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2022 North America Conference on Lung Cancer

ABSTRACT BOOK

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TABLE OF CONTENTS

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Oral Sessions

Oral Abstract Education Session 01 (OA01)
Chicago Ballroom ABCD | September 24, 2022, 15:00 - 16:40

OA01.01:
Second Primary Lung Cancer among Lung Cancer Survivors Who Never Smoked

Dr. Eunji Choi[1], Chloe Su[1,2], Dr. Julie Wu[3], Dr. Jacqueline Aredo[4], Dr. Joel Neal[3,5], Dr. Ann Leung[6], Dr. Leah Backhus[7], Dr. Loïc Marchand[8], Dr. Su-Ying Liang[9], Dr. Iona Cheng[4], Dr. Heather Wakelee[3,5], Dr. Summer Han[1,2,5,10]

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Background: Lung cancer among those who never smoked in their lifetime accounts for 25% of the lung cancers diagnosed in the U.S. With advances in early detection and treatment, lung cancer survivors are rapidly increasing in number. These survivors have a high risk of second primary lung cancer (SPLC), with a 4-6 times higher incidence than the initial primary lung cancer (IPLC) in the general population. Prior studies reported the incidence rate and risk factors for SPLC among lung cancer survivors who ever smoked. However, few have examined the incidence of SPLC among survivors who never smoked. We evaluate and compare the SPLC incidence among never- vs. ever-smoking lung cancer survivors.

Methods: The Multiethnic Cohort Study (MEC) is a population-based prospective cohort of 214,862 adults aged 45-75 years, followed since 1993. IPLC and SPLC were identified via linkage to SEER for 1993-2017. We applied the Aalen-Johansen estimator to calculate the cumulative incidence of IPLC in the entire study cohort and the cumulative incidence of SPLC among the IPLC patients. The standardized incidence ratio (SIR) was calculated as the SPLC incidence (observed SPLC cases over the person-year of IPLC patients), divided by IPLC incidence (observed IPLC cases over the person-year of the entire cohort) by smoking status.

Results: Among 214,862 participants, 7,234 (3.36%) developed IPLC over 4,112,936 person-years. Of the 7,234 IPLC patients, 167 (2.28%) developed SPLC over 17,074 person-years. The 10-year cumulative incidence of IPLC was 2.40% (95% confidence interval [2.31-2.49]) among those who ever smoked, which was 8 times higher than those who never smoked (0.33%, [0.30-0.37]). However, the 10-year cumulative incidence of SPLC following IPLC diagnosis remained as high among never-smoking IPLC patients (2.86%, [1.51-4.21]) as ever-smoking patients (2.75%, [2.27-3.23]). The SIR analysis showed that the SPLC incidence among IPLC patients was 5.6 times higher than the IPLC incidence in the entire MEC cohort (SIR: 5.56, [4.75-6.47]). However, the SIR was substantially higher among those who never smoked (SIR: 14.66, [8.82-22.89]) vs. ever smoked (SIR: 3.53, [2.98-4.16]).

Discussion: This study is the first to examine and compare the patterns of SPLC incidence among lung cancer survivors who never vs. ever smoked. Our finding suggests that the risk of SPLC remains as high among never-smokers as ever-smokers once an individual is diagnosed with IPLC. Future work is needed to identify the risk factors for SPLC among never-smokers to help develop a targeted surveillance strategy for never-smoking lung cancer survivors.

OA01.02:
Smoking Recidivism in a Low Dose Lung Cancer Screening Program Despite Point of Care Counseling

Dr Katy Marino[1], Jasmin Cotoco[1], Dr Claudia Barone[1], Patricia Franklin[1], Dr Jason Muesse[1], Dr. Matthew Steliga[1], Dr. Lauren Johnson[1]

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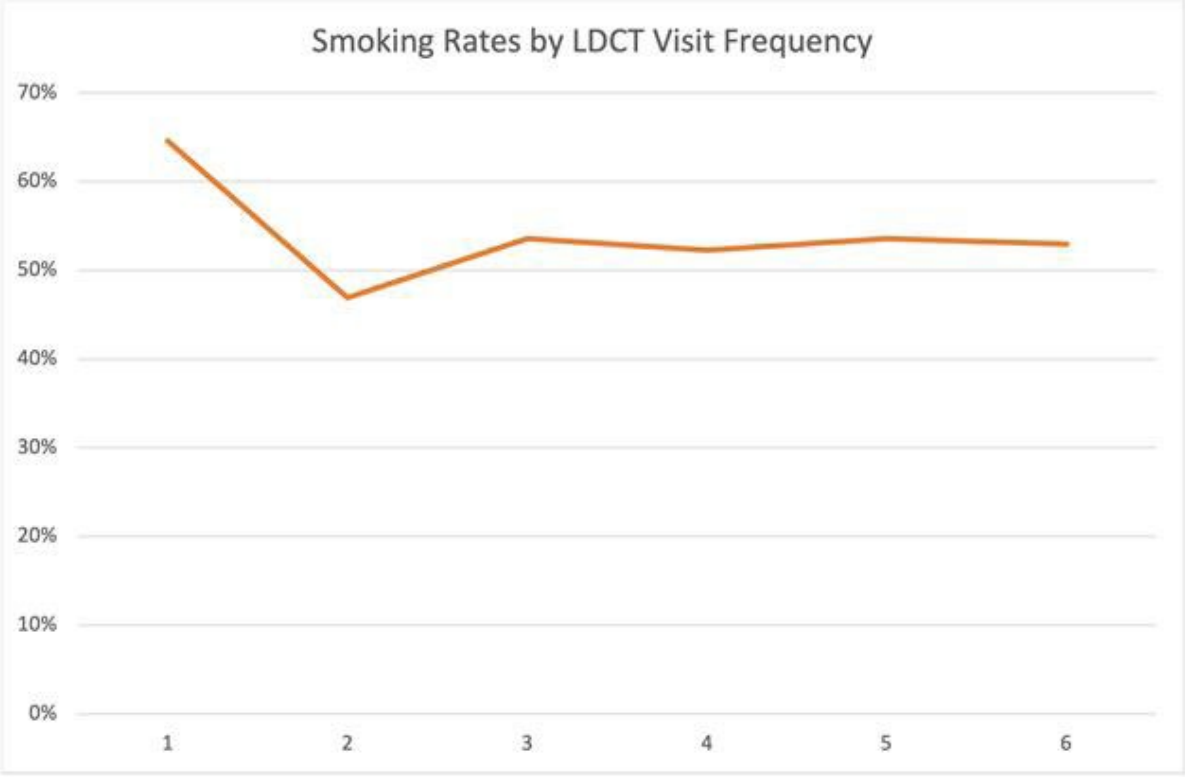
Background: Many patients who are undergoing Low Dose CT (LDCT) lung cancer screening continue to use tobacco. Cessation programs which are integrated into screening workflow can help patients quit, but further information was sought out as to whether this effect was greater with more visits, or if the efficacy of cessation efforts waned, and relapse was common.
Methods: A retrospective review of a prospectively collected database at a single institution lung cancer screening program was queried for smoking status by visit frequency. All patients referred for LDCT are screened for tobacco use and if still smoking, are met at the time of the scan for cessation support. All patient data was included for the entire history of the screening program (2014-2022), and analyzed for smoking status, gender, age, rurality (by zip code), whether they received counseling, and the number of scans.

Results: A total of 3561 LDCT scans were done over a consecutive seven-year period. The overall rate of smoking at the time of the scan was 56.7% (n=2020/3561). Expectedly, the smoking rate was the highest for those patients receiving their first LDCT scan. Upon enrollment, 64.6% (1072/1660) were smoking at the time of the first scan. Of those who went on to receive a second scan, smoking rate dropped to 46.9% (471/1004) demonstrating efficacy of the interventions three months to a year later. Unfortunately, relapse is common with nicotine addiction, and slightly higher smoking rates were demonstrated with those receiving further scans: third scan- 53.6% (238/444), fourth- 52.3% (127/243), fifth 53.6% (67/125), and sixth or more 52.9% (45/85).

Conclusions: Nicotine addiction is challenging to treat, and while evidence-based strategies such as pharmacotherapy and personalized counseling are effective, and our opt-out framework with point of care delivery is well accepted, relapse and/or continued use is possible. Persistent smoking and relapse after prior cessation further underscore the importance of asking patients at every single visit about tobacco use. Potential limitations may include that those receiving more scans may have increased pack years and this could be further evaluated as a predictor of lower quit rates. Furthermore societal, economic, and other pressures have changed over this time period due to a pandemic, and these external stressors / pressures may have influenced relapse rates in the latter 2.5 years. This persistence further demonstrates that ongoing support is needed for all screened patients at every visit.



OA01.04:
First-Line Nivolumab + Ipilimumab + Chemotherapy in Metastatic NSCLC: CheckMate 9LA 3-Year Update

Dr. David Paul Carbone[17], Dr. Luis G. Paz-Ares[1], Dr. Tudor-Eliade Ciuleanu[2], Dr. Manuel Cobo-Dols[3], Dr. Jaafar Bennouna[4], Dr. Ying Cheng[5], Dr. Hideaki Mizutani[6], Dr. Alejo Lingua[7], Dr. Felipe Reyes[8], Dr. Niels Reinmuth[9], Dr. Juliana Menezes[10], Dr. Jacek Jassem[11], Dr. Svetlana Protsenko[12], Dr. Kynan Feeney[13], Dr. Emmanuel de la Mora Jimenez[14], Dr. Shun Lu[15], Dr. Thomas John[16], Dr. Xiaoqing Zhang[18], Dr. Nan Hu[18], Dr. Martin Reck[19]

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Background: In CheckMate 9LA (NCT03215706), first-line nivolumab (NIVO) + ipilimumab (IPI) with 2 cycles of chemotherapy (chemo) improved overall survival (OS) versus chemo alone (4 cycles) in patients with metastatic non-small cell lung cancer (mNSCLC). Here, we report updated efficacy and safety results with a 3-year minimum follow-up (previous presentation: Paz-Ares ASCO2022 #LBA9026).

Methods: Adults with stage IV/recurrent NSCLC and no known sensitizing EGFR/ALK alterations were randomized 1:1 to NIVO (360 mg Q3W) + IPI (1 mg/kg Q6W) + 2 cycles of chemo (n=361) or 4 cycles of chemo alone (n=358). Patients were stratified by tumor PD-L1 expression, sex, and histology. Patients with non-squamous mNSCLC in the chemo-alone arm could receive pemetrexed maintenance. Assessments included OS, progression-free survival (PFS), objective response rate, and safety.

Results: At a minimum follow-up of 36.1 months (database lock: 15-Feb-2022), patients continued to derive long-term, durable OS benefit with NIVO+IPI+chemo versus chemo (median OS, 15.8 versus 11.0 months; HR, 0.74 [95% CI, 0.62–0.87]); 3-year OS rate was 27% versus 19%. OS benefit with NIVO+IPI+chemo versus chemo was observed across most subgroups, including by histology (Table) and tumor PD-L1 expression level. Among patients with tumor PD-L1 ≥1%, median OS was 15.8 versus 10.9 months (HR, 0.74 [95% CI, 0.60–0.93]); 3-year OS rate was 28% versus 19%. Among patients with tumor PD-L1 <1%, median OS was 17.7 versus 9.8 months (HR, 0.67 [95% CI, 0.51–0.88]); 3-year OS rate was 25% versus 15%. Additional efficacy outcomes will be presented. No new safety signals were identified.

Conclusions: With 3-years' minimum follow-up, first-line NIVO+IPI+chemo demonstrated long-term, durable efficacy benefit versus chemo, further supporting this treatment option for previously untreated patients with mNSCLC.

Table. Summary of efficacy outcomes by histology

	Squamous		Non-squamous	
	NIVO + IPI + chemo (n = 115)	Chemo (n = 112)	NIVO + IPI + chemo (n = 246)	Chemo (n = 246)
Median OS, months	14.5	9.1	17.8	12.0
HR (95% CI)	0.64 (0.48-0.86)		0.80 (0.65-0.98)	
3-year OS rate, %	24	11	28	23
3-year PFS rate, %	9	4	15	6
Objective response rate, n (%)	56 (49)	35 (31)	81 (33)	55 (22)
Median duration of response, months	10.8	3.9	17.5	7.5
Responders with ongoing response ≥3 years, %	17	6	27	20

OA01.05:
Three-year Outcomes per PD-L1 Status and Continued Cemiplimab Beyond Progression + Chemotherapy: EMPOWER-Lung 1

Prof. Marina Chiara Garassino[1], Saadettin Kilickap[2], Mustafa Özgüroğlu[3], Ahmet Sezer[4], Mahmut Gumus[5], Igor Bondarenko[6], Miranda Gogishvili[7], Marina Nechaeva[8], Michael Schenker[9], Irfan Cicin[10], Ho Gwo Fuang[11], Yaroslav Kulyaba[12], Mikhail Dvorkin[13], Kasimova Zyuhal[14], Roxana-Ioana Scheusan[15], Xuanyao He[16], Manika Kaul[16], Emmanuel Okoye[16], Yuntong Li[16], Siyu Li[16], Jean-Francois Pouliot[16], Frank Seebach[16], Israel Lowy[16], Giuseppe Gullo[16], Petra Rietschel[16]

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Background: In the EMPOWER-Lung 1 trial, cemiplimab monotherapy provided a significantly improved overall survival (OS) vs chemotherapy in patients with newly diagnosed advanced non small cell lung cancer. We are reporting the 3-year survival and objective response rate (ORR) data of the trial. Also, we are presenting the first efficacy data of patients who continued cemiplimab at progression with the addition of histology-specific chemotherapy. Some of these results were previously presented in ESMO 2022.

Methods: Patients were randomized 1:1 to cemiplimab 350 mg IV every 3 weeks for 2 years or investigator's choice of chemotherapy. A subgroup of patients who were initialy randomized to cemiplimab and experienced progression, confirmed by a blinded independent review committee (BIRC), continued cemiplimab with the addition of up to 4 cycles of chemotherapy. To be included in the post progression analysis, patients had to receive at least one dose of chemotherapy and have at least one scan following progression. Response to continued cemiplimab + chemotherapy was assessed by BIRC against a new baseline, defined as the last scan prior to the first dose of chemotherapy.

Results: At median follow-up of 37.1 months (range: 24.0-56.5), median OS in the PD-L1 ≥50% population was 26.1 months (22.1-31.8) for cemiplimab (N=284) vs 13.3 months (10.5-16.2) for chemotherapy (N=281), with hazard ratio (HR) of 0.57 (0.46-0.71); median progression free survival (mPFS) was 8.1 months (6.2-8.8) vs 5.3 months (4.3, 6.1), HR 0.51 (0.42-0.62). The difference in ORR was greatest for cemiplimab vs chemotherapy in patients with PD-L1≥90% (60.6% vs 17.9%; Odds Ratio [OR] 7.08), followed by PD-L1>60%,<90% (43.8% vs 22.2%; OR 2.72), and PD-L1 ≥50%,≤60% (34.4% vs 22.9%; OR 1.75). OS and PFS benefit with cemilplimab were similarly correlated with PD-L1 status. 64 patients continued cemiplimab + chemotherapy at the time of cemiplimab progression. The addition of chemotherapy resulted in a 31.3% ORR and an OS of 15.1 months (11.3-18.7). 19 (29.7%) patients had serious treatment-emergent adverse events (TEAEs), and 3 patients each with TEAE-induced discontinuation of study treatment or death. No new safety signal were observed in the whole, or continued cemiplimab, populations.

Conclusions: At 3 year follow-up, higher PD-L1 expression is still associated with improved outcomes for cemiplimab vs. chemotherapy as reflected by the main endpoints of ORR, PFS and OS, despite a high crossover rate. Continued cemiplimab with the addition of chemotherapy at the time of first progression provides a meaningful ORR and durable OS benefits.

OA01.07:
Sunvozertinib in NSCLC Patients with EGFR Exon20 Insertion Mutations

Dr. Lyudmila Bazhenova[1], Dr. James Chih-Hsin Yang, Dr. Mengzhao Wang, Dr. Paul Mitchell, Dr. D. Ross Camidge, Dr. Jian Fang, Dr. Weiqi Nian, Dr. Chao-Hua Chiu, Dr. Jianying Zhou, Dr. Yanqiu Zhao, Dr. Wu-Chou Su, Dr. Tsung-Ying Yang, Dr. Viola W. Zhu, Dr. Michael Millward, Dr. Yun Fan, Dr. Wen-Tsung Huang, Dr. Ying Cheng, Dr. Liyan Jiang, Dr. Li Zheng, Dr. Pasi A. Janne

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Background: Sunvozertinib (DZD9008) is a rationally designed EGFR Exon20ins inhibitor with wildtype selectivity. Results from the ongoing phase 1/2 studies showed sunvozertinib's strong anti-tumor activity and encouraging safety profile. Based on these data, sunvozertinib was granted the Breakthrough Therapy Designation by both US FDA and China NMPA. Here we present sunvozertinib's safety and efficacy results in advanced NSCLC patients with EGFR Exon20ins post platinum-based chemotherapies.

Method: Data from the ongoing WK-KONG1 (NCT03974022) and WU-KONG2 (CTR20192097) studies were pooled together for the analysis. Anti-tumor activity was assessed according to RECIST1.1 by investigator and retrospectively confirmed by IRC. The causality of adverse events was judged by investigator.

Results: As of April 3, 2022, a total of 71 locally advanced or metastatic NSCLC patients with EGFR Exon20ins mutations whose disease had progressed on or after platinum-based chemotherapy were enrolled into WU-KONG1 and WU-KONG2 studies, dosed with sunvozertinib (50 mg to 400 mg, once daily). Median age: 59; M/F: 36/62; 38% with baseline brain metastasis; subjects received 1 to10 lines of prior treatment; including platinum-based chemotherapy (71, 100%), EGFR TKIs (27, 38%), PD(L)-1 (24, 33.8%), and others. Anti-tumor activity was observed at the dose level of 100 mg and above. The best objective response rate was 45.9% and confirmed ORR was 40.5% for 300 mg group by the data cutoff date. CNS activity was observed, which was consistent with the preclinical studies. In addition, preliminary data showed tumor response in treatment naïve subjects (1 of 2 was observed to be PR) from a separate cohort. The common TEAEs of sunvozertinib were similar to those reported by other EGFR inhibitors and majority were CTCAE grade 1 or 2.

Conclusion: The data suggest sunvozertinib is active in both treatment naïve and prior platinum-based chemo treated NSCLC patients with EGFR Exon20ins. as well as in patients with CNS metastasis. Two pivotal studies (NCT03974022 and China CTR20211009) are ongoing and the updated data will be presented at the meeting. Sunvozertinib is also planned for development in treatment naïve NSCLC patients with EGFR Exon20ins in the first-line setting, either as monotherapy or combination with other agents.

OA01.08:
Clinical Response to Tepotinib According to Circulating Tumor (ct)DNA Biomarkers in Patients with Advanced/Metastatic NSCLC with High-level MET Amplification (METamp) Detected by Liquid Biopsy (LBx)

Dr. Xiuning Le[1], Luis G. Paz-Ares[2], Jan Van Meerbeeck[3], Santiago Viteri[4], Carlos Cabrera-Galvez[5], David Vincente Baz[6], Young-Chul Kim[7], Jin-Hyoung Kang[8], Christopher Stroh[9], Dilafruz Juraeva[10], Rolf Bruns[11], Gordon Otto[12], Andreas Johne[13], Paul K Paik[14,15]

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Background: Tepotinib, a potent, highly selective, oral, MET inhibitor showed meaningful activity in patients with advanced/metastatic NSCLC with high-level METamp by LBx in VISION. Exploratory biomarker analyses are presented herein.

Methods: Patients had 0–2 prior therapy lines, high-level METamp by LBx (Guardant360®; MET copy number ≥2.5), and no MET exon 14 skipping or EGFR/ALK alterations. Patients received tepotinib 500 mg (450 mg active moiety) QD. Primary endpoint was objective response by independent review; data cut-off: August 20, 2021. Exploratory biomarker analysis included LBx at baseline, on treatment, and end of treatment. Early molecular response was defined as undetectable METamp 6–8 weeks on treatment.

Results: 24 patients were enrolled (median age: 63.4 years; smokers: 88%; ECOG PS 1: 88%; adenocarcinoma: 67%). Treatment duration was ≥1 year in five patients and ≥2 years in two patients (both ongoing). Overall, objective response rate (ORR) was 41.7% (95% CI: 22.1, 63.4) (Table). ORR was 71.4% (29.0, 96.3) in treatment-naïve patients (n=7), and 27.3% (6.0, 61.0) and 33.3% (4.3, 77.7) in patients receiving tepotinib as second- (n=11) or third-line (n=6), respectively.
Baseline biomarker analyses according to clinical benefit (CR/PR/SD [n=11] vs PD/NE [n=13]) showed association with better outcomes in patients with focal METamp, or without MYCamp or RB1 mutation (Table). Low baseline ctDNA mutant allele frequency was associated with better outcomes.
Treatment-related adverse events included edema (composite term; any grade: 46%; Grade 3: 13%) and constipation (any grade: 17%; Grade ≥3: 0%).

