screening program, while the other struggled to overcome significant implementation barriers. Increased time spent with patients, disruption to normal workflows, and Medicaid reimbursement policies presented challenges at both sites. Supportive, engaged leaders and knowledgeable champions who provided clear implementation guidance improved staff engagement and were able to train, guide, and motivate staff throughout the intervention. A slow, stepwise implementation process allowed one site's project champions to pilot test new processes and resolve issues before scaling up. This pilot study provides critical insights into the necessary resources and steps for successful lung cancer screening program implementation in underserved settings. Future efforts can build upon these findings and identify and address possible facilitators and barriers to screening program implementation.

[Variation in Eligible Patients' Agreeing to and Receiving Lung Cancer Screening: A Cohort Study](#)

Am J Prev Med. 2020 Dec 17;S0749-3797(20)30502-X. doi: 10.1016/j.amepre.2020.10.014. Online ahead of print. N Joseph Leishman 1 , Renda S Wiener 2 , Angela Fagerlin 3 , Rodney A Hayward 4 , Julie Lowery 5 , Tanner J Caverly 6

INTRODUCTION: Little is known about how clinicians make low-dose computed tomography lung cancer screening decisions in practice. Investigators assessed the factors associated with real-world decision making, hypothesizing that lung cancer risk and comorbidity would not be associated with agreeing to or receiving screening. Though these factors are key determinants of the benefit of lung cancer screening, they are often difficult to incorporate into decisions without the aid of decision tools.

METHODS: This was a retrospective cohort study of patients meeting current national eligibility criteria and deemed appropriate candidates for lung cancer screening on the basis of clinical reminders completed over a 2-year period (2013-2015) at 8 Department of Veterans Affairs medical facilities. Multilevel mixed-effects logistic regression models (conducted in 2019-2020) assessed predictors (age, sex, lung cancer risk, Charlson Comorbidity Index, travel distance to facility, and central versus outlying decision-making location) of primary outcomes of agreeing to and receiving lung cancer screening. **RESULTS:** Of 5,551 patients (mean age=67 years, 97% male, mean lung cancer risk=0.7%, mean Charlson Comorbidity Index=1.14, median travel distance=24.2 miles), 3,720 (67%) agreed to lung cancer screening and 2,398 (43%) received screening. Lung cancer risk and comorbidity score were not strong predictors of agreeing to or receiving screening. Empirical Bayes adjusted rates of agreeing to and receiving screening ranged from 22% to 84% across facilities and from 19% to 85% across clinicians. A total of 33.7% of the variance in agreeing to and 34.2% of the variance in receiving screening was associated with the facility or the clinician offering screening. **CONCLUSIONS:** Substantial variation was found in Veterans agreeing to and receiving lung cancer screening during the Veterans Affairs Lung Cancer Screening Demonstration Project. This variation was not explained by differences in key determinants of patient benefit, whereas the facility and clinician advising the patient had a large impact on lung cancer screening decisions.

[Lung Cancer and Immunity Markers](#) Cancer Epidemiol Biomarkers Prev. 2020 Dec;29(12):2423-2430. doi: 10.1158/1055-9965.EPI-20-0716. Epub 2020 Aug 20. Raymond J Lim 1 2 , Bin Liu 1 , Kostyantyn Krysan 1 3 , Steven M Dubinett 4 2 3 5 6

An in-depth understanding of lung cancer biology and mechanisms of tumor progression has facilitated significant advances in the treatment of lung cancer. There remains a pressing need for the development of innovative approaches to detect and intercept lung cancer at its earliest stage of development. Recent advances in genomics, computational biology, and innovative technologies offer unique opportunities to identify the immune landscape in the tumor microenvironment associated with early-stage lung carcinogenesis, and provide further insight in the mechanism of lung cancer evolution. This review will highlight the concept of immunoediting and focus on recent studies assessing immune changes and biomarkers in pulmonary premalignancy and early-stage non-small cell lung cancer. A protumor immune response hallmarked by an increase in checkpoint inhibition and inhibitory immune cells and a simultaneous reduction in antitumor immune response have been correlated with tumor progression. The potential systemic biomarkers associated with early lung cancer will be highlighted along with current clinical efforts for lung cancer interception. Research focusing on the development of novel strategies for cancer interception prior to the progression to advanced stages will potentially lead to a paradigm shift in the treatment of lung cancer and have a major impact on clinical outcomes.

[Quantitative Emphysema on Low-Dose Computed Tomography of the Chest and Risk of Lung Cancer and Airflow Obstruction: An analysis of the National Lung Screening Trial](#) Chest. 2020 Dec 13;S0012-3692(20)35356-3. doi: 10.1016/j.chest.2020.12.004. Online ahead of print. Wassim W Labaki 1 , Meng Xia 2 , Susan Murray 2 , et al.

BACKGROUND: Lung cancer risk prediction models do not routinely incorporate imaging metrics available on low-dose computed tomography (LDCT) of the chest ordered for lung cancer screening. **RESEARCH QUESTION:** What is the association between quantitative emphysema measured on LDCT and lung cancer incidence and mortality, all-cause mortality, and airflow obstruction in individuals who currently or formerly smoked undergoing lung cancer screening? **STUDY DESIGN AND METHODS:** In 7,262 participants in the CT arm of the National Lung Screening Trial, % low attenuation area (%LAA) was defined as the percent of lung volume with voxels < -950 Hounsfield Units on the baseline exam. We built multivariable Cox proportional hazards models, adjusting for competing risks where appropriate, to test for association between %LAA and lung cancer incidence, lung cancer mortality and all-cause mortality with censoring at 6 years. We also built multivariable logistic regression models to test the cross-sectional association between %LAA and airflow obstruction on spirometry which was available in 2,700 participants. **RESULTS:** The median %LAA was 0.8% (interquartile range: 0.2%-2.7%). Every 1% increase in %LAA was independently associated with higher hazards of lung cancer incidence (HR 1.02; 95% CI 1.01-1.03; p=0.004), lung cancer mortality (HR 1.02; 95% CI 1.00-1.05; p=0.045) and all-cause mortality (HR 1.01; 95% CI 1.00-1.03; p=0.042). Among participants with spirometry, 892 had airflow obstruction. The likelihood of airflow obstruction increased with every 1% increase in %LAA (OR=1.07; 95% CI 1.06-1.09; p<0.001). A %LAA cutoff of 1% had the best discriminative accuracy for airflow obstruction in participants older than 65 years. **INTERPRETATION:** Quantitative emphysema measured on LDCT of the chest can be leveraged to improve lung cancer risk prediction and help diagnose COPD in individuals who currently or formerly smoked undergoing lung cancer screening.

[Racial disparities in occupational risks and lung cancer incidence: Analysis of the National Lung Screening Trial](#) Prev Med. 2020 Dec 7;143:106355. doi: 10.1016/j.ypmed.2020.106355. Online ahead of print. Hee-Soon Juon 1 , Alicia Hong 2 , Marcella Pimpinelli 3 , Madhuwani Rojulpote 4 , Russell McIntire 5 , Julie A Barta 6

The relationship between racial disparities in occupational risk and lung cancer diagnosis is not well defined. We examined occupational exposure to asbestos, silica, and other workplace chemicals, fumes, or dusts as reported in the National Lung Screening Trial (NLST). Descriptive analyses and multivariate logistic regression models were performed. Among the NLST study cohort, 3.9% were diagnosed with lung cancer. African-Americans had a higher rate of lung cancer diagnosis than White individuals (4.3% vs. 3.9%). About 28% reported at least one occupational exposure, including 6.5% exposed to silica and 4.7% to asbestos. African-Americans reported occupational exposure more frequently than White participants, including exposures to asbestos and silica. In a multivariate model, the interactions of all measures of occupational exposures and smoking status were significant. Current smokers with occupational exposures had higher odds of lung cancer diagnosis (aOR = 2.01, 95% CI = 1.76-2.30 for any exposure as well as higher odds after silica (aOR = 2.35, 95% CI = 1.89-2.91) or asbestos (aOR = 1.97, 95% CI = 1.52-2.56) exposure compared to former smokers without any exposures. African-Americans had higher odds of lung cancer diagnosis than White individuals (aOR = 1.24 to 1.25, 95% CI = 1.01-1.54). Our findings indicate that we need more effective public health prevention programs, especially for minorities who may have disproportionately greater occupational exposures due to socioeconomic constructs and barriers. Interventions may include education about occupational risks and lung cancer screening or instituting workplace policies for smoke-free environments with tobacco cessation support.

[Variation in Eligible Patients' Agreeing to and Receiving Lung Cancer Screening: A Cohort Study](#)

Am J Prev Med. 2020 Dec 17;S0749-3797(20)30502-X. doi: 10.1016/j.amepre.2020.10.014. Online ahead of print. N Joseph Leishman 1 , Renda S Wiener 2 , Angela Fagerlin 3 , Rodney A Hayward 4 , Julie Lowery 5 , Tanner J Caverly 6

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METHODS: This was a retrospective cohort study of patients meeting current national eligibility criteria and deemed appropriate candidates for lung cancer screening on the basis of clinical reminders completed over a 2-year period (2013-2015) at 8 Department of Veterans Affairs medical facilities. Multilevel mixed-effects logistic regression models (conducted in 2019-2020) assessed predictors (age, sex, lung cancer risk, Charlson Comorbidity Index, travel distance to facility, and central versus outlying decision-making location) of primary outcomes of agreeing to and receiving lung cancer screening. **RESULTS:** Of 5,551 patients (mean age=67 years, 97% male, mean lung cancer risk=0.7%, mean Charlson Comorbidity Index=1.14, median travel distance=24.2 miles), 3,720 (67%) agreed to lung cancer screening and 2,398 (43%) received screening. Lung cancer risk and comorbidity score were not strong predictors of agreeing to or receiving screening. Empirical Bayes adjusted rates of agreeing to and receiving screening ranged from 22% to 84% across facilities and from 19% to 85% across clinicians. A total of 33.7% of the variance in agreeing to and 34.2% of the variance in receiving screening was associated with the facility or the clinician offering screening. **CONCLUSIONS:** Substantial variation was found in Veterans agreeing to and receiving lung cancer screening during the Veterans Affairs Lung Cancer Screening Demonstration Project. This variation was not explained by differences in key determinants of patient benefit, whereas the facility and clinician advising the patient had a large impact on lung cancer screening decisions.

[Association between Medicaid expansion status and lung cancer screening exam growth: findings from the ACR lung cancer registry](#) Clin Imaging. 2020 Dec 3;73:79-85. doi:

10.1016/j.clinimag.2020.11.056. Online ahead of print. Neal Gupta 1, Ethan J Halpern 2, Vijay M Rao 2
PURPOSE: To determine if Medicaid expansion is associated with increased volumes of lung cancer screenings. **METHODS:** A quasi-experimental study was performed to compare the annual growth rates in lung cancer screenings between states that expanded Medicaid (n = 31) versus those that did not (n = 17). Using the American College of Radiology Lung Cancer Screening Registry, we calculated the average annual growth rate between 2016 and 2019 for both groups. Secondary analyses between these two groups also included calculations of the percentages of studies considered appropriate by USPSTF criteria. **RESULTS:** No significant difference was identified in the average annual growth in lung cancer screenings between Medicaid expanding and non-expanding states (57.6%, 50.3%, P = 0.51). No difference was observed in the percentage of studies considered appropriate (Medicaid expanding = 89.6%, non-expanding = 90.2%, P = 0.72). At baseline, there were socioeconomic differences between both groups of states. Medicaid expanding states had a more urban population (76.5% versus 67.9%, P = 0.05) and higher average incomes (\$56,947, \$49,876, P < 0.05). **CONCLUSION:** No association is found between Medicaid expansion and increasing volumes of lung cancer screening exams. Although no data is available in the registry for screening exams before the implementation of Medicaid expansion (2014), most nationwide estimates of lung screening rates report a low baseline (<5%). Furthermore, despite being advantaged in other ways, such as with a more urban population or with higher incomes, the Medicaid expansion cohort does not demonstrate a higher growth rate. These findings suggest Medicaid expansion alone will not increase lung cancer screenings.

[Computational identification of biomarker genes for lung cancer considering treatment and non-treatment studies](#) BMC Bioinformatics. 2020 Dec 3;21(Suppl 9):218. doi: 10.1186/s12859-020-3524-8.

Mona Maharjan 1, Raihanul Bari Tanvir 1, Kamal Chowdhury 2, Wenrui Duan 3, Ananda Mohan Mondal 4

BACKGROUND: Lung cancer is the number one cancer killer in the world with more than 142,670 deaths estimated in the United States alone in the year 2019. Consequently, there is an overreaching need to identify the key biomarkers for lung cancer. The aim of this study is to computationally identify biomarker genes for lung cancer that can aid in its diagnosis and treatment. The gene expression profiles of two different types of studies, namely non-treatment and treatment, are considered for discovering biomarker genes. In non-treatment studies healthy samples are control and cancer samples are cases. Whereas, in treatment studies, controls are cancer cell lines without treatment and cases are cancer cell lines with treatment. **RESULTS:** The Differentially Expressed Genes (DEGs) for lung cancer were isolated from Gene Expression Omnibus (GEO) database using R software tool GEO2R. A total of 407 DEGs (254 upregulated and 153 downregulated) from non-treatment studies and 547 DEGs (133 upregulated and 414 downregulated) from treatment studies were isolated. Two Cytoscape apps, namely, CytoHubba and MCODE, were used for identifying biomarker genes from functional networks developed using DEG genes. This study discovered two distinct sets of biomarker genes - one from non-treatment studies and the other from treatment studies, each set containing 16 genes. Survival analysis results show that most non-treatment biomarker genes have prognostic capability by indicating low-expression groups have higher chance of survival compare to high-expression groups. Whereas, most treatment biomarkers have prognostic capability by indicating high-expression groups have higher chance of survival compare to low-expression groups. **CONCLUSION:** A computational framework is developed to identify biomarker genes for lung cancer using gene expression profiles. Two different types of studies - non-treatment and treatment - are considered for experiment. Most of the biomarker genes from non-treatment studies are part of mitosis and play vital role in DNA repair and cell-cycle regulation. Whereas, most of the biomarker genes from treatment studies are associated to ubiquitination and cellular response to stress.

