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Timeliness of Lung Cancer Care From the Point of Suspicious Image at an Urban Safety Net Hospital by Demographic and Clinical Factors

N. Siddiqi, Y. Lin, K. Jenkins, G. Pan, A. Liu, K.S. Mak, U. Tapan, and K. Suzuki; *Boston Medical Center, Boston University School of Medicine, Boston, MA*

Purpose/Objective(s): Timeliness of care is an important metric for lung cancer patients, and care delays in the safety-net setting have been described. However, timeliness from the point of the suspicious image is not well-studied. Herein, we evaluate time intervals in the workup of lung cancer at an urban, safety net hospital and assess for disparities by demographic and clinical factors.
Materials/Methods: We performed a retrospective analysis of patients with lung cancer between 2015-2020. Median times from suspicious image to first treatment (I-T), suspicious image to diagnosis (I-D) and diagnosis to treatment (D-T) were calculated. Date of suspicious image was defined as the date that the imaging study prompting cancer-targeted workup resulted. Date of diagnosis was defined as date that biopsy first resulting in histologic diagnosis of lung cancer was performed. Non-parametric tests were applied to assess for intergroup differences in time intervals.
Results: A total of 687 patients were included in the final analysis, of whom 370 (53.9%) were male. By race, 328 (47.7%) were white, 248 (36.1%) were black, 47 (6.9%) were Hispanic, and the remaining 64 (9.3%) were of other racial groups. There were 235 stage I (34.2%), 54 stage II (7.9%), 125 stage III (18.2%), and 273 stage IV (39.7%) patients. I-T, I-D, and D-T for the entire cohort was 78, 34, and 32 days, respectively. Among females, the I-T was 87 days as compared to 72 days for males ($p<0.01$). By stage, the I-Ts were 106, 110, 81, and 41 days for stages I, II, III, and IV, respectively ($p<0.01$). The I-D was 40.5 and 45 days for black and Hispanic patients as compared to 28 and 23 days for white and Asian patients respectively ($p<0.05$, Table 1).
Conclusion: Advanced stage at presentation and male gender were associated with more timely treatment from the point of suspicious imaging while non-black or Hispanic race were associated with more timely lung cancer diagnosis without significant impact on time to treatment. Future analyses should seek to elucidate the drivers of differences in timeliness of care by these characteristics and assess for the impact of timeliness disparities on patient outcomes in the safety net setting.

Abstract 1 - Table 1 Time Intervals by Patient Factors

	I-T (days)		I-D (days)		D-T (days)	
	Median (25-75% IQR)	P-value	Median (25-75% IQR)	P-value	Median (25-75% IQR)	P-value
Factor						
Gender						
Males	72 (40-108)	<0.01	33 (7-69)	0.30	39 (7.5-54)	0.48
Females	87 (42.25-144.5)		34 (7-84)		42 (10-61)	
Race						
White	78 (35-125)	0.324	28 (7-74.25)	0.03	42.5 (7.75-57.25)	0.48
Black	81.5 (51-127)		40.5 (7-81.5)		37 (15.5-53)	
Hispanic	78 (37-141)		45 (9-89)		47 (11-55)	
Asian	69 (38.75-104)		23 (12.5-49.75)		41.5 (3.5-51)	
Unknown/ Other	66 (21.25-106.75)		10 (5-40.5)		37.5 (16.75-65.75)	
Stage						
I	106 (74-155)	<0.01	63 (6.5-85.5)	<0.01	43 (11-60.25)	0.59
II	110 (57.75-141.75)		38 (5.75-75.75)		49 (5-58)	
III	81 (53.5-107)		27 (7-75)		36 (10-59)	
IV	41 (22.5-71)		9 (7-66.5)		37 (9-54)	

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Use of *AVATS*, Awake Video Assisted Thoracic Surgery, to Redefine Operability in Lung Cancer Patients With Extremely Poor Pulmonary Function

A.S. Klijian,[1] and K. Bagheri[2]; [1]*Sharp & Scripps Hospital Systems, San Diego, CA,* [2]*Sharp Grossmont Hospital, La Mesa, CA*

Purpose/Objective(s): Surgery is the treatment for early NSC lung cancer in patients with normal pulmonary status but is excluded in poor pulmonary function. *AVATS*, Awake Video Assisted Thoracic Surgery, under local with sedation has been used in a variety of conditions. We wanted to see if patients with NSCCA and poor pulmonary reserve could benefit from *AVATS*.
Materials/Methods: Over 2300 AVATS have been performed, with a sub group of 502 resections with poor pulmonary status. Wedges, segments

and even lobectomy has been performed without significant morbidity/mortality. Pre-op PFT in these 502 patients showed FEV1 less than 0.8 (some under 0.5.) These patients would not tolerate general anesthesia and/or single lung ventilation. *AVATS* without affords surgical option. All had staging PET/CT scans. 83 Split function V/Q studies were used. Resections included 48 wedges, 123 segments, 21 bi-segments, 308 lobes, and 2 bi-lobectomies. No central venous, or epidural catheters were used. Only 15 arterial lines and only 8 urinary catheters were used. All had two year follow-up. Post-op PFT was available on 338.

Results: 502 patients with NSCCA with poor pulmonary reserve were offered *AVATS*. Comorbidities included: hypertension (390); CAD (262)-90 s/p CABG, 118 s/p stent; diabetes (108); COPD (382)-112 steroid dependent; smoking (438) with 12 active smokers; atrial fib (60)- 52 on anticoagulation; renal failure (79)-32 requiring dialysis; hepatic failure (28); thyroid disease (3); prior stroke (8). 502 patients with FEV1 less than 0.8 successfully had *AVATS* resection with 24-month follow-up. No deaths were seen. Avg. length of stay was 1.2 days. Thirty-eight had new onset atrial fib (all managed medically,) 1 had IV phlebitis. The use of dexmedetomidine allowed evaluation intra-op of the presence air leak significantly eliminating post-op air leak. Only 3 patients required >2 day chest tube for air leak. Five had readmission, all due to unrelated issues (2 for exacerbation of CHF, 2 for non-thoracic procedures, and 1 for diabetes.) AVATS, often via 1 small incisions, reduces pain minimizing narcotic usage. All received peri/post-operative IV acetaminophen, and if tolerated IV ketorolac minimizing nausea and alteration of sensorium, improving patient satisfaction. There was no stroke, UTI, DVT, PE, pneumothorax, pneumonia, hospital acquired infections, or prolonged (> 3 day) air leak. 338 patients had post-op PFT, the majority without reduction of FEV1 (39 had less than 10% reduction of FEV1 without clinical manifestation.)

Conclusion: *AVATS* is safe in select patients previously deemed inoperable often with improved outcomes compare with patients with good pulmonary status having VATS or robotic resection under general anesthesia. *AVATS* allows surgery in patients with poor pulmonary function with improved outcomes/patient satisfaction, shorter length of stay and presumably lower costs.

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A Nested Case-Control Study of Lung Cancer for Immune Biomarkers

U. Sivagnanalingam,[1,2] P.L. Beatty,[2] C. Jacqueline,[2] M. Dracz,[2] J. Adams-Haduch,[3] R. Wang,[3] J.M. Yuan,[3,4] and O.J. Finn[2,3]; [1]*University of Pittsburgh School of Medicine, Pittsburgh, PA,* [2]*University of Pittsburgh Department of Immunology, Pittsburgh, PA,* [3]*UPMC Hillman Cancer Center, Pittsburgh, PA,* [4]*University of Pittsburgh Graduate School of Public Health, Department of Epidemiology, Pittsburgh, PA*

Purpose/Objective(s): Smoking is the leading cause of lung cancer, which is the leading cause of cancer mortality worldwide, with 1.2 million deaths a year. Lung cancer has a very poor prognosis; over half of people diagnosed die within one year of diagnosis and the 5-year survival is less than 18%. Prior to cancer development, smokers develop multiple lung problems associated with chronic inflammation, which can promote progression to cancer. The aim of the study was to examine if immune competence would enhance or reduce the risk of lung cancer development among high-risk smokers. The hypothesis is that smokers who developed lung cancer would have a higher frequency of chronic inflammation induced myeloid-derived suppressor cells (MDSC) and/or regulatory T cells (Treg), three years or more prior to lung cancer diagnosis (baseline), compared to smokers who remained cancer-free. Additionally, smokers who developed cancer would have higher levels of certain inflammatory cytokines at baseline.

Materials/Methods: A case-control study of incident lung cancer was conducted within the participants of the Pittsburgh Lung Screening Study (PLuSS), a longitudinal low-dose CT screening study for early detection of lung cancer among smokers with a history of heavy smoking (median 47 pack-years of cigarette smoking). Cases consisted of 40 current or former smokers who developed lung cancer during follow-up after repeated blood draws and the control group consisted of 40 PLuSS participants, free of cancer, who were individually matched to the index case by age, sex, smoking status, and year of blood draw. Live peripheral blood mononuclear cells (PBMC) were thawed and analyzed for MDSC, CD4 T cells, and Treg by flow cytometry. Cytokines and chemokines were quantified in two repeated serum samples per subject using the next generation multiplex immunoassays.

Results: There was no statistically significant difference in overall MDSC percentage of PBMC nor in subtypes (PMN-MDSC, M-MDSC and e-MDSC) between cases and controls. There was also no difference found for Tregs. However, CD4 T cells were elevated in lung cancer cases and were associated with an increased risk of lung cancer overall (odds ratio [OR] = 2.61, 95% confidence interval [CI] = 0.73-9.32, p trend = 0.1409). Lung cancer cases had significantly higher levels of serum inflammatory cytokines IL-17A and Il-12/IL-23p40 at both early (median 84 months) and late time points (7 months prior to cancer diagnosis) (all *P*s < 0.05).

Conclusion: Lung cancer cases are associated with elevated levels of CD4 T cells and pro-inflammatory cytokines, specifically IL-17A and IL-12/IL-23p40, as early as 7 years before cancer diagnosis. The study has the potential to identify immune cells and soluble factors that mediate lung cancer development in smokers and could be used as early biomarkers for risk assessment or early diagnosis of lung cancer.

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Toxicity and Survival Outcomes From Intensity Modulated Proton Therapy-Based Re-Irradiation in Patients With Non-Small Cell Lung Cancer

P. Mohindra,[1,2] A. Saeed,[1] M.A.L. Vyfhuis,[2,3] K. Scilla,[4] J.K. Molitoris,[1,2] C.B. Simone, II[5,6] C. Rolfo,[7] and R. Mehra[4]; [1]*Department of Radiation Oncology, University of Maryland School of Medicine, Baltimore, MD,* [2]*Maryland Proton Treatment Center, Baltimore, MD,* [3]*Chesapeake Oncology Hematology Associates, Baltimore, MD,* [4]*Division of Medical Oncology, University of Maryland School of Medicine, Baltimore, MD,* [5]*New York Proton Center, New York, NY,* [6]*Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY,* [7]*Center for Thoracic Oncology, Icahn School of Medicine at Mount Sinai, New York, NY*

Purpose/Objective(s): Cumulative radiation doses to organs-at-risk is the primary limiting factor when delivering thoracic reirradiation (reRT). Intensity-modulated proton therapy (IMPT) offers a unique dosimetric advantage allowing for dose-escalation while limiting normal tissue irradiation. Given the limited published data, we analyzed toxicity and survival outcomes of non-small cell lung cancer (NSCLC) patients with prior radiation history undergoing IMPT-based definitive reRT.

Materials/Methods: A single-institution retrospective IRB-approved analysis was conducted of 62 consecutive patients treated with IMPT-reRT between from 2016-2020. Median dose of prior RT was 60.2 Gy EQD2 (range 30-126 Gy EQD2). Median time between initial and reirradiation courses was 30 months (range 3.5 − 562 months). Median IMPT-reRT dose was 62.2 Gy (RBE) EQD2 (range 40.1 − 99.7 Gy RBE EQD2). Patients received conventionally fractioned (n=37), twice-daily (n=6), or hypofractionated (n=19) reirradiation. The majority had full overlap with the previous radiation field (N=49, 79%), were centrally located (N=42, 58%), and involved nodal irradiation (N=47, 76%). Concurrent chemotherapy was delivered in 27 (44%) patients. Treatment related toxicities were analyzed in relationship to re-RT dosimetric parameters in 30 patients whose initial RT plan was available. Kaplan-Meier method and Cox Proportional Hazard was used to estimate overall survival (OS) and freedom from local progression (FFLP) calculated from the start of reRT.

Results: Grade 3 acute toxicities were seen in 6 (9%) patients (pulmonary [N=3], esophageal/skin/fatigue [N=1 each]). With a median follow-up from the start of reirradiation of 12.5 months, 8 (13%) patients experienced a grade 3 late toxicity (esophageal [N=4], pulmonary [N=3] and cardiac [N=1]). Two (3%) grade 5 toxicities were observed. None of the analyzed

dosimetric parameters (lung, heart, esophageal, target) correlated with grade 3 or more toxicity. CTV size greater than 150 cm^3 exhibited a trend of association with grade 3+ toxicity HR = 3.2 (95% CI: 0.88 − 12.1; p=0.08). Median FFLP was not reached and median OS was 22.6 months (95% CI, 16.5 − 22.1 months). On univariate analysis variables associated with improved OS were higher reirradiation dose, cumulative radiation dose >135 Gy, and smaller CTV (< 150 cc). However, on MVA only CTV size retained statistical significance (HR = 3.56; 95% CI, 1.10 − 11.48; p=0.03).

Conclusion: This is the largest series to date reporting outcomes for NSCLC patients treated with IMPT-reRT which demonstrated acceptable risk (<15%) of grade 3 or higher late toxicity with durable local control and prolonged survival. In contrast to limited published literature, no specific dosimetric parameters were significantly correlated with risk of toxicity.