Conclusions: Tepotinib showed meaningful activity, especially in first line, in the first trial of a MET inhibitor in EGFR WT NSCLC with high-level METamp to enroll based on a convenient LBx assay. Serial LBx could monitor molecular response and evaluate resistance.

Biomarker analyses		ORR, n (%) [95% CI]	mDOR, months (95% CI)	mPFS, months (95% CI)	mOS, months (95% CI)
Overall		10 (41.7) [22.1, 63.4]	14.3 (2.8, ne)	4.2 (1.4, 15.6)	7.5 (4.0, 15.6)
*MET*amp	Focal (n=14)	8 (57.1) [28.9, 82.3]	ne (2.9, ne)	15.6 (1.4, ne)	15.6 (6.4, ne)
	Non-focal (n=10)	2 (20.0) [2.5, 55.6]	3.0 (2.8, ne)	1.4 (0.6, 4.1)	2.2 (0.6, 6.1)
Baseline *MYC*	Diploidy (n=18)	10 (55.6) [30.8, 78.5]	14.3 (2.8, ne)	13.6 (1.4, ne)	14.3 (5.7, ne)
	Amp (n=6)	0 [0, 46.0]	ne (ne, ne)	1.4 (0.8, ne)	3.1 (0.8, ne)
Baseline *RB1*	WT (n=19)	10 (52.6) [28.9, 75.6]	14.3 (2.8, ne)	4.5 (1.4, ne)	8.3 (4.4, 24.1)
	Mutation (n=5)	0 [0, 52.2]	ne (ne, ne)	1.4 (1.4, ne)	4.9 (2.2, ne)
Early molecular response	Responder (n=14)	10 (71.4) [41.9, 91.6]	14.3 (2.8, ne)	13.6 (4.1, ne)	14.9 (6.1, ne)
	Non-responder (n=4)	0 [0, 60.2]	ne (ne, ne)	1.8 (1.4, ne)	4.9 (2.2, ne)

Amp, amplification; CI, confidence interval; DOR, duration of response; m, median; *MET*amp; *MET* amplification; ne, not estimable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; WT, wild type.

OA01.09:
Adjuvant Osimertinib in Resected EGFR-Mutated Stage IB–IIIA Non-Small Cell Lung Cancer: Updated ADAURA Results

Dr. Roy S. Herbst[1], Yi-Long Wu[2], Christian Grohe[3], Thomas John[4], Margarita Majem[5], Jie Wang[6], Terufumi Kato[7], Jonathan W. Goldman[8], Sang-We Kim[9], Chong-Jen Yu[10], Huu Vinh Vu[11], Guzel Mukhametshina[12], Charuwan Akewanlop[13], Filippo de Marinis[14], Frances A. Shepherd[15], Damien Urban[16], Marta Stachowiak[17], Ana Bolanos[18], Xiangning Huang[19], Masahiro Tsuboi[20]

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Background: Osimertinib, a third-generation EGFR-tyrosine kinase inhibitor (EGFR-TKI) that potently and selectively inhibits EGFR-TKI sensitising and EGFR T790M resistance mutations, has demonstrated efficacy in EGFR-mutated (EGFRm) non-small cell lung cancer (NSCLC), including central nervous system metastases. Adjuvant osimertinib was approved for treatment of patients with completely resected stage IB-IIIA EGFRm NSCLC based on results (data cut-off 17 Jan 2020) of the Phase III ADAURA trial (NCT02511106), which showed a statistically significant and clinically meaningful disease-free survival (DFS) benefit with adjuvant osimertinib vs placebo (DFS HR in stage IB-IIIA, 0.20; 99.12% CI, 0.14, 0.30; p<0.001). Fewer patients had disease recurrence with osimertinib (11%) vs placebo (46%) and there was a clinically meaningful improvement in central nervous system DFS (intracranial DFS) with osimertinib (HR, 0.18; 95% CI 0.10, 0.33; p<0.0001) vs placebo. We will report updated exploratory analyses of DFS and recurrence patterns after 2 years added follow up.

Methods: Eligible patients (≥18 years [≥20 in Japan/Taiwan], WHO PS 0/1, completely resected EGFRm stage IB-IIIA [AJCC 7th edition] NSCLC; adjuvant chemotherapy allowed) were randomised 1:1 to osimertinib 80 mg once daily or placebo for up to 3 years. The primary endpoint was investigator assessed DFS in stage II-IIIA; secondary endpoints included DFS in stage IB-IIIA, overall survival and safety. Patterns of recurrence and central nervous system DFS were pre-specified exploratory endpoints.

Results: Expected June 2022. An updated exploratory DFS analysis will be reported for patients with stage II-IIIA and stage IB-IIIA disease, including landmark DFS rates, plus an additional post-hoc analysis of DFS by stage based on AJCC 8th edition staging. Updated DFS in predefined subgroups, including by disease stage and adjuvant chemotherapy use, will be reported, as well as an updated safety summary. Updated recurrence data with extended follow-up will be presented, with a focus on central nervous system.

Conclusions: With 2 years further follow-up, a continued DFS benefit was sustained with osimertinib vs placebo, consistent with the primary analysis. These mature data reinforce adjuvant osimertinib as standard of care for patients with EGFRm stage IB–IIIA NSCLC after complete tumour resection and adjuvant CT, when indicated.

Previously presented at ESMO 2022, Final Publication Number: 2809, Masahiro Tsuboi et al. - Reused with permission

Poster Discussion Sessions

Poster Discussion (PPD01)
Chicago Ballroom ABCD | September 24, 2022, 16:40 - 17:40

PPD01.01:
Patterns of Use of Medical Cannabis in Lung Cancer and Other Cancer Patients

Dr. Deepti Behl[1]

[1]*Sutter Health, 2800 L Street, United States*

Background: Many patients with lung cancer and other malignancies report using cannabis for various medical reasons. Cannabis use is legal in the state of California but remains a Schedule 1 drug on the federal list with drugs such as heroin and LSD. The purpose of this study was to assess the prevalence, reasons for use, methods of use, and perceived benefits of medical cannabis in adults seen in oncology clinics in Northern California.

Methods: Patients received a questionnaire or scanned a QR code on their phone when they checked in for their appointment. Patients who used cannabis were asked questions regarding the mode of ingestion, perceived benefits, types of underlying cancer, and estimated monthly cost.

Results: A total of 1,778 surveys were completed. 481 (27%) patients with a mean age of 59.21 ± 13.44 stated that they used cannabis for medical reasons.

Table 1. Demographics of patients with cancer who stated that they used medical cannabis (N=481)

n (%)	**Race**	
Sex	White	Asian/Pacific Islander
Male	389 (81.4)	18 (3.8)
194 (40.3)	Black	Middle Eastern
Female	21 (4.4)	3 (0.6)
287 (59.7)	Hispanic	Other
	33 (6.9)	14 (2.9)

A significant number of patients with lung cancer used cannabis (92 patients- 19%), as did patients with breast cancer (110 patients-23%) and prostate cancer (63 patients-13.2%).

Of the 481 patients with all cancers reporting use of cannabis for medical reasons, 146 patients (34.6%) had a diagnosis of metastatic cancer and 130 (27.3%) were undergoing chemotherapy. The most often stated reasons for use were appetite (34.8%) pain (50.8%), sleep (59.3%), nausea (36.2 %); and anxiety/mood (45.5%).

Over 60% of the patients used edibles. A smaller percentage preferred vaping (28.3%) or smoking (41.8%) or using cannabis topically (22.8%). Over 63% of patients stated they used more than one method. Most patients reported positive results, with improved appetite reported by 57% (n=321), 2) improved nausea 56.3% (n=316), 3) improved sleep 79% (n=353), 4) improvement in neuropathy symptoms 47.1% (n=289), improved mood 71.3% patients (n=321) and 5) improved pain in 68.7% patients (n=233). 239 (48.6%) of patients spent $100 or less per month on marijuana whereas 14% spent between $100 and $200 per month.

Conclusions: Medical cannabis was used by approximately one-fourth of all cancer patients in our study. The majority reported cannabis helped improve their symptoms. Further research regarding mechanism of actions and associated risks is warranted.

PPD01.02:
Identifying Physical, Social, Emotional, and Medical Needs of Lung Cancer Survivors with Advanced Non-Small Cell Lung Cancer

Ms. Mattea Miller, Dr. Mary Boulanger, Mr. Matthew Guo, Ms Michelle Turner, Sarah Olson, Cyd Eaton, Dr. Melinda Hsu, Assoc. Prof. Joy Feliciano

Background: Current survivorship research mostly focuses on early-stage non-small cell lung cancer survivors (NSCLCS), however NSCLCS with advanced disease at diagnosis (aNCSLCS) have increased survival. Survivorship programs are beneficial, yet little is known about the physical, psychosocial, and medical needs of aNCSLCS

Methods: aNSCLCS alive ≥1 year from diagnosis and treated at Johns Hopkins were invited to complete across-sectional survey of needs of 4 subscales (physical, social, emotional, and medical) rated on a 5-point Likert scale (1=no need, 5=highest need). Demographic and clinical information were patient-reported and from chart review. Multiple regression models identified factors significantly associated with greater number of needs on each subscale.

Results: 97 surveys were included in analysis. 46% of aNCSLCS were 2-5 years from diagnosis, 64% were female, 74% had household income > $75,000, most were Caucasian (73%), non-Hispanic (98%), married (81%), retired (52%), current/former smokers (52.58%), had private insurance (84%), or had never received palliative care consultation (77%).

A majority of aNCSLCS reported physical needs of fatigue (77%), sleep disturbance (65%), memory and concentration issues (60%), weakness (53%), and hair or skin changes (54%). The most common social and emotional needs reported were managing daily activities (42%), defining a new sense of normal (77%), living with uncertainty (82%), fear of recurrence (77%), and managing difficult emotions (70%). Multivariate analysis identified factors associated with higher needs (Table 1).

Conclusions: We found that aNCSLCS have significant unmet physical, emotional, and social needs. Patients with younger age, current/former smoking status, more recent diagnosis, more lines of systemic therapy, and lower household income have greater needs. These results identify gaps in survivorship care which will be crucial to address as the number of aNCSLCS continues to increase.

Table 1. Clinical and demographic factors independently associated with needs.

Characteristic	Physical needs		Social needs		Emotional needs	
	β	P value	β	P value	β	P value
Age ≥ 65 vs <65	NS	NS	-3.85	.0002	-2.77	.006
Current / former smoker vs. never	NS	NS	NS	NS	2.06	.041
Time since diagnosis 1-2 yrs. Vs. >5 yrs. 2-5 yrs. vs. >5 yrs.	NS	NS	 2.83 2.09	 .0051 .038	NS	NS
Lines of systemic therapy 1-2 vs. 0 3+ vs 0	3.07 3.29	.002 .001	NS 2.80	NS .0056	NS	NS
Income <30,000 vs. >75,000 30,000-75,000 vs. >75,000	NS	NS	 4.52 3.20	 <.0001 .0016	NS	NS

- NS – non-significant findings

Poster Discussion (PPD02)
Chicago Ballroom ABCD | September 24, 2022, 16:40 - 17:40

PPD02.01:
Comprehensive Genomic Profiling (CGP) for Diagnostic Clarity in Pulmonary Large-Cell Neuroendocrine Carcinoma (LCNEC)

Dr. Umit Tapan[1], Dr. Kira Raskina[2], Dr. Richard Huang[2], Dr. Alexa Schrock[2], Dr. Jacob Sands[3], Dr. Geoffrey Oxnard[2], Dr. Hanna Tukachinsky[2]

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Background: LCNEC is an uncommon subtype of lung cancer believed to represent a spectrum of tumors that resemble both small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Reports by groups including MSKCC have proposed genomic LCNEC subtypes based on alterations in RB1 and MEN1. We aimed to validate this genomic subtyping in a large cohort of LCNEC samples tested with widely available CGP.

Methods: An institutional database was queried to identify tissue specimens (TBx) submitted for CGP during routine clinical care (8/2014 - 1/2022) with a disease ontology of LCNEC (N = 1,144). TBx were profiled with FoundationOne® (F1) or F1CDx, using hybrid-capture technology to detect genomic alterations (GAs) in 324+ cancer-related genes. Bayesian information criterion was used for latent class analysis (LCA) model selection.

Results: Targetable NSCLC driver alterations were seen rarely. 91/1,144 (8.0%) harbored KRAS G12C (49, 4.3%), HER2 amplification (16, 1.3%), EGFR (14, 1.2%), RET (5), ALK (3), NTRK1/2 (3), BRAF V600E (1), and MET (1). LCA identified 5 genomic subtypes of LCNEC: two commonly harbored RB1 GAs; two had GAs consistent with squamous histology (CDKN2A/B/MTAP loss, CCND1/FGF3/4/19 amplification); one was enriched for adenocarcinoma GAs (KRAS, STK11, NKX2-1, NFKBIA). MEN1 GAs were rare overall and were not recognized as a distinct subtype. Based on these data, we propose a refinement of the MSKCC classification where, hierarchically (Figure 1): (a) RB1 GAs define a SCLC-like subtype, comprising 475 (42%) of LCNEC, (b) KRAS, STK11, CDKN2A, CCND1 GAs rule-in a NSCLC-like subtype of 377 (33%), and (c) MEN1 GAs define a carcinoid-like subtype of 27 (3%). 265 (23%) biopsies remained unclassified. Prognostic implications of these LCNEC subsets will be explored.

Conclusions: CGP can detect targetable drivers and can help distinguish biologically distinct subtypes of LCNEC to potentially inform recommended treatment regimens for this challenging tumor type.

Figure 1. Latent class analysis (LCA)-informed definitions of SCLC-like, NSCLC-like, and carcinoid-like genomic subtypes of LCNEC. The top heatmap contains the genes used to define the subtypes. The bottom heatmap shows genes which had a prevalence >15% in at least one LCA cluster. Genes are in order of prevalence in the NSCLC-like subgroup. Asterisks denote significance of enrichment in the SCLC-like versus NSCLC-like group (* FDR <0.001, ** FDR <0.0001). Bottom row shows prevalence of tumor mutational burden (TMB) >10 mut/Mb.

PPD02.02:
Tepotinib + Gefitinib in Patients with EGFR-Mutant NSCLC with MET Amplification (METamp): Final Analysis of INSIGHT

Dr. Richard OHara[1], Dr. Chong Kin Liam[2], Dr. Azura Rozila Ahmad[3], Dr. Te-Chun Hsia[4], Dr. Jianying Zhou[5], Dr. Dong-Wan Kim[6], Dr. Ross Andrew Soo[7], Dr. Ying Cheng[8], Dr. Shun Lu[9], Dr. Sang Won Shin[10], Dr. James Chih-Hsin Yang[11], Dr. Yiping Zhang[12], Dr. Jun Zhao[13], Rolf Bruns[14], Andreas Johne[15], Dr. Yi-Long Wu[16]

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Background: In the INSIGHT trial primary analysis (NCT01982955; median follow-up: 21.8 months), tepotinib (a highly selective, once daily [QD] MET inhibitor) + gefitinib improved efficacy versus chemotherapy in patients with EGFR-mutant NSCLC, and resistance to anti-EGFR therapy due to METamp. Here, we report final analyses from INSIGHT (data cut-off: September 3, 2021; median follow-up: 57.5 months).
Previously presented at AACR 2022.

Methods: Patients with EGFR-mutant (T790M-negative) NSCLC and anti-EGFR resistance, with METamp (MET gene copy number ≥5 and/or MET:CEP7 ≥2 by FISH) and/or MET overexpression (IHC 2+/3+), were randomized to tepotinib 500 mg (450 mg active moiety) + gefitinib 250 mg QD or chemotherapy. Primary endpoint was progression-free survival (PFS) per investigator. Preplanned analyses evaluated patients with METamp.

Results: 19/55 randomized patients (34.5%) had METamp (MET IHC 3+, n=17; median age: 60.4 years; never-smokers: 68.4%; prior EGFR inhibitors: gefitinib [57.9%], afatinib [21.1%], erlotinib [10.5%], and icotinib [10.5%]). Median duration of tepotinib + gefitinib was 11.3 months (range: 1.1–56.5), with treatment duration >1 year in six patients (31.6%), and >4 years in three patients (15.8%). Two patients continued treatment outside the study (total duration >5 years).
Tepotinib + gefitinib improved PFS (hazard ratio [HR] 0.13; 90% confidence interval [CI]: 0.04, 0.43), overall survival (OS; HR 0.10; 90% CI: 0.02, 0.36), objective response rate, and duration of response versus chemotherapy (Table).
Treatment-related Grade ≥3 adverse events occurred in seven patients (58.3%) with tepotinib + gefitinib, and five (71.4%) with chemotherapy; most reported (>20%) were increased amylase and increased lipase (both 33.3%) with tepotinib + gefitinib, and anemia, decreased white blood cell count, and decreased neutrophil count (all 28.6%) with chemotherapy.

Conclusions: Tepotinib + gefitinib greatly improved PFS and OS versus chemotherapy in patients with EGFR-mutant NSCLC

Table. Summary of efficacy data in patients with *MET* amplification

Endpoint		Tepotinib + gefitinib (n=12)	Chemotherapy (n=7)	HR/OR (90% CI)
PFS Median, months (90% CI)	Investigator	16.6 (8.3, 22.1)	4.2 (1.4, 7.0)	HR 0.13 (0.04, 0.43)
	IRC	19.3 (5.6, 22.1)	4.2 (1.4, 7.0)	HR 0.16 (0.05, 0.52)
ORR n (%) [90% CI]	Investigator	8 (66.7) [39.1, 87.7]	3 (42.9) [12.9, 77.5]	OR 2.67 (0.37, 19.56)
	IRC	9 (75.0) [47.3, 92.8]	3 (42.9) [12.9, 77.5]	OR 4.00 (0.51, 31.38)
DOR Median, months (90% CI)	Investigator	19.9 (7.0, ne)	2.8 (2.8, ne)	-
OS* Median, months (90% CI)		37.3 (21.1, 52.1)	13.1 (3.3, 22.6)	HR 0.10 (0.02, 0.36)

*Post-study therapy included an EGFR inhibitor ± a MET inhibitor in two patients in each arm (tepotinib + gefitinib arm: osimertinib ± cabozantinib [n=1], gefitinib + cabozantinib [n=1]; chemotherapy arm: erlotinib, afatinib, and osimertinib ± crizotinib [n=1], osimertinib [n=1]). Post-study chemotherapy was received by one patient in the tepotinib + gefitinib arm, and two patients in the chemotherapy arm.

CI, confidence interval; DOR, duration of response; HR, hazard ratio; IRC, independent review committee; ne, not estimable; OR; odds ratio; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

PPD02.03:
Tepotinib in Patients with MET Exon 14 (METex14) Skipping NSCLC: Analysis of All Patients From VISION Cohorts A and C

Prof. Marina Chiara Garassino[1,2], Dr. Michael Thomas[3], Dr. Enriqueta Felip[4], Dr. Hiroshi Sakai[5], Dr. Xiuning Le[6], Dr. Remi Veillon[7], Dr. Egbert F. Smit[8], Dr. Julien Mazieres[9], Dr. Alexis B. Cortot[10], Dr. Jo Raskin[11], Santiago Viteri[12], Dr. James Chih-Hsin Yang[13], Dr. Myung-Ju Ahn[14], Dr. Yi-Long Wu[15], Dr. Rui Ma[16], Dr. Jun Zhao[17], Dr. Aurora O'Brate[18], Dr. Karin Berghoff19, Rolf Bruns[20], Gordon Otto[21], Dr. Paul Paik[22,23]

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Background: Tepotinib, a MET TKI, is approved for the treatment of METex14 skipping NSCLC. Here, we report analysis of all patients with METex14 skipping in the Phase II VISION study (Cohort A: >2-years' follow-up; confirmatory Cohort C: >9-months' follow-up); data cut-off February 20, 2022.

Previously presented at WCLC 2022.

Methods: Patients with advanced/metastatic METex14 skipping NSCLC, received tepotinib 500 mg (450 mg active moiety) once daily. Primary endpoint was objective response by IRC using RECIST v1.1. Pre-planned exploratory analysis of brain lesions was conducted by IRC using RANO-BM criteria.

Results: Patients in Cohorts A+C (N=313) had a median age of 72.0 years (range: 41–94), 49.2% were male, 62.3% were white, 33.9% were Asian, 47.6% had smoking history, 80.5% had adenocarcinoma histology, and 73.8% had ECOG PS 1.
In treatment-naïve patients (1L; n=164), objective response rate (ORR) was 56.1% (48.1, 63.8) and median duration of response (mDOR) was 46.4 months (13.8, not estimable [ne]); in previously treated patients (2L+; n=149), ORR was 45.0% (36.8, 53.3) and mDOR was 12.4 months (9.5, 18.5) (Table). 43 patients with brain metastases were evaluable by RANO-BM (1L, n=23; 2L+, n=20); 30 (69.8%) received prior brain radiotherapy or surgery. Intracranial (i) disease control rate was 88.4% (74.9, 96.1) with i-progression-free survival of 20.9 months (5.7, ne). In patients with target lesions only (n=15), iORR was 66.7% (38.4, 88.2) with iDOR ne (0.9, ne). Treatment-related adverse events (TRAEs) occurred in 91.7% of patients (Grade ≥3 34.2%); including (≥15%) peripheral edema (any grade/Grade ≥3: 66.5/10.9%), nausea (23.3/0.6%), hypoalbuminemia (23.0/3.2%), diarrhea (22.4/0.3%), and increased blood creatinine (21.7/0.6%). Permanent discontinuation due to TRAEs occurred in 14.7% of patients.