This study discovered a list of biomarkers, which would help experimental scientists to design a lab experiment for further exploration of detail dynamics of lung cancer development.

[Protocol to evaluate an enterprise-wide initiative to increase access to lung cancer screening in the Veterans Health Administration](#) Clin Imaging. 2020 Dec 26;73:151-161. doi:

10.1016/j.clinimag.2020.11.059. Online ahead of print. Jennifer A Lewis¹, Lucy B Spalluto², Claudia I Henschke³, David F Yankelevitz³, et al.

INTRODUCTION: The Veterans Affairs Partnership to increase Access to Lung Screening (VA-PALS) is an enterprise-wide initiative to implement lung cancer screening programs at VA medical centers (VAMCs). VA-PALS will be using implementation strategies that include program navigators to coordinate screening activities, trainings for navigators and radiologists, an open-source software management system, tools to standardize low-dose computed tomography image quality, and access to a support network. VAMCs can utilize strategies according to their local needs. In this protocol, we describe the planned program evaluation for the initial 10 VAMCs participating in VA-PALS.

MATERIALS AND METHODS: The implementation of programs will be evaluated using the Consolidated Framework for Implementation Research to ensure broad contextual guidance. Program evaluation measures have been developed using the Reach, Effectiveness, Adoption, Implementation and Maintenance framework. Adaptations of screening processes will be assessed using the Framework for Reporting Adaptations and Modifications to Evidence Based Interventions. Measures collected will reflect the inner settings, estimate and describe the population reached, adoption by providers, implementation of the programs, report clinical outcomes and maintenance of programs. Analyses will include descriptive statistics and regression to evaluate predictors and assess implementation over time.

DISCUSSION: This theory-based protocol will evaluate the implementation of lung cancer screening programs across the Veterans Health Administration using scientific frameworks. The findings will inform plans to expand the VA-PALS initiative beyond the original sites and can guide implementation of lung cancer screening programs more broadly.

[Rapid EGFR Mutation Detection Using the Idylla Platform: Single-Institution Experience of 1200 Cases Analyzed by an In-House Developed Pipeline and Comparison with Concurrent Next-Generation Sequencing Results](#) J Mol Diagn. 2020 Dec 18;S1525-1578(20)30584-5. doi:

10.1016/j.jmoldx.2020.11.009. Online ahead of print. Amir Momeni-Boroujeni¹, Paulo Salazar¹, Tao Zheng¹, et al.

Mutations in the epidermal growth factor receptor (EGFR) are the most common targetable alterations in lung adenocarcinoma. To facilitate rapid testing, we incorporated the Idylla EGFR assay as screening method before next-generation sequencing (NGS). We describe our validation and experience using an in-house developed analysis pipeline, enhanced with a manual review algorithm. Results are compared with corresponding NGS results. In all, 1249 samples were studied. Validation demonstrated 98.57% (69/70) concordance with the reference methods. The limit of detection varied from 2% to 5% variant allele frequency if total EGFR quantitation cycle was between 20 and 23. Of 1179 clinical cases, 23.41% were EGFR positive by Idylla. Concurrent NGS was successfully performed on 94.9% (799/842) of requests. Concordance of Idylla with NGS was 98.62% (788/799) and 98.50% (787/799) using our in-house and Idylla analysis pipelines, respectively. Discordances involved missed mutations by both assays associated with low tumor/low input. Incorporating a manual review algorithm to supplement automated calls improved accuracy from 98.62% to 99.37% and sensitivity from 94.68% to 97.58%. Overall reporting time, from receipt of material to official clinical report, ranged from 1 to 3 days. We conclude that Idylla EGFR testing enables rapid and sensitive screening without compromising subsequent comprehensive NGS, when required. Automated calling, enhanced with a manual review algorithm, reduces false-negative calls associated with low tumor/low input samples

NSCLC - SURGERY

[Prognosis of segmentectomy and lobectomy for radiologically aggressive small-sized lung cancer](#)

Eur J Cardiothorac Surg. 2020 Dec 1;58(6):1245-1253. doi: 10.1093/ejcts/ezaa231. Atsushi Kamigaichi 1 Yasuhiro Tsutani 1 , Takahiro Mimae 1 , et al.

OBJECTIVES: The purpose of this study was to determine the radiological characteristics of aggressive small-sized lung cancer and to compare the outcomes between segmentectomy and lobectomy in patients with these lung cancers. **METHODS:** A series of 1046 patients with clinical stage IA1-IA2 lung cancer who underwent lobectomy or segmentectomy at 3 institutions was retrospectively evaluated to identify radiologically aggressive small-sized (solid tumour size ≤ 2 cm) lung cancers. Prognosis of segmentectomy was compared with that of lobectomy in 522 patients with radiologically aggressive small-sized lung cancer using propensity score matching. **RESULTS:** Multivariable analysis showed that increasing consolidation-to-tumour ratio on preoperative high-resolution computed tomography (CT) ($P = 0.037$) and maximum standardized uptake on 18 fluoro-2-deoxyglucose positron emission tomography/CT ($P = 0.029$) was independently associated with worse recurrence-free survival. Based on analysis of the receiver operating characteristic curve, radiologically aggressive lung cancer was defined as a radiologically solid (consolidation-to-tumour ratio ≥ 0.8) or highly metabolic (maximum standardized uptake ≥ 2.5) tumour. Among patients with radiologically aggressive lung cancer, no significant statistical differences in 5-year recurrence-free (81% vs 90%; $P = 0.33$) and overall (88% vs 93%; $P = 0.76$) survival comparing lobectomy ($n = 392$) to segmentectomy ($n = 130$) were observed. Among 115 propensity-matched pairs, 5-year recurrence-free survival and overall survival were similar between patients who underwent lobectomy and those who underwent segmentectomy (83.3% and 88.3% vs 90.9% and 94.5%, respectively). **CONCLUSIONS:** Difference in survival was not identified with segmentectomy and lobectomy in patients with radiologically aggressive small-sized lung cancer with high risk of recurrence.

[County-Level Social Vulnerability is Associated with Worse Surgical Outcomes Especially Among Minority Patients](#)

Ann Surg. 2020 Dec 18; Publish Ahead of Print. doi: 10.1097/SLA.0000000000004691. Online ahead of print. Adrian Diaz 1 , J Madison Hyer, Elizabeth Barmash, Rosevine Azap, Anghela Z Paredes, Timothy M Pawlik

OBJECTIVE: We sought to characterize the association between patient county-level vulnerability with postoperative outcomes. **SUMMARY BACKGROUND DATA:** While the impact of demographic-, clinical- and hospital-level factors on outcomes following surgery have been examined, little is known about the effect of a patient's community of residence on surgical outcomes. **METHODS:** Individuals who underwent colon resection, coronary artery bypass graft (CABG), lung resection, or lower extremity joint replacement (LEJR) were identified in the 2016-2017 Medicare database, which was merged with CDC vulnerability index (SVI) dataset at the beneficiary level of residence. Logistic regression models were utilized to estimate the probability of postoperative complications, mortality, readmission, and expenditures. **RESULTS:** Among 299,583 Medicare beneficiary beneficiaries who underwent a colectomy ($n = 88,778$, 29.6%), CABG ($n = 109,564$, 36.6%), lung resection ($n = 30,401$, 10.1%), or LEJR ($n = 70,840$, 23.6%). Mean SVI score was 50.2 (SD: (25.2)); minority patients were more likely to reside in highly vulnerable communities (low SVI: $n = 3,531$, 5.8% vs. high SVI: $n = 7,895$, 13.3%; $p < 0.001$). After controlling for competing risk factors, the risk-adjusted probability of a serious complication among patients from a high versus low SVI county was 10-20% higher following colectomy (OR 1.1 95%CI 1.1-1.2) or CABG (OR 1.2 95%CI 1.1-1.3), yet there no association of SVI with risk of serious complications following lung resection (OR 1.2 95%CI 1.0-1.3) or LEJR (OR 1.0 95%CI 0.93-1.2). The

risk-adjusted probability of 30-day mortality was incrementally higher among patients from high SVI counties following colectomy (OR 1.1 95%CI 1.1-1.3), CABG (OR 1.4, 95%CI 1.2-1.5), and lung resection (OR 1.4 (95%CI 1.1-1.8), yet not LEJR (OR 0.95 95%CI 0.72-1.2). Black/minority patients undergoing a colectomy, CABG, or lung resection who lived in highly socially vulnerable counties had an estimate 28-68% increased odds of a serious complication and a 58-60% increased odds of 30-day mortality compared with a black/minority patient from a low socially vulnerable county, as well as a markedly higher risk than white patients (all $p > 0.05$). **CONCLUSION:** Patients residing in vulnerable communities characterized by a high SVI generally had worse postoperative outcomes. The impact of social vulnerability was most pronounced among black/minority patients, rather than white individuals. Efforts to ensure equitable surgical outcomes need to focus on both patient-level, as well as community-specific factors.

[Comparative Effectiveness of Surgical Approaches for Lung Cancer](#) J Surg Res. 2020 Dec 9;S0022-4804(20)30756-3. doi: 10.1016/j.jss.2020.10.020. Online ahead of print. Adwairy Manerikar 1 , Melissa Querrey 1 , Emily Cerier 1 , Samuel Kim 1 , David D Odell 1 , Lorenzo L Pesce 1 , Ankit Bharat 2

BACKGROUND: The magnitude of association and quality of evidence comparing surgical approaches for lung cancer resection has not been analyzed. This has resulted in conflicting information regarding the relative superiority of the different approaches and disparate opinions on the optimal surgical treatment. We reviewed and systematically analyzed all published data comparing near- (30-d) and long-term mortality for minimally invasive to open surgical approaches for lung cancer. **METHODS:** Comprehensive search of EMBASE, MEDLINE, and the Cochrane Library, from January 2009 to August 2019, was performed to identify the studies and those that passed bias assessment were included in the analysis utilizing propensity score matching techniques. Meta-analysis was performed using random-effects and fixed-effects models. Risk of bias was assessed via the Newcastle-Ottawa Scale and the ROBINS-I tool. The study was registered in PROSPERO (CRD42020150923) prior to analysis. **RESULTS:** Overall, 1382 publications were identified but 19 studies were included encompassing 47,054 patients after matching. Minimally invasive techniques were found to be superior with respect to near-term mortality in early and advanced-stage lung cancer (risk ratio 0.45, 95% confidence interval [CI] 0.21-0.95, $I^2 = 0\%$) as well as for elderly patients (odds ratio 0.45, 95% CI 0.31-0.65, $I^2 = 30\%$), but did not demonstrate benefit for high-risk patients (odds ratio 0.74, 95% CI 0.06-8.73, $I^2 = 78\%$). However, no difference was found in long-term survival. **CONCLUSIONS:** We performed the first systematic review and meta-analysis to compare surgical approaches for lung cancer which indicated that minimally invasive techniques may be superior to thoracotomy in near-term mortality, but there is no difference in long-term outcomes.

[Safety of patients and providers in lung cancer surgery during the COVID-19 pandemic](#) Eur J Cardiothorac Surg. 2020 Dec 1;58(6):1222-1227. doi: 10.1093/ejcts/ezaa332. Stephanie H Chang 1 , Michael Zervos 1 , Amie Kent 1 , Abraham Chachoua 2 , Costas Bizekis 1 , Harvey Pass 1 , Robert J Cerfolio 1

OBJECTIVES: The coronavirus disease 2019 (COVID-19) pandemic has resulted in patient reluctance to seek care due to fear of contracting the virus, especially in New York City which was the epicentre during the surge. The primary objectives of this study are to evaluate the safety of patients who have undergone pulmonary resection for lung cancer as well as provider safety, using COVID-19 testing, symptoms and early patient outcomes. **METHODS:** Patients with confirmed or suspected pulmonary malignancy who underwent resection from 13 March to 4 May 2020 were retrospectively reviewed. **RESULTS:** Between 13 March and 4 May 2020, 2087 COVID-19 patients were admitted, with a median daily census of 299, to one of our Manhattan campuses (80% of hospital capacity). During this time, 21 patients (median age 72 years) out of 45 eligible surgical candidates underwent pulmonary resection-13

lobectomies, 6 segmentectomies and 2 pneumonectomies were performed by the same providers who were caring for COVID-19 patients. None of the patients developed major complications, 5 had minor complications, and the median length of hospital stay was 2 days. No previously COVID-19-negative patient (n = 20/21) or healthcare provider (n = 9: 3 surgeons, 3 surgical assistants, 3 anaesthesiologists) developed symptoms of or tested positive for COVID-19. **CONCLUSIONS:** Pulmonary resection for lung cancer is safe in selected patients, even when performed by providers who care for COVID-19 patients in a hospital with a large COVID-19 census. None of our patients or providers developed symptoms of COVID-19 and no patient experienced major morbidity or mortality.