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Impact of Mesothelioma Histologic Subtype and Use of Cancer-Directed Surgery on Outcomes in the National Cancer Database

A. Mansur, A. Potter, R. Meyerhoff, M. Lanuti, and C.F.J. Yang; *Massachusetts General Hospital, Boston, MA*

Purpose/Objective(s): To evaluate the impact of malignant pleural mesothelioma (MPM) histology subtype and the use of surgery on overall survival.

Materials/Methods: Multivariable Cox proportional hazards modeling and propensity score-matched analysis was performed to evaluate the overall survival of patients with stage I-IIIA MPM who underwent cancer-directed surgery or nonoperative management stratified by subtype of MPM. Patients who were coded in the National Cancer Database (NCDB) as not having undergone surgery because surgery "was contraindicated due to patient risk factors (comorbid conditions, advanced age, progression of tumor prior to planned surgery, etc.)" were excluded from analysis.

Results: Of 6,778 patients who had stage I−IIIA MPM during the study period, histologic subtype was epithelioid in 4,783 patients (70%), sarcomatoid in 1,060 patients (16%), and biphasic in 935 patients (14%). Median survival was 17 months in the epithelioid group, 5 months in the sarcomatoid group, and 11 months in the biphasic group ($P < 0.01$). Among patients who underwent surgery, median survival was 26 months in the epithelioid group, 9 months in the sarcomatoid group, and 15 months in the biphasic group ($P < 0.01$). In multivariable analysis, cancer-directed surgery was associated with improved survival in the epithelioid (adjusted hazard ratio [aHR] 0.75 [95% CI: 0.68-0.82]; $P < 0.01$) and biphasic (aHR 0.78 [95% CI: 0.64-0.95]; $P = 0.02$) groups but not in the sarcomatoid (aHR 0.82 [95% CI: 0.64-1.05]; $P = 0.11$) group, when compared to nonoperative management. Propensity-score matching was used to create 2 groups of 725, 109, and 174 patients with epithelioid, sarcomatoid, and biphasic MPM, respectively, each of whom received cancer-directed surgery or nonoperative management and were well-matched with regard to 12 common prognostic covariates including comorbidities, clinical stage, and T and N status. Surgery was associated with improved median survival in the epithelioid (21.9 months [95% CI: 20.1-23.9] vs. 16.8 months [95% CI: 15.4-17.8]; $P < 0.01$) and biphasic (12.2 months [95% CI: 11.3-14.6] vs. 10.7 months [95% CI: 9.5-11.9]; $P < 0.01$) groups but not in the sarcomatoid (7.8 months [95% CI: 6.2-11.7] vs. 6.9 months [95% CI: 6.0-7.9]; $P < 0.01$) group.

Conclusion: In this national analysis, we found that cancer-directed surgery is associated with significantly improved survival for stage I-IIIA MPM patients with epithelioid and biphasic histologies. Patients with sarcomatoid histology have poor prognosis and do not benefit from cancer-directed surgery. Our findings support current National Comprehensive Cancer Network (NCCN) guidelines recommending surgery for only epithelioid and biphasic histologies.

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Hot Spot Not Hot Enough? Differences in Local Control for Non-Small Cell Lung Cancer Treated With Stereotactic Body Radiotherapy Based on Maximum Point Dose within the Planning Target Volume

E.L. Braschi, A.N. De Leo, C.G. Morris, and A.R. Yeung; *Department of Radiation Oncology, University of Florida College of Medicine, Gainesville, FL*

Purpose/Objective(s): One of the defining characteristics of stereotactic body radiation therapy (SBRT) is the creation of a steep dose gradient, resulting in a higher dose centrally within the planning target volume (PTV) than at the periphery. However, there is no consensus regarding objectives for the maximum point dose delivered to the PTV. In this study, we investigated whether higher relative maximum doses within the PTV were associated with improved tumor control.

Materials/Methods: We performed a single-institution retrospective review of patients with early-stage, node-negative NSCLC who received curative-intent SBRT between 2005 and 2018. Patients with biopsy-proven NSCLC or presumed NSCLC based on radiographic findings were included. All patients underwent four-dimensional computed tomography (CT) for radiation planning and were treated with a free-breathing technique, utilizing an internal target volume (ITV) to account for tumor motion during the respiratory cycle. The PTV was defined as a 5-mm expansion from the ITV. We calculated the relative maximum dose to the PTV from a ratio of the maximum point dose delivered within the PTV to the prescription dose. We analyzed outcomes using the Kaplan-Meier method and used a log-rank test to assess prognostic impact.

Results: The study population consisted of 175 patients and 186 individual lung nodules with a median follow-up time of 2.6 (range, 0.1 − 12) years for all patients and 3.5 (range, 0.2 − 8.4) years for living patients. The median age was 70.2 (range, 43 − 90) years, and the median maximum tumor diameter was 1.9 (range, 0.7 − 5.6) cm. Most tumors were peripheral with only 9.7% (n=18) centrally located. The median prescription dose was 50 (range, 48 − 62.5) Gy in 5 (range, 4-10) fractions. The median relative maximum dose delivered to the PTV was 110%. Among the entire cohort, the 3-year rates (95% CI) of local control (LC), cause-specific survival, and overall survival were 81.0% (73.8% − 86.5%), 72.4% (64.5 − 79.1%), and 48.3% (40.7% − 55.9%), respectively. The 3-year rate of LC was superior among patients treated with a maximum point dose ≥ 110% vs. < 110% (86% vs. 74%, p=0.03). The difference in 3-year LC was more pronounced between a maximum point dose ≥ 120% vs. < 120% (94% vs. 79%, p = 0.05). The maximum point dose was significant for LC on multivariate analysis (p = 0.03).

Conclusion: Patients with early-stage NSCLC treated with SBRT with a relative maximum dose in the PTV of at least 110% demonstrated improved local control. Thus, more homogeneous SBRT plans may compromise the ablative treatment. Further studies should clarify specific objectives for the maximum point dose delivered to the PTV.

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FLT-PET/CT in Non-Small Cell Lung Cancer Treated With SBRT- A Pilot Study

S.C. Lewis,[1,2] A.J. Hope,[3] M. Chan,[4] J. Weiss,[5] H. Raziee,[1] A. Bezjak,[6] J. Cho,[7] A. Sun,[1] B.H. Lok,[8] S. Raman,[1] J.P. Bissonnette,[9] D. Vines,[10] and M.E. Giuliani[1]; [1]*Department of Radiation Oncology, University of Toronto,*

Toronto, ON, Canada, [2]Radiation Medicine Program, Princess Margaret Cancer Centre, Toronto, ON, Canada, [3]Department of Radiation Oncology, Princess Margaret Cancer Center/University of Toronto, Toronto, ON, Canada, [4]Princess Margaret Cancer Centre, Toronto, ON, Canada, [5]Department of Radiation Oncology, University of Toronto,, Toronto, ON, Canada, [6]Radiation Medicine Program, Princess Margaret Cancer Center, University of Toronto, Toronto, ON, Canada, [7]Radiation Medicine Program, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, [8]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, [9]University of Toronto, Toronto, ON, Canada, [10]Radiation Medicine Program, Princess Margaret Cancer Centre, Toronto, ON, Canada

Purpose/Objective(s): To prospectively assess the value of FLT-PET in differentiating tumor recurrence from radiation-induced lung fibrosis. The primary objective was to compare FLT uptake in three cohort of patients: 1) before SBRT, 2) stable lung fibrosis after SBRT, and 3) suspicious/proven local recurrence. The secondary objective was to optimize FLT PET imaging sequences for lung cancer patients and compare FLT uptake in 4D (respiratory sorted) versus free-breathing FLT-PET scans.

Materials/Methods: Early-stage (T1-2N0M0 or T3N0M0 limited to the chest wall as per 7th edition American Joint committee on cancer staging manual) presumed or biopsy-proven non-small cell lung carcinoma, aged more than 18 years and planned for SBRT at the institution or followed up after SBRT with radiographic findings of fibrosis or recurrence were considered eligible for the study. Patients were assigned to one of three study cohorts. All patients underwent imaging with FLT PET CT- prior to SBRT in cohort 1 and at fibrosis or recurrence in cohort 2 and 3. The planned sample size was 20 patients in each cohort, 60 patients in total. The FLT PET SUV variables like SUV max, SUV mean, SUV2Dpeak, SUV3Dpeak, SUV 50 and SUV95 were compared between the three cohorts using Kruskal Wallis test. The correlation of 4D phased matched and 3D PET SUV variables was performed using spearman correlation coefficient. Statistical significance was set at $p<0.05$.

Results: Forty one patients were accrued in the study (20 in cohort 1, 16 in cohort 2 and 5 in cohort3). The median age of the entire cohort was 77 years (range 46-89). Majority were diagnosed with stage I lung cancer (86%) and 48Gy in 4 fractions was the most commonly used dose fractionation (59%). A 4D FLT PET was performed in 35 patients. There was no significant difference in the FLT uptake SUV variables between 4D (respiratory sorted) versus free-breathing scans (r=0.8-1). Using the 3D FLT PET information, SUV peak, SUV mean, SUV max were significantly lower in fibrosis cohort compared to recurrence and pretreatment cohorts (Table 1). The delayed FLT PET values SUV 50 and 95 values in recurrence cohort were significantly similar to pretreatment cohort and significantly different compared to fibrosis.

Conclusion: FLT PET may be helpful in differentiating SBRT related fibrosis from recurrence. This study was limited by the small sample size in recurrence cohort and larger validation studies are needed to ascertain utility of FLT PET to confirm the findings.

Abstract 7 - Table 1 3D FLT PET SUV Variables Across the Cohorts

Variable	Cohort 1 (n=20)	Cohort 2 (n=16)	Cohort 3 (n=5)	P value
SUV 3D peak				
Median(Range)	2.5 (0.9-6.1)	1.7 (0.8-3.9)	2.8 (1-6)	0.015
SUV mean				
Median(Range)	1.7 (0.7-3.4)	1.1 (0.7-1.5)	1.6 (1.1-2.3)	0.0011
SUV max				
Median(Range)	3 (1.1-7)	2 (0.8-4.1)	3.7 (1.7-7.6)	0.0093
SUV95				
Median(Range)	2.8 (1-5.8)	1.6 (0.8-2.8)	2.8 (1.4-3.8)	0.0019

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Comparison of National Comprehensive Cancer Network and American College of Surgeons Commission on Cancer Lymph Node Sampling Guidelines for Non-Small Cell Lung Cancer

B. Heiden,[1,2] D. Eaton,[3] S.H. Chang,[2,3] Y. Yan,[2,3] M. Schoen,[3,4] B. Meyers,[1] B. Kozower,[1] and V. Puri[1,3]; *[1]Division of Cardiothoracic Surgery, Department of Surgery, Washington University School of Medicine, St. Louis, MO, [2]Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, St. Louis, MO, [3]VA St. Louis Health Care System, St. Louis, MO, [4]Division of Hematology and Medical Oncology, Department of Internal Medicine, Saint Louis University School of Medicine, St. Louis, MO*

Purpose/Objective(s): Current guidelines conflict regarding adequate lymph node sampling during lung cancer surgery. The National Comprehensive Cancer Network (NCCN) guidelines recommend sampling at least 3 N2 and 1 N1 stations while the American College of Surgeons Commission on Cancer (CoC) guidelines recommend sampling at least 10 total lymph nodes. We sought to compare these guidelines in a cohort of Veterans with clinical stage I non-small cell lung cancer (NSCLC).

Materials/Methods: We performed a retrospective cohort study using a uniquely compiled dataset from the Veterans Health Administration (VHA) consisting of adults with clinical stage I NSCLC receiving surgery (2006-2016). We assembled a team of researchers who extracted lymph node sampling information from pathology reports and operative notes over a period in excess of 20 months. We defined sampling adequacy based on current guidelines from the NCCN ($\geq$3 N2 + 1 N1 station) and CoC ($\geq$10 lymph nodes). Our primary outcomes of interest were pathologic upstaging, disease-free survival, and overall survival.

Results: A total of 9575 patients were included in the current study. Of these, 3556 (37.1%) patients met NCCN guidelines and 3250 (33.9%) patients met CoC guidelines. Upstaging was observed in 1236 (12.9%) individuals. Adherence to either NCCN (adjusted odds ratio [aOR] 1.299, 95% CI 1.130-1.492) or CoC (aOR 1.637, 95% CI 1.425-1.881) guidelines was associated with higher likelihood of upstaging. With a median follow-up of 6.14 years, recurrence was observed in 2260 (23.6%) patients. While adherence to NCCN guidelines was associated with lower risk of recurrence (adjusted hazard ratio [aHR] 0.867, 95% CI 0.785-0.958), adherence to CoC guidelines was not associated with disease recurrence (aHR 0.928, 95% CI 0.839-1.028). Adherence to NCCN (aHR 0.932, 95% CI 0.874-0.994) or CoC (aHR 0.931, 95% CI 0.871-0.996) guidelines were associated with improved overall survival.

Conclusion: These data suggest that adherence to NCCN sampling guidelines may mitigate the risk of recurrence in clinical stage I NSCLC. Improving adherence to either guideline, however, may significantly improve long-term survival in patients with clinical stage I NSCLC undergoing surgical treatment.