Conclusion: In VISION – the largest clinical trial of a MET inhibitor in METex14 skipping NSCLC – tepotinib showed robust and durable efficacy across treatment lines, and promising intracranial activity was observed.

Line of therapy	Cohorts A+C	ORR, % (95% CI)	mDOR, months (95% CI)	mPFS, months (95% CI)	mOS, months (95% CI)
1L	n=164	56.1 (48.1, 63.8)	46.4 (13.8, ne)	12.6 (9.6, 17.7)	19.1 (13.7, 23.7)
2L+	n=149	45.0 (36.8, 53.3)	12.4 (9.5, 18.5)	11.0 (8.2, 13.7)	19.6 (15.2, 22.3)
Overall	n=313	50.8 (45.1, 56.5)	18.0 (12.4, ne)	11.2 (9.5, 13.8)	19.3 (15.8, 22.3)

1L, first line; 2L+, second-or-later line; CI, confidence interval; mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; ne, not estimable; ORR, objective response rate.

Poster Discussion (PPD03)
Chicago Ballroom ABCD | September 24, 2022, 16:40 - 17:40

PPD03.01:
Adjuvant Radiation Therapy in Clinical Stage III (N2) Non-Small Cell Lung Cancer after Neoadjuvant Chemotherapy

Assoc. Prof. Takefumi Komiya[1], Dr. Shinkichi Takamori

[1]*University at Buffalo, Buffalo, United States*

Background: Based on previous meta-analysis and recent two large phase III trials, guidelines do not recommend routine use of adjuvant radiation in completely resected stage I-III non-small cell lung cancer (NSCLC). However, these studies primarily enrolled those who have not received neoadjuvant chemotherapy. Role of postoperative radiation therapy (PORT) especially in persistent N2 after neoadjuvant chemotherapy remains unclear.

Materials & Methods: Using National Cancer Database (NCDB), patients with clinical stage III NSCLC diagnosed between 2004 and 2017 were screened. Eligibility criteria included pathologically diagnosed NSCLC, clinical stage III, clinical N2, neoadjuvant multi-agent chemotherapy, complete resection (R0), and information regarding post-surgical N2 status (persistent vs downstaged), PORT, and AJCC staging version (6th vs 7th). Those who have received neoadjuvant radiation or PORT with less than 45Gy as total dose were excluded. Kaplan-Meier and Logrank tests were used for survival analyses. All statistical analyses were two-sided, and $p<0.05$ was required for statistical significance.

Results: A total of 1,855 patients met the eligibility criteria for analysis. In the overall cohort, there was a significant difference in overall survival (OS) between persistent N2 (Group P: N=854) and downstaged N (Group D: N=1,001). Use of adjuvant radiation showed non-significant detrimental effect in OS in the overall and group D (univariate p-values 0.27 and 0.077, respectively); however, it demonstrated a significant improvement in OS in group P ($p=0.004$). Multivariate analysis in group P also supported the finding of univariate analysis ($p=0.028$). These findings were verified by propensity-score matching analysis (Univariate, $p=0.0347$).

Conclusion: This large-scale retrospective analysis suggests that PORT may have a role in persistent N2 disease after neoadjuvant chemotherapy. Further investigations are warranted.

Poster Discussion (PPD04)
Chicago Ballroom ABCD | September 24, 2022, 16:40 - 17:40

PPD04.01:
Survival Associations of T Cell Clusters with Immunotherapy in Mesothelioma

Dr. Aakash Desai[1], Dr. Farhad Kosari[1], Dr. Maria Disselhorst[2], Dr. Alireza Agahi[1], Dr. Jun Yin[1], Dr. Tobias Peikert[1], Dr. Julia Udell[1], Sarah Johnson[1], James Smadbeck[1], Dr. Stephen Murphy[1], Alexa McCune[1], Giannoula Karagouga[1], Janet Schaefer Klein[1], Dr. Mitesh Borad[3], Dr. John Cheville[1], Dr. George Vasmatzis[1], Dr. Paul Baas[2], Dr. Aaron Mansfield[1]

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Introduction: Immune checkpoint blockade therapy (ICBT) is a first-line treatment option for patients with pleural mesothelioma with the approval of ipilimumab and nivolumab. It has been challenging to identify predictive biomarkers of benefit with ICBT in mesothelioma given its low tumor mutation burden. Since ICBTs enable adaptive anti-tumor immune responses, we investigated T-cell receptor (TCR) associations with survival outcomes from participants of two ICBT clinical trials.

Methods: We sequenced TCR complementarity determining region 3 (CDR3) to identify unique clones, which were then clustered, since recent advances suggest that similar TCR sequences share antigen specificity. Our study cohort included patients with pleural mesothelioma who were treated with nivolumab (NivoMes, NCT02497508) or nivolumab and ipilimumab (INITIATE, NCT03048474) in second or later lines of therapy. TCR sequencing was performed with the ImmunoSEQ assay in 49 and 39 pre- and post-treatment patient peripheral blood mononuclear cell (PBMC) samples, respectively. These data were integrated with TCR sequences found in bulk RNAseq data by the TRUST4 program in 42 and 31 pre- and post-treatment tumor biopsy samples, respectively, and the sequences from over 600 healthy controls. We used GIANA to identify TCR clusters. Associations of TCR clusters with overall survival (OS) were determined by cox proportional hazard analysis.

Results: We identified approximately 12,200, 4.2 million, and 2.1 million CDR3 amino acid sequences and corresponding variable chains in tumor biopsies, PBMCs, and healthy controls, respectively. ICBT enhanced T-cell infiltration and clonal diversity in tumors. Furthermore, a high number of shared TCR clones between tissue and PBMCs was associated with improved survival ($p = 0.01$). To potentially select anti-tumor clusters, we filtered for clusters that were (1) not found in healthy controls (2) recurrent in multiple patients with mesothelioma, and (3) more prevalent in post- than pre-treatment samples. This approach identified that two TCR clusters not previously reported in public CDR3 databases that were significantly associated with OS (HRs 0.23 and 0.19, $p < 0.006$).

Conclusion: We identified two unique TCR clusters that were associated with survival upon treatment with ICBT in patients with pleural mesothelioma. Enhanced shared T cell clones between tumor and PBMC was also associated with improved survival. These TCR clusters may enable approaches for antigen discovery and inform future targets for design of adoptive T cell therapies.

PPD04.02:
First-Line Nivolumab + Ipilimumab (NIVO+IPI) in Metastatic NSCLC: 5-Year Survival in CheckMate 227

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Background: In CheckMate 227 part 1 (NCT02477826), first-line NIVO+IPI demonstrated long-term, durable overall survival (OS) benefit versus chemotherapy (chemo) in patients with metastatic NSCLC (mNSCLC). Here we present 5-year outcomes (previous presentation: Brahmer ASCO2022 #LBA9025).

Methods: Adults with previously untreated stage IV/recurrent NSCLC and no known EGFR/ALK alterations were stratified by histology. Patients with tumor PD-L1 ≥1% were randomized 1:1:1 to NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W), NIVO (240 mg Q2W), or chemo. Patients with tumor PD-L1 <1% were randomized 1:1:1 to NIVO+IPI, NIVO (360 mg Q3W)+chemo, or chemo. Patients were treated until progression, toxicity, or ≤2 years for immunotherapy. Assessments included OS in all randomized patients by tumor PD-L1 expression and patients who completed 2 years of therapy, and safety.

Results: Minimum follow-up was 61.3 months (database lock, 15-Feb-2022). In patients with tumor PD-L1 ≥1% (n=1189), continued long-term OS benefit was seen with NIVO+IPI versus chemo (HR, 0.77 [95% CI, 0.66–0.91]); 5-year OS rates were 24% (NIVO+IPI), 17% (NIVO), and 14% (chemo). OS benefit also continued in patients with tumor PD-L1 <1% (n=550) for NIVO+IPI versus chemo (HR, 0.65 [95% CI, 0.52–0.81]); 5-year OS rates were 19% (NIVO+IPI), 10% (NIVO+chemo), and 7% (chemo). OS by histology is summarized (Table). Among patients with tumor PD-L1 ≥1% who completed the 2-year regimen (NIVO+IPI: n=50; NIVO: n=44), 5-year OS rates were 72% and 72%. Among patients with tumor PD-L1 <1% who completed the 2-year regimen (NIVO+IPI: n=16; NIVO+chemo: n=23), 5-year OS rates were 56% and 64%.

Conclusions: With 5-years' minimum follow-up, first-line NIVO+IPI continues to provide long-term, durable OS benefit versus chemo in mNSCLC, regardless of tumor PD-L1 expression or histology.

Table. Efficacy of NIVO+IPI versus chemo by histology

	Squamous		Non-squamous	
	NIVO + IPI	Chemo	NIVO + IPI	Chemo
PD-L1 ≥1%, n	118	118	278	279
Median OS, months	14.8	9.2	19.4	17.2
HR (95% CI)	0.69 (0.52-0.91)		0.82 (0.67-0.99)	
5-year OS rate, %	15	5	28	18
PD-L1 <1%, n	46	46	141	140
Median OS, months	16.3	8.5	17.5	13.1
HR (95% CI)	0.52 (0.34-0.82)		0.70 (0.54-0.90)	
5-year OS rate, %	18	4	19	8

PPD04.03:
Risk of Further Progression or Death among Non-small Cell Lung Cancer Patients with Durable Disease Control Enrolled in Immunotherapy Trials

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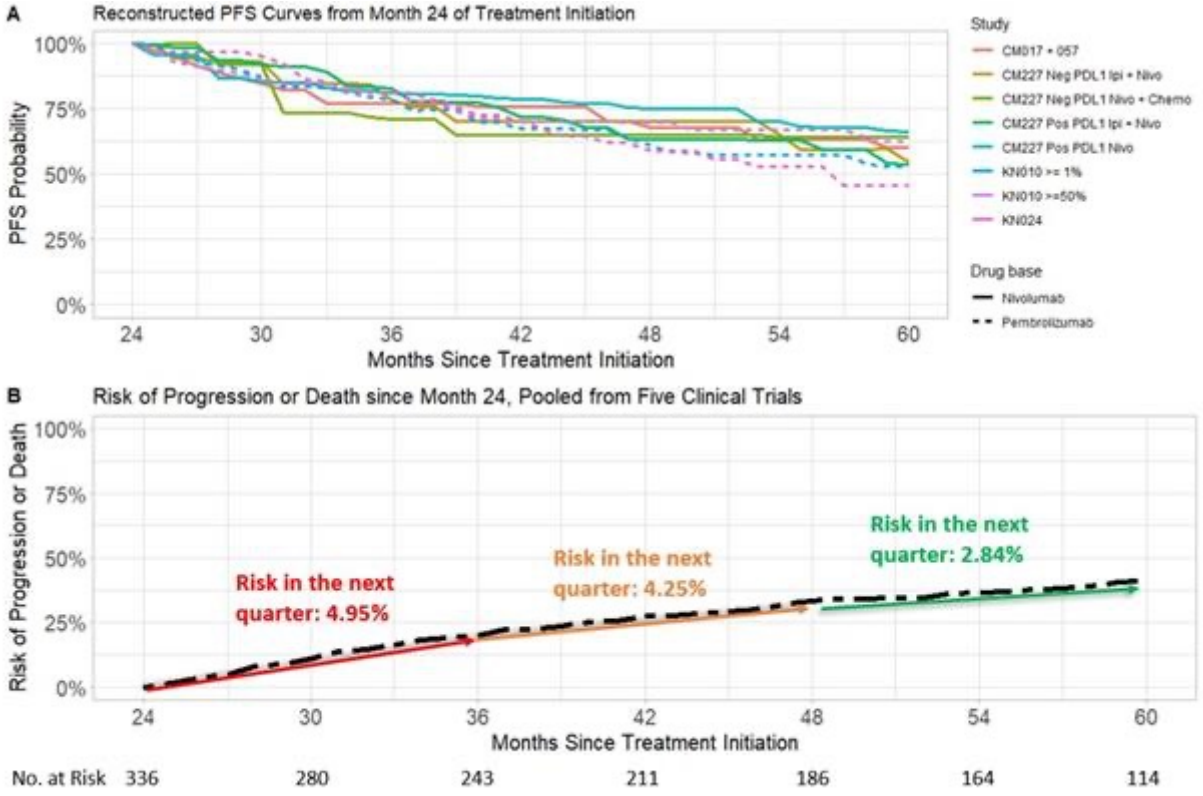
Background: Durable disease control in non-small cell lung cancer with immune checkpoint inhibitors has been reported. However, the optimal surveillance interval is largely unknown for this cohort of patients. With pooled data extracted from published clinical trials of five-year follow-up, this study aims to describe the risk of further progression or death (P or D) among patients whose disease have not progressed for 24 months.

Methods: We used Engauge Digitizer to extract P or D data from published progression-free survival (PFS) curves of Keynotes 024, 018 and Checkmates 227, 017, 057. Extracted data were pooled to construct risk of P or D curve for patients who have not progressed for two years in the immunotherapy arm. Number of censored cases were estimated with published number at risk. Risk of P or D in the next quarter was estimated.

Results: Out of 2427 aggregated patients, a total of 336 (13.8%) patients were alive and progression-free at month 24. Despite different PD-L1 status, lines of treatment and immunotherapy regimen, PFS curves were similar from month 24 onward across trials (Figure 1A). The pooled three-year rate of progression-free survival from month 24 was 59.0%. The estimated risk of P or D in the next three months was 4.95% from month 24 to 36, 4.25% from month 36 to 48, and 2.84% from month 48 to 60, respectively (Figure 1B).

Conclusion: The quarterly progression risk is less than 5% in patients who are progression free for more than 24 months, supporting surveillance longer than current every three months. However, nearly half of those patients are still at risk of further P or D in the subsequent 3 years. Further studies are needed for risk stratification.



Poster Sessions

Poster Viewing Reception (PP01)
Chicago Ballroom FGH | Exhibit Hall | September 24, 2022, 17:40 - 18:55

PP01.01:
PEOPLE (NTC03447678), a Phase II Trial to Test Biomarkers of Response to Pembrolizumab as First-Line Treatment inAdvanced NSCLC Patients with PD-L1>50%.

Dr. James Dolezal[1], MD Giuseppe Lo Russo[2], MD Claudia Proto[2], Arsela Prelaj[2], Monica Ganzinelli[2], Roberta Mortarini[2], Valter Torri[3], Roberto Ferarra[2], Luca Agnelli[2], Silvia Brich[2], Prof. Marina Chiara Garassino[1]

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Introduction: Efficacy of pembrolizumab in PD-L1<50% has been reported without no reliable biomarkers. The aim of this trial was to identify potential new immune biomarkers associated with PFS in NSCLC patients with PD-L1<50% treated with first-line pembrolizumab.

Methods: Advanced treatment-naïve NSCLC patients with PD-L1<50% were enrolled. Gene expression profiling was performed using nCounter® PanCancer IO 360™ Panel (Nanostring) on baseline tissue. Circulating immune profiling was performed by determination of absolute cell counts with multiparametric flow cytometry on freshly isolated whole blood samples at baseline and at first radiological evaluation. Gut bacterial taxonomic abundance was obtained by shotgun metagenomic sequencing of stool samples at baseline. Pembrolizumab was administered at 200 mg flat dose every 3 weeks until 35 cycles, disease progression, or unacceptable toxicity. Omics data was analyzed with sequential univariate Cox Proportional Hazards regression predicting progression-free survival (PFS), with Benjamini-Hochberg multiple comparisons correction. Biological features significant with univariate analysis were analyzed with multivariate Least Absolute Shrinkage and Selection Operator (LASSO).

Results: From May 2018 to October 2020 65 patients were enrolled. Main characteristics were: male 67.6%, smokers 87.7%, PD-L1 positive 70.8%. Median follow-up and PFS were 26.4 and 2.9 months, respectively. Gene expression profile was performed in 48 patients, microbiome in 54 patients and circulating immune profiling in 56 patients at baseline and in 46 patients at first radiologic evaluation. LASSO multivariate analysis with optimal lambda of 0.28 showed high expression levels of IRF9 and COMP genes were associated with an unfavorable PFS (HR 3.03,1.52-6.02, p=0.08 and HR 1.22, 1.08 – 1.37, corrected p=0.06, respectively). High expression levels of CD244 (HR 0.74, 0.62- 0.67, p=0.05), PTPRC (HR 0.55, 0.38 – 0.81, p=0.098), KLRB1 (HR 0.76, 0.66 – 0.89, p=0.05) in tissue samples and NK cells/CD56dimCD16+ (HR 0.56, 0.41 – 0.76, p=0.006) in peripheral blood at baseline and non classical CD14dim CD16+ monocytes (HR 0.52, 0.36 – 0.75, p=0.004), eosinophils (CD 15+CD16-) (HR 0.62, 0.44 – 0.89, p=0.003) lymphocytes (HR 0.28, 0.15 – 0.5, p=0.001) in peripheral blood after first radiologic evaluation were associated to a favorable PFS. No microbiome features were selected by LASSO.

Conclusions: To the best of our knowledge, this is the first prospective trial in NSCLC with PD-L1<50% performed with a multi-omic approach able to identify immune cell subsets and expression levels of genes associated with PFS under first-line treatment with pembrolizumab. These preliminary data will be confirmed in a larger multicentric dataset. (Presented Asco 2022)

PP01.02:
Molecular Recurrence Risk Profiles in Patients with Early-Stage NSCLC: Current Standard of Care Compared to a Prognostic and Predictive 14-gene Expression Assay

Ms. Julie Hufham[1], Jennifer Aversano[1,2], Martina Doleshal[1,3], Dr. Douglas Harrington[1,4]

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Background: The National Comprehensive Cancer Network (NCCN) Guidelines recommend patients with stage IB-IIA non-small cell lung cancer (NSCLC) receive adjuvant therapy post-surgical resection if they have clinicopathologic features that are considered high-risk.1 These features are not validated to stratify risk or predict therapy benefit. NCCN recommends observation for stage IA patients, despite a 26% recurrence rate for stage I adenocarcinomas post-resection2, with no guidelines to stratify which IA patients could benefit from additional management. This study reports utilization of a commercial CLIA-certified 14-gene qPCR expression assay (DetermaRx), validated to evaluate recurrence risk and predict chemotherapy benefit in early-stage non-squamous NSCLC.3 This report analyzes the benefit of assessing molecular risk compared to NCCN high-risk features alone. The study expands a previously published report of 250 cases to a review of over 2000 cases.4

Methods: All non-squamous NSCLC specimens received between 2/2020 and 4/2022 were tested with DetermaRx in a CLIA-certified laboratory (Oncocyte). Pathologic stage, type, and number of NCCN high-risk features1 were obtained from pathology reports submitted with the specimens and compared to the molecular risk profile. Inclusion criteria for this analysis were stage I-IIA tumors in which only one specimen was sent for testing and all NCCN clinicopathological features were available.

Results: A total of 2,003 cases were sent from 205 centers with 75% coming from thoracic surgeons. Forty-four percent of cases resulted as molecular high/intermediate risk. Fifty-nine percent were stage IA according to AJCC 8th edition staging criteria; one-third of IA cases were molecular high/intermediate risk. Molecular high/intermediate risk cases were more likely to have at least one NCCN high-risk feature compared to molecular low risk. However, as previously published4, a significant number of cases considered high-risk by NCCN (defined as having at least one high-risk feature) were reclassified as low risk by the molecular assay, and cases with no NCCN high-risk features were reclassified as molecular high-risk.

Conclusion: Molecular risk classification may improve outcomes for early-stage NSCLC patients, particularly for stage IA patients. Current standard of care is potentially undertreating one-third of stage IA patients who may be at higher risk for recurrence and could benefit from additional treatment post-resection. Use of clinicopathologic features alone may lead to overtreatment by the current paradigm. A validated 14-gene expression assay that has previously been demonstrated to outperform NCCN high-risk features in assessing recurrence risk is a powerful tool for reclassifying recurrence risk for many early-stage patients in the clinical setting.

PP01.03:
Flagging High-Risk Individuals with a ML Model Improves NSCLC Early Detection in a USPSTF-Eligible Population.

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Background: The USPSTF recommends annual lung cancer screening with LDCT in adults aged 50 to 80 years who have a ≥20 pack-year smoking history and currently smoke or have quit within the past 15 years. Risk prediction models are an alternative approach to identify high-risk individuals for screening that may have advantages compared to age and smoking history-based selection. We compared the performance of two risk prediction models, LungFlag and modified PLCOm2012 (mPLCOm2012).