Anatomic resection has superior long-term survival compared with wedge resection for second primary lung cancer after prior lobectomy

Eur J Cardiothorac Surg. 2020 Dec 17;eaa443. doi: 10.1093/ejcts/eaa443. Online ahead of print. Mirza Zain Baig 1 , Syed S Razi 2 , Stephanie Stroever 3 , Joanna F Weber 1 , Cliff P Connery 4 , Faiz Y Bhora 1

OBJECTIVES: The extent of surgical resection for early-stage second primary lung cancer (SPLC) in patients with a previous lobectomy is unclear. We sought to compare anatomic lung resections (lobectomy and segmentectomy) and wedge resections for small peripheral SPLC using a population-based database. **METHODS:** The Surveillance, Epidemiology and End Results database was queried for all patients with ≤ 2 cm peripheral SPLC diagnosed between 2004 and 2015 who underwent prior lobectomy for the first primary and surgical resection only for the SPLC. American College of Chest Physicians guidelines were used to classify SPLC. Kaplan-Meier analysis and multivariable Cox regression were used to compare overall survival. **RESULTS:** A total of 356 patients met the inclusion criteria with 203 (57%) treated with wedge resection and 153 (43%) treated with anatomic resection. Significantly better median survival was observed with anatomic resection than with wedge resection using a Kaplan-Meier analysis (124 vs 63 months; $P < 0.001$). With multivariable Cox regression, improved long-term survival was observed for anatomic resection (hazard ratio: 0.44, confidence interval: 0.27-0.70; $P = 0.001$). Improvement in survival was demonstrated with wedge resection when lymph node sampling was done. Lastly, we calculated the average treatment effect on the treated with inverse probability weighting for a subgroup of patients and found that those with wedge resection and lymph node sampling had shorter long-term survival times. **CONCLUSIONS:** Anatomic resections may provide better long-term survival than wedge resections for patients with early-stage peripheral SPLC after prior lobectomy. Significant improvement in survival was observed with wedge resection for SPLC when adequate lymph node dissection was performed.

Multimodal Prehabilitation for Lung Cancer Surgery: A Randomized Controlled Trial

Ann Thorac Surg. 2020 Dec 12;S0003-4975(20)32108-1. doi: 10.1016/j.athoracsur.2020.11.022. Online ahead of print. Vanessa Ferreira 1 , Enrico Maria Minnella 2 , Rashami Awasthi 2 , Ann Gamsa 2 , Lorenzo Ferri 3 , David Mulder 3 , Christian Sirois 3 , Jonathan Spicer 3 , Severin Schmid 3 , Francesco Carli 4

BACKGROUND: To determine whether a multimodal prehabilitation program enhances post-operative functional recovery compared to multimodal rehabilitation. **METHODS:** Patients scheduled for non-small cell lung cancer resection were randomized to two groups receiving home-based moderate intensity exercise, nutritional counseling with whey protein supplementation and anxiety reducing strategies, either for four weeks before (PREHAB, n=52) or 8 weeks after surgery (REHAB, n=43). Functional capacity (FC) was measured by the six-minute walk test (6MWT) at baseline, immediately prior to surgery, four and eight weeks after surgery. All patients were treated according to Enhanced Recovery Pathway (ERP) guidelines. **RESULTS:** There was no difference in FC at any time point during the perioperative period between the two multimodal programs. By eight weeks after surgery, both groups returned to baseline FC and a similar proportion of patients (over 75%) in both groups had recovered to their baseline.

CONCLUSIONS: In patients undergoing surgical resection for lung cancer within the context of ERP, multimodal prehabilitation initiated four weeks prior to surgery is as effective in recovering FC as multimodal rehabilitation.

[Short-term local control after VATS segmentectomy and lobectomy for solid NSCLC of less than 2 cm](#) Thorac Cancer. 2020 Dec 3. doi: 10.1111/1759-7714.13766. Online ahead of print. Marc Darras # 1 , Amaya Ojanguren # 1 , Céline Forster 1 , Matthieu Zellweger 1 , Jean Yannis Perentes 1 2 , Thorsten Krueger 1 2 , Michel Gonzalez 1 2

INTRODUCTION: VATS pulmonary segmentectomy is increasingly proposed as a parenchyma-sparing resection for tumors smaller than 2 cm in diameter. The aim of this study was to compare short-term oncological results and local control in solid non-small cell lung cancers (NSCLCs) <2 cm surgically treated by intentional VATS segmentectomy or lobectomy. **METHODS:** This study was a single center retrospective study of consecutive patients undergoing VATS lobectomy (VL) or segmentectomy (VS) for solid <2 cm NSCLC from January 2014 to October 2019. Results In total, 188 patients with a median age of 65 years (male/female: 99/89) underwent VS (n = 96) or VL (n = 92). Segmentectomies in the upper lobes were performed in 57% and as a single segment in 55% of cases. There was no statistically significant difference between VS and VL in terms of demographics, comorbidities, postoperative outcomes, dissected lymph node stations (2.89 ± 0.95 vs. 2.93 ± 1 , $P = 0.58$), rate of pN1 (2.2% vs. 2.1%, $P = 0.96$) or pN2 upstaging (1.09% vs. 1.06%, $P = 0.98$). Adjuvant chemotherapy was given in 15% of patients in the VL and 11% in the VS group. During follow-up (median: 23 months), no patients presented with local nodal recurrence or on the stapler line (VS group). Three patients on VL and two in VS groups presented with recurrence on the remnant operated lung. New primary pulmonary tumors were diagnosed in 3.3% and 6.3% of patients in the VL and VS groups, respectively. **CONCLUSIONS:** Despite the short follow-up, our preliminary data shows that local control is comparable for VATS lobectomy and VATS segmentectomy for patients with NSCLC <2 cm.

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

[Update 2020: Management of Non-Small Cell Lung Cancer](#) Lung. 2020 Dec;198(6):897-907. doi: 10.1007/s00408-020-00407-5. Epub 2020 Nov 11. Mariam Alexander 1 , So Yeon Kim 2 , Haiying Cheng 3

The past decade has seen a revolution of new advances in the management of non-small cell lung cancer (NSCLC) with remarkable progresses in screening, diagnosis, and treatment. The advances in systemic treatment have been driven primarily by the development of molecularly targeted therapeutics, immune checkpoint inhibitors, and anti-angiogenic agents, all of which have transformed this field with significantly improved patient outcomes. This review will address updates in lung cancer screening, liquid biopsy, and immunotherapy in the front-line setting. We discuss recent advances and highlight the plethora of new approvals of molecular-targeted therapy for subgroups of NSCLC patients with sensitizing EGFR, ALK, ROS1, RET, BRAF V600E, MET, and NTRK alterations.

[The biomarkers related to immune related adverse events caused by immune checkpoint inhibitors](#) J Exp Clin Cancer Res. 2020 Dec 14;39(1):284. doi: 10.1186/s13046-020-01749-x. Xiao-Hui Jia 1 , Lu-Ying Geng 1 , Pan-Pan Jiang 1 , Hong Xu 1 , Ke-Jun Nan 1 2 , Yu Yao 1 , Li-Li Jiang 1 , Hong Sun 1 , Tian-Jie Qin 1 , Hui Guo 3 4 5

The enthusiasm for immune checkpoint inhibitors (ICIs), an efficient tumor treatment model different from traditional treatment, is based on their unprecedented antitumor effect, but the occurrence of immune-related adverse events (irAEs) is an obstacle to the prospect of ICI treatment. IrAEs are a discrete toxicity caused by the nonspecific activation of the immune system and can affect almost all tissues and

organs. Currently, research on biomarkers mainly focuses on the gastrointestinal tract, endocrine system, skin and lung. Several potential hypotheses concentrate on the overactivation of the immune system, excessive release of inflammatory cytokines, elevated levels of pre-existing autoantibodies, and presence of common antigens between tumors and normal tissues. This review lists the current biomarkers that might predict irAEs and their possible mechanisms for both nonspecific and organ-specific biomarkers. However, the prediction of irAEs remains a major clinical challenge to screen and identify patients who are susceptible to irAEs and likely to benefit from ICIs.

[Current therapy of KRAS-mutant lung cancer](#) Cancer Metastasis Rev. 2020 Dec;39(4):1159-1177. doi: 10.1007/s10555-020-09903-9. Aron Ghimessy 1 , Peter Radeckzy 1 , Viktoria Laszlo 2 3 , et al. KRAS mutations are the most frequent gain-of-function alterations in patients with lung adenocarcinoma (LADC) in the Western world. Although they have been identified decades ago, prior efforts to target KRAS signaling with single-agent therapeutic approaches such as farnesyl transferase inhibitors, prenylation inhibition, impairment of KRAS downstream signaling, and synthetic lethality screens have been unsuccessful. Moreover, the role of KRAS oncogene in LADC is still not fully understood, and its prognostic and predictive impact with regards to the standard of care therapy remains controversial. Of note, KRAS-related studies that included general non-small cell lung cancer (NSCLC) population instead of LADC patients should be very carefully evaluated. Recently, however, comprehensive genomic profiling and wide-spectrum analysis of other co-occurring genetic alterations have identified unique therapeutic vulnerabilities. Novel targeted agents such as the covalent KRAS G12C inhibitors or the recently proposed combinatory approaches are some examples which may allow a tailored treatment for LADC patients harboring KRAS mutations. This review summarizes the current knowledge about the therapeutic approaches of KRAS-mutated LADC and provides an update on the most recent advances in KRAS-targeted anti-cancer strategies, with a focus on potential clinical implications.

[Management of immune checkpoint therapy for patients with cancer in the face of COVID-19](#) J Immunother Cancer. 2020 Dec;8(2):e001593. doi: 10.1136/jitc-2020-001593. Chen Shen 1 2 , Qianru Li 1 , Yongchang Wei 3 , Yuting Li 4 , Jun Li 5 , Juan Tao 6 7
The COVID-19 outbreak caused by SARS-CoV-2 challenges the medical system by interfering with routine therapies for many patients with chronic diseases. In patients with cancer receiving immune checkpoint inhibitors (ICIs), difficulties also arise from the incomplete understanding of the intricate interplay between their routine treatment and pathogenesis of the novel virus. By referring to previous ICI-based investigations, we speculate that ICIs themselves are not linked to high-infection risks of respiratory diseases or inflammation-related adverse effects in patients with cancer. Moreover, ICI treatment may even enhance coronavirus clearance in some patients with malignant tumor by boosting antiviral T-cell responsiveness. However, the 'explosive' inflammation during COVID-19 in some ICI-treated patients with cancer was illustrated as exuberant immunopathological damage or even death. In case of the COVID-19 immunopathogenesis fueled by ICIs, we propose a regular monitor of pathogenic T-cell subsets and their exhaustion marker expression (eg, Th17 and interleukin (IL)-6-producing Th1 subsets with surface programmed death 1 expression) to guide the usage of ICI. Here we aimed to address these considerations, based on available literature and experience from our practice, that may assist with the decision-making of ICI administration during the pandemic.

[Treatment patterns and clinical outcomes in patients with advanced non-small cell lung cancer initiating first-line treatment in the US community oncology setting: a real-world retrospective observational study](#) J Cancer Res Clin Oncol. 2020 Dec 2. doi: 10.1007/s00432-020-03414-4. Online ahead of print. Eric Nadler 1 2 , Bhakti Arondekar 3 , Kathleen Marie Aguilar 4 , Jie Zhou 2 , Jane Chang 3 , Xinke Zhang 5 6 , Vivek Pawar 5 6

PURPOSE: Treatments for advanced non-small cell lung cancer (NSCLC) have evolved to include targeted and immuno-oncology therapies, which have demonstrated clinical benefits in clinical trials. However, few real-world studies have evaluated these treatments in the first-line setting. **METHODS:** Adult patients with advanced NSCLC who initiated first-line treatment with chemotherapy, targeted therapies (TT), or immuno-oncology-based regimens in the US Oncology Network (USON) between March 1, 2015, and August 1, 2018, were included and followed up through February 1, 2019. Data were sourced from structured fields of USON electronic health records. Patient and treatment characteristics were assessed descriptively, with Kaplan-Meier methods used to evaluate time-to-event outcomes, including time to treatment discontinuation (TTD) and overall survival (OS). Adjusted Cox regression analyses and inverse probability of treatment weighting (IPTW) were performed to control for covariates that may have affected treatment selection and outcomes. **RESULTS:** Of 7746 patients, 75.6% received first-line systemic chemotherapy, 11.7% received immuno-oncology monotherapies, 8.5% received TT, and 4.2% received immuno-oncology combination regimens. Patients who received immuno-oncology monotherapies had the longest median TTD (3.5 months; 95% confidence interval [CI], 2.8-4.2) and OS (19.9 months; 95% CI, 16.6-24.1). On the basis of multivariable Cox regression and IPTW, immuno-oncology monotherapy was associated with reduced risk of death and treatment discontinuation relative to other treatments. **CONCLUSION:** These results suggest that real-world outcomes in this community oncology setting improved with the introduction of immuno-oncology therapies. However, clinical benefits are limited in certain subgroups and tend to be reduced compared with clinical trial observations.

[Retrospective Observational Study of ALK-Inhibitor Therapy Sequencing and Outcomes in Patients with ALK-Positive Non-small Cell Lung Cancer](#) Drugs Real World Outcomes. 2020

Dec;7(4):261-269. doi: 10.1007/s40801-020-00207-6. David M Waterhouse 1 , Janet L Espirito 2 , Marc D Chioda 3 , Bismark Baidoo 2 , Jack Mardekian 3 , Nicholas J Robert 2 , Elizabeth T Masters 3

BACKGROUND: Data are sparse concerning the sequential use of multiple anaplastic lymphoma kinase (ALK) inhibitors for ALK-positive locally advanced or metastatic non-small cell lung cancer (NSCLC).

OBJECTIVE: This study investigated sequencing and outcomes among patients receiving multiple ALK inhibitors.