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Tepotinib in Patients with Advanced NSCLC with *MET* Amplification (*MET*amp)

X. Le,[1] R. O'Hara,[2] L. Paz-Ares,[3] J.P. Van Meerbeeck,[4] S. Viteri Ramirez,[5,6] C. Cabrera Galvez,[7] D. Vincente Baz,[8] Y.C. Kim,[9] J.H. Kang,[10] K.M. Schumacher,[11] N. Karachaliou,[11] S. Adrian,[11] R. Bruns,[12] and P. Paik[13,14]; *[1]Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, [2]EMD*

Serono, Inc., Rockland, MA, [3]Hospital Universitario 12 de Octubre - Servicio de Oncologia, Madrid, Spain, [4]Antwerp University Hospital (UZA), Antwerp, Belgium, [5]Instituto Oncológico Dr. Rosell, Hospital Universitario Dexeus, Grupo Quironsalud, Barcelona, Spain, [6]UOMI cancer center, Clínica Mi NovAliança, Lleida, Spain, [7]Hospital Universitari Sagrat Cor, Barcelona, Spain, [8]Hospital Universitario Virgen Macarena - Servicio de Oncologia, Seville, Spain, [9]Chonnam National University Hwasun Hospital, Hwasun-Gun, Korea, Republic of (South), [10]The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, Korea, Republic of (South), [11]Global Clinical Development, the healthcare business of Merck KGaA, Darmstadt, Germany, [12]Department of Biostatistics, the healthcare business of Merck KGaA, Darmstadt, Germany, [13]Weill Cornell Medical College, New York, NY, [14]Thoracic Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, NY

Purpose/Objective(s): *MET*amp, an oncogenic driver occurring in 1−5% of NSCLC cases, confers a poor prognosis and lacks approved targeted therapies. Tepotinib, a highly selective MET inhibitor, provided durable response in advanced NSCLC with *MET* exon 14 (*MET*ex14) skipping in VISION Cohort A. VISION Cohort B evaluated tepotinib in patients with advanced NSCLC and *MET*amp, as detected by a convenient and minimally invasive liquid biopsy (LBx) assay.

Materials/Methods: Patients with advanced NSCLC, ECOG PS 0−1, 0−2 prior therapy lines, *EGFR*/*ALK* wild-type status, no *MET*ex14 skipping, and *MET*amp by LBx (*MET* gene copy number ≥2.5) received oral tepotinib 500 mg QD (450 mg active moiety). Primary endpoint was objective response rate (ORR) (RECIST v1.1) by independent review committee (IRC). Duration of response (DOR), progression-free survival (PFS), and safety were secondary endpoints. The data cut-off was July 1, 2020.

Results: Of 24 enrolled patients, the median age was 63.4 years (range 38 −73), 21 patients were male (88%), 21 had ECOG PS 1, and 21 were smokers. Seven patients (29%) received tepotinib in first line (1L), 10 (42%) in second line (2L), and seven patients in third line (3L). As of November 2020, treatment was ongoing for >1 year in five patients (1L, n=2; 2L, n=2; 3L, n=1). The ORR was 42% (10/24 patients) overall, 71% (5/7) in 1L, 30% (3/10) in 2L and 29% (2/7) in 3L (Table). The median DOR was not estimable (NE). Five patients (20.8%) discontinued due to adverse events (AEs) considered unrelated to tepotinib. 16 patients reported treatment-related AEs (67%; Grade 3/4 in seven patients [29%]), including peripheral edema (nine patients [38%]; Grade 3/4 in two [8%]), generalized edema (four patients [17%]; Grade 3/4 in two [8%]), and constipation (four patients [17%]; none with Grade 3/4).

Conclusion: In the first study of a MET inhibitor in advanced NSCLC with *MET*amp prospectively detected by LBx, tepotinib had high and clinically meaningful activity, especially in 1L, and was generally well tolerated. Tepotinib warrants further evaluation in advanced NSCLC with *MET*amp.

Abstract 9 - Table 1

Endpoints by IRC	Overall (n=24)	1L (n=7)	2L (n=10)	3L (n=7)
Best overall response, n (%) Partial responses Stable disease Progressive disease Not evaluable	10 (42) 1 (4) 5 (21) 8 (33)	5 (71) 0 1 (14) 1 (14)	3 (30) 1 (10) 2 (20) 4 (40)	2 (29) 0 2 (29) 3 (43)
ORR, n (%) [95 CI]	10 (42)	5 (71)	3 (30)	2 (29)
	[22, 63]	[29, 96]	[7, 65]	[4, 71]
DOR 9-month event-free rate, % (95% CI) Median, months (95% CI)	67	60	100	NE
	(28, 88) NE	(13, 88) NE	(NE, NE) NE	(NE, NE) NE
	(2.8, NE)	(2.8, NE)	(NE, NE)	(3.2, NE)
PFS 9-month event-free rate, % (95% CI) Median, months (95% CI)	40	51	58	NE
	(19, 61) 4.2	(12, 81) NE	(18, 84) NE	(NE, NE) 1.4
	(1.4, NE)	(1.4, NE)	(1.0, NE)	(0.6, 4.5)

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Prospective Evaluation of Limited Stage Small Cell Lung Cancer (LS-SCLC) Fractionation Regimen Usage and Toxicity in a Large Statewide Quality Collaborative

S.G. Allen,[1] A.F. Dragovic,[1] H. Yin,[2] A.K. Bryant,[1] P. Paximadis,[3] M.M. Matuszak,[1] M. Schipper,[4] R.T. Dess,[1] J.A. Hayman,[1] M.M. Dominello,[5] L.L. Kestin,[6] I.S. Grills,[7] B. Movsas,[8] S. Jolly,[1] and D.P. Bergsma[1]; *[1]Department of Radiation Oncology, University of Michigan, Ann Arbor, MI, [2]University of Michigan, Ann Arbor, MI, [3]Department of Radiation Oncology, Spectrum Health Lakeland, St. Joseph, MI, [4]Department of Biostatistics, University of Michigan, Ann Arbor, MI, [5]Department of Radiation Oncology, Barbara Ann Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI, [6]Michigan Healthcare Professionals, 21st Century Oncology, Farmington Hills, MI, [7]Department of Radiation Oncology, Beaumont Health, Royal Oak, MI, [8]Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI*

Purpose/Objective(s): National guidelines on LS-SCLC treatment give preference to a hyperfractionated regimen of 45 Gy in 30 fractions (Fx) delivered twice-daily (BID) but allow for daily fractionation (QD) to 60-70 Gy in certain circumstances. Use of the BID regimen has been reportedly low, however this is based upon small retrospective series, national databases that lack radiation treatment specifics, or survey data. We sought to characterize the fractionation regimens used to treat LS-SCLC in actual practice across academic and community settings and analyze factors associated with fractionation and toxicity.

Materials/Methods: As part of a quality improvement initiative, the Michigan Radiation Oncology Quality Consortium prospectively collects clinical, dosimetric, and physician- and patient-reported outcomes data from patients treated for lung cancer at 29 institutions, which represent about 60% of the radiation oncology volume in the state. Between 2012 and 2021, 3,962 lung cancer cases were enrolled. Of those, 680 (17%) had SCLC histology and the 502 patients with LS-SCLC and known fractionation regimen represent the population studied here.

Results: Among the 502 LS-SCLC patients, 98% were current or former smokers (50 pack-year mean) and 98% received chemotherapy. In total, 73 (15%) were treated BID to a median dose of 45 Gy / 30 Fx (IQR same) and 429 (85%) were treated QD to a median dose of 60 Gy / 30 Fx (IQR 60-64.8 Gy / 30-36 Fx). The proportion of patients treated BID did not vary by practice setting or demographics except those treated BID were significantly more likely to be married or living with someone (64% vs 51%, p=0.035). There was no difference between the groups in baseline

clinical factors such as performance status, weight loss, comorbidities, or pulmonary function. QD treated patients were more likely to experience a treatment break due to toxicity (24% vs 6%, p<0.01) despite no differences in physician-reported toxicity or patient-reported swallowing difficulty at the end of treatment. However, BID treated patients did report twice the rate of difficulty swallowing solids at 1 month (42% vs 19%, p<0.01).

Conclusion: Despite evidence in its favor, the twice-daily fractionation regimen for LS-SCLC remains infrequently prescribed (15%) in a large multicenter prospectively collected cohort. BID treated patients were more likely to be married or living with someone, perhaps relating to the logistic burden of BID treatment. Despite similar end of treatment toxicity, QD treated patients had more treatment breaks. However, BID treated patients had twice the rate of swallowing difficulty at 1 month suggesting BID toxicity may peak later than QD toxicity, which is consistent with prior reports. Analysis of late toxicity, chemotherapy specifics, and additional physician- and patient-reported outcomes is ongoing.

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Impact of Cardiac Dose on Overall Survival in Lung Stereotactic Body Radiotherapy (SBRT) Compared to Conventionally Fractionated Radiotherapy for Locally Advanced Non-Small Cell Lung Cancer (LA-NSCLC)

J. Anderson,[1] M. Fatyga,[2] S.E. Schild,[3] J. Li,[4] and J. Hu[5]; *[1]Department of Radiation Oncology, Mayo Clinic, Phoenix, AZ, [2]Department of Radiation Oncology, Mayo Clinic Arizona, Phoenix, AZ, [3]Mayo Clinic Arizona Department of Radiation Oncology, Phoenix, AZ, [4]Georgia Institute of Technology, Atlanta, GA, [5]Arizona State university, Tempe, AZ*

Purpose/Objective(s): To examine possible association between heart irradiation and overall survival (OS) in lung SBRT patients and to compare observed associations with cardiac toxicity models previously derived in LA-NSCLC patient studies.

Materials/Methods: 197 Patients treated with lung SBRT at Mayo Clinic Arizona were selected for this IRB approved study. Multivariate Cox model with Akaike Information Criterion (AIC) was used to select patient specific covariates associated with OS. Heart dosimetry was represented by indices, which is a percentage of volume exposed to dose D or greater. A multivariate Cox models with patient specific covariates and single index per model was used to find a range of doses which were predictive for OS. A digital subdivision of the heart was further used to determine spatial distribution of doses which were predictive for OS. A coarse subdivision divided hearts into 4 segments, while fine subdivision divided hearts into 64 segments. Knowledge constrained Fused Lasso operator was used to derive a more complete model which correlated heart dosimetry with OS. Results of statistical analysis were compared to predictions of a model of cardiac toxicity in LA-NSCLC patients.

Results: Higher age (p<0.001), higher stage (p<0.001) and squamous cell histology (p=0.001) were associated with reduced OS. Whole heart DVH analysis did not reveal associations between heart irradiation and reduced OS. Coarse subdivision of the heart into four segments revealed that the irradiation of two inferior segments of the heart with low doses was associated with reduced OS, in the right-inferior segment (HR = 1.012/1%, p=0.02), and in the left-inferior segment (HR = 1.01/1%, p=0.04). Maximum dose in the right-inferior segment of the heart was also associated with reduced OS (HR = 1.02/Gy, p=0.02). Fine subdivision of the heart into 64 segments revealed that approximately 25% of heart volume in the inferior part of the heart (15/64 segments), when irradiated to doses in the 1Gy − 5Gy range, were predictive for reduced OS (HR=1.01/1%, p=0.01). A previously derived model of cardiac toxicity in LA-NSCLC patients did not predict a reduction of OS due to heart irradiation in lung SBRT patients, because of relatively low doses to the heart in most lung SBRT patients.

Conclusion: Doses lower than 5Gy in the inferior segments of the heart may be associated with reduced overall survival in patients treated for lung lesions with SBRT. Stage and histology of the disease, as well as patients age, were also associated with overall survival. Comparisons of cardiac toxicity patterns in LA-NSCLC patients and lung SBRT patients suggest different etiology of cardiac toxicity in the two groups.

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Poster Q&A Sessions

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Effect of Antibiotic Therapy on Immunotherapy Outcomes for Non-Small Cell Lung Cancer: Analysis From the Veterans Health Administration

W.A. Stokes,[1,2] M. Behera,[1] R. Jiang,[1] D.A. Gutman,[3] Z. Huang,[1] A. Burns,[3] N. Sebastian,[2] V.V. Sukhatme,[4] M. Lowe,[1,5] S. Ramalingam,[1,6] V.P. Sukhatme,[4] and D. Moghanaki[7]; *[1]Winship Cancer Institute of Emory University, Atlanta, GA, [2]Department of Radiation Oncology, Emory University School of Medicine, Atlanta, GA, [3]Atlanta Veterans Affairs Health Care System, Decatur, GA, [4]Morningside Center for Innovative and Affordable Medicine, Emory University, Atlanta, GA, [5]Division of Surgical Oncology, Emory University School of Medicine, Atlanta, GA, [6]Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, GA, [7]Department of Radiation Oncology, University of California at Los Angeles, Los Angeles, CA*

Purpose/Objective(s): Dysregulation of gut microbiota induced by antibiotic therapy (Abx) may alter the anticancer immune response. Multiple small studies have associated Abx use with inferior outcomes in patients with non-small cell lung cancer (NSCLC) who were treated with immune checkpoint inhibitors (ICI). We investigated this association in a larger population of patients treated with ICI within the Veterans Health Administration.

Materials/Methods: We conducted a nested cohort study of Veterans diagnosed with NSCLC between 2010-2018 and treated with ICI. Abx exposure was defined as receipt of an Abx prescription within a window extending from 30 days before to 30 days after first ICI administration. Overall survival (OS), measured from start of ICI, was compared. Cox proportional hazard multivariate analysis (MVA) was used to identify factors associated with OS. A separate cohort of Veterans with stage IV NSCLC who received docetaxel without ICI was similarly analyzed.

Results: 3,634 Veterans received ICI, mostly nivolumab (59.1%) or pembrolizumab (35.1%), with a median age of 69, male gender in 97.0%, white race in 73.0%, adenocarcinoma in 47.8%, and stage IV disease at diagnosis in 40.9%. In this nested cohort, 1,240 (34.1%) were exposed to Abx, with beta-lactams (30.1% of Abx recipients) the most common agent. Abx receipt was associated with male gender, greater comorbidity burden, and non-receipt of chemotherapy (all $p \leq 0.044$). Abx were associated with worse OS on MVA (HR 1.38, 95%CI 1.27-1.49, $p<0.001$) and in a propensity-

matched matched subset (HR 1.37, 95%CI 1.26-1.50, $p<0.001$). Among 764 Veterans with stage IV disease receiving docetaxel, Abx were also associated with worse OS on MVA (HR 1.26, 95%CI 1.11-1.44, $p<0.001$) and in a propensity-score matched subset (HR 1.22, 95%CI 1.07-1.40, $p=0.004$). In a *post-hoc* pooled analysis of the 1,681 Abx-exposed Veterans from the ICI and stage IV docetaxel cohorts, ICI receipt was associated with worse OS as compared to docetaxel receipt (HR 1.15, 95%CI 1.00-1.31, $p=0.044$); no such difference was observed in a pooled analysis of 2,910 unexposed Veterans (HR 0.99, 95%CI 0.88-1.12, $p=0.904$). However, a test for heterogeneity of Abx effect by ICI/docetaxel did not attain statistical significance (interaction $p=0.062$).