Methods: Data from a large US health system including 6,505 case patients with non-small cell lung cancer (NSCLC) and 189,597 contemporaneous NSCLC-free controls were used to evaluate the performance of an optimized version of a previously published machine-learning model (LungFlag) to detect NSCLC among individuals who meet the USPSTF criteria compared to the performance of mPLCOm2012. The model used existing routine out-patient lab measurements, smoking history, comorbidities, and demographic data.

Results: Data were analyzed using the area under the receiver operating characteristic curve (AUC), and diagnostic sensitivity on the USPSTF screen-eligible population (Table). The risk predictor was calculated for a 3–12-month window prior to the diagnosis date (Dx) using cut-offs yielding specificity levels of 97%, 95% or 90%.

Conclusion: The LungFlag model was more accurate for early diagnosis of NSCLC than mPLCOm2012, demonstrating the potential to help prevent lung cancer deaths through early detection among USPSTF population.

NSCLC Stage	AUC		Sensitivity @ Specificity Level					
			Sens @ 97% Spec		*Sens @ 95% Spec*		*Sens@ 90% Spec*	
	LungFlag	PLCOm2012	LungFlag	PLCOm2012	LungFlag	PLCOm2012	LungFlag	PLCOm2012
Stage 0 (in situ)	0.840 [0.770,0.890]	0.770 [0.710,0.850]	26.5 [11.5,46.3]	23.5 [10.0,38.7]	44.1 [26.7,61.3]	23.5 [10.3,41.2]	55.9 [37.9,69.7]	35.3 [18.8,53.1]
Stage I	0.793 [0.770,0.822]	0.747 [0.722,0.775]	21.4 [16.8,26.6]	11.0 [7.4,15.2]	28.5 [24.1,35.2]	16.7 [12.6,21.9]	42.7 [38.3,49.7]	31.7 [25.5,37.2]
Stage II	0.824 [0.785,0.852]	0.764 [0.729,0.808]	26.6 [18.1,34.7]	18.8 [12.7,26.5]	32.0 [24.0,41.3]	25.0 [17.6,33.8]	44.5 [35.7,54.6]	33.6 [25.7,42.4]
Stage III	0.777 [0.746,0.805]	0.739 [0.709,0.770]	16.7 [11.2,21.2]	15.9 [11.2,20.6]	24.7 [18.5,29.6]	18.8 [13.9,24.0]	40.2 [32.6,45.8]	33.1 [26.5,39.0]
Stage IV	0.753 [0.733,0.775]	0.726 [0.704,0.748]	15.5 [12.2,19.1]	11.7 [9.0,14.9]	21.7 [17.3,25.4]	17.4 [12.8,21.3]	33.1 [28.1,38.0]	29.1 [24.1,33.0]
Total	**0.772 [0.757,0.788]**	**0.735 [0.718,0.749]**	**17.7 [15.2,20.5]**	**12.1 [9.6,14.1]**	**23.7 [21.2,26.8]**	**18.0 [14.7,20.3]**	**37.5 [33.6,40.5]**	**29.5 [26.5,33.2]**

PP01.04:
Hispanic Patients are at Higher Risk for Delayed Time to Surgery Following Identification of a Solid Lung Nodule

Dr. Donna Phan[1,2], Dr. Rachel Riccardi[1], Dr. Gbalekan Dawodu[1], Dr. Jorge Rodriguez Quintero[1], Dr. Brandon Ferrell[1], Dr. Syeda Sarosh Sohail[1], Patricia Friedmann[1,2], Dr. Neel Chudgar[1], Dr. Brendon Stiles[1,2]

[1]Montefiore Medical Center, 3450 Wayne Ave, Apt 23d, United States, [2]Albert Einstein College of Medicine, Bronx, United States

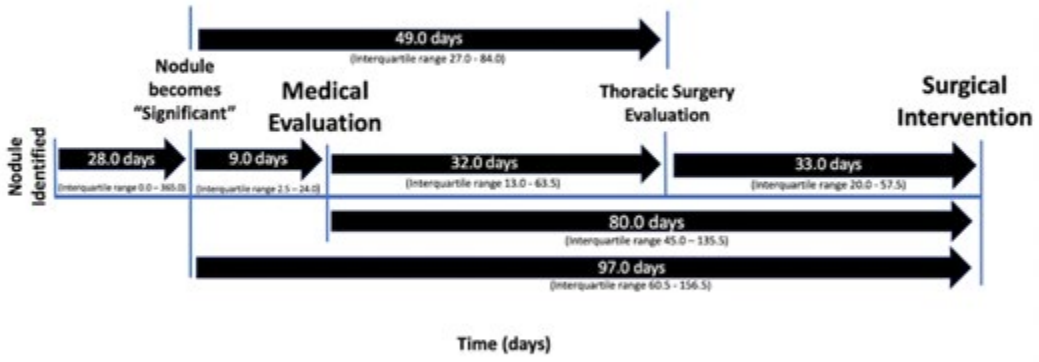
Background: The majority of lung cancer cases are diagnosed at advanced stages of disease. Receiving timely care is crucial in disparate populations with reduced access to care. The purpose of this study was to delineate timelines of care after identification of suspicious lung nodules and examine factors associated with delays.

Methods: This is a single center, retrospective review of resections for primary lung cancers at a large urban medical center between 2018 and 2020. Pathology other than non-small cell lung cancer and those receiving neoadjuvant therapy were excluded. Time to surgery (TTS) was the period from when a nodule was identified as "significant" to the date of surgery. A "significant" nodule was one which triggered referral for evaluation given concern for malignancy, in contrast to surveillance. Delayed TTS was defined as greater than 8 weeks (56 days).

Results: Of 210 patients identified, 149 met inclusion criteria. The majority were female (n=91, 61.1%) and minorities (Hispanic [n=57, 38.3%], Black [n=49, 32.2%]). The median age 68.0 years (interquartile range (IQR), 62.0-75.0), and the majority were insured through Medicare (n=85, 57.0%). Most patients experienced delayed TTS (n=114, 76.5%); median TTS was 97.0 days (IQR, 60.5-156.5, Figure 1). They had prompt medical evaluations with median time to medical evaluation (consultation with pulmonology or medical oncology) being 9 days (IQR, 2.5-24.0), while median time to initial thoracic surgery evaluation was 49 days (IQR, 27.0-84.0). All but one patient were referred to thoracic surgery after medical evaluation. On multivariate analysis of demographic factors, Hispanic patients (adjusted odds ratio 3.69 [CI 1.25-10.9]), demonstrated greater risk of delayed TTS.

Conclusions: Hispanic patients in our population are at a significantly increased risk of experiencing delayed TTS. Targeting this populations with educational initiatives and earlier referral to thoracic surgery during nodule evaluation may expedite care and improve lung cancer outcomes.

Figure 1. Median Times between Evaluations



PP01.05:
Impact of PD-L1 Status on Survival on Immunotherapy Monotherapy in Real-World Patients with Poor Performance Status: A US Nationwide Veterans Affairs Study

Dr. Julie Wu[1], Chloe Su1, Dr. Jennifer La[2], June Corrigan[2], Dr. Millie Das[1], Dr. Nhan Do[2], Dr. Mary Brophy[2], Dr. Sara Ahmed[3], Dr. Summer Han[1], Dr. Nathanael Fillmore[2], Dr. Michael Kelley[3]

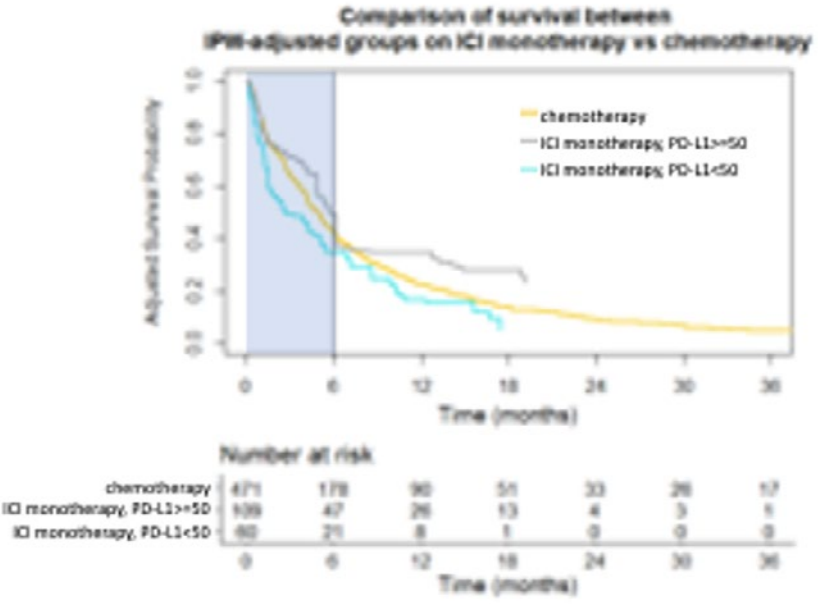
[1]Stanford University, Palo Alto, United States, [2]VA Boston Healthcare System, Boston, United States, [3]VA National Oncology Program, Durham, United States

Introduction: Patients with Eastern Cooperative Oncology Group performance status (PS) of 2 or greater were excluded from immune checkpoint inhibitor (ICI) trials in non-small cell lung cancer (NSCLC). We aim to assess how PD-L1 status affects survival on ICI monotherapy versus chemotherapy in patients with trial-ineligible PS using nationwide real-world data.

Methods: We used retrospective, multi-center data from the Veterans Affairs (VA) Precision Oncology database and VA Corporate Data Warehouse. We compared patients with advanced NSCLC who initiated first-line ICI monotherapy between 1/1/2019 and 12/30/2021, stratified by PD-L1 status (>=50% or <50%), to a historic cohort who initiated first-line chemotherapy between 1/1/2015 and 12/30/2018. All had PS>=2 documented in the period starting from 60 days prior to 14 days after therapy initiation. Patients were followed until 5/10/2022. To evaluate the causal effects of treatment, the two treatment groups were balanced using inverse probability weighting (IPW) on the following baseline covariates: age, frailty, smoking history, histology, and PS score. Overall survival of re-weighted groups was compared using Kaplan-Meier analysis and restricted mean survival times (RMST). To evaluate early versus late effects of treatment on survival, we use time censoring to calculate the IPW-adjusted Cox regression hazard ratio (aHR) at less than 6 months and 6 months or greater.

Results: 471 patients on chemotherapy (75% with PS 2, 22% PS 3, 3% PS 4) were followed for a median of 4.8 years. Median follow-up for 169 patients on ICI monotherapy (66% with PS 2, 32% PS 3, 2% PS 4) was 1.26 years. Among patients on ICI, 109 (64.5%) had PD-L1>=50%. When patients on chemotherapy were compared to patients on ICI, there were no significant survival differences at 12 months (RMST, chemotherapy 5.86mo vs ICI 5.92mo, p=0.91). However, among patients with PD-L1<50%, ICI monotherapy was associated with early increased mortality relative to chemotherapy (aHR within 6 months, 1.6, 95%CI 1.1-2.4, p=0.023) that lessened over time (aHR among patients who survived 6 months, 1.1, 95%CI 0.52-2.2, p=0.87). In contrast, among patients with PD-L1>=50%, ICI monotherapy was associated with comparable survival to chemotherapy in the first six months (aHR <6mo, 0.92, 95%CI 0.76-1.3, p=0.60) with also a late benefit (aHR >=6mo, 0.49, 95%CI 0.28-0.87, p=0.015).

Conclusion: Among patients with trial-ineligible PS, there was no significant difference in 12-month survival on ICI monotherapy and chemotherapy. However, ICI monotherapy is associated with early harm among patients with PD-L1<50% and late benefit among patients with PD-L1>=50%.



PP01.06:
Circulomic Variables may Predict Pathologic Staging Preoperatively in Treatment-Naïve Non-Small Cell Lung Cancer

Dr. Nathaniel Deboever[1], Dr Michael Eisenberg[1], Dr Wayne Hofstetter[1], Dr Reza Mehran[1], Dr Ravi Rajaram[1], Dr David Rice[1], Dr Jack Roth[1], Dr Boris Sepesi[1], Dr Stephen Swisher[1], Dr Ara Vaporciyan[1], Dr Garrett Walsh[1], Dr. Mara Antonoff[1]

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Background: Therapeutic options in non-small cell lung cancer (NSCLC) are stage-dependent, and, consequently, changes in an individual's stage carries potential for substantial alterations in management. Disturbance of the circulomic inflammasome from oncologic pressures may affect platelets in a quantitative manner, and ultimately lead to changes in tumor characteristics associated with disease overstaging or understaging. Our objective was to identify circulomic characteristics associated with a change in stage among chemotherapy-naïve patients with resectable NSCLC.

Methods: Retrospective review of a prospectively maintained thoracic surgery database was performed, identifying chemotherapy-naïve patients who underwent resection of NSCLC between 1998-2021. Clinicopathologic characteristics were gathered; circulomic variables comprised of platelet, and lymphocyte count from the last blood draw prior to resection. Platelet to lymphocyte ratio (PLR) was calculated. Two multivariate models (MVA) were built to evaluate variables that might affect upstaging or downstaging. Surgical era adjustment was performed.

Results: 4400 patients met inclusion criteria (median age: 66.9 years) among whom the sex distribution was fairly equal (2316 female, 52.6%). The most common histopathology identified was adenocarcinoma (n=2619, 59.5%). The most frequent clinical and pathologic stages were both I (n=3026, 68.8% and n=2392, 54.4%, respectively). Among these patients, 1050 (23.9%) were upstaged, while 300 (6.8%) were downstaged. Squamous histology was associated with decreased upstaging (Odds Ratio [OR]=0.665, 95% Confidence Interval [CI]: 0.549-0.806, p<0.001), and increased upstaging (OR=1.521, CI: 1.144-2.022, p=0.004, Table). Moreover, patients with elevated PLR were at reduced risk of being upstaged (OR= 0.760, CI: 0.653-0.883, p<0.001), and, in fact, were more likely to be downstaged (OR=1.410, CI 1.093-1.821, p=0.008).

Conclusion: PLR appears to impact likelihood of upstaging and downstaging in chemotherapy-naïve patients with resectable NSCLC. Along with clinicopathologic characteristics, circulomic variables may provide insight relating to pathologic staging prior to resection. These results may guide patient counseling, as well as referral patterns for adjuvant therapy.

Variables	Upstaging		Downstaging	
	OR (95%CI)	p value	OR (95%CI)	p value
PLR (Above median value)	0.760 (0.653-0.883)	<0.001	1.410 (1.093-1.821)	0.008
Age (Increasing)	NS		0.986 (0.975-0.997)	0.017
Histopathology				
Adenocarcinoma	Reference		Reference	
Squamous Cell	0.665 (0.549-0.806)	<0.001	1.521 (1.144-2.022)	0.004
Other	0.842 (0.688-1.030)	0.095	0.785 (0.537-1.147)	0.211
VATS (Yes)	0.732 (0.619-0.867)	<0.001	0.613 (0.453-0.828)	0.001
Margin (Positive)	NS		2.691 (1.634-4.435)	<0.001
Tumor Size (increasing)	1.164 (1.124-1.206)	<0.001	NS	
Lymphovascular Invasion (Yes)	2.917 (2.474-3.441)	<0.001	NS	
Extranodal Invasion (Yes)	2.886 (1.830-4.551)	<0.001	NS	

Table: Binomial Logistical Regression models investigating clinicopathologic and circulomic variables that impact upstaging or downstaging in chemotherapy naïve patients with resectable non-small cell cancer. Abbreviations: OR: Odds Ratio, 95%CI: 95% Confidence Interval, PLR: Platelet to Lymphocyte Ratio, NS: Not Significant, VATS: Video Assisted Thoracoscopic Surgery.

PP01.07:
Identifying Patient Barriers to Adherence in Lung Cancer Screening

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Background: Lung cancer remains the leading cause of cancer death despite the decade since results of the National Lung Screening Trial, which afforded opportunity for lung cancer screening (LSC) for high-risk patients. While screening contributed to the slowly increasing 5-year survival rates in this patient population there remain a large portion of eligible patients who have not participated. In addition, patients who begin the LCS process fail to follow up are unable to receive the full benefits of LCS. Published adherence rates among LCS programs average 55%. Barriers to adherence rates are not well known. We aimed to identify barriers to adherence in patients undergoing LCS in a tertiary care cancer center.

Methods: An investigation of patients enrolled in The Center for Lung Cancer Prevention and Screening at Stony Brook Medicine's LCS program who were identified as non-adherent in follow up identified 332 patients in 2017-2019. The program's protocol involves an initial reminder letter, two follow up calls and a certified-letter to maximize adherence and identify reasons for non-adherence. Notes from these calls were reviewed to determine barriers to LCS adherence .

Results: Patients enrolled in LCS through 2019 numbered 1211. Charts of the non-adherent LCS patients were reviewed. Barriers were identified with the following frequencies:

1. **Patient** left the practice but continues with LCS elsewhere(41%).
2. **Patient** unable to be screened due to illness (18%).
3. **Lost** to follow up (9%).
4. **Patient** refused with explanations (14%) of the patients that were identified as #4 the barriers identified were as follows:
5. **Patient** does not see the need (50%), patient does not agree with frequency (20%), patient concerned about radiation (10%), patient felt claustrophobic in CAT scanner (4%), cost (1%), no further explanation (15%)
6. **Patient's** insurance changed and patient had LCS elsewhere (18%)

Conclusions: Of the 1211 patients, 332(27%) were identified as non-adherent. Inquiry regarding "barriers" allowed us to determine that 59% were adherent undergoing LCS elsewhere and 18% no longer met criteria for LCS. This information led to a final non-adherence rate of 23%.

This investigation shed light on the importance of barrier evaluation for both the success of a LCS program and patient feedback. The outcomes included clarification of adherence rates as well as important details of the reasons patients refused follow up. Foresight of potential barriers may equip health care providers to enquire and address such issues in a LCS program. Further investigation is warranted.

PP01.08:
Circulating Genetically Abnormal Cells Predicts Risk of Lung Cancer in Individuals with Indeterminant Pulmonary Nodules

Dr. Benjamin A Katchman[1], Shahram Tahvilian[1], Joshua D Kuban[2], David F Yankelevitz[3], Daniel Leventon[1], Claudia I Henschke[3], Jeffrey Zhu[3], Lara Baden[1], Rowena Yip[3], Fred R Hirsch[3], Rebecca Reed[1], Ashely Brown[1], Allison Muldoon[1], Michael Trejo[1], Michael J Donovan[1], Paul C Pagano[1]

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Background: Identification of lung cancer at earlier stages results in a more favorable clinical outcome. National screening trials have demonstrated that computed tomography (CT) could identify lung nodules at an earlier, more curable stage. However, CT scans, while highly sensitive have poor specificity resulting in approximately 60% of patients to have a diagnosis of an indeterminant nodule. Additionally, 40% of patients that undergo pulmonary biopsies, do not have lung cancer, suggesting that improved diagnostic tools are needed to compliment current screening and risk profile calculators. LungLB™ is a liquid biopsy test that identifies rare genetically abnormal cells found in blood to aid in the clinical assessment of patients with indeterminant lung nodules.

Methods : The LungLB™ test is a 4-color fluorescence in-situ hybridization assay for detecting rare genetically abnormal cells from peripheral blood. A blinded, prospective correlational study was performed on 151 participants scheduled for a pulmonary nodule biopsy and to receive the LungLB™ blood test. Mann-Whitney, Fisher's Exact and Chi-Square were used to assess correlation of LungLB with biopsy results. The Receiver operator characteristics area under the curve (AUC), sensitivity, specificity along with the were evaluated and compared to CT, positron emission tomography (PET), and the Mayo Risk Model.

Results: Out of the 151 total patients, as a preliminary analysis, a subset with Stage I Lung Cancer (N=62) were compared against patients with benign disease (N=39) to determine the sensitivity and specificity of the LungLB™ test for the early detection of lung cancer. Clinical variables including previous cancer, smoking history, lesion size, and nodule appearance were collected. LungLB™ achieved a 74% sensitivity and 74% specificity with an area under the curve (AUC) of 0.81 for predicting early-stage lung cancer.

Conclusions: Early clinical performance of the LungLB™ test supports a role in the discrimination of benign from malignant pulmonary nodules. Additional clinical validation and utility studies are ongoing.