PATIENTS AND METHODS: This was a retrospective observational cohort study of adult patients with ALK-positive NSCLC treated with available first- and second-generation ALK inhibitors from 1 September 2011 to 31 December 2017. Duration of therapy (DOT) and overall survival (OS) were assessed with the Kaplan-Meier method. A multivariable linear regression analysis was performed to assess if DOT with a preceding ALK inhibitor was predictive of DOT for subsequent ALK inhibitor treatments. **RESULTS:** A total of 410 patients were analyzed: 57% received 1 ALK inhibitor; 35%, 2 ALK inhibitors; and 8%, 3-4 ALK inhibitors. Among those receiving > 1 ALK inhibitor (n = 177), 60% received a crizotinib-led sequence and 39% an alectinib-led sequence. Nearly 60% of the overall population received chemotherapy prior to their first ALK inhibitor. Median OS for the study population was 28 months, 15 months in patients who received 1 ALK inhibitor, 42 months in patients who received 2 ALK inhibitors, and 56 months in patients who received 3-4 ALK inhibitors. Longer DOT of the first ALK inhibitor was associated with increased DOT of the second (p < 0.0001), and longer DOT of the second ALK inhibitor was associated with increased DOT of the third (p < 0.0001). **CONCLUSIONS:** This study provides initial information on real-world treatment patterns following the introduction of new ALK inhibitors, and supports the use of sequential ALK therapies.

[The role of nivolumab combined to immunotherapy and/or chemotherapy in the first-line treatment of advanced Non Small Cell Lung Cancer](#) Expert Opin Biol Ther. 2020 Dec 31;1-7. doi:

10.1080/14712598.2021.1869209. Online ahead of print. Danilo Rocco 1 , Luigi Della Gravara 2 , Ciro Battiloro 1 , Cesare Gridelli 3

INTRODUCTION: One of the latest breakthroughs in the treatment of advanced Non Small Cell Lung Cancer (NSCLC) is represented by PD-1/PD-L1-targeting Immune Checkpoint Inhibitors (ICIs). However, only a limited subset of advanced NSCLC patients can receive first-line ICI monotherapy (advanced NSCLC patients without driver mutations and with a PD-L1 expression $\geq 50\%$ or $\geq 1\%$) and naïve ICI-respondent patients represent an even more limited subgroup of patients, which eventually experience progression of disease after approximately 7-11 months. Therefore, different strategies are being evaluated to obtain a higher response rate and a more durable clinical response in this setting. A very encouraging one is represented by ICI-combination therapies, i.e. the use of an ICI combined to cytotoxic chemotherapy and/or another immunotherapeutic agent. **AREAS COVERED:** This paper aims to assess currently available data from trials evaluating nivolumab-based first-line combination therapies. **EXPERT OPINION:** Nivolumab-based combinations regimens will represent one of the standard treatments for naïve advanced NSCLC patients in a near future. However, in order to fully exploit these combination therapies, additional studies assessing potential predictive and/or prognostic biomarkers are required to better clarify which patients are more likely to benefit from these regimens, alongside with studies investigating safer and more durable second-line treatments.

[RET inhibition in novel patient-derived models of RET-fusion positive lung adenocarcinoma reveals a role for MYC upregulation](#) Dis Model Mech. 2020 Dec 14;dmm.047779. doi:

10.1242/dmm.047779. Online ahead of print. Takuo Hayashi ^{1 2 3}, Igor Odintsov ^{1 2}, Roger S Smith ^{1 2 4}, et al.

Multi-kinase RET inhibitors, such as cabozantinib and RXDX-105, are active in lung cancer patients with RET fusions; however, the overall response rates to these two drugs are unsatisfactory compared to other targeted therapy paradigms. Moreover, these inhibitors may have different efficacies against RET rearrangements depending on the upstream fusion partner. A comprehensive preclinical analysis of the efficacy of RET inhibitors is lacking due to a paucity of disease models harboring RET rearrangements. Here we generated two new patient-derived xenograft (PDX) models, one new patient-derived cell line, one PDX-derived cell line, and several isogenic cell lines with RET fusions. Using these models, we re-examined the efficacy and mechanism of action of cabozantinib and found that this RET inhibitor was effective at blocking growth of cell lines, activating caspase 3/7 and inhibiting activation of ERK and AKT. Cabozantinib treatment of mice bearing RET-fusion-positive cell line xenografts and two PDXs significantly reduced tumor proliferation without adverse toxicity. Moreover, cabozantinib was effective at reducing growth of a lung cancer PDX that was not responsive to RXDX-105. Transcriptomic analysis of lung tumors and cell lines with RET alterations showed activation of a MYC signature and this was suppressed by treatment of cell lines with cabozantinib. MYC protein levels were rapidly depleted following cabozantinib treatment. Taken together, our results demonstrate that cabozantinib is an effective agent in preclinical models harboring RET rearrangements with three different 5' fusion partners (CCDC6, KIF5B and TRIM33). Notably, we identify MYC as a protein that is upregulated by RET expression and down-regulated by cabozantinib treatment, opening up potentially new therapeutic avenues for combinatorial targeting RET-fusion driven lung cancers. The novel RET fusion-dependent preclinical models described herein represent valuable tools for further refinement of current therapies and the evaluation of novel therapeutic strategies.

[Updated Overall Survival in a Randomized Study Comparing Dacomitinib with Gefitinib as First-Line Treatment in Patients with Advanced Non-Small-Cell Lung Cancer and EGFR-Activating Mutations](#) Drugs. 2020 Dec 17. doi: 10.1007/s40265-020-01441-6. Online ahead of print.

Tony S Mok ¹, Ying Cheng ², Xiangdong Zhou ³, et al.

BACKGROUND: ARCHER 1050, an ongoing, randomized, open-label, phase III trial of dacomitinib versus gefitinib in newly diagnosed patients with advanced non-small-cell lung cancer (NSCLC) and an EGFR-activating mutation, reported significant improvement in overall survival (OS) with dacomitinib. **OBJECTIVE:** This paper reports an updated OS analysis of ARCHER 1050 after an extended follow-up. **PATIENTS AND METHODS:** In this multinational, multicenter trial, adults (aged ≥ 18 years or ≥ 20 years in Japan and Korea) with newly diagnosed NSCLC and EGFR mutation (exon 19 deletion or exon 21 L858R substitution), and no history of central nervous system metastases, were randomized 1:1 to receive dacomitinib 45 mg/day (n = 227) or gefitinib 250 mg/day (n = 225). Randomization was stratified by race and EGFR mutation type. An ad hoc updated analysis of OS was conducted at the protocol-defined cut-off of 48 months from first dosing of the last enrolled patient (13 May 2019). **RESULTS:** After a median follow-up of 47.9 months, 133 (58.6%) patients had died in the dacomitinib arm and 152 (67.6%) in the gefitinib arm. The hazard ratio (HR) for OS was 0.748 (95% CI 0.591-0.947; two-sided P = 0.0155); median OS was 34.1 months with dacomitinib versus 27.0 months with gefitinib. The HR for OS in patients with dose reduction(s) in the dacomitinib arm (n = 154) compared with all patients in the gefitinib arm was 0.554 (95% CI 0.420-0.730); median OS was 42.5 months for patients with dose reduction(s) in the dacomitinib arm. The most common adverse events were diarrhea (87.7%), paronychia (61.7%), dermatitis acneiform (49.3%), and stomatitis (43.6%) with dacomitinib, and diarrhea (55.8%) and alanine aminotransferase increased (40.2%) with gefitinib. **CONCLUSIONS:** The OS benefit from first-line treatment with dacomitinib versus gefitinib was maintained after extended follow-up in patients with advanced NSCLC with EGFR-activating mutations.

Opioids impair Nivolumab outcomes: a retrospective propensity score analysis in non-small-cell lung cancer BMJ Support Palliat Care. 2020 Dec 8;bmjspcare-2020-002480. doi: 10.1136/bmjspcare-2020-002480. Online ahead of print. Yoshihiko Taniguchi 1 , Akihiro Tamiya 2 , Yoshinobu Matsuda 3 , Yuichi Adachi 4 , Takatoshi Enomoto 4 , Kouji Azuma 5 , Shunichi Kouno 6 , Akihiro Tokoro 3 , Shinji Atagi 7

OBJECTIVES: Opioids are often administered for cancer-related pain relief. However, few reports have evaluated the association between opioids and immune checkpoint inhibitor treatment for patients with non-small-cell lung cancer (NSCLC). The aim of this retrospective study was to reveal the effect of opioids on the prognosis of patients harbouring NSCLC treated with nivolumab. **METHODS:** The medical records of consecutive patients with NSCLC receiving nivolumab at our institution were retrospectively reviewed. We collected clinical data at the time of nivolumab treatment initiation. Propensity score matching (PSM) was performed to minimise potential selection bias. We compared clinical outcomes with and without baseline opioid use. **RESULTS:** Of the 296 patients identified in the study, after PSM, 38 cases with opioid use and matched 38 cases without opioid use were selected. The overall response rate was significantly lower in patients with opioid use than in those without (2.63%, 95% CI 0.47% to 13.49%, vs 21.05%, 95% CI 11.07% to 36.35%; p=0.0284). The median progression-free survival in patients with opioid use was significantly shorter than that in patients without (1.17, 95% CI 0.93 to 1.73 months, vs 2.07 95% CI 1.23 to 4.73 months; p=0.002). The median overall survival in patients with opioid use was significantly shorter than that in patients without (4.20, 95% CI 2.53 to 6.20 months, vs 9.57, 95% CI 2.23 to not reached months; p=0.018). **CONCLUSIONS:** Patients with NSCLC receiving regular opioid administration at nivolumab treatment initiation had a worse nivolumab treatment outcome than patients without opioid use.

[Stereotactic Body Radiotherapy Versus Delayed Surgery for Early-stage Non-small-cell Lung Cancer](#)

Ann Surg. 2020 Dec;272(6):925-929. doi: 10.1097/SLA.0000000000004363. Nicholas R Mayne 1 , Belle K Lin 2 , Alice J Darling 1 , Vignesh Raman 1 , Deven C Patel 3 , Douglas Z Liou 3 4 , Thomas A D'Amico 1 , Chi-Fu Jeffrey Yang 5

OBJECTIVE: To evaluate the overall survival of patients with operable stage IA non-small-cell lung cancer (NSCLC) who undergo "early" SBRT (within 0-30 days after diagnosis) versus "delayed" surgery (90-120 days after diagnosis). **SUMMARY OF BACKGROUND DATA:** During the COVID-19 pandemic, national guidelines have recommended patients with operable stage IA NSCLC to consider delaying surgery by at least 3 months or, alternatively, to undergo SBRT without delay. It is unknown which strategy is associated with better short- and long-term outcomes. **METHODS:** Multivariable Cox proportional hazards modeling and propensity score-matched analysis was used to compare the overall survival of patients with stage IA NSCLC in the National Cancer Data Base from 2004 to 2015 who underwent "early" SBRT (0-30 days after diagnosis) versus that of patients who underwent "delayed" wedge resection (90-120 days after diagnosis). **RESULTS:** During the study period, 570 (55%) patients underwent early SBRT and 475 (45%) underwent delayed wedge resection. In multivariable analysis, delayed resection was associated with improved survival [adjusted hazard ratio 0.61; (95% confidence interval (CI): 0.50-0.76)]. Propensity-score matching was used to create 2 groups of 279 patients each who received early SBRT or delayed resection that were well-matched with regard to baseline characteristics. The 5-year survival associated with delayed resection was 53% (95% CI: 45%-61%) which was better than the 5-year survival associated with early SBRT (31% [95% CI: 24%-37%]). **CONCLUSION:** In this national analysis, for patients with stage IA NSCLC, extended delay of surgery was associated with improved survival when compared to early treatment with SBRT.

[An Automated knowledge-based planning routine for stereotactic body radiotherapy of peripheral lung tumors via DCA-based volumetric modulated arc therapy](#)

J Appl Clin Med Phys. 2020 Dec 3. doi: 10.1002/acm2.13114. Online ahead of print. Justin Visak 1 , Gary Y Ge 1 , Ronald C McGarry 1 , Marcus Randall 1 , Damodar Pokhrel 1

PURPOSE: To develop a knowledge-based planning (KBP) routine for stereotactic body radiotherapy (SBRT) of peripherally located early-stage non-small-cell lung cancer (NSCLC) tumors via dynamic conformal arc (DCA)-based volumetric modulated arc therapy (VMAT) using the commercially available RapidPlan™ software. This proposed technique potentially improves plan quality, reduces complexity, and minimizes interplay effect and small-field dosimetry errors associated with treatment delivery. **METHODS:** KBP model was developed and validated using 70 clinically treated high quality non-coplanar VMAT lung SBRT plans for training and 20 independent plans for validation. All patients were treated with 54 Gy in three treatments. Additionally, a novel k-DCA planning routine was deployed to create plans incorporating historical three-dimensional-conformal SBRT planning practices via DCA-based approach prior to VMAT optimization in an automated planning engine. Conventional KBPs and k-DCA plans were compared with clinically treated plans per RTOG-0618 requirements for target conformity, tumor dose heterogeneity, intermediate dose fall-off and organs-at-risk (OAR) sparing. Treatment planning time, treatment delivery efficiency, and accuracy were recorded. **RESULTS:** KBPs and k-DCA plans were similar or better than clinical plans. Average planning target volume for validation was 22.4 ± 14.1 cc (7.1-62.3 cc). KBPs and k-DCA plans provided similar conformity to clinical plans with average absolute differences of 0.01 and 0.01, respectively. Maximal doses to OAR were lowered in both KBPs and k-DCA plans. KBPs increased monitor units (MU) on average 1316 ($P < 0.001$) while k-DCA reduced total MU on average by 1114 ($P < 0.001$). This routine can create k-DCA plan in less than 30 min. Independent Monte Carlo calculation demonstrated that k-DCA plans showed better agreement

with planned dose distribution. **CONCLUSION:** A k-DCA planning routine was developed in concurrence with a knowledge-based approach for the treatment of peripherally located lung tumors. This method minimizes plan complexity associated with model-based KBP techniques and improve plan quality and treatment planning efficiency.