Conclusion: Abx are associated with worse OS among NSCLC patients receiving either ICI or cytotoxic chemotherapy; however, this decrement appears larger among ICI recipients. These findings suggest Abx may have a detrimental effect on immunotherapy outcomes.

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Plasma Cell-Free RNA PD-L1 Expression and Clinical Outcomes With Immunotherapy

S. Jayananda, M. Muzaffar, P. Namireddy, N. Sharma, and P. Walker; *East Carolina University, Greenville, NC*

Purpose/Objective(s): Programmed death ligand-1 (PD-L1) expression is predictive of immunotherapy benefit. However, tissue PD-L1 protein immunohistochemical testing can be fraught with tissue acquisition and heterogeneity limitations. PD-L1 expression by RNA sequencing can be performed by both tissue and plasma with tissue PD-L1 protein correlations. What has not been well characterized is the correlation of plasma cfRNA PD-L1 and clinical outcomes with immunotherapy. Plasma cfRNA PD-L1 expression was evaluated and correlated with immunotherapy benefit in advanced non-small cell lung cancers (NSCLC).

Materials/Methods: Patients with advanced NSCLC undergoing plasma next-generation sequencing including plasma cfRNA PD-L1 testing in a CLIA and CAP accredited laboratory were retrospectively identified and evaluated at a single institution. Plasma PD-L1 positive patients underwent a de-identified chart abstraction to identify those patients with advanced NSCLC treated with front line immunotherapy regimens and those who received cytotoxic chemotherapy alone.

Results: 16 patients with plasma PD-L1 expression treated with front line immunotherapy regimens including single-agent immune checkpoint inhibitors and combinatorial chemo-immune or chemo-immune-bevacizumab regimens, were assessed for overall survival (OS). 11 patients with plasma PD-L1 expression who received chemotherapy alone were identified and evaluated as a non-immunotherapy OS comparison. Median OS for the immunotherapy treated patients was 13 months with a 30% 3-year landmark OS versus 4 months median OS and a 10% 3-year landmark OS for those treated with chemotherapy alone. Comparative log-rank test p-value 0.0091 and a hazard ratio of 0.36 (95%-CI 0.13-0.99).

Conclusion: Plasma cfRNA PD-L1 expression is predictive of a statistically significant survival benefit from immunotherapy treatment compared to chemotherapy in the first line treatment of advanced NSCLC. The 3-year landmark OS of 30% parallels tissue PD-L1 directed immunotherapy-based treatment outcomes. The clinical utility of plasma cfRNA PD-L1 to overcome tissue acquisition and PD-L1 protein heterogeneity limitations and to study the dynamic nature of PD-L1 expression with non-immune cancer treatments and potential immunotherapy response monitoring are undergoing ongoing research.

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DREAM3R: DuRvalumab With chEmotherapy as First Line treAtment in Advanced Pleural Mesothelioma: A Phase 3 Randomised Trial

P. Forde,[1] H. Kindler,[2] M. Zauderer,[3] Z. Sun,[4] S. Ramalingam,[5] V. Anagnostou,[6] J.R. Brahmer,[7] A.K. Nowak,[8] P.S. Kok,[9] C. Brown,[9] S. Yip,[9] A. Cook,[10] W.J. Lesterhuis,[11] B.G.M. Hughes,[12] N. Pavlakis,[13] M.R. Stockler,[14] and K.J. O'Byrne[15]; *[1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]University of Chicago, Chicago, IL, [3]Memorial Sloan Kettering Cancer Center, New York, NY, [4]ECOG-ACRIN Biostatistics Center, Frontier Science Foundation, Boston, MA, [5]Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, GA, [6]Bloomberg-Kimmel Institute for Cancer Immunotherapy, Johns Hopkins, Baltimore, MD, [7]Department of Oncology, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, [8]Medical School, University of Western Australia, Perth, WA, Australia, [9]NHMRC Clinical Trials Centre, University of Sydney, Sydney, NSW, Australia, [10]National Centre for Asbestos Related Diseases, University of Western Australia; Medical School, University of Western Australia, WA, WA, Australia, [11]National Centre for Asbestos Related Diseases, University of Western Australia, WA, WA, Australia, [12]University of Queensland, Brisbane, QLD, Australia, [13]Royal North Shore Hospital, Sydney, NSW, Australia, [14]University of Sydney, Sydney, Australia, [15]Princess Alexandra Hospital and Queensland University of Technology, Queensland, QLD, Australia*

Purpose/Objective(s):

- Platinum-based chemotherapy with pemetrexed is an appropriate first line treatment option for unresectable malignant pleural mesothelioma (MPM)
- The DREAM[1] and PrE0505[2] Phase II trials combined durvalumab (PD-L1 inhibitor) with a platinum and pemetrexed both exceeding prespecified response with acceptable toxicity
- CheckMate 7433 recently reported an overall survival benefit with ipilimumab plus nivolumab vs. chemotherapy (HR 0.74, 95% CI 0.50 to 0.91). However, this benefit was less apparent in the 75% of patients with epithelioid histology (HR 0.86, 95% CI 0.69 to 1.08)
- Clinical trials to further explore optimal first line treatment for MPM with immunotherapy are needed

Materials/Methods: International, open label, randomised (2:1), multicentre, phase 3 trial

- 480 patients (320 durvalumab and chemotherapy, 160 chemotherapy) to be recruited over 27 months and followed for another 24 months
- This provides over 85% power if the true hazard ratio for overall survival is 0.70 with 2-sided alpha of 0.05, assuming a median survival of 15 months in the chemotherapy group, 21.4 months in the durvalumab and chemotherapy group, with an allowance for crossover

Results: TBD

Conclusion: TBD

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Salvage Radiosurgery for Recurrent Cardiac Sarcoma: A Case Report

S.N. Shah,[1] W. Knotts,[2] and S.A. Shah[1]; [1]*Christiana Care Health System, Newark, DE,* [2]*Christiana Care, Newark, DE*

Purpose/Objective(s): Primary cardiac sarcoma is a rare malignant tumor that arises from the cardiac myocardium. Surgical resection is the standard of care and median survival after a R0 resection is typically 6 to 12 months. However, after local recurrence, patients are frequently inoperable with a poor prognosis. The role of salvage chemotherapy and radiation is not well defined. A few case reports have described local control for up to eight months after hypo-fractionated radiosurgery.

Materials/Methods: A 53 year old female presented in October 2017 with acute congestive heart failure and underwent complete surgical resection of undifferentiated pleomorphic sarcoma of the left atrium followed by 6 cycles of adjuvant doxorubicin/hydroxydaunorubicin and ifosfamide. An MRI scan demonstrated an asymptomatic, 24 mm, recurrent atrial mass. The patient elected to proceed with salvage frameless robotic radiosurgery system stereotactic body radiosurgery. We fused CT, MRI, and PET imaging modalities in order to determine the target volume. The tumor was treated with a dose of 7200 cGy in 15 fractions to the 84% isodose line utilizing spine tracking with 4D CT to determine the ITV. Fractionation was used in order to achieve acceptable maximal doses to the main stem bronchus and esophagus. Repeat cardiac MRI at four weeks showed in-field local progression with greater protrusion into the left atrium. The tumor volume doubled in size with invasion of the left ventricle. The patient elected to proceed with salvage frameless robotic radiosurgery system treatment. 2500 cGy in 1 fraction was prescribed to the 76% isodose line in June of 2019.

Results: She tolerated treatment well without any acute toxicity. The patient was subsequently treated with a variety of chemotherapy regimens including TKIs and immunotherapy. Unfortunately, the patient relapsed in December with metastases in the spine and the pelvis. She underwent palliative radiation therapy to multiple bony sites with a partial response. She resumed chemotherapy treatment with TKIs but passed away in June 2020 due to septic shock without evidence of local failure.

Conclusion: Fractionated SBRT was ineffective at controlling our patient's cardiac sarcoma. Our patient demonstrated local control of disease at twelve months after salvage 25 Gy in one fraction radiosurgery without any evidence of cardiac toxicity. High dose single fraction radiosurgery is a reasonable palliative option for long term local control of unresectable cardiac sarcomas.

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Surgical Outcomes for Early-Stage Non-Small Cell Lung Cancer at Facilities With Stereotactic Body Radiation Therapy Programs

Y.A. Syed,[1] W.A. Stokes,[2] M. Rupji,[3] Y. Liu,[4] O. Khullar,[5] N. Sebastian,[2] K.A. Higgins,[6] J.D. Bradley,[7] W.J. Curran, Jr[6] S. Ramalingam,[8] J. Taylor,[9] M. Sancheti,[5] F. Fernandez,[2] and D. Moghanaki[10]; [1]*Winship Cancer Institute, Emory University, Atlanta, GA,* [2]*Winship Cancer Institute of Emory University, Atlanta, GA,* [3]*Biostatistics and Bioinformatics Shared Resource, Winship Cancer Institute, Emory University, Atlanta, GA,* [4]*Department of Biostatistics and Bioinformatics, Rollins School of Public Health, Emory University, Atlanta, GA,* [5]*Department of Surgery, Emory University School of Medicine, Atlanta, GA,* [6]*Department of Radiation Oncology, Winship Cancer Institute of Emory University, Atlanta, GA,* [7]*Emory University, Atlanta, GA,* [8]*Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, GA,* [9]*Department of Radiation Oncology, Sidney Kimmel Medical College & Cancer Center at Thomas Jefferson University, Philadelphia, PA,* [10]*Department of Radiation Oncology, University of California at Los Angeles, Los Angeles, CA*

Purpose/Objective(s): Patients undergoing surgery for early-stage non-small cell lung cancer (NSCLC) may be at high-risk for post-operative mortality. Access to stereotactic body radiation therapy (SBRT), a less invasive alternative, may facilitate more appropriate patient selection for surgery.

Materials/Methods: An analysis of all patients with early-stage NSCLC reported to the National Cancer Database between 2004-2015 was performed. Post-operative mortality rates were derived using vital status data. Utilization of SBRT was defined by each facility's SBRT Experience in years and SBRT-to-Surgery Volume Ratios, defined by quartiles. Multivariable logistic regression with backward elimination was used to test for the associations between facility-level SBRT utilization and post-operative mortality. Interaction testing of independent covariates was performed to assess the effect of SBRT utilization across subgroups.

Results: The study cohort consisted of 202,542 patients who underwent surgical resection of clinical stage T1-T2 N0 M0 NSCLC between 2004-2015. The 90-day post-operative mortality rate declined significantly during the study period from 4.6% to 2.6% ($p < 0.001$). During this period, the proportion of facilities that utilized SBRT increased from 4.6% to 77.5% ($p < 0.001$) and the proportion of patients treated with SBRT increased significantly from 0.7% to 15.4% ($p < 0.001$). On multivariable analysis, lower 90-day post-operative mortality rates were observed among patients who underwent resection at facilities with greater than six years of SBRT Experience (OR 0.84, CI 0.76-0.94, $p = 0.003$) and SBRT-to-Surgery Volume Ratios above 17% (OR 0.85, CI 0.79-0.92, $p < 0.001$). Additional covariates associated with 90-day mortality included higher surgical volume, geographic region, year of diagnosis, age, sex, race, insurance status, facility type, Charlson-Deyo score, clinical T stage, histology, anatomic location, surgery type, and prior malignancy. Interaction testing between these covariates was negative, demonstrating that findings were consistent across subgroups.

Conclusion: Patients who underwent surgical resection for early-stage NSCLC at facilities with higher SBRT Experience and SBRT-to-Surgery Volume Ratios had lower rates of post-operative mortality. These findings suggest that the availability of SBRT may improve allocation of patients to surgery or SBRT, particularly for higher-risk patients. The observation of higher post-operative mortality rates at facilities without an SBRT program merits further investigation.

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Accounting for Operability Status in Retrospective Comparisons of Surgery vs. SBRT for Early-Stage NSCLC

J. Lorenz,[1] D. Moghanaki,[2] H. Keshava,[3] D.H. Harpole,[4] J.D. Bradley,[5] K.A. Higgins,[6] C.G. Rusthoven, Jr[7] and W.A. Stokes[8]; *[1]Winship Cancer Institute, Department of Radiation Oncology, Emory University, Atlanta, GA, [2]Atlanta Veterans Affairs Health Care System, Atlanta, GA, [3]University of California Irvine, Irvine, CA, [4]Duke School of Medicine, Durham, NC, [5]Emory University, Atlanta, GA, [6]Department of Radiation Oncology, Winship Cancer Institute of Emory University, Atlanta, GA, [7]Department of Radiation Oncology, University of Colorado School of Medicine, Aurora, CO, [8]Winship Cancer Institute of Emory University, Atlanta, GA*

Purpose/Objective(s): Patients receiving stereotactic body radiotherapy (SBRT) for early-stage non-small cell lung cancer (NSCLC) are typically inoperable, in concordance with consensus guidelines that advocate surgical resection as standard of care for operable patients. This differential treatment allocation complicates retrospective comparisons of surgery with SBRT by introducing the potential for confounding by operability. Accounting for operability status in these comparisons offers one solution to mitigate this source of bias; however, it is unknown what proportion of published analyses do so. We conducted a meta-research study to characterize whether published retrospective series comparing surgery with SBRT for ES- NSCLC account for operability status.