PP01.09:
Genotypic Characteristics and Resistance Mutations in Advanced ALK+ NSCLC: The ALK-PATHFINDER Study

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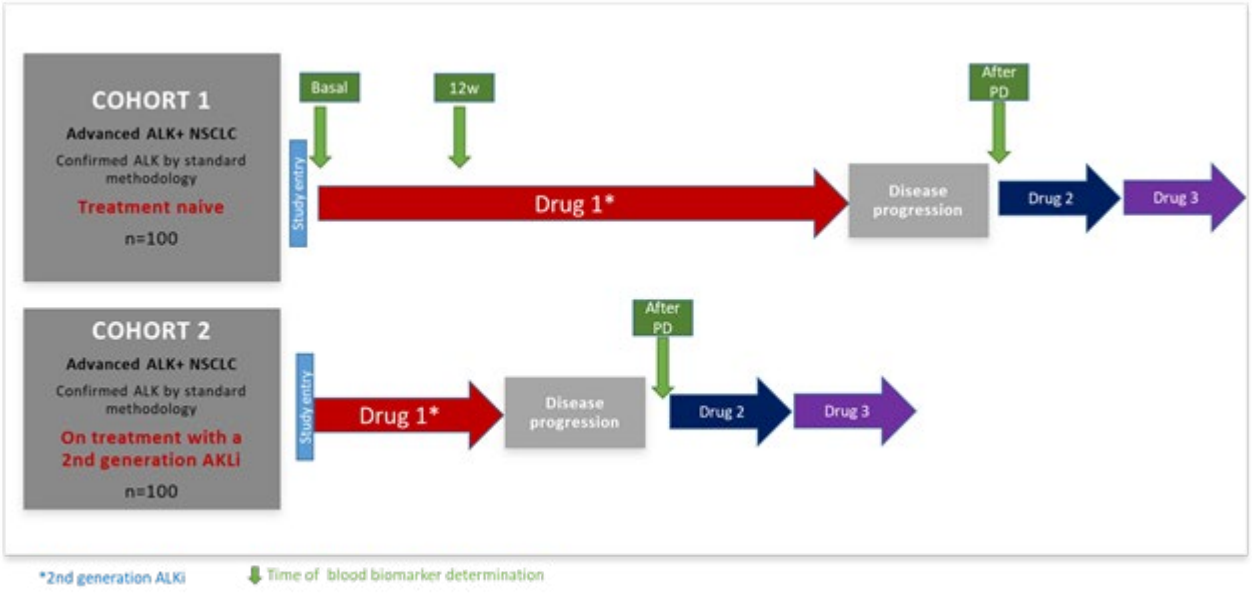
Background: ALK rearrangements occur in approximately 5% of advanced non-small cell lung cancer (NSCLC) patients. The current standard initial therapy is a second-generation ALK tyrosine kinase inhibitor (TKI), such as alectinib or brigatinib, which has shown great improvements in response rates, progression-free survival and overall survival. However, most patients relapse due to acquired resistance mechanisms including secondary mutations in ALK kinase domain, such as G1202R and I1171N. Indeed, ALK mutations are more frequent in patients treated with second generation inhibitors than with first-generation (53-54% under alectinib or ceritinib, 71% under brigatinib vs. 20% under crizotinib). In addition, the optimal sequence of ALK inhibitors has not been established yet, but the selection of the most suitable subsequent line according to ALK resistance mutations must be a key strategic approach for the therapeutic decision-making process for these patients.

Trial Design: The ALK-PATHFINDER study is a two-cohort and multicenter observational study in advanced ALK-positive NSCLC patients. Cohort 1 will prospectively include patients that are treatment naïve, whereas cohort 2 will include patients who are already on treatment with a second-generation ALK inhibitor. A sample size of approximately 100 patients is planned for each cohort (figure 1). The primary endpoint of this study is to describe initial and longitudinally genotypic characteristics of patients through circulating free/tumor DNA (cf/ctDNA) by comprehensive NGS, and evaluate its influence in progression free survival (PFS), pattern of tumor spread and overall survival (OS). This trial will run in 30 sites in Spain and recruitment st arted in September 2021. Currently, 20 patients with blood sample collected have been enrolled. The recruitment is expected to be completed by September 2023.



PP01.10:
A Randomized, Open-Label Phase 2 Study of the TORC 1/2 Inhibitor Sapanisertib in Relapsed/Refractory (R/R) NFE2L2 (NRF2)-Mutated and Wild-Type (WT) Squamous Non-Small Cell Lung Cancer (sqNSCLC)

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Background: Activation of the transcription factor NRF2 increases the expression of genes that regulate defense against reactive oxygen species and cellular stress, which is implicated in tumorigenesis of several cancer types. NRF2 activation in tumor cells has also been found to accelerate metabolic inactivation of certain antitumor agents and decrease intracellular drug concentrations, promoting drug resistance and tumor growth. Aberrant activation of NRF2 results from gain-of-function mutations in NFE2L2 (the gene that encodes NRF2) or loss-of-function mutations in KEAP1 (a negative regulator of NRF2) leading to upregulated signaling through the mTOR pathway. This event occurs early in NSCLC tumorigenesis and is associated with poor prognosis in patients with metastatic sqNSCLC. sqNSCLC cell lines harboring NFE2L2 or KEAP1 mutations have demonstrated selective sensitivity to the dual TORC1/2 inhibitor sapanisertib, compared to TORC1-only inhibitors (Paik et al. ASCO 2020). In a phase 2 trial, single agent sapanisertib was well tolerated and led to an overall response rate (ORR) of 25%, disease control rate (DCR) of >90%, and median progression-free survival (PFS) of 8.9 months in 12 patients with NFE2L2-mutated sqNSCLC (Paik et al. ASCO 2020). Preclinical data and encouraging early clinical activity formed the rationale for conducting this phase 2 study to evaluate the efficacy and further refine the dose of sapanisertib monotherapy in patients with R/R NFE2L2-mutant and wild-type (WT) sqNSCLC (NCT05275673).

Methods: This multicenter, randomized, open-label study will enroll approximately 50 patients with histologically or cytologically documented stage IV sqNSCLC in 2 arms: NFE2L2-mutant cohort (Group A) or NFE2L2-WT cohort (Group B). Patients must have disease that progressed during or after prior systemic therapy for metastatic disease, including a platinum doublet and immune checkpoint inhibitor. Additional eligibility criteria include measurable disease per RECIST v1.1, and ECOG performance status 0-1. Study-eligible mutation in NFE2L2 or NFE2L2-WT status will be determined via next generation sequencing. Both Group A and Group B patients (NFE2L2-mutated) will be randomized to sapanisertib 3 mg once daily or 2 mg twice daily in 21-day cycles. The primary endpoints are investigator-assessed ORR per RECIST v1.1 and safety. Secondary endpoints are duration of response, PFS, and overall survival. Exploratory endpoints include PK/PD and biomarker analyses. Findings from this study will inform on the optimal dose/schedule and further confirm previously shown efficacy and safety of sapanisertib in patients with metastatic R/R NFE2L2-mutated sqNSCLC and evaluate its activity in NFE2L2-WT sqNSCLC.

PP01.11:
Furmonertinib is an Oral, Irreversible, Highly Brain-Penetrant Pan-EGFR Inhibitor with Activity Against Classical and Atypical EGFR Mutations

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Background: Furmonertinib is an oral, highly brain-penetrant pan-EGFR mutant selective inhibitor that contains a trifluoroethoxypridine group, predicted to improve binding to the hydrophobic pocket within the EGFR kinase domain. A randomized Phase 3 frontline study in patients with classical EGFR mutations (exon 19 deletions [exon19del], L858R) demonstrated clinical superiority over gefitinib. Promising clinical activity was observed in patients with atypical EGFR mutations such as EGFR exon 20 insertions (exon20ins). Here we present the nonclinical data supporting broad activity across EGFR activating mutations (classical and atypical) and HER2 exon20ins, and antitumor activity in the CNS.

Methods: Furmonertinib and its active metabolite, AST5902, were tested in cell lines and in murine xenograft models to evaluate antitumor activity. Furmonertinib and AST5902 concentrations in brain tissue were measured to determine brain penetration. Furmonertinib activity in treating CNS disease was assessed in PC-9 luc brain orthotopic model harboring EGFR exon19del mutation.

Results: Furmonertinib and AST5902 demonstrated potent inhibition of lung cancer cell lines with classical EGFR mutations, including exon19del or L858R with or without T790M resistance mutations (IC50 range of 0.8 nM to 2.9 nM). Utilizing engineered Ba/F3 cells, furmonertinib and AST5902 demonstrated activity across a panel of EGFR mutations, including atypical mutations such as exon20ins (eg, D770_N771insSVD [IC50 of ~48 nM]) and other atypical mutations such as G719x or E709x (IC50 range of 12.1 nM to 31.6 nM). Furmonertinib also demonstrated activity against HER2 exon20ins mutations (eg, V777_G778insGC [IC50 = 25 nM]).

In murine tumor xenograft models with EGFR or HER2 exon20ins mutations, furmonertinib exhibited dose-dependent antitumor activity. In murine models with EGFR exon20ins mutation, furmonertinib 30 mg/kg and 50 mg/kg PO QD for 14 days was well tolerated and resulted in tumor growth inhibition (TGI) of 49.6% and 90.14%, respectively. In a model harboring EGFR G724S atypical mutation, furmonertinib 30 mg/kg and 50 mg/kg resulted in TGI of 114% and 123%, respectively. In a single dose mice PK study, brain-to-plasma ratio of furmonertinib and AST5902 were 3.31 and 0.76, respectively, indicating that furmonertinib is highly brain-penetrant. In a PC-9-LuC human orthotopic transplantation tumor model (EGFR exon19del), furmonertinib 10 mg/kg and 30 mg/kg had significant antitumor activity, with TGI of 90.20% and 100.49%, respectively.

Conclusions: Furmonertinib exhibits broad preclinical activity against both classical and atypical EGFR mutations, as well as HER2 exon20ins mutations. Furmonertinib is also active in treating CNS disease in animal models. Furmonertinib is currently being evaluated in global clinical trials (NCT05364073).

PP01.12:
Increasing Diagnosis of Ground Glass Nodules and Semi-Solid Lung Lesions on Chest CT Scans over the Past Decade

Dr. Gavitt Woodard[1], Dr. Lynn Tanoue[1], Dr. Frank Detterbeck[1], Dr. Daniel Boffa[1], Dr. Vincent Mase[1], Dr. Justin Blasberg[1], Dr. Andrew Dhanasopon[1], Dr. Babina Gosangi[1], Dr. Leah Traube[1], Dr. Anna Bader[1]

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Background: The increased use of cross-sectional computerized tomography (CT) frequently identifies a growing number of lung nodules and adenocarcinoma spectrum lung lesions which require a growing volume of CT scan interpretations, follow up imaging studies, and consultations with pulmonologists or thoracic surgeons. We report here the frequency of finding a ground glass nodule or semi-solid lung lesion (GGN/SSL) following the creation of a lung cancer screening program.

Methods: A retrospective review of a centralized radiology database for the Yale New Haven Hospital health system was performed including all chest CT scans of adults age 35 and greater between 2013-2021. All types of outpatient chest CT scans were included; with and without IV contrast, chest CT done as part of a chest/abdomen/pelvis exam, and initial and follow-up lung cancer screening CT scans. Final radiology reports were searched for the terms “ground glass nodule” “subsolid” and “semisolid” (GGN/SSL) to identify reports with findings concerning for an adenocarcinoma spectrum lesion. In-patient CT scans and the words “ground glass” and “ground glass opacity” were intentionally not used in order to avoid including lesions thought to be infectious.

Results: A total of 148,405 CT scans were performed between 2013-2021, with a steadily increasing number every year from 10,794 in 2013 to 20,364 performed in the year 2021. Of the 2021 CT scans, 1720 (8.4%) were lung cancer screening CT scans. In 2021 there was a 10.3% chance of any chest CT reporting a GGN/SSL and a 9.9% chance in a screening chest CT, representing a total of 2100 GGN/SSL reported on CT scans in a single year. The frequency with which a lung cancer screening CT scan identified a GGO/SSL has stayed relatively constant since 2014, ranging between 9.6-12.7%, however identification of GGO/SSN in CT scans done for other reasons has increased steadily from 5.9% in 2013 to10.3% in 2021. The chance of finding a GGO/SSN increased with age, with patients age 80-89 having a 14.7% rate of GGN/SSL findings.

Discussion: The total number of CT scans done as well as the number of CT scans with GGN/SSL findings has more than doubled between 2013 to 2021. Among both chest CT scans and lung cancer screening CT scans there is approximately a 10% chance of identifying a GGN/SSL with increased likelihood among older patient populations.

PP01.13:
Low Screening Rates in Patients Ultimately Diagnosed with Advanced NSCLC

Dr. Danielle Dressler[1], Dr. Joseph Fuchs[1], Philip Silberman[2], Dr. Masha Kocherginsky[2], Dr. Zequn Sun[2], Dr. Yanis Boumber[2], Dr. Young Kwang Chae[2], Dr. Nisha Mohindra[2], Dr. Avanthi Ragam[3], Dr. Chetan Vakkalagadda[2], Prof. Jyoti Patel[2]

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Background: Early diagnosis of lung cancer with screening low-dose computed tomography (LDCT) in high risk populations improves lung and all-cause mortality. LDCT was first recommended by the USPTF in 2013 for screening 55-80-year-olds with a 30 pack-year tobacco history who are active smokers or have quit within the past 15 years. This recommendation was expanded in 2021 for 50-80-year-olds with a 20 pack-year or greater tobacco history. As part of our analysis of healthcare delivery at our system, Northwestern Medicine, we investigated tobacco history for our patients with advanced NSCLC to identify the proportion of patients who would have been eligible for screening and detection of early-stage disease prior to their diagnosis of metastatic NSCLC.

Methods: We queried the Northwestern Medicine Enterprise Data Warehouse for all patients with a new diagnosis of lung cancer between January 1, 2019 and December 31, 2020 at Northwestern Memorial Hospital and two affiliated community hospitals. A total of 864 patients with a new diagnosis of lung cancer were identified, we further selected for those with a diagnosis of stage IV disease at presentation.

Results: 191 patients had a diagnosis of stage IV NSCLC, among which 78.5% (150/191) were active or former smokers with a median tobacco history of 35 pack-years. Of the 151 patients, 141 had available data. 54/141 (38.3%) were eligible for LDCT based on 2013 USPSTF recommendations, and 61/141 (43.3%) using 2021 guidelines at time of diagnosis. Only 4 (7.4%) eligible patients had LDCT at any time prior to diagnosis. Although 4 patients had screening, 3 did not follow USPTF guidelines for follow up and had prolonged gaps between scans. Five (9.3%) patients had CT screening for other lung diseases that led to diagnosis and 1 (1.9%) patient did not complete ordered screening.

Conclusions: Despite public health recommendations to screen active and former smokers for lung cancer, at our academic institution and affiliated hospitals, most patients did not receive appropriate screening. This is concerning, as screening CT has been shown to reduce lung cancer mortality. 2021 USPTF lung cancer screening guidelines were updated to ensure a larger screening population, especially as women and people of color tend to have a lower tobacco burden at lung cancer diagnosis. Our data suggest that more work is needed to identify systems, tools, and actions to ensure maximal screening of appropriate patients prior to late-stage presentation.

PP01.14:
The Utilization of Molecular Risk Stratification of Early-Stage Non-Small Cell Lung Cancer to Identify Increase Failure Despite Complete Surgical Resection

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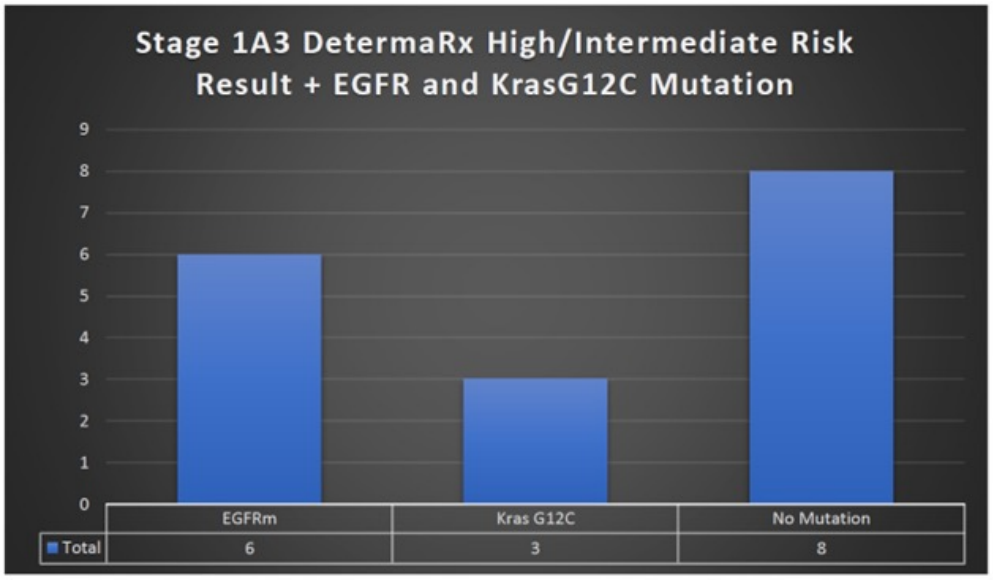
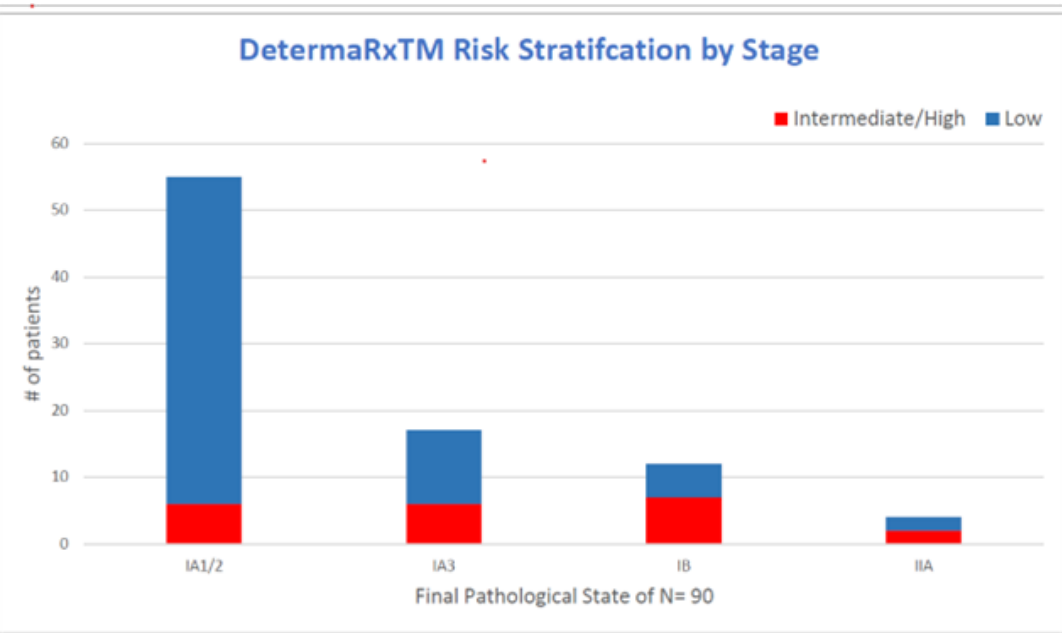
Objective: Lung cancer is the leading cause of cancer related deaths worldwide. 40,000 individuals are diagnosed, annually, with early-stage non-small cell lung cancer (NSCLC). Despite complete surgical resection, 30-50% patients fail 5-year survival. Early-stage NSCLC patients who are not candidates for adjuvant treatment per existing guidelines may conceal occult metastasis and have disease reoccurrence. Epidermal Growth Factor Receptor mutations (EGFRm) are an oncogene mutation in non-squamous NSCLC and are a prevalent risk for central nervous system (CNS) metastasis. The AJCC 8th Edition utilizes only clinicopathologic characteristics despite adoption of molecular biomarkers in the management of NSCLC. Early stage IA3 may neglect size criteria at 3cm of a stage IB but may biologically behave as IB, though stage drift to lower stage by National Comprehensive Cancer Network (NCCN) will not recommend adjuvant therapy. Our goal is to further discern the subset of resected Stage IA3 which may benefit from adjuvant therapy. A 14 gene quantitative polymerase chain reaction expression assay demonstrates ability to stratify risk IA,IB, and IIA non-squamous into low, intermediate, and high risk. Such results may significantly impact physician treatment decisions in the new classification of IA3.

Methods: A review of 90 consecutive patients experienced complete pulmonary resection for early-stage NSCLC. A 14 gene molecular stratification test ,the Oncocyte (Irvine, CA) DetermaRx +EGFR test was utilized for the stratification and identification of possible increased reoccurrence.

Results: Sixty-seven patients (74%) were staged IA, with 17 being stage IA3 (25%). 6 of the 17 stage IA3 (35%) registered as intermediate to high risk. Six of the staged IA3 demonstrated EGFRm and 3 possessed Kras G12C.

Conclusion: Data suggests there is a 20-34% chance of reoccurrence for early-stage NSCLC. As well as EGFRm positive non-squamous NSCLC possess several clinicopathological and molecular factors identified as association with increased recurrence rate. In resectable NSCLC, the consequence of disease recurrence is a significant threat, many patients reoccur or die within 5 years. Initial metastatic recurrence following surgical resection occurs in multiple sites in approximately 40% of patients. Molecular profiling of completely resected stage IA3 more accurately stratifies risk than current NCCN guidelines, as well as with EGFRm being a prevalent driver of disease across stages I-III, should be considered in identifying increased risk patients who might improve with adjuvant chemotherapy/targeted therapy recommendations.