Whole Brain Radiotherapy With and Without Concurrent Erlotinib in NSCLC with Brain

Metastases: a multicentre, open-label, randomized, controlled phase 3 Trial Neuro Oncol. 2020 Dec 17;noaa281. doi: 10.1093/neuonc/noaa281. Online ahead of print. Zhenzhou Yang 1 2 , Yan Zhang 3 , Rongqing Li 4 , Abulimiti Yisikandaer 5 , Biyong Ren 6 , Jianguo Sun 7 , Jianjun Li 8 , Long Chen 9 , Ren Zhao 10 , Juying Zhang 11 , Xuefeng Xia 12 , Zhongxing Liao 13 , David P Carbone 14

BACKGROUND: Erlotinib combined with whole brain radiotherapy (WBRT) demonstrated a favorable objective response rate in a phase 2 single-arm trial of non-small cell lung cancer (NSCLC) patients with brain metastases. We assessed whether concurrent erlotinib with WBRT is safe and benefits patients in a phase 3, randomized trial. **METHODS:** NSCLC patients with two or more brain metastases were enrolled and randomly assigned (1:1) to WBRT (n=115) or WBRT combined with erlotinib arms (n=109). The primary endpoint was intracranial progression-free survival (iPFS) and cognitive function (CF) was assessed by Mini-Mental State Examination (MMSE). **RESULTS:** A total of 224 patients from 10 centers across China were randomized to treatments. Median follow-up was 11.2 months. Median iPFS for WBRT concurrent erlotinib was 11.2 months versus 9.2 months for WBRT-alone (p=0.601). Median PFS and overall survival (OS) of combination group were 5.3 versus 4.0 months (p=0.825) and 12.9 versus 10.0 months (p=0.545), respectively, compared with WBRT-alone. In EGFR-mutant patients, iPFS (14.6 versus 12.8 months; p=0.164), PFS (8.8 versus 6.4 months; p=0.702) and OS (17.5 versus 16.9 months; p=0.221) were not significantly improved in combination group over WBRT-alone. Moreover, there were no significant differences in patients experiencing MMSE score change between the treatments.

CONCLUSION: Concurrent erlotinib with WBRT didn't improve iPFS and excessive CF detriment either in the intent-to-treat (ITT) population or in EGFR-mutant patients compared with WBRT-alone, suggesting that while safe for patients already taking the drug, there is no justification for adding concurrent EGFR-TKI with WBRT for the treatment of brain metastases.

SMALL CELL LUNG CANCER - SCLC

Mechanisms of small cell lung cancer metastasis EMBO Mol Med. 2020 Dec 9;e13122. doi: 10.15252/emmm.202013122. Online ahead of print. Julie Ko 1 2, Monte M Winslow 2 3, Julien Sage 1 2 Affiliations expand

Metastasis is a major cause of morbidity and mortality in cancer patients. However, the molecular and cellular mechanisms underlying the ability of cancer cells to metastasize remain relatively poorly understood. Among all solid tumors, small cell lung cancer (SCLC) has remarkable metastatic proclivity, with a majority of patients diagnosed with metastatic disease. Our understanding of SCLC metastasis has been hampered for many years by the paucity of material from primary tumors and metastases, as well as the lack of faithful pre-clinical models. Here, we review recent advances that are helping circumvent these limitations. These advances include methods that employ circulating tumor cells from the blood of SCLC patients and the development of diverse genetically engineered mouse models of metastatic SCLC. New insights into the cellular mechanisms of SCLC metastasis include observations of cell fate changes associated with increased metastatic ability. Ongoing studies on cell migration and organ tropism promise to expand our understanding of SCLC metastasis. Ultimately, a better molecular understanding of metastatic phenotypes may be translated into new therapeutic options to limit metastatic spread and treat metastatic SCLC.

[CBL0137 increases the targeting efficacy of Rovalpituzumab tesirine against tumour-initiating cells in small cell lung cancer](#) Br J Cancer. 2020 Dec 1. doi: 10.1038/s41416-020-01192-x. Online ahead of print. Daniel J Lindner 1 , Gary Wildey 2 , Yvonne Parker 1 , Afshin Dowlati 2 , George R Stark 3 , Sarmishtha De 4

Small cell lung cancer (SCLC) is characterised by high relapse rates. Tumour-initiating cells (TICs) are responsible for drug resistance and recurrence of cancer. Rovalpituzumab tesirine (Rova-T), a potent humanised antibody-drug conjugate, selectively targets delta-like protein 3, which is highly expressed in SCLC TICs. The experimental drug CBL0137 (CBL) inhibits the histone chaperone FACT (facilitates chromatin transcription), which is required for the expression of transcription factors that are essential for TIC maintenance. Rova-T and CBL each target SCLC TICs as single agents. However, acquired or intrinsic resistance to single agents is a major problem in cancer. Therefore, we investigated the potential effect of combining Rova-T and CBL in SCLC to eradicate TICs more effectively. Our preclinical studies report a novel and highly translatable therapeutic strategy of dual targeting TICs using Rova-T in combination with CBL to potentially increase survival of SCLC patients.

[Trilaciclib prior to chemotherapy and atezolizumab in patients with newly diagnosed extensive-stage small cell lung cancer: a multicentre, randomised, double-blind, placebo-controlled phase II trial](#) Int J Cancer. 2020 Dec 21. doi: 10.1002/ijc.33453. Online ahead of print. Davey Daniel 1 , Vladimer Kuchava 2 , Igor Bondarenko 3 , et al.

Trilaciclib is an intravenous CDK4/6 inhibitor administered prior to chemotherapy to preserve haematopoietic stem and progenitor cells and immune system function from chemotherapy-induced damage (myelopreservation). The effects of administering trilaciclib prior to carboplatin, etoposide and atezolizumab (E/P/A) were evaluated in a randomised, double-blind, placebo-controlled phase II study in patients with newly diagnosed extensive-stage small cell lung cancer (ES-SCLC) (NCT03041311). The primary endpoints were duration of severe neutropenia (SN; defined as absolute neutrophil count $<0.5 \times 10^9$ cells per L) in cycle 1 and occurrence of SN during the treatment period. Other endpoints were prespecified to assess the effects of trilaciclib on additional measures of myelopreservation, patient-reported outcomes, antitumour efficacy and safety. Fifty-two patients received trilaciclib prior to E/P/A and 53 patients received placebo. Compared with placebo, administration of trilaciclib resulted in statistically significant decreases in the mean duration of SN in cycle 1 (0 versus 4 days; $p < 0.0001$) and occurrence of SN (1.9% versus 49.1%; $p < 0.0001$), with additional improvements in red blood cell and platelet measures and health-related quality of life (HRQoL). Trilaciclib was well tolerated, with fewer grade ≥ 3 adverse events compared with placebo, primarily due to less high-grade haematological toxicity. Antitumour efficacy outcomes were comparable. Administration of trilaciclib versus placebo generated more newly expanded peripheral T-cell clones ($p = 0.019$), with significantly greater expansion among patients with an antitumour response to E/P/A ($p = 0.002$). Compared with placebo, trilaciclib administered prior to E/P/A improved patients' experience of receiving treatment for ES-SCLC, as shown by reduced myelosuppression, and improved HRQoL and safety profiles. This article is protected by copyright. All rights reserved.

[Combination of tissue and liquid biopsy molecular profiling to detect transformation to small cell lung carcinoma during osimertinib treatment](#) Ther Adv Med Oncol. 2020 Dec 18;12:1758835920974192. doi: 10.1177/1758835920974192. eCollection 2020. Julie A Vendrell 1 , Xavier Quantin 2 , Isabelle Serre 3 , Jérôme Solassol 4

BACKGROUND: Histological transformation of advanced non-small cell lung cancer (NSCLC) to small cell lung cancer (SCLC) is one of the mechanisms of resistance to third-generation tyrosine kinase inhibitors (TKIs), such as osimertinib. This acquired TKI resistance is linked to the high degree of tumor heterogeneity and adaptive cellular signaling pathways, including epidermal growth factor receptor

(EGFR)-dependent pathways, observed in NSCLC. **METHODS:** Here, we investigated a series of paired pre- and post-histological transformation biopsies obtained from three patients initially having a NSCLC with an EGFRactivating mutation treated with first-generation TKI, who then received osimertinib as second-line after EGFR T790M resistance and, lastly, developed a histological transformation to SCLC. Both tissue and liquid biopsies were analyzed using large panel sequencing approaches at various time points to reconstruct the clonal evolutionary history of the tumor. **RESULTS:** Our complementary analysis of tumor tissue and circulating tumor DNA samples allowed us to better characterize the histological and molecular alterations associated with resistance to osimertinib. SCLC transformation was linked to the presence of several concomitant gene alterations, including EGFR, TP53 and RB1, but also to specific signal bypass, such as EGFR and MET amplifications and activation of the PI3K/AKT/mTOR pathway. **CONCLUSION:** Our report emphasizes the mutational landscape of SCLC histological transformation and highlights the importance of combining tissue and liquid biopsy profiling before and during osimertinib treatment to predict such histological transformation.

[Recent advances in small cell lung cancer: the future is now?](#) *Minerva Endocrinol.* 2020 Dec 17. doi: 10.23736/S0391-1977.20.03213-7. Online ahead of print. Andrea Luciani ¹, Miriam Blasi ², Leonardo Provenzano ², Sabrina Zonato ², Daris Ferrari ²

Small cell lung cancer is a relevant clinical issue as it is a highly malignant cancer, often diagnosed in advanced stage. Similarly to non-small cell lung cancer, tobacco smoking is currently the main risk factor. Its incidence, at least in males, has declined over the past decades, due to the worldwide decreased percentage of active smokers. The typical small cells of this tumor type are characterized by a high proliferation index, chromosomal deletions such as 3p(14-23) involving the tumor-suppressor gene FHIT, alterations of the MYC or Notch family proteins and the frequent expression of neuroendocrine markers. The combination of thoracic radiotherapy and chemotherapy is the standard treatment for limited stage disease, while platinum-based chemotherapy is the most effective choice for extensive stage disease. Unfortunately, whatever chemotherapy is used, the results are disappointing. No regimen has proved to be effective in the long run, indeed small cell lung cancer rapidly progresses after a frequent initial strong response, and the mortality rate remains still high. The advent of immunotherapy is actually changing the landscape in oncology. As well as in other cancers, recent trials have demonstrated the efficacy of the combination of immune checkpoint inhibitors and chemotherapy, opening new perspectives for the future of our patients.

[Liquid Biopsy in Small Cell Lung Cancer-A Route to Improved Clinical Care?](#) *Cells.* 2020 Dec 3;9(12):2586. doi: 10.3390/cells9122586. Matt Church ¹, Louise Carter ^{1 2}, Fiona Blackhall ^{1 2}

Small cell lung cancer (SCLC) has a particularly poor prognosis despite the high initial response to first-line systemic therapy, and there is a well-recognised lack of meaningful treatments beyond the second line. A number of reasons have been put forward to explain this, including a lack of common, easily-druggable genetic mutations in SCLC and rarity of high-quality tissue samples due to late presentation. Liquid biopsies, including circulating tumour cells (CTCs) and circulating tumour DNA (ctDNA) are increasingly used as surrogates for tumour tissue and have the advantage of being easily obtained serially to inform on the biology of disease progression and acquired chemoresistance, and may provide a pathway to improve care in this notoriously refractory disease. Here we discuss the current evidence behind these liquid biopsy methods in SCLC, and how they could be employed in future clinical care.

[FDA Approval Summary: Lurbinectedin for the Treatment of Metastatic Small Cell Lung Cancer](#) *Clin Cancer Res.* 2020 Dec 7. doi: 10.1158/1078-0432.CCR-20-3901. Online ahead of print. Sonia Singh ¹, Adnan A Jaigirdar ², Flora Mulkey ², et al.

On June 15, 2020, the FDA granted accelerated approval to lurbinectedin for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy. Approval was granted on the basis of the clinically meaningful effects on overall response rate (ORR) and duration of response (DOR), and the safety profile observed in a multicenter, open-label, multicohort clinical trial (PM1183-B-005-14, NCT02454972), referred to as Study B-005, in patients with advanced solid tumors. The trial included a cohort of 105 patients with metastatic SCLC who had disease progression on or after platinum-based chemotherapy. The confirmed ORR determined by investigator assessment using RECIST 1.1 in the approved SCLC patient population was 35% [95% confidence interval (CI): 26-45], with a median DOR of 5.3 (95% CI: 4.1-6.4) months. The drug label includes warnings and precautions for myelosuppression, hepatotoxicity, and embryo-fetal toxicity. This is the first drug approved by the FDA in over 20 years in the second line for patients with metastatic SCLC. Importantly, this approval includes an indication for patients who have platinum-resistant disease, representing an area of particular unmet need.