Materials/Methods: We queried PubMed for manuscripts reporting primary data from retrospective comparisons of overall survival (OS) between patients undergoing surgery versus SBRT for early-stage NSCLC. There were two outcomes of interest: (1) whether the manuscript reported whether allocation to SBRT was based on a determination of patient operability; and (2) whether each manuscript reported a direct OS comparison between operable SBRT patients and surgically-treated patients. χ^2 analysis was used to measure associations between outcomes and categorical variables of interest, including temporal (year of publication), journal-specific (specialty focus, impact factor), cohort-specific (nationality, source), and author-specific (specialty) factors, with a pre-specified $p<0.10$ level of statistical significance.

Results: Our search yielded 3,072 initial results, of which 61 analyses met our screening criteria. Twenty-one of 61 analyses (34.4%) reported operability status influencing treatment allocation. These analyses were significantly more likely to be published in journals with a surgical focus (52.4 vs 20%) and impact factor <5 (81.0 vs 57.5%), to contain patient cohorts from Asia (47.6 vs 27.5%) and from institutional datasets (81.0 vs 55.0%), and to have a radiation oncologist as first (42.9 vs 25.0%) or senior (42.9 vs 27.5%) author. Seven (13.7%) of 61 analyses directly compared OS between operable SBRT patients and patients undergoing surgery. These analyses were significantly more likely to be published in surgery-focused journals (71.4 vs 25.9%) and to contain cohorts from the National Cancer Database (57.1 vs 11.1%).

Conclusion: Nearly two-thirds of peer-reviewed retrospective studies that have compared OS between surgery and SBRT for early-stage NSCLC lack information on patient operability status, and nearly 90% lack a direct comparison between operable SBRT patients and those receiving surgery. Randomized comparisons of surgery versus SBRT in operable cohorts are ongoing, and the results are awaited.

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Prediction of Regional and Distant Failure After Definitive Thoracic Stereotactic Body Radiation Therapy (SBRT) Using Pre-Treatment CT-Based Radiomic Analysis

J. Bae,[1] E. Zabrocka,[2] C. Rodriguez,[1] D.L. Payne,[3] R. Cattell,[1] S. Ryu,[1] P. Prasanna,[2] and K.M. Mani[1]; *[1]Department of Biomedical Informatics, Stony Brook University, Stony Brook, NY, [2]Department of Radiation Oncology, Stony Brook University Hospital, Stony Brook, NY, [3]Department of Radiology, Stony Brook University Hospital, Stony Brook, NY*

Purpose/Objective(s): Patients with early-stage non-small cell lung cancer (NSCLC) have the option of either lobectomy or definitive SBRT, both of which provide excellent local control. However, a tangible portion still suffer regional failure (RF) in the lymph nodes (LNs), or distant failure (DF) outside the thorax. Those receiving SBRT are at a further disadvantage as a LN dissection can identify occult nodal spread at the time of surgery. Thus predicting the risk of RF/DF, particularly for those treated with SBRT, remains an essential issue. Here we seek to assess whether CT-based radiomics (quantitative, sub-visual cues) could provide such insight.

Materials/Methods: We identified patients who received definitive lung SBRT between 2014-2019, had a pre-treatment CT chest (CT1) within 3 months prior, and had at least 12 months of follow-up. Charts were assessed for RF and DF. A pre-trained U-Net model was used to segment right and left lungs from CT1 for radiomic feature extraction. 304 radiomic signatures (Gabor wavelet, Haralick, and CoLlAGe) were extracted, filtered, and used to train Linear Discriminant Analysis (LDA) machine learning classifiers for RF and DF prediction tasks. Features from the ipsilateral (Ip) and contralateral (Con) lung were analyzed separately to assess for their comparative utility. Leave-one-out cross validation method was utilized. To serve as a control, a baseline LDA classifier was trained using canonical clinical features (Clin) including performance status, tumor stage, age, and tumor location.

Results: 89 stage I-II NSCLC patients with 90 lesions who received definitive SBRT were included. Median dose was 48 Gy (range: 40-54 Gy) in 3-5 fractions, prescribed to the 100% isodose line. RF was identified in 12 (13%) lesions, while DF was found in 21 (23%) lesions. Radiomic features significantly outperformed the baseline approach in both RF (AUC=0.65 vs. 0.46) and DF (AUC=0.66 vs. 0.57). There was no significant difference between features from the ipsilateral vs. contralateral lung.

Conclusion: CT-based radiomic analysis predicted RF and DF more accurately than clinical features alone. The similar performance between the ipsilateral and contralateral lung suggests there may be features intrinsic to the parenchyma contributing to disease recurrence. Further studies should assess whether different ROIs, including the hilum/mediastinum or peritumoral region, are more informative.

Abstract 106 - Table 1 Time Intervals by Patient Factors

		Sensitivity	Specificity	AUC
RF	Ip	0.60±0.02	0.61±0.02	0.63±0.02
	Con	0.62±0.02	0.63±0.04	0.65±0.03
	Clin	0.34±0.03	0.56±0.02	0.46±0.02
DF	Ip	0.57±0.01	0.77±0.02	0.66±0.01
	Con	0.58±0.03	0.61±0.02	0.66±0.03
	Clin	0.53±0.01	0.6±0.02	0.57±0.01

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Dosimetric Comparison of Arms Up Versus Arms Down Positions for Lung SBRT

T. Carpenter, J.P. Santoro, J.W. Lischalk, D.W. Ebling, M.C. Repka, M. Witten, and J.A. Haas; *Perlmutter Cancer Center NYU Langone Long Island, Mineola, NY*

Purpose/Objective(s): Reproducible patient positioning is integral to the safe and accurate delivery of radiation therapy. Commonly, lung patients are simulated with their arms up (AU) to improve dose conformality by utilizing lateral gantry angles. However, the AU position can be uncomfortable and difficult to maintain, especially in the early stage lung SBRT patient cohort, who tend to be older and less physically fit. For these patients, the physical discomfort from the AU position can lead to decreased accuracy in patient positioning and possibly treatment delivery. We sought to evaluate any potential dosimetric differences between simulating and treating SBRT lung patients in the standard AU position versus a more comfortable arms down (AD) position.

Materials/Methods: A sample of 10 patients undergoing lung SBRT on a noncoplanar robotic radiosurgery platform were selected. Patients were originally simulated, planned, and treated in the AD position. For ease of comparison, all treatments were replanned to 50 Gy (10 Gy x 5 fractions) regardless of tumor location. For each patient a new plan was then generated subtracting out the arms to reproduce the commonly used AU simulation position. Dosimetric quantities such as PTV coverage, PTV conformality, and other commonly accepted normal tissue constraints were compared. *Paired t-tests* of various plan metrics were calculated with a <0.05 threshold of significance.

Results: All plans were able to achieve adequate target coverage without violating any standard normal tissue constraints. There was no statistically significant differences observed for plans calculated in the AD versus AU positions for PTV V50Gy, lung V20Gy, esophagus D0.03cc, chest wall V30Gy, proximal bronchus D0.03cc, and distal bronchus D0.03cc. There was a statistically significant difference observed for the cord 0.03cc and cord 0.35cc doses in favor of the AD position, though in all cases the cord constraints were met. The median cord D0.35cc was 557cGy for AU verses 216cGy for AD. The median cord D0.03cc was 606cGy for AU verses 252cGy for AD.

Conclusion: There is no major dosimetric difference between treatment plans generated in the AU and AD positions. The exception was cord dose metrics, which showed a favorable decrease in median D0.03cc and D0.35cc in the AD position. Given the increased ease of positioning, which we believe leads to improved reproducibility and ultimately accuracy of treatment, we believe that simulating and treating patients in the AD position can be advantageous for lung SBRT treatments.

Abstract 107 - Table 1 Time Intervals by Patient Factors

Constraint	p-value	CI (95%) (Up-Down)
PTV V50Gy	0.236	[-1.6cc, 0.45cc]
Lung V20Gy	0.769	[-0.37cc, 0.28cc]
Esophagus D0.03cc	0.901	[-291cGy, 326cGy]
Chest Wall V30Gy	0.875	[-2.3cc, 2.0cc]
Proximal Bronchus D0.03cc	0.963	[-136cGy, 130cGy]
Distal Bronchus D0.03cc	0.215	[-82cGy, 321cGy]
Cord D0.03cc	**<0.01**	**[-428cGy, -153cGy]**
Cord D0.35cc	**<0.01**	**[-401cGy, -154cGy]**

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Comparing Clinicopathologic Factors and Survival in Stage III Adenocarcinoma and Squamous Cell Carcinoma of the Lung Following Definitive Chemoradiotherapy

S. Abel,[1] A. Colonias,[1] S. Beriwal,[1] B. Weksler,[2] G. Finley,[3] S. Long,[3] and R.E. Wegner[1]; [1]*Division of Radiation Oncology, Allegheny Health Network Cancer Institute, Pittsburgh, PA,* [2]*Department of Thoracic Surgery, Allegheny Health Network, Pittsburgh, PA,* [3]*Allegheny Health Network Cancer Institute, Pittsburgh, PA*

Purpose/Objective(s): Non-small cell lung carcinoma (NSCLC) represents a diverse array of malignancies with the primary histologic subtypes of adenocarcinoma (ADC) and squamous cell carcinoma (SCC). Nearly one third of patients diagnosed with NSCLC will present with stage III disease. In patients with unresectable disease, the current standard is definitive chemoradiotherapy (CRT) followed by immunotherapy. Even though the systemic therapeutic landscape has changed based on histological subtype, radiation treatment remains the same for all NSCLC. Also it remains unclear whether certain clinicopathologic factors are associated with either histology or if histology influences survival outcomes following definitive CRT. Therefore, we analyzed the national cancer database (NCDB) to compare overall survival (OS) in Stage III NSCLC patients with ADC and SCC treated with definitive CRT.

Materials/Methods: We queried the NCDB for patients diagnosed with Stage III ADC or SCC of the lung between the years 2004 − 2015 who were treated non-surgically with concurrent CRT to a definitive dose (60-74 Gy). Univariable and multivariable analyses identified characteristics predictive of OS. Survival was calculated using Kaplan Meier method. Multivariable logistic regression was performed to identify clinicopathologic variables associated with each histology.

Results: Ultimately 17,015 Stage III NSCLC patients with either SCC (n=9,406) or ADC (n=7,609) were eligible for analysis. Univariable analysis demonstrated a median OS of 24 months and 20 months (p<0.0001) and 3-year OS rates of 36% and 30% (p<0.0001) in patients diagnosed with ADC and SCC, respectively. Patients with SCC were more likely to be older (OR: 1.14, 95% CI: 1.07-1.23), have higher comorbidity scores (OR: 1.60, 95% CI: 1.43-1.80), left sided tumors (OR: 1.23, 95% CI: 1.14-1.31), and T4 lesions [OR: 2.68, 95% CI: 2.40-2.99, (p<0.0001, for all)]. Patients with SCC were less likely to have N2 (OR: 0.83, 95% CI: 0.72-0.94) or N3 disease (OR: 0.53, 95% CI: 0.46-0.62) and to receive treatment at an academic treatment facility (OR: 0.90, 95% CI: 0.84-0.97). Younger age, lower comorbidity score, higher radiation dose (i.e. ≥ 70 Gy), female sex, lower T stage, lower N stage, and ADC histology were associated with improved OS on multivariable comparison (p<0.01, for all).

Conclusion: Compared to ADC, SCC was associated with higher T stage, lower N stage, older patients with greater comorbidity scores, and left sided tumors. Both median, as well as, 3-year and 5-year OS rates were inferior in patients with SCC compared to ADC. Prospective studies are needed to validate these findings and potentially identify radiotherapeutic strategies that may improve outcomes in this histologic subset.

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IGNYTE: A Phase 1/2 Multi-Cohort Clinical Trial of RP1 ± Nivolumab in Patients with Non-Small Cell Lung Cancer and Other Solid Tumors

H. Emamekhoo,[1] S. Patel,[2] E. Rodriguez,[3] M.K. Riaz,[4] G. Giaccone,[5] M. Furqan,[6] J.J. Sacco,[7] P. Bommareddy,[8] S. Raza,[8] S. He,[8] K. Harrington,[9] and M.R. Middleton[10]; [1]*University of Wisconsin Carbone Cancer Center, Madison, WI,* [2]*UC San Diego, Moores Cancer Center, Dept of Hematology/Oncology, La Jolla, CA,* [3]*Thoracic Oncology Division, Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL,* [4]*Division of Hematology Oncology, University of Cincinnati, Cincinnati, OH,* [5]*Weill-Cornell Medical Center, New York, NY,* [6]*University of Iowa Hospitals & Clinics, Iowa City, IA,* [7]*Medical Oncology, Clatterbridge Cancer Centre, & Department of Molecular and Clinical Cancer Medicine, University of Liverpool, Liverpool, United Kingdom,* [8]*Replimune, Woburn, MA,* [9]*Institute of Cancer Research, The Royal Marsden NHS Foundation Trust National Institute of Health Research Biomedical*

Research Center, London, United Kingdom, [10]University of Oxford, Oxford, United Kingdom

Purpose/Objective(s): RP1 is an enhanced potency oncolytic HSV-1 which expresses a fusogenic glycoprotein (GALV-GP R-) and granulocyte macrophage colony stimulating factor (GM-CSF). In pre-clinical studies, RP1 demonstrated a potent GALV-GP R-enhanced anti-tumor activity and immunogenic cell death and initial clinical data in a range of tumor types has been promising, including in patients with anti-PD1 failed disease. The Phase 1 part of the study demonstrated a tolerable safety profile for RP1 and RP1 combined with nivolumab (nivo) and determined the recommended phase 2 dose (RP2D). The objective of the Phase 2 part of the study is to evaluate the safety and efficacy of RP1 combined with nivo in patients (pts) with a range of advanced solid tumors, including anti-PD-1/PD-L1-failed non-small-cell lung cancer (NSCLC).