DetermaRxTM Risk Stratifcation by Stage
Intermediate/High
Low
60
50
40
30
20
10
0
# of patients
IA1/2
IA3
IB
IIA
Final Pathological State of N= 90

PP01.15:
Circulating Tumor DNA (ctDNA) Level: a Prognostic Biomarker for Clinical Outcomes in Non-Small Cell Lung Cancer (NSCLC) Patients Across Diverse Therapy Classes

Mrs. Layla Mowlavi[1], Jiemin Liao[1], Caroline Weipert[1], Estelamari Rodriguez[2], Prof. Christian Rolfo[3], Han-Yu Chuang[1], Dr. Sean Gordon[1]

[1]Guardant Health, United States, [2]Sylvester Comprehensive Cancer Center, University of Miami, [3]The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai

Background: Liquid biopsy provides a less invasive alternative to tissue biopsy for comprehensive genomic profiling (CGP) and also contains additional information in the form of ctDNA level. Qualitative and quantitative ctDNA level has been shown to be indicative of tumor burden. Less is known about how ctDNA level, as estimated from a single blood collection, correlates with outcome of late-stage metastatic NSCLC patients undergoing different treatments.

Methods: Patients with NSCLC were identified via the Guardant INFORM database and grouped by the timing of Guardant360 liquid biopsy test relative to their start of metastatic first line (1L) therapy into "Pre 1L" (90 days prior to 1L), "Early 1L" (90 days after start of 1L), or "Late 1L" (90-190 days after start of 1L). Kaplan-Meier and Cox proportional hazards (CPH) were used for real world overall survival (rwOS) analyses. Gender and age were included as covariates in CPH. A threshold value of 4% was used to define ctDNA high/low when ctDNA level (highest variant allele fraction) was used as a categorical variable and patients without detected ctDNA were categorized as "TND".

Results: ctDNA level was significantly prognostic of outcome, including all blood collection timepoints for immune checkpoint inhibitor (ICI) and chemotherapy cohorts when modeled as a continuous variable. ctDNA level was also significantly prognostic when modeled as a categorical variable in all cases except Late 1L ICI TND (small sample size) and chemotherapy Early 1L ctDNA low. TND patients had the best outcomes with hazard ratios ranging from 0.26 to 0.46.

Conclusions: In addition to providing a less invasive alternative to tissue biopsy for CPG, highest variant allele fraction on the Guardant360 liquid test, and particularly lack of detectable ctDNA, provides prognostic information and may be useful in identifying patients who could benefit from more/less aggressive treatment.

Table 1. 1L rwOS by timing of blood collection in 1L EGFR-TKI, ICI, and chemotherapy cohorts.

Cohort	G360 timing	CPH HR	CPH HR, p-value	Logrank p-value
EGFR TKI	pre-1L ctDNA low	0.65 [0.54-0.77]	< 0.005	< 0.005 low (n=932) vs high (n=780)
EGFR TKI	pre-1L TND	0.33 [0.21-0.53]	< 0.005	< 0.005 TND (n=115) vs high (n=780)
EGFR TKI	Early 1L ctDNA low	0.63 [0.42-0.97]	0.03	0.03 low (n=158) vs high (n=83)
EGFR TKI	Early 1L TND	0.34 [0.19-0.63]	< 0.005	< 0.005 TND (n=44) vs high (n=83)
EGFR TKI	Late 1L ctDNA low	0.56 [0.40-0.78]	< 0.005	< 0.005 low (n=234) vs high (n=137)
EGFR TKI	Late 1L TND	0.26 [0.15-0.44]	< 0.005	< 0.005 TND (n=63) vs high (n=137)
ICI	pre-1L ctDNA low	0.73 [0.62-0.87]	< 0.005	< 0.005 low (n=1149) vs high (n=543)
ICI	pre-1L TND	0.46 [0.32-0.65]	< 0.005	< 0.005 TND (n=140) vs high (n=543)
ICI	Early 1L ctDNA low	0.41 [0.27-0.62]	< 0.005	< 0.005 low (n=162) vs high (n=75)
ICI	Early 1L TND	0.34 [0.14-0.81]	0.01	0.01 (n=16) TND vs high (n=75)
ICI	Late 1L ctDNA low	0.55 [0.36-0.86]	0.01	0.01 low (n=122) vs high (n=71)
ICI	Late 1L TND	0.43 [0.18-1.03]	0.06	0.05 TND (n=16) vs high (n=71)
Chemotherapy	pre-1L ctDNA low	0.64 [0.56-0.74]	< 0.005	< 0.005 low (n=1,795) vs high (n=851)
Chemotherapy	pre-1L TND	0.34 [0.26-0.44]	< 0.005	< 0.005 TND (n=278) vs high (n=851)
Chemotherapy	Early 1L ctDNA low	0.73 [0.53-1.01]	0.06	0.03 low (n=402) vs high (n=123)
Chemotherapy	Early 1L TND	0.45 [0.29-0.71]	< 0.005	< 0.005 TND (n=95) vs high (n=123)
Chemotherapy	Late 1L ctDNA low	0.60 [0.46-0.77]	< 0.005	< 0.005 low (n=374) vs high (n=213)
Chemotherapy	Late 1L TND	0.38 [0.24-0.62]	< 0.005	< 0.005 TND (n=57) vs high (n=213)

PP01.16:
Improving Access to Early Palliative Care Delivery for Patients with an Advanced Thoracic Malignancy Through an Embedded Onco-Palliative Clinic Model

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Introduction: Early integration of palliative care (PC) with standard oncology care is driving the development of innovative PC delivery models.

Methods: This was a single institution retrospective study of outpatient PC before and after the opening of an embedded thoracic oncology-palliative clinic at The Ohio State University (Franklin County, Ohio). All patients in the pre-intervention cohort had access to outpatient PC through a freestanding clinic while the post-intervention cohort had access to the freestanding and embedded clinics. Using time-to-event analyses, we evaluated differences in time intervals from first medical oncology visit to PC referral and first PC visit between the two cohorts.

Results: In the post-intervention cohort, 75 of 358 patients (20.9%) were referred to outpatient PC compared to 33 of 359 patients (9.2%) in the pre-intervention cohort ($p < 0.01$). PC referrals for patients outside of Franklin and adjacent counties increased from 4.0% (10/251) to 14.2% (33/232) after opening the embedded clinic ($p < 0.01$). Completion percentages of PC referrals increased from 57.6% to 76.0% in the pre- vs post-intervention cohorts (HR = 1.69, 95% CI: (1.0, 2.8); $p = 0.05$). Median time from palliative referral order to first PC visit decreased from 29 days to 20 days ($p = 0.05$). Similarly, median time from the first oncology visit to PC referral completion decreased from 103 days to 41 days ($p = 0.08$).

Conclusion: Implementation of an embedded palliative clinic model increases access for early PC among patients with thoracic malignancies particularly for those traveling farther for cancer care.

PP01.17:
Sotorasib in Advanced KRAS p.G12C–Mutated NSCLC with Treated or Untreated Brain Metastases: Safety and Efficacy Data from the Global Expanded Access Program (EAP)

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Introduction: The sotorasib EAP provided compassionate use of sotorasib, a first-in-class KRAS G12C inhibitor, prior to local regulatory approvals. An abstract presenting data on the safety and efficacy of sotorasib in patients with advanced KRAS p.G12C–mutated NSCLC from 2 global protocols under the EAP (Amgen study 20190436 [study-436] and 20190442 [study-442]) was submitted to ESMO 2022. Herein we provide focused analyses on the safety and efficacy of patients with previously treated or untreated brain metastases.

Methods: Patients, including those with ECOG PS 2, treated or untreated brain metastases, and additional co-morbidities, enrolled in 6 countries (USA, ITA, BRA, ISR, ESP, TWN) across 52 centers. The EAP was primarily designed to assess the safety of sotorasib 960 mg QD. Real-world progression-free survival (rwPFS) was estimated for study-436 (designed for long-term follow-up) based on time from start of treatment to end of protocol sotorasib due to disease progression, any death before new anti-cancer therapy, or end of commercial sotorasib, whichever occurred earlier.

Results: Under 2 EAP protocols, 137 patients received sotorasib. Median prior lines of therapy were 2 (up to 7); 29 (21%) patients had ECOG PS 2, and 36 (26%) had brain metastases (75% treated, 25% untreated). Baseline characteristics were similar in patients with and without brain metastases. Incidences of treatment-related adverse events (TRAEs), including grade ≥3 TRAEs, were comparable for patients with and without brain metastases at baseline. For patients with and without brain metastases, the median treatment duration on protocol sotorasib was 2.8 months and 3.9 months, and the rwPFS was 4.7 (95% CI, 2.7-7.6) and 6.7 (95% CI, 4.6-9.1) months, respectively.

Conclusions: In this focused analysis on patients with brain metastases in the sotorasib EAP, safety and efficacy data were similar across patients with and without brain metastases. Additional data on treated brain metastases will be presented.

Table 1

Study-436	Brain metastases at baseline (n=24)	No brain metastases at baseline (n=68)
Baseline characteristics		
Median age, years (range)	67 (51–87)	68 (46–81)
Median prior lines of therapy	2	2
ECOG performance score		
0	3 (12.5)	9 (13.2)
1	15 (62.5)	41 (60.3)
2	6 (25.0)	18 (26.5)
Treatment-related adverse event (TRAE)		
Overall	19 (79.2)	43 (63.2)
Grade ≥3	5 (20.8)	13 (19.1)
Leading to sotorasib discontinuation	0 (0.0)	4 (5.9)
Leading to sotorasib reduction or interruption	6 (25.0)	11 (16.2)
Efficacy		
Treatment duration on protocol sotorasib, months (95% CI)	2.8 (2.6–4.8)	3.9 (3.2–4.6)
Median rwPFS, months (95% CI)[a,b]	4.7 (2.7–7.6)	6.7 (4.6–9.1)

[a]In study-436, 30/92 (33%) patients switched to commercial supply. Patients who discontinued commercial supply were deemed to have progressed.
[b]Median follow-up was 7.4 months; data cut-off date: April 1, 2022

PP01.18:
Surgical Resection after Targeted Therapy in Stage IV NSCLC: Nuances and Considerations

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Background: The treatment landscape for operative resection of Stage IV non-small cell lung cancer (NSCLC) is rapidly expanding, with recent evidence demonstrating feasibility and efficacy of pulmonary resection as a component of local consolidative therapy (LCT) in oligometastatic disease. However, the operative details and technical complexity of surgical resection following targeted therapy in Stage IV disease have not been explored, particularly in a population of patients including oligo- as well as polymetastatic disease. Thus, we aimed to characterize the intraoperative nuances of pulmonary resection in this cohort.

Methods: Patients were identified who underwent pulmonary resection as a component of LCT in prospective trials of LCT (including surgery and/or radiation) following targeted therapy. These trials included patients with either activating EGFR mutations or ALK fusions, who received osimertinib and brigatinib, respectively, prior to LCT. All operations took place between 06/2018-04/2022. Intraoperative findings of complexity were systematically collected immediately postoperatively in 4 domains using 5-point scales. In addition, data regarding surgical approach, extent of resection, use of advanced surgical techniques, operative duration, and aspects of post-operative convalescence were reviewed. Variables were descriptively analyzed.

Results: In these trials, 21 patients underwent pulmonary resection, which was approached minimally invasively in 2 (9.5%). Procedures included 17 (81.0%) lobectomies, 2 (9.5%) wedges, and 2 (9.5%) segmentectomies. Surgeons reported the operations as overall severely difficult in 16 (76.2%). Adhesions were reported as severe in about one-third of the cases (6, 28.6%). Mediastinal nodal dissection was noted as severely impacted in 11 (52.4%) cases, and surgeons indicated in the majority of cases (17, 81.0%) severe hilar fibrosis contributing to complexity of vascular dissection. These findings led to frequent advanced maneuvers in 5 patients (23.8%), and included chest wall resection (n=5, 23.8%), change in surgical approach (n=1, 4.8%), proximal pulmonary artery control (n=1, 4.8%), and extended resection in 1 (4.8%). Mean operative duration and blood loss remained typical, at 255 min (interquartile range [IQR]: 145-255) and 200 mL (IQR: 100-200), respectively, with 1 (4.8%) patient needing intraoperative transfusion. There were no operative mortalities or postoperative ICU admissions. Median postoperative chest tube duration was likewise typical at 2.48 days (IQR: 1.38-3.46).

Conclusion: Indications for pulmonary resection in metastatic NSCLC are expanding, and, in the setting of LCT after targeted therapy, these operations may be particularly complex. However, these operations are feasible, and surgical teams should consider allocation of appropriate time, resources, and expertise to optimize operative outcomes.

PP01.19:
Volatile Organic Compound Biomarkers Identification for Prediction of Lung Cancer Based on Exhaled Breath Analysis

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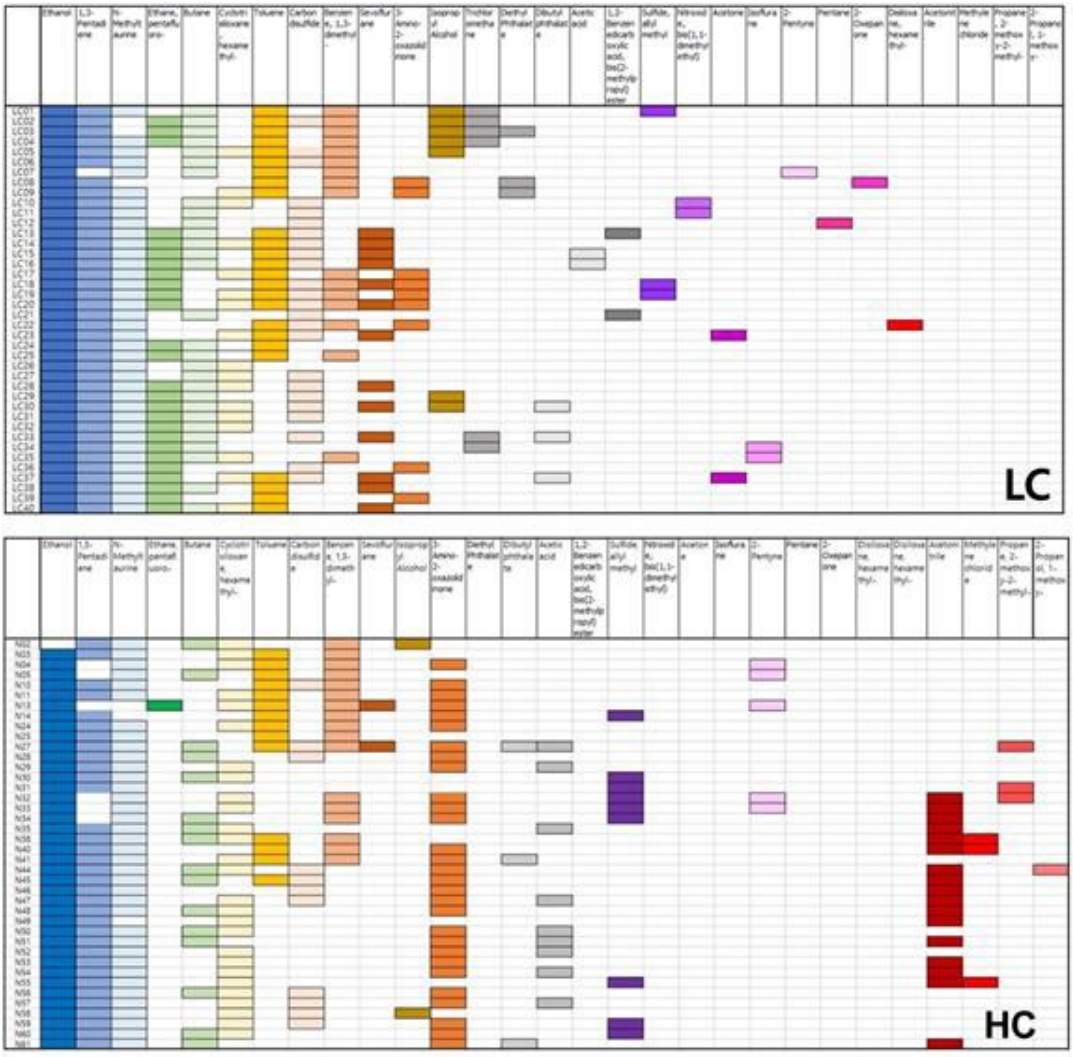
Background: Breath analysis is a promising noninvasive technique that offers a wide range of opportunities to facilitate early diagnosis of lung cancer. The aim of this study is to identify volatile organic compound (VOC) biomarkers in lung cancer.

Methods: Exhaled breath samples of 200 subjects including 100 with lung cancer (LC) and 100 healthy controls (HC) were analyzed through thermal desorption coupled with gas chromatography-mass spectrometry (TD-GC-MS) to obtain the metabolic information from volatile organic compounds (VOCs). Comparisons of VOCs between LC and HC were performed with the Mann-Whitney U test. Multivariate analysis and cross validation were used to identify exhaled biomarkers

Results: The analysis revealed that 25 and 23 VOCs discriminated LC from HC, respectively. LC patients displayed significantly increased levels of oxygenated VOCs such as ethane, toluene, carbon disulfide and sevoflurane. ($p<0.05$) And 3 amino 2-oxazolidone was significantly lower in LC than HC. ($p<0.05$) The calculated diagnostic indices showed a large area under the curve (AUC) to distinguish HC from LC (AUC: 0.827, 95 % CI: 0.768-0.886).

Conclusion: VOC biomarkers of breath of the LC patients was significantly different from that of both LC and HC. We concluded that the VOC in exhaled breath has a potential to help improve early diagnosis of LC.



PP01.20:
Trial in Progress: Screening for High Frequency Malignant Disease (SHIELD)

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Background: Cancer screening implementation in asymptomatic adults has positively impacted global cancer mortality rates. However, significant screening adherence gaps exist, especially in lung cancer where screening adherence rates are as low as ~5%. By reducing access barriers inherent to current screening options, a blood-based multi-cancer screening test with clinically significant performance in cancers where early detection and intervention can save lives may improve access and clinical outcomes Effective test evaluation in screen relevant populations requires studies designed to enroll individuals across multiple cancer types, considering prevalence rates for the evaluated cancers, allowing overlap in screen-eligible populations, and ensuring representation from diverse ethnicities and geographies.

Methods: SHIELD (Screening for High Frequency Malignant Disease; NCT#05117840) is a prospective, observational, multi-center basket study in the United States and Europe uniquely designed to recruit individuals across multiple cancer types. The study's primary objective is to evaluate the performance of a blood-based multi-cancer screening test (GuardantLUNAR-2, Guardant Health, USA) to detect cancer in screen-relevant individuals compared to the reference standard cancer screening modality. The study is recruiting eligible individuals into multiple cohorts with specified pathways for cancer screening. Within each cohort, Eligible individuals consent to whole blood collection within 90-days of the standard of care screening method. Clinical diagnoses, e.g cancer, are made per standard of care. Primary outcomes: sensitivity, specificity, negative and positive predictive value of the test compared to the standard of care screening modality. Secondary outcomes: number of screen-detected cancers, early- (stage I/II) and late-stage (stage III/IV), per 1000 screened individuals. Outcomes are collected at one and two-years to investigate the possibility of incidental non-screen relevant cancers and interval screen-relevant cancers not reaching clinical threshold for detection at initial screening. Additional cancer specific follow-up is designed per cohort. The first enrolling cohort, cohort A, is focused on those who meet guideline criteria for lung cancer screening with low dose CT. Additional cancer-risk cohorts will begin enrolling as the study expands and are designated cohort B, C, etc.

Cohort A: Eligibility criteria are aligned with lung cancer screening guidelines; age 50-80 years with > 20 pack-year smoking history who are current smokers or have quit < 15 years prior, without a cancer history, preinvasive lung lesions, or current treatment for pneumonia. Cohort A enrollment, targeting 9,000 subjects over 24 months at up to 120 global sites, began in January 2022. As of June 2022, 27 study sites have been activated and are enrolling.

PP01.21:
Utilization of Pre- and Post-Stereotactic Body Radiotherapy (SBRT) Neutrophil-to-Lymphocyte (NLR) Ratios and Platelet-to-Lymphocyte (PLR) Ratios as Prognostic Factors in Early-Stage Non-Small Cell Lung Cancer

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Background: SBRT is the standard of care in medically inoperable early-stage NSCLC. Pre-treatment NLR and PLR have been reported to be prognostic factors for patients with lung cancer in predicting overall survival (OS). While large field radiation therapy is known to cause significant lymphopenia, the effects are lesser known after SBRT where a smaller radiation field is usually utilized. This retrospective study assessed the effect of SBRT on pre- and post-treatment NLR, PLR, and OS with long-term follow-up.