[A Call to Action: Dismantling Racial Injustices in Preclinical Research and Clinical Care of Black Patients Living with Small Cell Lung Cancer](#) Cancer Discov. 2020 Dec 14. doi: 10.1158/2159-

8290.CD-20-1592. Online ahead of print. Portia L Thomas^{1 2}, Chioma J Madubata³, Melinda C Aldrich^{4 5 6}, Montessa M Lee⁷, Taofeek K Owonikoko⁸, John D Minna^{9 10 11}, Charles M Rudin¹², Julien Sage^{13 14}, Christine M Lovly^{15 16}

Small cell lung cancer (SCLC) is an aggressive disease with dismal survival rates and limited therapeutic options. SCLC development is strongly associated with exposure to tobacco carcinogens. However, additional genetic and environmental risk factors that contribute to SCLC pathogenesis are beginning to emerge. Here, we specifically assess disparities pertaining to SCLC in Black populations. In contrast to non-small cell lung cancer, preliminary data suggest that Black individuals may actually be at a lower risk of developing SCLC relative to white individuals. This difference remains unexplained but urgently needs to be verified in larger data sets, because it could provide important new insights and approaches to understanding this recalcitrant tumor. Importantly, little biological information exists on SCLC in Black individuals, and few patient-derived preclinical SCLC models from diverse ancestries are available in the laboratory. Unfortunately, we note strikingly low numbers of Black participants in clinical trials testing new treatments for SCLC. Evidence further indicates that care for patients with SCLC may vary between communities with a large fraction of Black patients and those without. Together, these observations underscore the need to better investigate genetic, environmental, and socioeconomic factors associated with SCLC development, preclinical research, clinical care, and outcomes.

PALLIATIVE AND SUPPORTIVE CARE

[Depression, smoking, and lung cancer risk over 24 years among women](#) Psychol Med. 2020 Dec 3;1-10. doi: 10.1017/S0033291720004390. Online ahead of print. Claudia Trudel-Fitzgerald¹, Emily S Zevon¹, Ichiro Kawachi¹, Reginald D Tucker-Seeley², Laura D Kubzansky¹

BACKGROUND: Studies evaluating depression's role in lung cancer risk revealed contradictory findings, partly because of the small number of cases, short follow-up periods, and failure to account for key covariates including smoking exposure. We investigated the association of depressive symptoms with lung cancer risk in a large prospective cohort over 24 years while considering the role of smoking.

METHODS: Women from the Nurses' Health Study completed measures of depressive symptoms, sociodemographics, and other factors including smoking in 1992 (N = 42 913). Depressive symptoms were also queried in 1996 and 2000, whereas regular antidepressant use and physician-diagnosed depression were collected starting in 1996. Multivariable Cox regression models estimated hazard ratios (HRs) and 95% confidence intervals (CIs) of lung cancer risk until 2016. **RESULTS:** We identified 1009

cases of lung cancer. Women with the highest v. lowest level of depressive symptoms had an increased lung cancer risk (HR_{sociodemographics-adjusted} = 1.62, 95% CI 1.34-1.95; HR_{fully-adjusted} = 1.25, 95% CI 1.04-1.51). In a test of mediation, lifetime pack-years of smoking accounted for 38% of the overall association between depressive symptoms and disease risk. When stratifying by smoking status, the elevated risk was evident among former smokers but not current or never smokers; however, the interaction term suggested no meaningful differences across groups (p = 0.29). Results were similar or stronger when considering time-updated depression status (using depressive symptoms, physician diagnosis, and regular antidepressant use) and chronicity of depressive symptoms. **CONCLUSIONS:** These findings suggest that greater depressive symptoms may contribute to lung cancer incidence, directly and indirectly via smoking habits, which accounted for over a third of the association.

Artificial neural networks for simultaneously predicting the risk of multiple co-occurring symptoms among patients with cancer Cancer Med. 2020 Dec 22. doi: 10.1002/cam4.3685. Online ahead of print.

Wenhui Xuyi 1, Hsien Seow 2 3, Rinku Sutradhar 1 2 4

Patients with cancer often exhibit multiple co-occurring symptoms which can impact the type of treatment received, recovery, and long-term health. We aim to simultaneously predict the risk of three symptoms: severe pain, moderate-severe depression, and poor well-being in order to flag patients who may benefit from pre-emptive early symptom management. This was a retrospective population-based cohort study of adults diagnosed with cancer between 2008 and 2015. We developed and tested an Artificial Neural Network (ANN) model to predict the risk of multiple co-occurring symptoms within 6 months after diagnosis. The ANN model derived from a training cohort was assessed on an independent test cohort for model performance based on sensitivity, specificity, accuracy, AUC, and calibration. The mutually exclusive training and test cohorts consisted of 35,606 and 10,498 patients, respectively. The area under the curve for the risk of experiencing severe pain, moderate-severe depression, and poor well-being were 71%, 73%, and 70%, respectively. Patient characteristics at highest risk of simultaneously experiencing these three symptoms included: those with lung cancer, late stage cancer, existing chronic conditions such as osteoarthritis, mood disorder, hypertension, diabetes, and coronary disease. Patients with over a 40% risk of severe pain also had over a 70% risk of depression, and over a 55% risk of poor well-being. Our ANN model was able to simultaneously predict the risk of pain, depression, and lack of well-being. Accurate prediction of future symptom burden can serve as an early indicator tool so that providers can implement timely interventions for symptom management, ultimately improving cancer care and quality of life.

Patterns of Specialty Palliative Care Utilization Among Patients Receiving Palliative Radiotherapy

J Pain Symptom Manage. 2020 Dec 28;S0885-3924(20)30969-6. doi:

10.1016/j.jpainsymman.2020.12.018. Online ahead of print. Jie Jane Chen 1, Bhupendra Rawal 2, Monica S Krishnan 3, Lauren M Hertan 4, Diana D Shi 3, Claudia S Roldan 3, Mai Anh Huynh 3, Alexander Spektor 3, Tracy A Balboni 5

CONTEXT: Palliative radiotherapy (RT) is frequently used to ameliorate cancer-associated symptoms and improve quality of life. **OBJECTIVES:** To examine how palliative care (PC) as a specialty is integrated at the time of RT consultation for patients with advanced cancer. **METHODS:** We retrospectively reviewed 162 patients with metastatic cancer who received palliative RT at our institution (7/2017-2/2018). Fisher's exact test identified differences in incidence of receiving any specialty PC. Logistic regression analyses determined predictors of receiving PC. **RESULTS:** Of the 74 patients (46%) who received any specialty PC, 24 (32%) initiated PC within 4 weeks of RT consultation. The most common reasons for specialty PC initiation were pain (64%) and goals of care/end-of-life care management (23%). Referrals to specialty PC were made by inpatient care teams (48.6%), medical oncologists (48.6%), radiation oncologists (1.4%), and self-referring patients (1.4%). Patients with pain at

RT consultation had a higher incidence of receiving specialty PC (58.7% vs. 37.4%, $p=0.0097$). There was a trend towards decreased PC among patients presenting with neurological symptoms (34.8% vs. 50%, $p=0.084$). On multivariable analysis, receiving specialty PC significantly differed by race (non-white vs. white, $OR=6.295$ [95% CI 1.951-20.313], $p=0.002$), cancer type (lung vs. other histology, $OR=0.174$ [95% CI 0.071-0.426], $p=0.0006$), and RT consultation setting (inpatient vs. outpatient, $OR=3.453$ [95% CI 1.427-8.361], $p=0.006$). **CONCLUSION:** Fewer than half of patients receiving palliative RT utilized specialty PC. Initiatives are needed to increase PC, especially for patients with lung cancer and neurological symptoms, and to empower radiation oncologists to refer patients to specialty PC.

[Association of Exercise Behavior with Overall Survival in Stage I-III A Lung Cancer](#) Ann Am Thorac Soc. 2020 Dec 16. doi: 10.1513/AnnalsATS.202003-235OC. Online ahead of print. Duc M Ha 1 2 , Chan Zeng 1 , Edward D Chan 3 , Mark Gray 1 , Peter J Mazzone 4 , Jonathan M Samet 5 , John F Steiner 1 6

RATIONALE: Exercise assessments may help predict outcomes for patients diagnosed with lung cancer. **OBJECTIVES:** We examined the relationship between pre-diagnosis exercise behavior and clinical outcomes among stage I-III A lung cancer patients. **METHODS:** In a retrospective cohort study of patients with stage I-III A lung cancer at Kaiser Permanente Colorado who had at least one Exercise Vital Sign (EVS) assessment - a questionnaire tool to help promote exercise in chronic disease management - within the year prior to diagnosis, we defined exercise behavior as active (any minutes/week of moderate-to-vigorous intensity physical activity) or inactive (no moderate-to-vigorous physical activity). The outcomes were: 1) overall survival (OS); and 2) acute health care utilization (AHCU). We used the Kaplan-Meier method, and Cox proportional hazard, and negative binomial regression models to analyze the effects of exercise on outcomes, adjusting for demographic, socioeconomic, clinical, and lung cancer characteristics. **RESULTS:** Among 552 lung cancer patients, 230 (42%) were identified as physically active prior to their cancer diagnosis. There was no significant difference in the stage distribution between active and inactive patients. The median survival times were 2.4 years for the active group and 1.8 years for inactive patients ($P<0.001$). The mean rates (standard deviations) of AHCU were 1.09 (1.55) and 2.31 (5.61) per person-year for active and inactive groups, respectively ($P<0.01$). Active exercise, compared to inactivity, was associated with better OS [hazard ratio (HR) 0.52 (0.39, 0.69)] and lower AHCU [rate ratio (RR) 0.63 (0.49, 0.80)] in unadjusted analyses, and better OS [HR 0.62 (0.45, 0.86)] but not statistically significant lower AHCU [RR 0.82 (0.65, 1.04)] in adjusted analyses. **CONCLUSIONS:** Pre-diagnosis active exercise was associated with better OS following diagnosis with stage I-III A lung cancer. Exercise assessments may help predict outcomes, risk-stratify patients for curative intent therapy, and identify those who would benefit from increased physical activity and exercise.

[Optimising patient fitness: strategies to reduce the effects of cancer cachexia in patients with advanced lung cancer](#) Curr Opin Support Palliat Care. 2020 Dec;14(4):304-308. doi:

10.1097/SPC.0000000000000525. Iain Phillips 1 , Samantha Kestenbaum

PURPOSE OF REVIEW: Outcomes for patients with advanced lung cancer have traditionally been very poor. This patient group are often comorbid, less fit and experience multiple symptoms. This review discusses strategies for minimizing the impact of cachexia on patients with advanced lung cancer. This is timely, as in recent years there has been a rapid increase in available systemic therapy options, with the potential of long-term survival for some patients. **RECENT FINDINGS:** The review discusses current strategies in combating cachexia, including: symptom control, systemic therapy for cancer and for cachexia, nutritional interventions and exercise interventions. It discusses current clinical trials, combining interventions and the paradigm of prehabilitation. **SUMMARY:** It is likely that the optimal way of minimizing the impact of cachexia in advanced lung cancer is through a combination of early interventions including symptom management.

[Perspectives of bereaved partners of lung cancer patients on the role of mindfulness in dying and grieving: A qualitative study](#) Palliat Med. 2021 Jan;35(1):200-208. doi: 10.1177/0269216320967281.

Epub 2020 Dec 14. Melanie Pj Schellekens 1, Desiree Gm van den Hurk 2, Ellen Tm Jansen 3, Marije L van der Lee 1, Judith B Prins 4, Miep A van der Drift 2, Anne Em Speckens 3

BACKGROUND: Mindfulness-Based Stress Reduction (MBSR) has been shown to reduce psychological distress in cancer patients but not their partners. Whether MBSR can support patients and partners in coping with the dying and grieving process is less well examined. **AIM:** We aimed to gain more insight in the role of mindfulness in the dying and grieving process from the perspective of the partner after the patient's death. **DESIGN:** As part of a pilot study or subsequent randomized controlled trial, partners had participated together with the patient in MBSR. After the patient's death partners were invited for qualitative in-depth interviews. Data from the interviews was analyzed using the grounded theory approach. **SETTING/PARTICIPANTS:** Interviews were conducted with 11 partners in their homes, on average 11 months after the patient's death (SD = 7.8). **RESULTS:** Mindfulness helped couples to allow and regulate difficult thoughts and feelings, which in turn helped them to accept the patient's impending death. It also facilitated them to enjoy things together and communicate more openly. For a few couples, however, participation was physically too burdensome or emotionally too confrontational. During the partners' grieving process, mindfulness helped allowing difficult thoughts and feelings, and taking the time to grieve, which helped them to take good care of themselves, giving them faith in the future. **CONCLUSION:** The present study showed that MBSR can facilitate lung cancer patients and their partners in accepting the forthcoming death and openly communicating about this, which can support a peaceful death and healthy grieving process.