Materials/Methods: The Phase 2 portion of this multi-center, open label clinical trial is enrolling approximately 270 pts across five cohorts, including 30 pts in an anti-PD-1/PD-L1-failed NSCLC cohort, as well as patients with anti-PD1 failed and naïve melanoma, non-melanoma skin cancers and MSI-H/dMMR tumors. Pts in the Ph 2 portion receive up to 10 mL of RP1 intratumorally into one or more superficial or deep seated/visceral lesions by imaging guidance at the RP2D identified in the Phase 1 portion of the study (1×10^6 PFU/mL × 1 followed by 1×10^7 PFU/mL × 7, Q2W). Following the first dose of RP1, nivo (240 mg IV Q2W for 4 months then 480 mg IV Q4W for up to 2 years) is subsequently administered in combination. Pts may receive up to 8 additional doses of RP1 if they meet protocol-specified criteria. Tumor assessments are performed Q8W. The primary objectives of the Ph 2 part of the study are to assess the safety, tolerability, and overall response rate (ORR) of RP1 in combination with nivo. Secondary objectives include duration of response, complete response rate, disease control rate, PFS, 1-year and 2-year survival rates. Exploratory objectives include biodistribution and shedding analysis of RP1 and biomarker studies, including analyses of tumor biopsies and blood samples. Enrollment is currently ongoing in the US, UK and EU.

Results: TBD/NA (Trial-in-Progress)

Conclusion: TBD/NA (Trial-in-Progress)

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*MET*ex14 ctDNA Dynamics & Resistance Mechanisms Detected in Liquid Biopsy (LBx) From Patients (pts) With *MET*ex14 Skipping NSCLC Treated With Tepotinib

P. Paik,[2,3] R. O'Hara,[1] R. Veillon,[4] E. Felip,[5] A. Cortot,[6] H. Sakai,[7] J. Mazières,[8] M. Thomas,[9] N. Reinmuth,[10] J. Raskin,[11] P. Conte,[12] M. Garassino,[13] W.T. Iams,[14] F. Griesinger,[15] D. Kowalski,[16] C. Stroh,[17] D. Juraeva,[18] J. Scheuenpflug,[19] A. Johne,[20] and X. Le[21]; *[1]Weill Cornell Medical College, New York, NY, [2]Thoracic Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, NY, [3]EMD Serono, Inc., Rockland, MA, [4]CHU Bordeaux, Service des Maladies Respiratoires, Bordeaux, France, [5]Department of Oncology, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, [6]Univ. Lille, CHU Lille, CNRS, Inserm, Institut Pasteur de Lille, Canther, Lille, France, [7]Department of Thoracic Oncology, Saitama Cancer Center, Saitama, Japan, [8]CHU de Toulouse, Institut Universitaire du Cancer, Toulouse, France, [9]Thoraxklinik, University Heidelberg and Translational Lung Research Center Heidelberg (TLRC-H), The German Center for Lung Research (DZL), Heidelberg, Germany, [10]Department of Thoracic Oncology, Asklepios Clinics Munich-Gauting, Gauting, Germany, [11]Department of Pulmonology and Thoracic Oncology, Antwerp University Hospital (UZA), Edegem, Belgium, [12]Department of Surgery, Oncology and Gastroenterology; University of Padova and Oncologia Medica 2, Istituto Oncologico Veneto, I.R.C.C.S., Padova, Italy, [13]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IL, Italy, [14]Division of Hematology/Oncology, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, [15]Department of Hematology and Oncology, University Department Internal Medicine-Oncology, Pius-Hospital, University Medicine Oldenburg, Oldenburg, Germany, [16]Department of Lung Cancer and Thoracic Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland, [17]Translational Innovation Platform, Oncology, the healthcare business of Merck KGaA, Darmstadt, Germany, [18]Translational Medicine, Department of Bioinformatics, the healthcare business of Merck KGaA, Darmstadt, Germany, [19]Clinical Biomarkers and Companion Diagnostics, the healthcare business of Merck KGaA, Darmstadt, Germany, [20]Global Clinical Development, the healthcare business of Merck KGaA, Darmstadt, Germany, [21]Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*

Purpose/Objective(s): In VISION Cohort A, tepotinib showed robust and durable clinical activity in pts with *MET*ex14 skipping NSCLC. Here, we present biomarker analyses on serial LBx samples.

Materials/Methods: LBx samples at baseline (BL), Week 6, 12, and end of treatment (EOT) were analyzed (73 genes). Investigator (INV)-assessed clinical outcome was evaluated per BL biomarker profiles and molecular response (MR; >75% depletion from BL in *MET*ex14 variant allele frequency [VAF] ctDNA confirmed in 2 consecutive samples) or molecular progression (MP; VAF increase >0 from BL). Per INV, acquired resistance was investigated in EOT samples.

Results: Of 99 LBx pts, median age was 72 yrs (range 49−88), 53% were male, 44% never smokers, and 85% had adenocarcinoma. INV ORR was 53% (95% CI: 42, 63); ORR in first line (1L; n=44) was 59% (43, 74) and 47% (33, 61) in ≥2L (n=55). 94 pts had BL biomarker profiles, similar in 1L to ≥2L except for *EGFR*amp (1/43 [2%] vs 8/51 [16%]). Location/type of *MET*ex14 alteration did not affect outcomes. 1 pt with concomitant *MET* M1250T had a 17.3-month PFS. A trend toward improved efficacy was seen with concomitant *MET*amp (6/8 responses). Tepotinib response occurred in pts with wt or mutant *TP53*, but there was a trend for longer mDOR and mPFS with wt*TP53*. Concomitant oncogenic mutations were rare: 3 pts with *KRAS*, *NRAS* alterations (no responses) and 5 with *PI3K/AKT* alterations (3 responses). 65 pts had 2 consecutive on-treatment samples (30 1L, 35 ≥2L): 46 (71%) had confirmed MR, 5 (8%) had confirmed MP, and 14 (22%) had no change in VAF/lacked confirmation. MR was associated with clinical response and MP with no response/short PFS (Table). 52 pts with progression had EOT LBx samples. Emerging *MET* resistance mutations (Y1230H/C & D1228H/N) occurred in 7 pts (13%): all responders and 5 had PFS >10 months. Non-MET-driven resistance mechanisms will be presented.

Conclusion: LBx biomarker analysis from the largest on-treatment data set for a MET inhibitor in *MET*ex14 skipping NSCLC showed that ctDNA depletion in *MET*ex14 VAF is associated with improved clinical response in pts treated with tepotinib. Serial LBx could help monitor responses, understand resistance and guide dose-adjustment strategies to improve outcomes and quality of life.

Abstract 110 - Table 1 Time Intervals by Patient Factors

Treatment line, confirmed molecular status	All, MR	All, MP	1L, MR	1L, MP	≥2L, MR	≥2L, MP
n (%)	46 (71)	5 (8)	20 (67)	4 (11)	26 (74)	1 (3)
ORR, n (%)	35 (76)	0	18 (90)	0	15 (58)	0
mDOR, months (95% CI)	14 (9.8, NE)	-	18 (7.23, NE)	-	14 (9.69, NE)	-
DCR, n (%)	42 (91)	3 (60)	18 (90)	2 (50)	24 (92)	1
mPFS, months (95% CI)	11.0 (8.6, 17.7)	5.5 (2.8, NE)	19.7 (9.67, NE)	4.8 (2.8, NE)	9.9 (6.9, 13.8)	5.8

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Upfront Treatment With Osimertinib vs. Osimertinib and Radiotherapy for Patients With EGFR-Positive Non-Small Cell Lung Cancer Brain Metastases

A.E. Dohm,[1] J. Tang,[2] M.N. Mills,[1] B.A. Perez,[2] T.J. Robinson,[1] B. Creelan,[2] H.H.M. Yu,[1] D.E. Oliver,[1] and K.A. Ahmed[1]; [1]*H. Lee Moffitt Cancer Center and Research Institute, Department of Radiation Oncology, Tampa, FL,* [2]*H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Purpose/Objective(s): Given the improved central nervous system penetration of 3rd generation tyrosine kinase inhibitors, such as osimertinib, the role of upfront radiation therapy (RT) in the setting of brain metastases (BM) has been brought into question. We sought to retrospectively evaluate outcomes at our institution for patients with EGFR-positive NSCLC treated with osimertinib as the upfront treatment for new or progressing BM versus osimertinib in combination with intracranial RT.

Materials/Methods: This single-institution retrospective analysis of EGFR-positive NSCLC with new or progressing BM included a total of 92 patients with 405 BM treated between 2013 to 2021 and followed until July 2021. Two BM treatment groups were evaluated: (1) patients treated with upfront osimertinib alone (n=58), and (2) patients treated with osimertinib combined with RT [either whole brain radiation therapy (WBRT) or stereotactic radiosurgery (SRS) prior or concurrently with osimertinib (n=34)]; both groups began treatment within 2 months of BM diagnosis. Time-to-event analysis was conducted with the Kaplan-Meier (KM) method, and outcomes included distant intracranial control (DIC), local control (LC), and overall survival (OS). Cox proportional hazards model was utilized for multivariate analysis (MVA) to identify correlations of clinical outcomes.

Results: Median follow-up from BM diagnosis was 13.2 months (0.8-48.9 months). Of the patients treated with osimertinib and RT, 17 were treated with SRS and 17 with WBRT. No significant differences in age (p=0.96), gender (p=0.42), DS-GPA (p=0.73), KPS (p=0.54, number (p=0.52) or volume (p=0.29) of BM, SRS dose (p=0.44), or number of systemic metastases (p=0.88) were noted between groups. No difference between osimertinib vs osimertinib and RT groups was noted for 12 month KM rates of DIC 84.9% and 68.7% (p=0.80); LC 99.6% and 93.1% (p=0.31); and OS 66% and 73.5% (p=0.). Of the 58 patients treated with upfront osimertinib, 19 patients with 77 lesions eventually required radiation for intracranial progression with 62 of those lesions being treated with SRS. Upon MVA, higher KPS (p=.001) and DS-GPA (p=0.002) were associated with increased OS and systemic metastasis at time of treatment with worse OS (p=0.001).

Conclusion: The results of this study support other preliminary data suggesting that upfront osimertinib alone may provide sufficient intracranial control to allow RT to be deferred until further intracranial progression. Prospective trials are needed to further guide treatment.

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Intracranial Activity of Tepotinib in Patients (pts) With *MET* exon 14 (*MET*ex14) Skipping NSCLC Enrolled in VISION

C.M. Bestvina,[1] J.D. Patel,[2] X. Le,[3] R. Veillon,[4] I. Anderson,[5] I. Demedts,[6] M. Garassino,[7] J. Mazières,[8] M. Morise,[9] E. Smit,[10] S.P. Eggleton,[11] A. O'Brate,[12] G. Otto,[13] R. Bruns,[14] K.M. Schumacher,[13] and P. Paik[15,16];

[1]University of Chicago Medical Center, Chicago, IL, [2]Lurie Cancer Center, Northwestern University-Feinberg School of Medicine, Chicago, IL, [3]Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, [4]CHU Bordeaux, Service des Maladies Respiratoires, Bordeaux, France, [5]St Joseph Heritage Healthcare, Santa Rosa, CA, [6]Department of Pulmonary Diseases, AZ Delta Hospital, Roeselare, Belgium, [7]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IL, Italy, [8]CHU de Toulouse, Institut Universitaire du Cancer, Toulouse, France, [9]Department of Respiratory Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan, [10]Department of Thoracic Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands, [11]Global Clinical Development, Merck Serono Limited, Feltham, UK, a subsidiary of the healthcare business of Merck KGaA, Darmstadt, Germany, [12]Global Medical Affairs, the healthcare business of Merck KGaA, Darmstadt, Germany, [13]Global Clinical Development, the healthcare business of Merck KGaA, Darmstadt, Germany, [14]Department of Biostatistics, the healthcare business of Merck KGaA, Darmstadt, Germany, [15]Weill Cornell Medical College, New York, NY, [16]Thoracic Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, NY

Purpose/Objective(s): Brain metastases (BMs), reported in 20−40% of pts with *MET*ex14 skipping NSCLC, present a high unmet need with a poor prognosis. Preclinical data from tepotinib, a highly selective MET inhibitor, demonstrated intracranial activity in MET-driven lung cancer orthotopic BM models. In VISION Cohort A (N=152), tepotinib had robust and durable clinical activity in pts with *MET*ex14 skipping NSCLC, with an objective response rate (ORR) of 45% and a median duration of response (mDOR) of 11.1 months. Here, we report the intracranial activity of tepotinib.

Materials/Methods: In VISION, pts with *MET*ex14 skipping NSCLC received oral tepotinib 500 mg QD (450 mg active moiety). Pts with BM (neurologically stable on symptomatic therapy with stable steroids, and pts with asymptomatic BM) were eligible. Primary endpoint was systemic ORR per RECIST v1.1; a subgroup analysis in pts with BM (determined by RECIST v1.1) was predefined. An ad-hoc retrospective analysis of brain lesions determined by CT/MRI was conducted by an independent review committee using RANO-BM criteria, which accounts for pts' clinical status and steroid use. Responses were determined in pts with ≥1 evaluable post-baseline tumor assessment. For those with non-measurable lesions per RANO-BM (enhancing and non-enhancing non-target lesions [NTLs]), disease control in the brain was defined as non-complete response (CR)/non-progressive disease (PD). Data cut-off was July 1, 2020.