Methods: We identified 48 patients undergoing SBRT for primary lung cancer between 2014 to 2017 from our institutional database who had a complete blood count prior to and within 1 week following SBRT. Variables collected include age, sex, stage, date and type of recurrence, pre- and post- SBRT absolute neutrophil count (ANC), lymphocyte and platelet count. NLR and PLR were calculated by dividing neutrophil count and platelet count with lymphocyte count, respectively. Paired t-test was used to compare differences in NLR and PLR pre- and post-SBRT using 3 as the cutoff ratio based on literature. OS was calculated using the Kaplan–Meier analysis.

Results: Median follow-up was 40.3 months (range 24.4 – 83.2 months). 52.1% of patients were male with median age at diagnosis of 67 years (range 55 – 82 years). 77.1% had stage IA/IB and 22.9% had node-negative stage II cancer. Mean lymphocyte count pre- and post-SBRT was 1.37x109/L and 0.9x109/L, respectively (p=0.003). Mean NLR pre- and post-SBRT was 4.56 and 6.08, respectively (p=0.002). Mean PLR pre- and post-SBRT was 181.8 and 276.1, respectively (p=0.00007). 58.3% of patients had an NLR >3 prior to starting SBRT. 23.4% of patients with a pre-treatment NLR >3 had local recurrence versus 16.4% with a pre-treatment NLR ≤3 (p=0.034). Median survival among patients with a pre-treatment NLR >3 versus ≤3 was 4.19 years and 4.52, respectively. Median survival among patients with a post-treatment NLR > 3 versus ≤3 was 4.13 years and 5.95, respectively (p=0.057). Pre- or post- treatment PLR correlation to OS was not statistically significant.

Conclusion: Even with smaller radiation fields like in SBRT, there is significant change in pre- and post-SBRT NLR and PLR values. Pre-treatment NLR > 3 was associated with significantly higher local recurrence compared to NLR ≤3. A higher post-SBRT NLR was associated with a borderline statistically significant decrease in OS. These findings warrant further investigation of the utility of pre- and post-SBRT NLR as an important prognostication factor.

PP01.22:
First Lung Cancer Screening Program in Greece - Initial Experience, Preliminary Data and Pitfalls

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Background: Poor prognosis of lung cancer is linked to its late diagnosis, typically in the advanced stage 4 in 50–70% of incidental cases. Lung Cancer Screening Programs provide low-dose lung CT screening to current and former smokers who are at high risk for developing this disease. Greece is an EU country, returning strong from a long period of economic recession, ranked 2nd place in overall age-standardized tobacco smoking prevalence in the EU. In December 2020, at the Metropolitan Hospital of Athens, we started the 1st Screening Program in the country. We present our initial results and pitfalls met.

Methods: A weekly outpatient clinic offers consultation to possible candidates. LDCT (≤3.0mGy), Siemens VIA, Artificial Intelligence multi-computer-aided diagnosis (multi-CAD) system and LungRADS (v.1.1) are used for the validation of any abnormal findings with semi-auto measurement of volume and volume doubling time. Patients get connected when necessary with the smoking cessation and Pulmonology clinic. USPSTF guidelines are used, (plus updated version). Abnormal CT findings are discussed by an MDT board with radiologists, pulmonologists/interventional pulmonologists, oncologists and thoracic surgeons. A collaboration with Fairlife Lung Cancer Care the first non-profit organization in Greece is done, in order to offer the program to population with low income too. An advertisement campaign was organized to inform family doctors and the people about screening programs, together with an anti-tobacco campaign.

Results: 106 people were screened, 74 males & 32 females (mean age 62yo), 27/106 had an abnormal finding (25%).
2 were diagnosed with a resectable lung cancer tumor (primary adenocarcinoma) of early-stage (1.8%).
2 with extended SCLC (lung lesion & mediastinal adenopathy).
1 with multiple nodules (pancreatic cancer not known until then).
3 patients with mediastinal and hilar lymphadenopathy (2 diagnosed with lymphoma, 1 with sarcoidosis).
19 patients were diagnosed with pulmonary nodules (RADS 2-3, 17%) - CT follow up algorithm.

Conclusions: We are presenting our initial results, from the first lung cancer screening program in Greece. Greece represents a country many smokers, who also started smoking at a young age, with a both public and private health sector, returning from a long period of economic recession. COVID-19 pandemia has cause practical difficulties along the way. LDCT with AI software, with an MDT board and availability of modern diagnostic and therapeutic alternatives should be considered as essential. A collaboration spirit with other hospitals around the country is being built, in order to share current experience and expertise.

PP01.23:
Outcomes of Stage IIIA Disease in NSCLC, Treated with Surgery - A Single Institution Experience

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Background: In NSCLC patients, the Stage group of IIIA-with N2 nodal status have always remained the subgroup of interest which requires multimodality management i.e, Accurate mediastinal staging, NACT, surgery, adjuvant chemotherapy and radiotherapy. Outcomes in the same group also significantly vary according to chosen treatment modalities.So we aim to study the outcomes of this subgroup patients treated with surgery at single tertiary care institute.

Methods: From 2012 to 2020, all patients with Stage IIIA-with N2 nodal status were analysed retrospectively for demographics, preoperative therapy, type of lung resection and received adjuvant treatment. mOS & mDFS among the cohort was analysed using the Kaplan-Meier survival plot.

Results: Out of total 244 surgically treated patients, 73(29.9%) patients were diagnosed with stage IIIA-N2 NSCLC. Male to female ratio was (M:F= 5:1), with mean age 57(33-78) of which (76.7%) were smokers, while rest (23.3%)were non-smokers. Majority of the patients had very good performance status at the time of diagnosis (ECOG 0-1 94.5%).Biopsy showed 25(34.2%) patients were diagnosed with adenocarcinoma, 35(47.9%) with squamous cell carcinoma, 2(2.7%) with NSCLC-NOS and 2(2.7%) with adenosquamous carcinoma.PET-CT was done in 64(87.6%) patients, mediastinal staging with EBUS-FNA was done only in 24(32.8%) due to resource constraints. Among these 55(75.3%) patients were found to have intraoperatively significant N2 station but only 21(28.7%)out of it were found to be pathologically positive N2 node. In our patients NACT was given in 52(71.2%) of the cases based on significant N2 on PET; NACT and RT in 2(2.7%) ; upfront surgery was done in 19(26%) patients who turned out to be negative on EBUS; adjuvant chemotherapy in 19(26%) and adjuvant CTRT was given in 12(17.8%) based on final histopathological report. Recurrence was found in 35(47.9%) patients, of which 19(26%) were systemic, 4(5.4%) locoregional and 4(5.4%) locoregional as well as systemic. Among the systemic recurrences most common was brain (17.1%) followed by Liver (11.4%) and bone (8.5%).mOS and mDFS in our patients was 37 months and 25 months, while 5-Year OS and DFS was found to be 31% and 27% respectively

Conclusion: Outcomes in Stage IIIA with N2 nodal station in NSCLC treated with surgery and chemoradiation is variable. Almost half of the patient showed recurrence very early post treatment, even after multimodality approach. Proper preoperative staging evaluation in the form of imaging and invasive mediastinal staging is of paramount importance to achieve best possible outcomes and guide treatment decision in this sub-group.

PP01.24:
5-Year Survival Outcomes of Lung Cancer Treated with Surgery: A Single Institution Experience

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Objectives: Lung cancer is one of the most common and lethal cancer worldwide, with incidence of 2.2 million and mortality rate of 1.8 million per annum. According to SEER database 5-year survival rates reported 25% in NSCLC. The purpose of this study was to analyse the characteristics of patients who have survived more than 5-years after surgical treatment for primary lung cancer in a single institute.

Methods: All patients with a diagnosis of lung cancer, surgically treated from 2012 to 2021 who reached 5-year survival in our institute were reviewed. A retrospective analysis was done to study demographic details, smoking status, clinical profile, histological subtypes, type of surgery and pathological characteristics in same patients.

Results:Out of 244 patients, there were 55(22.5%) who reached 5-year survival, majority being males (M:F= 3.6:1), with mean age 51(18-78)years. Smokers being 29(52.7%), while 26(47.2%) were non-smokers. Most common Symptom was cough(50.9%) followed by hemoptysis(40%), dyspnoea(34%) and chest pain(34%).Only 9(16.3%) patients were having co-morbidities and 51(92.7%) patients had very good performance status (ECOG 0-1) at presentation. Radiologically mean tumor size was 4.8cm(T2b) and most of the patients; 46(83.6%) were having N0-N1 nodal status. Most common pathological diagnosis was squamous cell carcinoma in 16(29.0%), followed by NET in 13(23.6%) , adenocarcinoma in 11(20.0%) ,adenosquamous in 2(3.6%) and 2(3.6%)poorly differentiated carcinoma.Pre-treatment staging was stage-I in 21(38.1%),stage-II in 22(40.0%) and Stage-III in 12(21.8%) patients. In these patients upfront surgery was done in 43(78.1%) while NACT was given in 12(21.8%) of which 6(10.9%) patients showed Complete response(CR) on final HPR. Lobectomy was done in 35(63.6%), pneumonectomy in 13(23.6%) and Bi-lobectomy in 4(7.2%) patients and for rest 3(5.4%)only sub-lobar resection was done; On final HPR, mean tumor size was 4.1cm(T2b). Out of all patients, only 13(23.6%)patients showed pathologically positive nodes, of which N1 station was in 8(14.5%), N2 station was in 4(7.2%). On final staging Pathological CR was in 6(10.9%) while stage-I was found in 19(34.5%), stage -II 17(30.9%) and stage III in 12(21.8%) patients. Adjuvant chemotherapy was given in 12(21.8%)patients and adjuvant CTRT was given in 3(5.4%) while, PORT was given in 2(3.6%)patients.

Conclusions:5-Year survival in lung cancer is achievable goal, especially in early-stage disease, when treated with timely surgical resection followed by multimodality treatment. Stage at presentation, pathological complete response after NACT, histological subtype, nodal involvement, final histopathological stage and patient's GC were found to be the most important factors influencing the 5-year survival in our cohort

PP01.25:
Incidence and Timing of Immune-Related Adverse Events in Patients with Non-Small Cell Lung Cancer Treated with Immune Checkpoint Inhibitor as Monotherapy or in Combination with Chemotherapy

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Background: Immune-checkpoint inhibitors (ICI) combined with chemotherapy is an FDA approved and standard approach for treating non-small cell lung cancer (NSCLC). Immune-related adverse events (irAEs) are a unique set of toxicities that occur with ICI and have been shown to be correlated with increased overall survival (OS). Most studies conducted to date have focused only on ICI without chemotherapy. In this study, 217 NSCLC patients treated first-line with either ICI alone or in combination with chemotherapy (ICI-Chemo) were evaluated to investigate differences in incidence, risk factors, effect on OS, or timing of irAEs between treatment groups.

Methods: We conducted a retrospective review of consecutive patients with metastatic NSCLC treated with either ICI alone or with chemotherapy between 2017 – 2021 at The Ohio State University Wexner Medical Center. Patient demographics, treatment history, tumor biomarker information and clinical outcomes were extracted from the medical records. Patient characteristics have been compared between the ICI and the ICI-Chemo using Chi-square test for the categorical variables and two-sample T test or Wilcoxon rank-sum test for the continuous variables. Overall survival (OS) was calculated from the date of ICI initiation until date of death from any cause or censored at loss to follow-up. Median OS with 95% confidence intervals was estimated using the Kaplan-Meier method. Log rank test was used to compare survival curves. P values less than 0.05 were considered to indicate statistical significance.

Results: Both ICI ($P < .001$) and ICI-Chemo ($P < .001$) groups had significantly better OS with irAEs. No significant differences were found in the incidence or timing of irAEs between treatment groups. ICI-Chemo patients were more likely to experience dose-interruption at any point in treatment ($P = .028$). ICI patients who continued treatment after irAEs had increased OS compared to those who discontinued treatment in the ICI cohort ($P = .021$).

Conclusion: The presence of irAEs were associated with significantly increased OS for both treatment groups. ICI patients were more likely to have positive programmed death ligand-1 due to approval indications. No significant differences were found in the incidence or timing of irAEs between ICI or ICI-Chemo groups. Patients who continued treatment despite irAEs had increased OS compared to those who discontinued treatment, suggesting that the underlying mechanism linking OS and irAEs may be different in ICI vs ICI-Chemo. Future studies are indicated to evaluate differences between ICI and ICI-Chemo regarding underlying mechanisms of action and clinical implications.

PP01.26:
Evaluation of Automated Sample Preparation System for Lymph Node Sampling

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Background: Rapid On-Site Evaluation has increased diagnostic yield of bronchoscopic transbronchial needle aspiration (TBNA) and endobronchial ultrasound (EBUS) procedures. High variability in sample quality may lead to lengthy procedures. We report the results of an automated sample preparation system, designed by ASPHealth, that combines both specimen deposition and staining in a compact/mobile unit.

Methods: We performed a prospective, single-center study of patients undergoing EBUS. After determination of cellular adequacy by a cytotechnologist, samples were split into conventional standard of care (SOC) slide preparation and preparation using the device (ASP). Time of sample preparation using both methods was recorded. Pathologists assessed the following metrics: nuclear and cytoplasmic quality, debris/artifact presence, staining quality, monolayer creation, and adequacy/diagnosis assessment ease. A score between 1 (lowest quality) and 3 (highest quality) was assigned to each. Samples containing only blood were removed.

Results: One to three lymph nodes were sampled from 60 patients with a total of 73 samples collected. The SOC mean sample preparation time was 147.7 seconds (SD 58.2) compared to mean preparation time of 48.3 seconds (SD 21.9) plus a machine run time of 156.4 seconds (SD 35.1) for the ASP slides. Table 1 shows the scores of each category. All samples showed diagnostic equivalency between the automated slides and conventional slides except for one.

Conclusions: Study results suggest that slides prepared by the automated system are of adequate quality for adequacy assessment with diagnostic concordance when compared to SOC slides.

Table 1:

Mean Score of Assessment Category	ASP (N=66)	SOC (N=60)	p value
Nuclear Detail and Quality (SD)	2.45 (0.67)	2.33 (0.69)	0.315
Cytoplasmic Detail and Quality (SD)	2.51 (0.67)	2.43 (0.68)	0.487
Amount of Debris Artifact	2.66 (0.62)	2.64 (0.55)	0.587
Monolayer (SD)	2.67 (0.48)	2.25 (0.69)	0.001
Staining (SD)	2.40 (0.53)	2.29 (0.59)	0.360
Ease of Adequacy Assessment (SD)	2.83 (0.43)	2.72 (0.59)	0.422
Ease of Diagnosis (SD)	2.85 (0.42)	2.71 (0.59)	0.203

PP01.27:
Real-World Effectiveness of Second-Line Therapies for Metastatic Non-Small Cell Lung Cancer

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Background: With the shift to immunotherapy (IO) in 1L (first line) regimens for advanced non-small cell lung cancer (aNSCLC), treatment patterns and outcomes in second-line (2L) are largely unknown. This study sought to describe 2L treatment patterns and clinical outcomes associated with 2L treatment regimens.

Methods: In this retrospective, multisite cohort study, community oncologists completed electronic case report forms for randomly selected stage IIIB/IV, EGFR-/ALK wild-type aNSCLC patients who initiated 1L therapy between 01/01/2016 and 12/31/2019 and received 2L systemic therapy following confirmed disease progression. From this cohort, two subgroups were examined: (a) 2L IO treated, (b) 2L non-IO treated. Follow-up was through November 2020. Demographics, clinical characteristics, treatment patterns, disease response, progression date, and date of death/last follow-up were collected. Overall response rate (ORR) was assessed by RECIST v1.1 criteria. Progression-free survival (PFS) and overall survival (OS) were calculated from initiation of 2L treatment using the Kaplan-Meier method. Although this study is descriptive in nature, post-hoc statistical comparisons of patient characteristics and clinical outcomes were made between the 2L IO and non-IO treated.

Results: A total of 194 patients initiated 2L therapy which included 93 treated with 2L IO (including 12 who received IO in both 1L and 2L) and 101 who did not receive IO in 2L. Median follow-up from 1L initiation was 23.7 months for the 2L IO treated and 20.0 months for the 2L non-IO treated (p=0.09). ORR was similar between 2L IO and non-IO treated cohorts (28.0% and 25.7%), but real-world PFS was significantly longer in 2L for IO treated at 8.4 months versus 5.1 months (p<0.001) in 2L non-IO treated. Median OS from 2L initiation was 13.5 months for IO and 7.7 months for non-IO (p<0.01), respectively. In the cohort treated with both 1L and 2L IO, a prolonged 2L PFS of 30.9 months was observed with no death occurred.

Conclusions: This study described treatment patterns and outcomes associated with 2L regimens among aNSCLC patients. We found 2L IO regimens appeared to have better PFS and OS than 2L non-IO treatments. In a small sample of patients who received IO in 1L and 2L, IO rechallenge use in 2L, resulted in favorable PFS and OS; further research with larger sample size is needed to verify this finding.

PP01.28:
Tumor Engraftment is Prognostic for Disease Recurrence in Resected Non-Small Cell Lung Cancer

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Background: A large percentage of patients undergoing curative intent resection for non-small cell lung cancer (NSCLC) recur. There are no established biomarkers that can identify patients who are likely to recur. Since tumor specimens that successfully engraft to form patient-derived xenografts (PDX) are likely to be more aggressive, we hypothesize that comprehensive proteogenomic characterization of tumors from patients with resected NSCLC that readily engraft would facilitate biomarker development and validation. We report results correlating engraftment with clinical outcomes.

Methods: Tumor tissue from patients undergoing curative intent surgery for NSCLC was collected for engraftment in nude mice through flank injection. Time to disease recurrence was calculated from time of diagnosis to time of disease recurrence. Patients were staged using AJCC 8th edition. Clinical data and outcomes were compared between patients whose tumors successfully engrafted with those that failed to engraft.

Results: A total of 100 patients who underwent curative intent surgical resection for NSCLC and had corresponding tumor specimens implanted for PDX generation were included in this retrospective analysis. Successful PDX engraftment was observed in 18% of patients. Median time to engraftment was 5 months (range: 0-14). The PDX engraftment rate varied by stage with 9% (4/43), 17% (5/30) and 36% (9/25) in patients with stage I, II and III disease, respectively. The median post-operative follow-up was 25.5 months (range: 0.5-48). Disease recurrence was 50% (9/18) in patients whose tumors developed a PDX compared to 21% (17/82) in patients whose tumors did not engraft ($p<0.05$). Recurrence rates by stage and engraftment status are summarized in Table 1.

Conclusion: Successful tumor PDX engraftment and development of a PDX is a high-risk feature that predicts for disease recurrence in patients with resected NSCLC. Characterizing the proteogenomic features that drive tumor engraftment could provide novel biomarkers to guide management of patients with resected NSCLC.

Table 1. Disease recurrence rates by stage and engraftment status.

	Engrafted	Failed to Engraft
All patients (regardless of stage)	50% (9/18)	21% (17/82)
Stage I	25% (1/4)	15% (6/39)
Stage II	60% (3/5)	12% (3/25)
Stage III	56% (5/9)	50% (8/16)

PP01.29:
Prevalence and Predictor of Significant Unmet Needs in Patients who were Surgically Resected for Non-Small Cell Lung Cancer

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Background: The aim of study is to identify the prevalence and predictors of unmet need in patients who were surgically resected for non-small cell lung cancer in Korea.

Methods: A total of 949 patients were recruited from January to October 2020 and completed survey questionnaires which includes Cancer Survivor's Unmet Needs (CaSUN-K), fear of cancer recurrence (FCR) inventory-Short Form, and European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30). Multivariable logistic regression was analyzed to determine potential predictors of significant unmet needs for each domain of CaSUN, which was defined by any of moderate or strong need.

Results: At least one significant unmet need were reported by 59.7% for information, 51.2% for comprehensive cancer care, 59.1% for existential survivorship, 38.9% for quality of life, 31.0% for relationship, and 22.6% for financial domain. Information needs were predicted by high fear of cancer recurrence (aOR 4.13, 95% CI 3.02-5.64), poor emotional function (1.93, 1.35-2.77), and poor cognitive function (1.65, 1.18-2.31).

Comprehensive Cancer Care needs were predicted by male (aOR 1.37, 95% CI 1.01-1.85), shorter time since the end of active treatment (<18 month, aOR 1.50, 95% CI 1.11-2.02), high fear of cancer recurrence (aOR 3.87, 95% CI 2.83-5.30), poor emotional function (1.70, 1.18-2.44), and poor social function (1.89, 1.34-2.66). Existential survivorship needs were predicted by shorter time since the end of active treatment (<18 month, aOR 1.55, 95% CI 1.12-2.14), high fear of cancer recurrence (aOR 5.99, 95% CI 4.32-8.30), poor physical function (1.64, 1.01-2.65), poor emotional function (1.65, 1.09-2.49), and poor social function (2.34, 1.59-3.44). Quality of life needs were predicted by shorter time since the end of active treatment (<18 month, aOR 1.59, 95% CI 2.79-5.46), high fear of cancer recurrence (aOR 3.90, 95% CI 2.79-5.46), poor emotional function (1.86, 1.30-2.65), and poor social function (2.00, 1.42-2.80). Relationship needs were predicted by high fear of cancer recurrence (aOR 4.39, 95% CI 3.02-6.39), poor emotional function (1.87, 1.31-2.68), and poor social function (1.79, 1.26-2.53). Financial needs were predicted by young age (<65, aOR 1.54, 95% CI 1.09-2.18), high fear of cancer recurrence (aOR 2.77, 95% CI 1.85-4.15), poor role function (1.56, 1.09-2.24), and poor emotional function (2.31, 1.60-3.35).