[Pre-radiotherapy pain intensity and health-related quality of life in patients with bone metastases at various vertebral levels](#) J Med Imaging Radiat Sci. 2020 Dec 18;S1939-8654(20)30382-9. doi:

10.1016/j.jmir.2020.11.014. Online ahead of print. Devin Hindle 1, ZhiHui Amy Liu 2, Tara Rosewall 3

PURPOSE: The spine is the most common site of bone metastasis from cancer and can be divided into 5 locational subsections, varying in mobility. The purpose of this research was to determine if the mobility of the metastases-bearing vertebral segment influenced pre-treatment pain intensity or health-related quality of life (HR-QoL) for patients about to receive palliative radiation therapy for painful spine metastasis. **METHODS:** This study was a retrospective chart review of patients referred to the Palliative Radiation Oncology Program, about to receive radiation therapy for vertebral metastasis between January 2014 and June 2016. The main variables included patient-reported Edmonton Symptom Assessment Score pain intensity, the EQ-5D score for HR-QoL and the location of the vertebral metastasis (categorized using the SINS mobility score (mobile, junctional, semi-rigid, or rigid)). Various patient, disease and treatment characteristics were also collected, and entered into a multivariate analysis. **RESULTS:** The eligible sample included 196 patients. Spinal metastases were distributed with approximately equal frequency (~27%) between the junctional, mobile and semi-rigid spine segments. Rigid spine was the least common site for spinal metastases (19%). Patients with metastatic disease in the mobile spine regions experienced greater pre-treatment pain compared to patients with disease in junctional subsections (Odds Ratio [OR] 1.37; p0.012). No relationship between HR-QoL and spinal mobility was found. Multivariate analysis also revealed that spinal metastases from a primary lung diagnosis reported worse pre-treatment pain compared to those from genitourinary cancers (OR 1.15; p0.05). Only age significantly influenced HR-QoL (75-95yrs vs. 35-55yrs; p0.041). **CONCLUSIONS:** Patients referred to an RT clinic for the treatment of painful spinal metastases have a different distribution of disease throughout the spine compared to those referred for surgery or SBRT. Those with metastases in mobile spine segments were more likely to experience severe pre-treatment pain than those with metastases in junctional segments. Although further corroboration is needed, our results suggest that the mobility of the metastasis-bearing

spinal section could be added to the existing list of predictors that aid clinicians in identifying patients that will benefit from closer follow-up or early intervention.

COMPLEMENTARY & ALTERNATIVE THERAPY

[Awareness and Use of Complementary and Alternative Medicine in Korean Lung Cancer Patients](#)

Tuberc Respir Dis (Seoul). 2020 Dec 8. doi: 10.4046/trd.2020.0098. Online ahead of print. Cheol-Kyu Park 6 7 , In-Jae Oh 6 7 , et al.

BACKGROUND: Complementary and alternative medicine (CAM) has been frequently used and its use continues to increase in lung cancer patients, despite insufficient scientific evidence. We analyzed the current status of the awareness and use of CAM in Korean lung cancer patients. **METHODS:** This study was a prospective survey-based study performed at seven medical centers in South Korea between August 2019 and October 2019. The survey included general patient characteristics, and the awareness and use of CAM. We analyzed the differences in the clinical parameters between patients aware and not aware of CAM and between CAM non-users and users. **RESULTS:** A total of 434 patients were included in this study. Among them, 68.8% of the patients responded that they were aware of CAM, and 30.9% of the patients said they experienced CAM. In univariate analysis, patients aware of CAM were younger with poor performance status, patients with advanced-stage lung cancer, those who received more systemic therapy, and those who received CCRT. By multiple logistic regression, younger age, poor performance status, advanced stage, and prior CCRT were independent risk factors for CAM awareness. There were no significant differences in the general characteristics and cancer-associated clinical parameters between CAM non-users and users. **CONCLUSIONS:** More lung cancer patients with younger age, poor performance status, advanced stage, and prior CCRT were aware of CAM. There were no significantly different characteristics between CAM users and non-users.

[Symptom burden and willingness to participate: implications for herbal clinical trials in lung cancer](#)

Ann Palliat Med. 2020 Dec 17;apm-20-865. doi: 10.21037/apm-20-865. Online ahead of print. Jie Liu 1 , Wei Hou 2 , Mithat Gönen 3 , Christina Seluzicki 4 , Susan Qing Li 4 , Jun J Mao 4

BACKGROUND: People with lung cancer are interested in using herbs for symptom management. However, well-designed clinical trials are lacking. We aimed to quantify symptom burden and willingness to participate in herbal clinical trials among this population. **METHODS:** We conducted a cross-sectional analysis using data collected from people with lung cancer at an oncology clinic at an academic cancer center. The primary outcome was self-reported willingness to participate in herbal research. We measured symptoms using the MD Anderson Symptom Inventory (MDASI). Multivariate logistic regression was performed to explore the relationship between demographic/ clinical factors, symptom burden, and willingness to participate in herbal studies. **RESULTS:** Among 288 participants, 55% were female, 42% were >65 years, 54% had stage IV cancer, and 86% had non-small cell lung cancer (NSCLC). Nearly half (46%) indicated willingness to participate in an herbal clinical trial. The most commonly reported moderate to severe symptoms (≥ 4 on the MDASI scale) were fatigue (57%), drowsiness (44%), disturbed sleep (43%), distress (42%), and dyspnea (36%). In multivariate analyses, higher education was significantly associated with willingness to participate in herbal studies (adjusted odds ratio 1.87, 95% confidence interval, 1.12-3.10, $P=0.016$), while symptom burden was not. **CONCLUSIONS:** People with lung cancer experience high rates of symptom burden. Nearly half of our participants expressed willingness to participate in an herbal clinical trial, particularly those with higher education. These findings can inform the design of future herbal clinical trials targeting common symptoms in lung cancer populations.

[Albanol B from Mulberries Exerts Anti-Cancer Effect through Mitochondria ROS Production in Lung Cancer Cells and Suppresses In Vivo Tumor Growth](#) Int J Mol Sci. 2020 Dec 14;21(24):9502. doi: 10.3390/ijms21249502. Thanh Nam Phan 1 , Okwha Kim 1 , Manh Tuan Ha 2 , Cheol Hwangbo 3 4 , Byung-Sun Min 2 , Jeong-Hyung Lee 1

Albanol B (ABN-B), an arylbenzofuran derivative isolated from mulberries, has been shown to have anti-Alzheimer's disease, anti-bacterial and antioxidant activities. The aim of this study was to investigate the anti-cancer effect of this compound against lung cancer cells. The results show that ABN-B inhibited the proliferation of four human lung cancer cell lines (A549, BZR, H1975, and H226) and induced apoptosis, based on the cleavage of caspase-7 and PARP (poly (ADP-ribose) polymerase), as well as the downregulation of Bcl-2. ABN-B also induced cell cycle arrest at G2/M by down-regulating the expression of CKD1 (cyclin-dependent kinase 1) and cyclin B1, but up-regulating p21 (cyclin-dependent kinase inhibitor 1) expression. Notably, ABN-B increased the production of mitochondrial reactive oxygen species (ROS); however, treatment with mito-TEMPO (a specific mitochondrial antioxidant) blocked ABN-B-induced cell cycle arrest at G2/M and apoptosis, as well as the up-regulation of p21 and down-regulation of CDK1 and cyclin B1 induced by ABN-B. At the molecular level, ABN-B-induced mitochondrial ROS production increased the phosphorylation levels of AKT (protein kinase B) and ERK1/2 (extracellular signal-regulated kinase 1/2), while the inhibition of these kinases blocked the ABN-B-induced up-regulation of p21 and down-regulation of CDK1 and cyclin B1. Moreover, ABN-B significantly suppressed tumor growth in Ex-3LL (Lewis lung carcinoma) tumor-bearing mice. Taken together, these results suggest that ABN-B can exert an anti-cancer effect by inducing apoptosis and cell cycle arrest at G2/M through mitochondrial ROS production in lung cancer cells.

[Effect of Traditional Chinese Medicine Injection on Cancer-Related Fatigue: A Meta-Analysis Based on Existing Evidence](#) Evid Based Complement Alternat Med. 2020 Dec 21;2020:2456873. doi: 10.1155/2020/2456873. eCollection 2020. Zhengkai Huang 1 , Qiang Zhang 2 , Yihua Fan 3 4 , Jiajing Zhou 5 , Mingkun Liang 1 6 , Xin Deng 7 , Jian Liang 1 8

METHODS: We systematically searched randomized controlled studies reported through March 2020 in PubMed, EMBASE, the Cochrane Central Register of Controlled Trials, Web of Science, China Biomedical Literature Database (CBM), the China National Knowledge Infrastructure (CNKI), Wanfang, and VIP databases. Two investigators independently screened the studies according to the predetermined criteria, extracted data, and evaluated the bias risk of the included studies, using RevMan5.3 software.

RESULTS: Twelve studies enrolling 1005 participants were included in this systematic review. We found that TCMJ could improve the clinical efficacy of CRF patients (RR = 1.24, 95% CI: 1.05-1.46, P=0.01), ameliorate fatigue status (RR = 1.44, 95% CI: 1.27-1.65, P < 0.00001), and improve quality of life (MD = 8.34, 95% CI: 3.31-13.37, P=0.001), but there was no statistical significance in the fatigue score (MD = -1.10, 95% CI: -2.23-0.04, P=0.06). Referring to the number of adverse events, the safety of TCMJ was good. Subgroup analysis showed that TCMJ could improve clinical efficacy, fatigue, and quality of life in a short time (≤ 4 weeks). Among them, tonic TCMJ could improve the clinical efficacy. TCMJ had advantages in improving fatigue of lung cancer and gastric cancer. In addition, life quality of lung cancer patients improved significantly. **CONCLUSION:** Current research evidence showed that TCMJ could improve the clinical efficacy, fatigue status, and life quality of patients with CRF. In addition, we found that TCMJ could improve the clinical efficacy of CRF patients in a short period of time. Tonic TCMJ could improve the clinical efficacy, but heat-clearing TCMJ could not. Life quality and fatigue status of lung cancer patients improved significantly. However, due to the sample size and quality of the included studies, the results of this analysis should be treated with caution. The above conclusions still need to be verified by more large-sample and high-quality randomized controlled trials.

[**Home Radon Testing in Rural Appalachia**](#) J Rural Health. 2020 Dec 31. doi: 10.1111/jrh.12552. Online ahead of print. Stacy R Stanifer 1 2 , Mary Kay Rayens 1 3 , Amanda Wiggins 1 , David Gross 4 , Ellen J Hahn 1 2 3

PURPOSE: This study compared differences in sociodemographic characteristics, personal risk perception of lung cancer, lung cancer worry, and synergistic risk perception among rural Appalachia residents who completed home radon testing with those who did not, after receiving a free long-term test kit at a rural primary care clinic. The study also examined the association between the Teachable Moment Model constructs and home radon testing. **METHODS:** The study was an exploratory correlational design with a convenience sample of (N = 58) adult participants recruited from 2 rural primary care clinics in Appalachia Kentucky. Participants completed a brief survey and were given a free long-term home radon test kit. Multiple logistic regression was used to determine characteristics associated with home radon testing. **FINDINGS:** Twenty-eight participants (48%) completed home radon testing. There were no differences in personal risk perception of lung cancer, lung cancer worry, or synergistic risk perception between those who completed home radon testing and those who did not. Age was the only significant factor associated with completion of radon testing (B = 0.077, P = .005). For every 5-year increase in age, participants were 47% more likely to test their home for radon. **CONCLUSION:** Providing free home radon test kits in the primary care setting shows promise in prompting radon testing in rural Appalachia. As radon-induced lung cancer risk increases with exposure over time, health care providers in rural Appalachia need to encourage patients of all ages to test their home for radon, especially those who smoke or report smoking in the home.

[**The associations of interstitial lung abnormalities with cancer diagnoses and mortality**](#) Eur Respir J. 2020 Dec 17;56(6):1902154. doi: 10.1183/13993003.02154-2019. Print 2020 Dec. Gisli T Axelsson 1 , Rachel K Putman 2 , Thor Aspelund 3 4 , et al.

An increased incidence of lung cancer is well known among patients with idiopathic pulmonary fibrosis. It is not known whether interstitial lung abnormalities, i.e. early fibrotic changes of the lung, are a risk factor for lung cancer in the general population. The study's objective was to assess whether interstitial lung abnormalities were associated with diagnoses of, and mortality from, lung cancer and other cancers. Data from the AGES-Reykjavik study, a cohort of 5764 older Icelandic adults, were used. Outcome data were ascertained from electronic medical records. Gray's tests, Cox proportional hazards models and proportional subdistribution hazards models were used to analyse associations of interstitial lung abnormalities with lung cancer diagnoses and lung cancer mortality as well as diagnoses and mortality from all cancers. There was a greater cumulative incidence of lung cancer diagnoses (p<0.001) and lung cancer mortality (p<0.001) in participants with interstitial lung abnormalities than in others. Interstitial lung abnormalities were associated with an increased hazard of lung cancer diagnosis (hazard ratio 2.77) and lung cancer mortality (hazard ratio 2.89) in adjusted Cox models. Associations of interstitial lung abnormalities with all cancers were found in models including lung cancers but not in models excluding lung cancers. People with interstitial lung abnormalities are at increased risk of lung cancer and lung cancer mortality, but not of other cancers. This implies that an association between fibrotic and neoplastic diseases of the lung exists from the early stages of lung fibrosis and suggests that interstitial lung abnormalities could be considered as a risk factor in lung cancer screening efforts.

[**Out-of-Pocket Costs for Tyrosine Kinase Inhibitors and Patient Outcomes in EGFR- and ALK-Positive Advanced Non-Small-Cell Lung Cancer**](#) JCO Oncol Pract. 2020 Dec 7;OP2000692. doi: 10.1200/OP.20.00692. Online ahead of print. Bernardo H L Goulart 1 2 3 , Joseph M Unger 2 3 , Shasank Chennupati 1 2 , Catherine R Fedorenko 1 2 , Scott D Ramsey 1 2 3

PURPOSE: We investigated the association of out-of-pocket (OOP) costs for tyrosine kinase inhibitors (TKIs) with overall survival (OS) in epidermal growth factor receptor (EGFR)- and anaplastic lymphoma kinase (ALK)-positive advanced non-small-cell lung cancer (NSCLC). We secondarily investigated associations of TKI OOP costs with TKI adherence, duration of therapy (DOT), and TKI discontinuation. **METHODS:** We used the Hutchinson Institute for Cancer Outcomes Research registry-claims database to identify patients with stage IV EGFR- or ALK-positive NSCLC; ≥ 1 claims for EGFR or ALK TKIs; and ≥ 3 -month survival from TKI initiation. We estimated the average monthly TKI OOP costs per patient up to 3 months from TKI initiation, categorizing patients into quartiles of TKI OOP costs ($Q1 < Q2 < Q3 < Q4$). We conducted landmark analysis at 3 months from TKI initiation to compare Q1-3 v Q4 TKI OOP costs with respect to OS, TKI DOT, TKI adherence, and TKI discontinuation. **RESULTS:** Seventy-eight and twenty-seven patients comprised the Q1-3 and Q4 groups, respectively. Median monthly TKI OOP costs were \$1,431 (Q1-3) v \$2,888 (Q4). Compared with Q1-3, Q4 patients had inferior OS (adjusted hazard ratio [HR], 1.85; [95% CI, 1.11 to 3.10], similar TKI DOT (adjusted HR, 1.06; 95% CI, 0.53 to 2.15), decreased TKI adherence (adjusted odds ratio [OR], 0.28; 95% CI, 0.10 to 0.76), and higher TKI discontinuation rate (adjusted OR, 8.75; 95% CI, 2.59 to 29.52). **CONCLUSION:** Among patients with advanced EGFR- and ALK-positive NSCLC, higher TKI OOP costs are associated with decreased TKI adherence, a higher likelihood of TKI discontinuation, and inferior survival.