Results: Per RECIST v1.1, 23 pts in Cohort A had BM at baseline. Systemic efficacy was consistent with the overall population (ORR 47.8% [95% CI: 26.8, 69.4], mDOR 9.5 months [95% CI: 5.5, not estimable]). 15 pts were evaluable by RANO-BM; 12 received prior radiotherapy for BM (median 6.4 weeks before tepotinib initiation [range 2.6−44]). Systemic best objective responses (BORs) were partial response (PR; n=9), stable disease (SD; n=3), and PD (n=3). Seven pts had measurable CNS disease per RANO-BM (all with prior radiotherapy); intracranial BORs were PR (n=5; including three with complete disappearance of target lesions), SD (n=1) and PD (n=1). Of eight pts with NTL only, seven achieved intracranial disease control and one had PD. Of the seven with disease control, three had a CR of the enhancing NTL.

Conclusion: Tepotinib demonstrated robust systemic activity in pts with *MET*ex14 skipping NSCLC with BM, complemented by intracranial activity in an ad-hoc analysis using RANO-BM. Small pt numbers, a large proportion of pts with prior radiotherapy for BM, and the retrospective nature of the analysis should be considered. A prospective evaluation of intracranial activity data from VISION Cohort C is ongoing.

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A Multi-Center, Open-Label, Randomized, Two-Arm Study, to Evaluate the Efficacy of Osimertinib with Early Intervention SRS Treatment Compared to the Continuation of Osimertinib Alone, in Patients with EGFR-Mutated NSCLC and Asymptomatic Brain Metastases

P.A. Blumenfeld,[1] G. Marwaha,[2] Y. Shoshan,[1] J. Feldman,[1] H. Nechushtan,[1] Y. Rottenberg,[1] N. Hirsch,[1] K. Sheva,[1] and A. Meirovitz[1]; [1]Hadassah Medical Center, Jerusalem 91120, Israel, [2]Rush University Medical Center, Chicago, IL

Purpose/Objective(s): Brain metastases (BM) develop in 50-70% of patients with EGFR mutant NSCLC and are a main cause of morbidity and mortality. While radiation therapy (stereotactic radiosurgery (SRS) or whole brain) remains a viable treatment option for the treatment of BM, often Osimertinib monotherapy is the treatment of choice in cases of asymptomatic BM due to its improved pharmacokinetic profile and excellent CNS penetration compared to first generation TKIs. In the recently published FLAURA trial, 77% of patients with brain metastases demonstrated an objective response rate with Osimertinib, 18% having a complete response. Various studies, however, have highlighted the benefit of combining TKI and SRS treatment as opposed to each treatment alone. The goal of this Phase III trial is to assess whether early intervention with SRS (2 months post-treatment initiation of Osimertinib) to active brain metastases (as visualized by MRI at this time point) will better control disease that did not completely respond to Osimertinib and in turn will delay brain progression (CNS-PFS).

Materials/Methods: Eligible patients will undergo baseline brain MRI, CT, cognitive assessments and a QOL questionnaire. Patients will be treated with Osimertinib for 2 months (8 weeks). At 2 months, a second MRI will be performed. One-hundred and sixty two asymptomatic or mildly symptomatic patients with <20 visualized BM will be randomized in a 1:1 ratio between the control arm consisting of continued Osimertinib and the SRS arm consisting of Osimertinib + SRS to all residual brain lesions. Recommended SRS doses are 20 Gy in 1 fraction to metastases ≤ 1.5 cm and 27Gy in 3 fractions to larger metastases. The primary endpoint is CNS-PFS, assessed by RECIST criteria, and secondary endpoints include whole body PFS, cognitive function, QOL, time to whole-brain radiation, and overall survival.

Results: Accrual has begun at the main study center.

Conclusion: This study will determine if addition of SRS to residual brain metastases two months post-treatment initiation of Osimertinib for selected patients with asymptomatic brain metastases results in improved oncologic, cognitive and QOL outcomes.

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Racial Disparities in Treatment and Outcome of Non-Small Cell Lung Cancer (NSCLC) Patients Across Different Facility Types

F. Zhu,[1] J. Shogan,[2] H. Wang,[1] and H. Ashamalla[1]; [1]*New York - Presbyterian Brooklyn Methodist Hospital, Brooklyn, NY,* [2]*New York - Presbyterian Brooklyn Methodist Hospital, Brooklyn, NY*

Purpose/Objective(s): We hypothesize that differential disparities exist in diagnosis, treatment and outcome among NSCLC patients of different races across different types and locations of treatment facilities.

Materials/Methods: The National Cancer Database was queried for cases of lung cancer from 2004-2016. Patients with invasive lung cancer were included. Exclusion criteria were unknown treatment status and unknown tumor size. Multivariate logistic and Cox model were used to assess effects of age, sex, race, facility type, facility location, insurance, education and income on stage, receipt of any treatment, time to receive treatment and outcome.

Results: Among 457,236 patients, 149,772 (32.8%), 241,471(52.9%) and 65,330 (14.3%) were treated at academic, community and integrated centers, respectively. After adjusting for co-founders, as shown in Table 1, Black (B) and Asian (A) race was associated with later stage but better outcomes. B race was associated with less treatment and delayed treatment. In academic facilities, B and A race had later stage, less and delayed treatment but better outcomes. In integrated facilities, B race had similar outcome as White (W) race. When compared to patients from Central facility location, those from West Coast and Mountain facility locations received less treatment (OR, 0.70 and 0.78, respectively, $P < 0.001$) and later treatment (HR, 0.83 and 0.91, respectively, $P < 0.001$); patients from Mountain facility locations had better outcomes (HR, 0.89, $P < 0.001$).

Conclusion: B and A patients were diagnosed at later stage and had less and delayed treatment. However, they had better outcomes stage for stage when compared to W patients. The reverse racial disparity between B and W patients was less in integrated facilities. Efforts to investigate these reverse racial disparities are warranted. Patients from Mountain facility locations had better outcomes than those from Central facility locations, despite less and later treatment. Investigation regarding the effects of facility location on outcome is warranted.

Abstract 114 - Table 1 MVA for Various End Points of Three Races among Three Types of Facilities

		Overall		Academic		Community		Integrated	
		OR	*P*	OR	*P*	OR	*P*	OR	*P*
Stage III&IV vs Stage I&II	B vs W	1.34	**<0.01**	1.41	**<0.01**	1.29	**<0.01**	1.26	**<0.01**
	A vs W	1.38	**<0.01**	1.40	**<0.01**	1.35	**<0.01**	1.37	**<0.01**
Receipt of Any Treatment	B vs W	0.84	**<0.01**	0.86	**<0.01**	0.85	**<0.01**	0.96	0.44
	A vs W	1.02	0.61	1.26	**<0.01**	0.84	**<0.01**	1.06	0.57
		HR	*P*	HR	*P*	HR	*P*	HR	*P*
Time to Receive Treatment	B vs W	0.85	**<0.01**	0.84	**<0.01**	0.88	**<0.01**	0.86	**<0.01**
	A vs W	1.00	0.99	1.04	**<0.01**	0.97	0.13	0.94	0.04
Overall Survival	B vs W	0.95	**<0.01**	0.95	**<0.01**	0.94	**<0.01**	0.98	0.27
	A vs W	0.66	**<0.01**	0.64	**<0.01**	0.68	**<0.01**	0.65	**<0.01**

Bold values are statistically significant.
For time to receive treatment, larger HR corresponds to earlier treatment.

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A Comparison of Overall Patient Reported Distress Levels in Appalachian Cancer Patients From Economically Distressed vs. Non-Economically Distressed Counties Receiving Radiation Therapy for Thoracic Malignancies

K. Finnegan,[1] N.St. Thomas,[1] D. Rosenweig,[2] and R.C. Miller[3]; [1]*Maryville College, Maryville, TN,* [2]*Philadelphia College of Medicine, Suwanee, GA,* [3]*University of Tennessee Medical Center, Knoxville, TN*

Purpose/Objective(s): Appalachia has historically been an impoverished region. Higher levels of poverty are positively correlated with poorer cancer outcomes, particularly with areas that had a strong coal mining industry. Our medical center primarily serves 21 counties located entirely within Appalachian, 11 of which are economically classified as having a "Distressed" or "At Risk" by the Appalachian Regional Commission (ARC). The patients traveling from these counties usually have longer commute times and reliable access to care can be challenging. The remaining 10 counties are deemed "Transitional" and no county is designated in ARC's economically successful "Competitive" or "Attainment" categories. Considering the correlation between poverty level and outcomes, we hypothesized that patients from the "Distressed" or "At Risk" counties would have higher overall distress levels compared to "Transitional" counties.

Materials/Methods: Of 479 patients receiving radiotherapy (RT) at our institution for lung cancer in 2019 and 2020, 79 sequential patients treated with RT without definitive surgery were identified who had their overall distress level prospectively measured using the NCCN distress instrument prior to starting RT. Patient demographics, tumor and treatment characteristics, and overall distress data were collected and mean values of distress between groups were assessed using Pearson's chi-squared test.

Results: There were no statistically significant differences in patient, tumor, or treatment characteristics between distressed and non-distressed counties, with the exception of cancer stage. 84% of patients coming from distressed counties had Stage I lung cancers (p=0.04). Patients coming from economically "At Risk" and "Distressed" counties had a median distress score of 2.8 (range 0 to 9); patients from "Transitional" counties had a median distress score of 3.3 (p-value = 0.5).

Conclusion: Our study did not find a statistically significant difference in overall distress levels between patients coming from areas of economic hardship. We hypothesize that a lung cancer diagnosis is one of many stressors facing our Appalachian patients coming from economically distressed regions. Additionally, the majority of patients referred for radiotherapy had Stage I cancers that were asymptomatic. Lung and heart diseases are also more prevalent in these poorer counties and may lead to an earlier subsequent diagnosis of lung cancer incidentally at an earlier age in some patients, which may in turn also result in a better cancer prognosis and prevent distress in the population we studied.

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Implementation of Standardized Lecture to Improve Radiation Oncology Knowledge in Multidisciplinary Lung Cancer Care Team: Initial Results of a Multi-Institutional Pilot Study

J.C. Ye,[1] F.F. Rizvi,[2] G. Welch,[3] T.O. Thomas, Jr[4] E. Weiss,[5] R.A. Chandra,[6] S. Gutiontov,[7] S.B. Motwani,[8] and M.D. Mattes[9]; [1]*Department of Radiation Oncology, University of Southern California Keck School of Medicine, Los Angeles, CA,* [2]*Robert Wood Johnson Medical School, New Brunswick, NJ,* [3]*Yale School of Medicine, New Haven, CT,* [4]*Department of Radiation*

Oncology, Edward Hines VA Hospital, Maywood, IL, [5]Virginia Commonwealth University Health, Department of Radiation Oncology, Richmond, VA, [6]Oregon Health and Science Univ, Portland, OR, [7]Department of Radiation and Cellular Oncology, University of Chicago Medical Center, Chicago, IL, [8]Rutgers University, New Brunswick, NJ, [9]Department of Radiation Oncology, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ

Purpose/Objective(s): Most lung cancer (LC) providers have had no exposure to radiation oncology (RO) in training and may not know when a patient should have RO consultation. Despite this, there is paucity of literature describing RO interdisciplinary educational initiatives in LC. In 2019, ASTRO began developing disease-site specific slide decks, the first of which was designed to teach the specialists about RO in management of LC. The deck has been downloaded over 1000 times since it was made public. The authors examined the feasibility of an introductory lecture using the slide deck and its impact on the providers' knowledge and practice. By understanding treatment modalities outside one's own, it is hoped that the providers can present a full spectrum of options needed for patient-centered decision-making.

Materials/Methods: Between November 2019 and May 2021, a total of 7 radiation oncologists offered lectures to attendings and fellows in pulmonology, thoracic surgery, and medical oncology at 8 academic institutions. Due to the pandemic, lectures were given both in-person as well as virtually. The participants were invited to take an anonymized pre-test online, consisting of demographics and 13 multiple choice questions about RO for LC. After the lectures, the attendees were asked to take a post-test identical to the pre-test, with two additional questions about knowledge gained, and comfort level in making appropriate referrals to RO.

Results: A total of 76 individuals completed the pre-test, and 25 completed the post-test. The vast majority of the participants have never had a RO rotation (86%), lecture (75%), or seen a LINAC (82%). The mean pre-test score was 53.5% (SD 17.6%), and the mean post-test score was 75.1% (SD 3.6%), ($p<0.001$). On the post-test, 12 participants(48.0%) reported feeling much more knowledgeable about the role of RO in LC treatment and 13 (52.0%) felt a little more knowledgeable. A total of 9 participants (36.0%) felt much more comfortable making appropriate referrals to RO after the lecture, whereas 15 (60.0%) felt a little more comfortable, and 1 (4.0%) felt not any more comfortable. The improvement in score and reported knowledge and comfort levels were similarly observed across all subspecialties and between attendings and fellows.

Conclusion: Introductory lecture on RO for LC given using a standard slide deck resulted in a statistically significant improvement in relevant knowledge of RO. Nearly all participants also reported improved comfort level in making appropriate referrals to RO. The current study demonstrates feasibility of implementing such lectures to multiple providers across various institutions even during a pandemic. An organized effort to provide such lectures at more institutions may result in more appropriate management and RO referral for LC patients, especially in practice settings where tumor board is not readily available.

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Impact of Radiation Therapy on Inpatient Outcomes Among Patients With Lung Cancer

C.R. Mudigonda,[1] C. Davila-Chapa,[1] P. Gutta,[1] H.P. Patel,[2] U. Grewal,[1] and K. Beedupalli[1]; [1]*LSU Health Sciences Center Shreveport, Shreveport, LA,* [2]*Louis A Weiss Memorial Hospital, Chicago, IL*

Purpose/Objective(s): Hospitalizations during cancer treatment not only disrupt treatment but are also associated with increased healthcare resource utilization and negatively impact patient quality of life. While the impact of chemotherapy on hospitalizations among patients with lung cancer has been well-studied, the effect of radiation therapy in hospitalized patients with lung cancer is poorly studied.

Materials/Methods: We interrogated the nationwide inpatient sample from 2015-2017 for admissions in patients with lung cancer with and without a history of radiation therapy using appropriate ICD-10 diagnosis codes. Data related to baseline characteristics and inpatient outcomes were collected and analyzed using data management and decision management software.

Results: A total of 896,245 hospitalizations among patients with lung cancer were identified, out of which, 10.97% (96,775) had undergone radiation therapy. The mean age for hospitalizations in the radiation therapy group was 74.97±10.71 years and 50.95% were males. Majority of the patients in the radiation group were Caucasians (77.56%) and 87.67% of the hospitalizations were unplanned. Medicare (63.70%) and private insurance (21.91%) were identified as the primary payers in majority of these admissions. Admissions in the radiation group were noted to have a higher incidence of hypothyroidism (10.64% vs 9.96%, $p<0.0001$), electrolyte imbalance (32.05% vs 31.84%, $p<0.0001$) and coagulopathy 8.18% vs 7.26%, $p<0.0001$). The radiation group also did not demonstrate an increased incidence of atrial fibrillation (15.28% vs 15.93%, $p=0.20$) and stroke (2.98% vs 3.44%, $p=0.06$). Admissions in the radiation group were found to have a decreased all-cause inpatient mortality (6.03% vs 8.25%, $p<0.0001$) and median total hospital charges ($9,240 vs $10,324, $p=0.009$) when compared to the group that did not receive radiation. However, no difference between the median length of stay was noted [4(2,7) vs 4(2,7)].

Conclusion: Unplanned admissions are common among patients with lung cancer after radiation therapy. Radiation therapy was found to be associated with hypothyroidism, electrolyte imbalance and coagulopathy. In line with recent evidence, thoracic radiation did not appear to increase the risk of atrial fibrillation and stroke in our analysis. Further prospective research studies are needed to find ways to reduce non-elective admissions in cancer patients who have received radiation therapy. Perhaps prompt recognition and intervention of hypothyroidism, electrolyte imbalances, and coagulopathies may help improve overall inpatient outcomes in these patients.

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Sarcoidosis or Sarcoid Reaction With Lung Cancer in Ethnic Han Chinese Patients: A Single Center Experience and Literature Review

X. He; *Tongji University, Shanghai, China*

Purpose/Objective(s): The aim of the present study was to analyze the clinical characteristics of the sarcoidosis (SA) or sarcoid reaction (SR) with lung cancer in ethnic Han Chinese patients.

Materials/Methods: A retrospective review based on discharge summaries from January 2004 to December 2014 was performed with tissue-proved at Shanghai Pulmonary Hospital and the cases report of Chinese patients had been revived. The clinical and follow-up data of those patients were collected and their clinical features, treatment and prognosis were analyzed.

Results: Of the 536 sarcoidosis patients, 1.31% (7/536) patients with lung cancer in our hospital. With the patients in literature, 12 patients had the SA or SR with lung cancer. Our report patients (median 60 yrs; 58.71±7.59 yrs) were significantly older than the patients with SA only (49.19±10.83 yrs, $P=0.002<0.05$). Our lung cancer patients with SA or SR were predominantly in women (F/M: 5/2). And the most common type was adenocarcinoma (100%, 7/7). The symptoms of those patients were not specific. 57.14% (4/7) had no symptoms,

28.57% (2/7) had cough, 14.29% (1/7) had chest pain. All patients presented lymph node involvement. The size of the lung cancer was from 0.5-6cm (2.47±1.90). The treatment of cancer and SA/SR did not influence each other. Our cases were followed up for 18 to 90 months (average 36 months) and were all alive during the follow-up period.

Conclusion: The incidence of SA/SR with lung cancer is not high in our subjects and easily associated with early stage of lung cancer. The biopsy of lung and lymph nodes is essential to accurate diagnose and the right TNM stage of lung cancer. The SA/SR may be a protective factor against lung cancer relapse.

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Indirect Treatment Comparison of Lurbinectedin vs. Other Second-Line Treatments for Small-Cell Lung Cancer

B. Rengarajan,[1] R. Hanvesakul,[2] C. Stack,[3] F. Wilson,[4] J. Park,[4] and A. Adeyemi[4]; [1]*Jazz Pharmaceuticals, Palo Alto, CA,* [2]*Jazz Pharmaceuticals, Oxford, CA, United Kingdom,* [3]*Jazz Pharmaceuticals, Philadelphia, PA,* [4]*PRECISIONheor, Vancouver, BC, Canada*

Purpose/Objective(s): Lurbinectedin received accelerated approval from the US Food and Drug Administration in 2020 for patients with metastatic small-cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy based on the results of a single-arm phase 2 basket trial . In this trial, lurbinectedin demonstrated an overall response rate (ORR) of 35.2% and a median overall survival (OS) of 9.3 months. Here, we performed an indirect treatment comparison of lurbinectedin vs relevant second-line treatments for SCLC by means of a network meta-analysis (NMA).

Materials/Methods: A systematic literature review (1990−Jan 2021) identified 3 randomized controlled trials (RCTs) of second-line SCLC therapies recommended by NCCN guidelines that met the criteria for the NMA. Unanchored matching-adjusted indirect comparison (MAIC) connected Study B-005 to the network of RCTs. The RCT with the most overlap with Study B-005 was used as the target population in the base case, and a MAIC was performed to estimate the relative treatment effect of lurbinectedin vs oral topotecan (central node of the network). Relative treatment effects from the MAIC were used as direct evidence in the NMA. Analyses were conducted in a Bayesian framework for OS and ORR using a fixed-effect NMA, and relative effectiveness was assessed with hazard ratios (HR) and odds ratio.

Results: The 3 RCTs included in the NMA were Baize 2020 (carboplatin/etoposide vs oral topotecan), and Eckardt 2007 and von Pawel 2001 (oral topotecan vs IV topotecan). In the base case, Baize 2020 was the target population, which consisted only of patients with platinum-sensitive disease (chemotherapy-free interval ≥90 day); therefore, the platinum-sensitive subgroup of Study B-005 was connected to the network. In the base case analysis, the HR for OS significantly favored lurbinectedin vs oral topotecan, IV topotecan, and carboplatin/etoposide (Table). There was a significant improvement in ORR for lurbinectedin vs oral topotecan; the ORR was similar for lurbinectedin vs carboplatin/etoposide (Table). Two sensitivity analyses were also conducted.

Conclusion: In the absence of head-to-head RCTs, indirect treatment comparisons provide a means of estimating the relative efficacy of lurbinectedin vs relevant comparators for the second-line treatment of SCLC. In this NMA, lurbinectedin showed a robust survival benefit for the second-line treatment of platinum-sensitive patients with SCLC compared with platinum rechallenge and vs oral and IV topotecan. Study B-005; NCT02454972

Abstract 119 - Table 1

Comparison	OS (HR, 95% CrI)	ORR (OR, 95% CrI)
Base Case (Platinum-sensitive)	0.43 (0.27, 0.67) 0.43 (0.26, 0.70) 0.42 (0.30, 0.58)	2.58 (1.12, 5.94) 2.36 (0.89, 6.23) 0.85 (0.40, 1.83)
Lurbinectedin vs oral topotecan		
Lurbinectedin vs IV topotecan		
Lurbinectedin vs carboplatin/etoposide		

*Analysis relies on strong assumptions.

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End of Life Care in Hospitalized Patients With Lung Cancer

T.S. Brown,[1] U. Grewal,[1] S.R. Thotamgari,[2] A.K. Ananthaneni,[2] C. Burnett,[2] S. Vutukuri,[2] and K. Beedupalli[1]; [1]*LSU Health Sciences Center Shreveport, Shreveport, LA,* [2]*LSU Health Science Center Shreveport, Shreveport, LA*

Purpose/Objective(s): Most patients with lung cancer lack access to palliative care support until later stages of their disease, resulting in needless aggressive care and healthcare resource utilization towards the end of life. We sought to study practices surrounding the delayed initiation of palliative care services in hospitalized patients with advanced lung cancer.

Materials/Methods: This retrospective cross-sectional analysis included hospitalized patients with advanced lung cancer that received palliative care consultation from July 2020- to March 2021 at our academic tertiary care medical center. Patients were categorized as 'early consult' if palliative care was initiated within 5 days of admission. ANOVA and Chi-square tests were used for analysis and a p value of <0.05 was considered statistically significant.

Results: A total of 43 patients were included for analysis, out of which, a majority of the patients had Stage IV non-small cell lung cancer (22/43, 52.3%). None (0%) had received palliative care support prior to admission and only 4.8% had advance care planning documentation. The average delay in palliative care consult from the time of admission was 5.69± 6.06 days. The length of stay following palliative care initiation and the total length of stay were 4.28±4.18 days and 10.35±6.31 days respectively. Patients with a total hospital stay >10 days were significantly older than patients with a length of stay <10 days (60.7±7.4 days vs 65.6±5.7 days, p=0.02). During their hospitalization, 66.6% (28/43) of the patients received invasive procedures; which did not change with early vs late initiation of palliative care during hospitalization (p=0.65). Majority of the patients were discharged to hospice (21/43, 48.8%), which was not facilitated by earlier inpatient palliative care consultation (p=0.11).

Conclusion: The current study shows that a vast majority of patients with advanced lung cancer lack access to adequate palliative care support and continue to receive aggressive care including prolonged hospitalization and invasive procedures towards the end of life. There is a need to introduce palliative care services earlier, on an outpatient basis to improve advance care planning discussions and prevent gratuitous procedures and aggressive care towards the end of life.

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Comprehensive Analyses Identify a Signature Based on Pyroptosis-Related Genes for Breast Cancer

Y. Zhou,[1,2] J. Zheng,[3] and N. Lin[1,2]; *[1]Hangzhou First People's Hospital, Hangzhou, China, [2]Key Laboratory of Clinical Cancer Pharmacology and Toxicology Research of Zhejiang Province, Cancer Center, Zhejiang University School of Medicine, Hangzhou, China, [3]Nanjing Medical University, Hangzhou, China*

Purpose/Objective(s): Pyroptosis, a newly pattern of specific programmed cell death, has been reported to participate in several cancers. However, the value of pyroptosis in breast cancer (BC) is still not clear. Herein, we explored a signature based on pyroptosis-related genes (PRGs) through comprehensive analyses for BC.

Materials/Methods: The prognostic signature containing six PRGs, which can divide BC patients into high and low-risk groups with different prognosis, was constructed and validated by two independent cohorts. By assessing immune status, we found that a total of 79 immune microenvironments differed between the two subgroups. 11 immune checkpoint genes (BTLA, TNFRSF9, ICOS, PDCD1, TIGIT, CTLA4, LAG3, CD274, TNFRSF4, HAVCR2, and SIRPA) showed disparate expression levels in the two groups. Besides, BRCA patients in high-risk group exhibited lower TIDE scores than those in low-risk group, indicating that BRCA patients with higher RSs were more sensitive to ICB therapy. GSEA revealed that the risk groups were associated with tumor-related and immune-associated pathways. Another mentionable result was that the univariate and multivariate Cox regression analysis demonstrated that the risk model was an independent prognostic factor for BC patients. The two risk groups were confirmed to be sensitive to several chemotherapeutic agents.

Results: We found six prognostic pryroptosis-relate genes (PRGs) from public database for BC. The PRG-signature based on the six PRGs was developed. In addition, we identified differences in enrichment pathways, immune microenvironment, immune checkpoints, and sensitivity to several chemotherapeutic agents between risk groups.

Conclusion: Our identified and validated risk model based on six pyroptosis-related genes is an independent prognostic factor for BC patients. Through comprehensive analyses, the findings of our study uncovered the potential biomarkers and therapeutic target for the risk model based on PRGs.

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Tumor Agnostic Models for NSCLC Drug Development

P. Hays; *Personalis Inc, San Mateo, CA*

Purpose/Objective(s): To demonstrate evidence-based methods for the establishment of tumor agnostic models for non-small cell lung carcinoma (NSCLC) drug development. Tumor agnostic drugs comprise targeted therapies or immunotherapies that target the cancer cell based on the malignancy's genetic alteration, rather than histological subtype. Thus, far three tumor agnostic drugs have been FDA-approved: the immunotherapy pembrolizumab for MMR-D; and targeted agents larotrectinib for tumors harboring the NRTK fusion, and entrectinib for ROS-1 positive tumors. The development and mechanistic details of these drugs and their applicability to NSCLC will be described.

Materials/Methods: Literature reviews will be conducted on biomedical literature databases (MEDLINE, PubMed, ASCO databases, etc.) with terms "tumor agnostic drugs", "NSCLC", "oncogenic drivers" "MMR-D alterations", "NRTK fusions", "ROS-1 positive", "pembrolizumab", Larotrectinib" and "entrectinib" "tumor agnostic clinical trials" "adverse events tumor agnostic".

Results: The tumor agnostic drugs enumerated here have efficacy for NSCLC, with manageable safety profiles. Data from open-label prospective clinical trials performed on NSCLC patients who harbor these genetic alterations with pembrolizumab, larotectinib, entrectinib demonstrated robust outcomes and manageable toxicity with median progression-free survival and median overall survival (as primary endpoints) being met, when compared to other therapies. As an example, entrectinib was evaluated in clinical studies with 51 adult NSCLC patients who were ROS1 positive. Overall response rate was 78%, with 5.9% of patients experiencing complete response, which persisted at a follow-up of 12 months. Common grade 1 side effects were fatigue, constipation, dizziness and diarrhea. More severe adverse events included congestive heart failure, cognitive impairment, and hepatotoxicity.

Conclusion: Elucidating and outlining the rich literature on tumor agnostic drugs for NSCLC sheds insight into the effective clinical management of tumor agnostic drugs for NSCLC and their unique role in precision medicine.

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