[Long-term exposure to fine particle elemental components and lung cancer incidence in the ELAPSE pooled cohort](#) Environ Res. 2020 Dec 2;193:110568. doi: 10.1016/j.envres.2020.110568.

Online ahead of print. Ulla Arthur Hvidtfeldt ¹, Jie Chen ², Zorana Jovanovic Andersen ³, et al.

BACKGROUND: An association between long-term exposure to fine particulate matter (PM_{2.5}) and lung cancer has been established in previous studies. PM_{2.5} is a complex mixture of chemical components from various sources and little is known about whether certain components contribute specifically to the associated lung cancer risk. The present study builds on recent findings from the "Effects of Low-level Air Pollution: A Study in Europe" (ELAPSE) collaboration and addresses the potential association between specific elemental components of PM_{2.5} and lung cancer incidence.

METHODS: We pooled seven cohorts from across Europe and assigned exposure estimates for eight components of PM_{2.5} representing non-tail pipe emissions (copper (Cu), iron (Fe), and zinc (Zn)), long-range transport (sulfur (S)), oil burning/industry emissions (nickel (Ni), vanadium (V)), crustal material (silicon (Si)), and biomass burning (potassium (K)) to cohort participants' baseline residential address based on 100 m by 100 m grids from newly developed hybrid models combining air pollution monitoring, land use data, satellite observations, and dispersion model estimates. We applied stratified Cox proportional hazards models, adjusting for potential confounders (age, sex, calendar year, marital status, smoking, body mass index, employment status, and neighborhood-level socio-economic status).

RESULTS: The pooled study population comprised 306,550 individuals with 3916 incident lung cancer events during 5,541,672 person-years of follow-up. We observed a positive association between exposure to all eight components and lung cancer incidence, with adjusted HRs of 1.10 (95% CI 1.05, 1.16) per 50 ng/m³ PM_{2.5} K, 1.09 (95% CI 1.02, 1.15) per 1 ng/m³ PM_{2.5} Ni, 1.22 (95% CI 1.11, 1.35) per 200 ng/m³ PM_{2.5} S, and 1.07 (95% CI 1.02, 1.12) per 200 ng/m³ PM_{2.5} V. Effect estimates were largely unaffected by adjustment for nitrogen dioxide (NO₂). After adjustment for PM_{2.5} mass, effect estimates of K, Ni, S, and V were slightly attenuated, whereas effect estimates of Cu, Si, Fe, and Zn became null or negative. **CONCLUSIONS:** Our results point towards an increased risk of lung cancer in connection with sources of combustion particles from oil and biomass burning and secondary inorganic aerosols rather than non-exhaust traffic emissions. Specific limit values or guidelines targeting these specific PM_{2.5} components may prove helpful in future lung cancer prevention strategies.

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

[Infection](#) JAMA Oncol. 2020 Dec 10;e206178. doi: 10.1001/jamaoncol.2020.6178. Online ahead of print. 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.

[COVID-19 related concerns of people with long-term respiratory conditions: a qualitative study](#)

BMC Pulm Med. 2020 Dec 9;20(1):319. doi: 10.1186/s12890-020-01363-9. Keir E J Philip 1 2 , Bradley Lonergan 3 , Andrew Cumella 4 , Joe Farrington-Douglas 4 , Michael Laffan 4 , Nicholas S Hopkinson 5 3 4

BACKGROUND: The COVID-19 pandemic is having profound psychological impacts on populations globally, with increasing levels of stress, anxiety, and depression being reported, especially in people with pre-existing medical conditions who appear to be particularly vulnerable. There are limited data on the specific concerns people have about COVID-19 and what these are based on. **METHODS:** The aim of this study was to identify and explore the concerns of people with long-term respiratory conditions in the UK regarding the impact of the COVID-19 pandemic and how these concerns were affecting them. We conducted a thematic analysis of free text responses to the question "What are your main concerns about getting coronavirus?", which was included in the British Lung Foundation/Asthma UK (BLF-AUK) partnership COVID-19 survey, conducted between the 1st and 8th of April 2020. This was during the 3rd

week of the UK's initial 'social distancing measures' which included advice to stay at home and only go outside for specific limited reasons. **RESULTS:** 7039 responses were analysed, with respondents from a wide range of age groups (under 17 to over 80), gender, and all UK nations. Respondents reported having asthma (85%), COPD (9%), bronchiectasis (4%), interstitial lung disease (2%), or 'other' lung diseases (e.g. lung cancer) (1%). Four main themes were identified: (1) vulnerability to COVID-19; (2) anticipated experience of contracting COVID-19; (3) pervasive uncertainty; and (4) inadequate national response. **CONCLUSIONS:** The COVID-19 pandemic is having profound psychological impacts. The concerns we identified largely reflect contextual factors, as well as their subjective experience of the current situation. Hence, key approaches to reducing these concerns require changes to the reality of their situation, and are likely to include (1) helping people optimise their health, limit risk of infection, and access necessities; (2) minimising the negative experience of disease where possible, (3) providing up-to-date, accurate and consistent information, (4) improving the government and healthcare response

[Using Social Media Data to Understand Consumers' Information Needs and Emotions Regarding Cancer: Ontology-Based Data Analysis Study](#) J Med Internet Res. 2020 Dec 7;22(12):e18767. doi: 10.2196/18767. Jooyun Lee 1 , Hyeoun-Ae Park 2 , Seul Ki Park 2 , Tae-Min Song 3

BACKGROUND: Analysis of posts on social media is effective in investigating health information needs for disease management and identifying people's emotional status related to disease. An ontology is needed for semantic analysis of social media data. **OBJECTIVE:** This study was performed to develop a cancer ontology with terminology containing consumer terms and to analyze social media data to identify health information needs and emotions related to cancer. **METHODS:** A cancer ontology was developed using social media data, collected with a crawler, from online communities and blogs between January 1, 2014 and June 30, 2017 in South Korea. The relative frequencies of posts containing ontology concepts were counted and compared by cancer type. **RESULTS:** The ontology had 9 superclasses, 213 class concepts, and 4061 synonyms. Ontology-driven natural language processing was performed on the text from 754,744 cancer-related posts. Colon, breast, stomach, cervical, lung, liver, pancreatic, and prostate cancer; brain tumors; and leukemia appeared most in these posts. At the superclass level, risk factor was the most frequent, followed by emotions, symptoms, treatments, and dealing with cancer.

CONCLUSIONS: Information needs and emotions differed according to cancer type. The observations of this study could be used to provide tailored information to consumers according to cancer type and care process. Attention should be paid to provision of cancer-related information to not only patients but also their families and the general public seeking information on cancer.

[Baseline Demographics and Clinical Characteristics Among 3471 US Patients Hospitalized with COVID-19 and Pulmonary Involvement: A Retrospective Study](#) Adv Ther. 2020 Dec;37(12):4981-4995. doi: 10.1007/s12325-020-01510-y. Epub 2020 Oct 12. Jennie H Best 1 , Shalini V Mohan 2 , Amanda M Kong 3 , Krish Patel 4 , John M Pagel 4 , Boris Ivanov 3 , Otis W Brawley 5 , Krutika Jariwala-Parikh 3 , James L Zazzali 2 , John Pauk 6

INTRODUCTION: Coronavirus disease 2019 (COVID-19) can present as a range of symptoms, from mild to critical; lower pulmonary involvement, including pneumonia, is often associated with severe and critical cases. Understanding the baseline characteristics of patients hospitalized with COVID-19 illness is essential for effectively targeting clinical care and allocating resources. This study aimed to describe baseline demographics and clinical characteristics of US patients hospitalized with COVID-19 and pulmonary involvement. **METHODS:** US patients with COVID-19 and pulmonary involvement during an inpatient admission from December 1, 2019, to May 20, 2020, were identified using the IBM Explorys® electronic health records database. Baseline (up to 12 months prior to first COVID-19 hospitalization) demographics and clinical characteristics and preadmission (14 days to 1 day prior to admission) pulmonary diagnoses were assessed. Patients were stratified by sex, age, race, and geographic

region. **RESULTS:** Overall, 3471 US patients hospitalized with COVID-19 and pulmonary involvement were included. The mean (SD) age was 63.5 (16.3) years; 51.2% of patients were female, 55.0% African American, 81.6% from the South, and 16.8% from the Midwest. The most common comorbidities included hypertension (27.7%), diabetes (17.3%), hyperlipidemia (16.3%), and obesity (9.7%). Cough (27.3%) and dyspnea (15.2%) were the most common preadmission pulmonary symptoms. African American patients were younger (mean [SD], 62.5 [15.4] vs. 67.8 [6.2]) with higher mean (SD) body mass index (33.66 [9.46] vs. 30.42 [7.86]) and prevalence of diabetes (19.8% vs. 16.7%) and lower prevalence of chronic obstructive pulmonary disease (5.6% vs. 8.2%) and smoking/tobacco use (28.1% vs. 37.2%) than White patients. **CONCLUSIONS:** Among US patients primarily from the South and Midwest hospitalized with COVID-19 and pulmonary involvement, the most common comorbidities were hypertension, diabetes, hyperlipidemia, and obesity. Differences observed between African American and White patients should be considered in the context of the complex factors underlying racial disparities in COVID-19.

[New Perspectives on Antimicrobial Agents: Remdesivir Treatment for COVID-19](#) Antimicrob Agents Chemother. 2020 Dec 16;65(1):e01814-20. doi: 10.1128/AAC.01814-20. Print 2020 Dec 16. Muneerah M Aleissa ¹, Emily A Silverman ², Luisa M Paredes Acosta ^{3 4}, Cameron T Nutt ^{3 4}, Aaron Richterman ⁵, Francisco M Marty ^{6 3 4}

Remdesivir was recently approved by the Food and Drug Administration for the treatment of hospitalized patients with coronavirus disease 2019 (COVID-19). Remdesivir is the prodrug of an adenosine analogue that inhibits viral replication of several RNA virus families, including Coronaviridae. Preclinical data in animal models of coronavirus diseases, including COVID-19, have demonstrated that early treatment with remdesivir leads to improved survival, decreased lung injury, and decreased levels of viral RNA. Recent clinical data have demonstrated the clinical activity of remdesivir in terms of faster time to recovery in patients with severe COVID-19 and higher odds of improved clinical status in patients with moderate COVID-19. Here, clinical trials published to date are presented and appraised. Remdesivir's potential benefits and its favorable adverse-event profile make it an option for the treatment of COVID-19. This article examines the available literature describing remdesivir's pharmacology, pharmacokinetics, and preclinical and clinical data.

[Canakinumab as treatment for COVID-19-related pneumonia: a prospective case-control study](#) Int J Infect Dis. 2020 Dec 29;S1201-9712(20)32597-2. doi: 10.1016/j.ijid.2020.12.073. Online ahead of print. Daniele Generali ¹, Giancarlo Bosio ², Fabio Malberti ³, et al.

OBJECTIVES: Canakinumab is an IL-1 β antibody that neutralizes the activity of IL-1 β . We studied the efficacy and safety of canakinumab in patients with moderate COVID-19-related pneumonia. **DESIGN:** The aim of our study was to evaluate the reduction in duration of hospitalization with adequate oxygen status. Forty-eight patients with moderate COVID-19-related pneumonia were asked to participate in the prospective case-control study; 33 patients (Cases) signed informed consent and received canakinumab (Cohort 1); 15 patients (Controls) refused to receive the experimental drug and received institutional standard of care (SoC), (Cohort 2). **RESULTS:** Hospital discharge within 21 days was seen in 63% of patients in Cohort 1 vs. 0% in Cohort 2 (median 14 vs 26 days, respectively; $p < 0.001$). There was significant clinical improvement in ventilation regimes following administration of canakinumab compared to Cohort 2 (Stuart-Maxwell test for paired data, $p < 0.001$). Patients treated with canakinumab experienced a significant increase in PaO₂:FiO₂ ($p < 0.001$) and reduction in lung damage by CT ($p = 0.01$), along with significant decreases in immune/inflammation markers that were not observed in Cohort 2. Only mild side effects were seen in patients treated with canakinumab; survival at 60 days was 90.0% (95% CI: 71.9-96.7) in patients treated with canakinumab and 73.3% (95% CI: 43.6-89.1) for Cohort 2.

CONCLUSIONS: Treatment with canakinumab in patients with COVID-19-related pneumonia rapidly restored normal oxygen status, decreased the need for invasive mechanical ventilation, and was associated with earlier hospital discharge and favorable prognosis versus SoC.