Conclusion: Significant unmet needs in many domains were associated with higher FCR and poor emotional function. Interventions to reduce unmet needs of cancer patients should be focused to relieve FCR and improve emotional functioning.

PP01.30:
Are Delays In The Diagnosis Of Lung Cancer Due To Patients First Seeking Treatment for Tuberculosis In Rural India?

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Background: Lung cancer is often presented late in diagnosis in India due to various factors, one such being receiving treatment for pulmonary tuberculosis. Lung cancer is associated with a poor prognosis, especially when diagnosed in the end stages. Pulmonary tuberculosis and lung cancer have multiple common symptoms, such as cough, expectoration, hemoptysis, weight loss, expectoration, and shortness of breath. Radiological findings can also be similar. A complete physical examination and a careful history must be elicited to help make a proper diagnosis. The author aimed to check the number of patients who received treatment for tuberculosis after experiencing symptoms instead of being referred to a specialist for lung cancer work-up.

Methods: 150 patients diagnosed with end-stage lung cancer confirmed by biopsy were studied retrospectively to check for rates of prior treatment for tuberculosis. The patients were asked to bring their medical records and why they waited before coming to a specialist.

Results: Of the 150 patients, 39 received treatment for tuberculosis prescribed to them by their local village physician. The 39 patients were further interviewed and said they had the preconceived notion that they were suffering from tuberculosis. The patients then went to their physicians asking for anti-tuberculosis medication. The physicians prescribed the medication and told the patients that they needed to complete the entire course of the tuberculosis treatment before they would feel better. Only 18 of the 39 patients had a chest x-ray taken.

Conclusion: Our study shows that patients with lung cancer in India can be misdiagnosed as having pulmonary tuberculosis. We consult that there must be more clinical awareness among the public and physicians alike about the possibility of lung cancer, especially in those with high-risk factors and preconceived notions. A high degree of clinical suspicion must also be needed for physicians to prevent a delay in the diagnosis of lung cancer and to avert unnecessary treatment with anti-tuberculosis medications.

PP01.31:
Real-World Treatment Outcomes of Amivantamab in Pre-Approval Access (PAA) Participants with Advanced Non-Small Cell Lung Cancer (NSCLC) with EGFR Exon 20 Insertion Mutations (ex20ins)

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Background: Amivantamab, an epidermal growth factor receptor (EGFR)-MET bispecific antibody, is approved for the treatment of patients with advanced EGFR ex20ins NSCLC that progressed on or after platinum-based chemotherapy. We present updated data on the real-world experience with amivantamab acquired through the global PAA program on a larger patient population with the inclusion of 4 additional countries and a longer follow-up period. The initial results were presented at the 2022 European Lung Cancer Congress on 210 patients.

Methods: Patients who were eligible for PAA (NCT04599712) had EGFR ex20ins NSCLC that progressed after platinum-based chemotherapy. Amivantamab (1050 mg; 1400 mg for bodyweight ≥80 kg) was administered intravenously once weekly for the first 4-week cycle, then every 2 weeks thereafter. Investigator assessment of response, based on radiologic and clinical judgement, was provided at the time of drug re-supply and was optional. Time to treatment discontinuation was analyzed using a Kaplan-Meier approach. Patients who did not request drug within 45 days from last supply were considered to have stopped treatment. Patients who transitioned to commercial amivantamab drug supply were censored at time of commercial supply.

Results: As of 10 June 2022, 380 patients had initiated treatment with amivantamab in the PAA program across 215 sites in 23 countries; 57.9% from Asia, 26.8% from Europe, 11.6% from North America, and 3.7% from South America. The median age was 63 years (range, 24–86), and the median number of prior lines was 2 (range, 1–9), with 60.5% of patients heavily pretreated with ≥2 prior lines. Median time to treatment discontinuation was 5.13 months (95% CI, 4.2–7.0), with 28% of patients still on treatment at 12 months. Among 205 patients (53.9%) with response information available, 64 (31.2%) achieved partial responses. Frequency and response by site of exon 20 insertion will be reported at the time of the meeting.

Conclusion: The real-world experience of amivantamab from the PAA program was consistent with that observed from the registrational clinical trial (NCT02609776). Patients who entered the amivantamab PAA program were heavily pretreated, underscoring the high unmet need for patients with EGFR ex20ins NSCLC.

PP01.32:
Proteasome Hyperactivity as a Targetable Vulnerability in Oncogenic Missense TP53 Mutated NSCLC.

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Background: Despite advances in targeted approaches and immunotherapy, lung cancer remains the leading cause of cancer mortality in the United States and worldwide. This is partly because these novel treatments are not applicable to all patients and are often associated with primary or secondary resistance. This highlights the need for continued search for new therapeutic strategies for patients with non-small cell lung cancer (NSCLC). Gain-of-function (GOF) oncogenic TP53 mutations, which are present in 20-30% of NSCLC, are harbingers of poorer prognosis and subdued responses to therapy. To date, strategies aimed at directly targeting mutant p53 have not been successful. Here, we provide evidence of proteasome hyperactivity in GOF mutant p53 NSCLC and show that this could be a targetable vulnerability specific to this subset of NSCLC.

Methods: Lung cancer cell lines with GOF oncogenic mutant p53 and wildtype p53 were used in this study. An isogenic cell line set in which a p53 null cell line was stably transfected to express either wildtype p53 or the GOF p53-R273H was used to determine mutant TP53 dependency of the proteasome hyperactivity, as determined by the proteasome activity functional assay and RNA-sequencing. Proteasome pathway activation in NSCLC tumors was predicted using gene expression data from The Cancer Genome Atlas (TCGA). TCGA analysis was performed using the cBio portal platform as well as downloaded data from TCGA. Cell viability studies and apoptosis assays were used to measure vulnerabilities to proteasome inhibitors. Statistical analysis was performed using GraphPad Prism software.

Results: Functional assays revealed a statistically significant increase in proteasome activity in GOF p53 cell lines. The mutant p53 dependency of this effect was confirmed using the isogenic lung cancer cell line model described above. RNA-sequencing data analysis showed statistically significant upregulation of the proteasome genes in the isogenic model with stable expression of the R273H mutant compared to p53-null control. TCGA data analysis revealed increased expression of the proteasome genes in the mutant p53-bearing NSCLC. Importantly, when compared to wildtype p53 cell lines, lung cancer cell lines with mutant p53 showed increased susceptibility to proteasome inhibitors.

Conclusion: The cumulative evidence of the proteasome hyperactivity and increased susceptibility of mutant p53 lung cancer cell lines to proteasome inhibition suggest that proteasome hyperactivity could be a targetable vulnerability in mutant p53 lung cancer. Proteasome inhibition could be used as an indirect targeting strategy to increase susceptibility of mutant p53 NSCLC to other targeted and chemotherapeutic approaches.

PP01.33:
Serum Autoantibodies may help Identify Individuals with Actionable Pulmonary Nodules on LDCT Scan.

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Background: Blood-based biomarkers can serve as a simple and cost-effective method, when used in conjunction with USPSTF guidelines, for selecting LDCT screening. Due to B-cell amplification, autoantibodies are found at a higher concentration in blood than their corresponding neoantigens, making them potentially valuable as early detection biomarkers. We hypothesize, circulating autoantibody targets can be utilized for 'pre-screening' individuals for LDCT testing.

Methods: As a training cohort, 148 serum specimens were obtained from our institutional biorepository and split into sample pools. 3-10 serum samples were combined to make each sample pool, and 2-4 sample pools were created per pathologically distinct cohort. The 'Actionable' cohorts were comprised of early-stage lung malignancies (Stage IA-IIB), including groups of adenocarcinoma (AdCa) (n = 35), squamous cell carcinoma (SqCa) (n=27), or carcinoid (n = 24) histologies, or patients with pathologically-diagnosed non-malignant lesions >6mm (Benign) (n=32). The 'Non-Actionable' cohort (n= 30) consisted of individuals who met USPSTF criteria for lung cancer screening and had no nodules on LDCT scan. Using high-density protein microarrays, (HuProt; CDI laboratories), circulating levels of 21,000 candidate autoantibodies were determined for each sample pool. Empirical Bayesian statistics were run to determine differential expression of each of the 21,000 autoantibodies within each comparison of interest (AdCa versus Non-Actionable microarrays, SqCa versus Non-Actionable, Carcinoid versus Non-Actionable, Benign versus Non-Actionable). 20 markers were chosen based on level of significance within a comparison and if they were significant for more than one comparison. Luminex immunobead assays were developed for the 20 autoantibodies. These assays were used to evaluate serum specimens from a distinct validation LDCT screening cohort consisting of individuals with either 'Actionable' (n=469) or 'Non-Actionable' (n= 377) lesions. The resulting datasets were analyzed via Mann-Whitney Rank Sum test (2-sided) to evaluate candidate biomarker performance for discerning 'Actionable' versus 'Non-Actionable' cohorts.

Results: Protein microarrays identified 501 candidate biomarkers differentially expressed in the training cohort ($p<0.01$). From these findings, 20 autoantibodies were selected for further analysis: CFAP36, DCD, DR1, GPBP1, HNRNPD, IKZF5, KEAP1, MED21, MIDIP1, MYBPH, NAP1L5, NAT9, NIP30, PJA2, PNMA1, RAB27A, SGPL1, TAF10, Ubiquillin 2, ZNF696. Luminex assays were developed for the 20 biomarkers and tested against the validation cohort. Twelve proteins were differentially expressed (p-values <.05) between the actionable and non-actionable validation cohorts: DCD, GPBP1, HNRNPD, KEAP1, MED21, MIDIP1, NAT9, PJA2, PNMA1, RAB27A, SGPL1, and ZNF696.

Conclusion: Novel circulating autoantibodies may have the potential to select patients with "Actionable" lesions on lung cancer screening LDCT scans.

PP01.34:
Induction of Tertiary Lymphoid Structures in Non-Small Cell Lung Cancer Improves B and T Cell Anti-Tumor Immunity

Miss Hye Mi Kim[1], Miss Dongyan Liu[1], Miss Ayana Ruffin[1], Miss Alexandra McDonough[1], Mr Caleb Lampenfeld[1], Mrs Sheryl Kunning[1], Dr Ashwin Somasundaram[1], Dr Laura Stabile[1], Dr Tullia Bruno[1]

[1]University Of Pittsburgh, UPMC Hillman Cancer Center, Department of Immunology, Pittsburgh, United States Induction of Tertiary Lymphoid Structures in Non-Small Cell Lung Cancer Improves B and T Cell Anti-Tumor Immunity

Background: Tertiary lymphoid structures (TLS) are lymphoid aggregates that often form locally in tissues with chronic infection, autoimmune disease, and cancer. As such, TLS correlate with favorable prognosis in patients with solid tumors, including non-small-cell lung cancer (NSCLC). Further, TLS have recently been associated with superior response to immune checkpoint blockade (ICB). B cells are predominantly located within TLS and correlate with improved survival and ICB response. Despite the therapeutic promise of B cells and TLS, they have not been investigated as immunotherapeutic targets. Moreover, a mechanistic understanding of TLS formation and function in cancer is lacking.

Methods: Our studies in NSCLC include investigation of human cancer for unique factors that promote or inhibit TLS formation paired with a physiologically relevant, carcinogen (NNK) induced murine model of lung cancer that spontaneously forms TLS. Specifically, we utilized multispectral imaging (Vectra Polaris) with spatial transcriptomics (Nanostring Digital Spatial Profiler) to interrogate TLS in NSCLC patients. We also utilized these state-of-the-art platforms to uncover new pathways to improve TLS formation and B and T cell function. We paired these studies with our carcinogen induced murine model as well as other subcutaneous murine models to test if TLS induction and maturation was increased with an oncolytic virus that targets TLS-initiating factors.

Results: According to transcriptomics, tumor-associated TLS have decreased TLS-initiating and maturation factors such as CXCL13, IL-21, CD40, and LTβ/LIGHT in comparison to normal lymphoid tissues. In addition, gene signature of TLS tends to be more regulatory as its proximity to tumor increases. Thus, using an oncolytic virus that targets CXCL13, IL-21, CD40 and LTβR/LIGHT, we have interrogated TLS formation over time. As a result, tumor infiltrating B cells was increased and tumor burden was decreased even in a tolerogenic mouse model.

Conclusion: These studies will increase our understanding of TLS formation for improved immunotherapies in NSCLC patients and will potentially provide therapeutic interventions that could be administered prior to cancer development.

PP01.35:
Validation of a High-Specificity Blood-Based Autoantibody Test to Detect Lung Cancer in Pulmonary Nodules

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Background: Evaluation of indeterminate pulmonary nodules (IPNs) is a clinical challenge, with over 1.6 million identified annually. Here, we performed an additional clinical validation of a 7-autoantibody (AAb) plasma panel, Nodify CDT® (CDT), previously shown to identify likely malignant IPNs, using a prospectively collected, retrospective blinded evaluation.

Methods: The CDT blood test measures AAbs targeting p53, NY-ESO-1, MAGE A4, GBU4-5, CAGE, HuD, and SOX2. Depending on the concentration of circulating AAbs, samples are classified as No Significant Level of Autoantibodies Detected , Moderate Level or High Level (HL), which are associated with increased likelihood of lung cancer. We identified patients from a single center that met the clinical use criteria (8-30 mm diameter, age ≥40 years and no cancer history). Test classifications were correlated with clinical outcomes (≥1year follow-up).

Results: From 621 nodules, 213 qualified for analysis, resulting in a lung cancer prevalence of 59% (126/213). Following testing, patient pre-test risk was adjusted using the likelihood ratios for CDT (Figure 1). Thirty-four (16%) were positive by CDT (22/34 cancer), resulting in a specificity of 87% (79-93%), sensitivity of 17% (12-25%), and positive predictive value (PPV) of 67% (50-81%). The HL cutoff (6%, 13/213) performed at a 95% (89-98%) specificity, 7% (4-13%) sensitivity and PPV of 69% (42-87%). The test identified NSCLC across stages for 47% (9/19) of stage I, 11% (2/19) of stage II, 21% (4/19) of stage IIIA and 21% (4/19) stage IV cases. The two SCLC cases detected (2/2, 100%) were limited stage.

Conclusion: AAbs detected by CDT testing can identify likely malignant IPNs with high specificity and PPV, confirming previously reported performance. Elevated AAbs identified early-stage NSCLC and SCLC, indicating the potential to accelerate time to diagnosis. Further clinical trials are ongoing to understand the clinical utility of incorporating blood biomarkers to expedite early-stage lung cancer diagnosis.

Table.

Outcomes by Target Lesion Shrinkage						
	Brigatinib (n=124)[a]			Crizotinib (n=125)[a]		
	None–50%	51%–75%	76%–100%	None–50%	51%–75%	76%–100%
PFS,[b,c] mo						
Overall, n (%)	20 (16)	34 (27)	70 (56)	44 (35)	38 (30)	43 (34)
Events, n (%)	12 (60)	23 (68)	33 (47)	33 (75)	29 (76)	24 (56)
Median (95% CI)	3 (2–17)	11 (7–19)	44 (25–NE)	4 (4–9)	9 (7–13)	27 (13–NE)
HR (95% CI)	Reference	0.58 (0.29–1.18)	0.23 (0.12–0.46)	Reference	0.68 (0.41–1.12)	0.26 (0.15–0.45)
Baseline brain metastases, n (%)	5 (13)	9 (24)	24 (63)	16 (46)	10 (29)	9 (26)
Events, n (%)	2 (40)	7 (78)	15 (63)	11 (69)	8 (80)	7 (78)
Median (95% CI)	NE (1–NE)	13 (5–24)	27 (21–NE)	5 (2–9)	9 (2–12)	11 (4–NE)
HR (95% CI)	Reference	2.95 (0.60–14.53)	1.08 (0.25–4.72)	Reference	0.81 (0.32–2.03)	0.65 (0.25–1.68)
Prior CT, n (%)	10 (30)	5 (15)	18 (55)	17 (52)	8 (24)	8 (24)
Events, n (%)	5 (50)	3 (60)	11 (61)	12 (71)	7 (88)	6 (75)
Median (95% CI)	16 (2–NE)	9 (5–NE)	38 (18–NE)	9 (3–21)	12 (4–24)	17 (4–NE)
HR (95% CI)	Reference	1.62 (0.38–6.99)	0.64 (0.22–1.86)	Reference	0.95 (0.37–2.44)	0.60 (0.22–1.62)
OS,[b] mo						
Overall, n (%)	20 (16)	34 (27)	70 (56)	44 (35)	38 (30)	43 (34)
Events, n (%)	11 (55)	12 (35)	12 (17)	25 (57)	12 (32)	8 (19)
Median (95% CI)	28 (7–NE)	NE (35–NE)	NE (NE)	38 (19–NE)	NE (41–NE)	NE (NE)
HR (95% CI)	Reference	0.39 (0.17–0.89)	0.15 (0.07–0.35)	Reference	0.43 (0.21–0.85)	0.23 (0.10–0.50)
Baseline brain metastases, n (%)	5 (13)	9 (24)	24 (63)	16 (46)	10 (29)	9 (26)
Events, n (%)	2 (40)	3 (33)	5 (21)	7 (44)	6 (60)	4 (44)
Median (95% CI)	NE (1–NE)	NE (12–NE)	NE (NE)	NE (12–NE)	37 (14–NE)	NE (4–NE)
HR (95% CI)	Reference	0.92 (0.15–5.52)	0.47 (0.09–2.40)	Reference	1.37 (0.46–4.10)	0.91 (0.26–3.10)
Prior CT, n (%)	10 (30)	5 (15)	18 (55)	17 (52)	8 (24)	8 (24)
Events, n (%)	7 (70)	3 (60)	1 (6)	9 (53)	5 (63)	1 (13)
Median (95% CI)	22 (3–NE)	14 (7–NE)	NE (NE)	39 (13–NE)	39 (13–24)	NE (4–NE)
HR (95% CI)	Reference	0.86 (0.22–3.33)	0.05 (0.01–0.42)	Reference	1.01 (0.34–3.02)	0.18 (0.02–1.45)

CI, confidence interval; CT, chemotherapy; HR, hazard ratio; NE, not estimable; OS, overall survival; PFS, progression-free survival
[a] Evaluable patients; [b] Kaplan-Meier estimate; [c] Blinded, independent review committee (BIRC)-assessed

PP01.36:
Blood-Based Biomarker Testing in Advanced Non-Small Cell Lung Cancer: Adoption, Biomarker Assessment, and Therapy Selection

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Background: Oncologists now have both Food and Drug Administration approved tissue- and blood-based biomarker testing to understand patients' genomics and make therapy recommendations. We studied the temporal trends in blood-based testing adoption and the implications of blood-based testing on biomarker assessment, biomarker status, and first-line therapy selection.

Methods: We conducted a retrospective analysis using the Flatiron Health electronic health record-derived deidentified nationwide longitudinal database. We studied patients with a de novo advanced diagnosis of non-small cell lung cancer (NSCLC) from January 2016 to July 2021 and at least one tissue or blood-based genomic biomarker result prior to first-line treatment (LOT1). Patients were categorized based on their genomic results before LOT1 as: tissue-only, blood-only, or tissue+blood. Genomic biomarkers studied included variants in ALK, BRAF, EGFR, KRAS, and ROS1. PD-L1 IHC testing was considered independently.

Results: 9,621 patients met the inclusion criteria. The tissue-only, blood-only and tissue+blood cohorts represented 76%, 12% and 12% of the study sample, respectively. The percentage of patients with blood-based testing (alone or with tissue-based testing) increased from 11% in 2016 to 38% in 2021. The tissue+blood cohort had the highest rate of testing for all five biomarkers at 94% compared to 86% and 41% in the blood-only and tissue-only cohorts, respectively. PD-L1 IHC missingness was highest in the blood-only genomic cohort at 48% compared to 18% in the tissue-only and 11% in the tissue+blood cohorts. Among patients tested for all five biomarkers, the probability of at least one positive biomarker was 35% in the blood-only, 46% in the tissue-only, and 47% in the tissue+blood cohorts. Targeted therapy rates among biomarker positive patients were not different across the tissue- and blood-only cohorts except for EGFR, where blood-only had higher use of matched LOT1 targeted therapies (95% vs. 85%; $p<0.01$). Overall, 14% of ALK+ patients, 16% of EGFR+ patients and 27% of ROS1+ patients did not receive matched FDA-approved LOT1 targeted therapy.

Conclusion: Blood-based biomarker testing adoption is accelerating, providing a pragmatic option when tissue is unavailable. While blood-based testing increases the probability a patient is tested for all five biomarkers, the lower positivity rates in this cohort may be partly driven by the lower sensitivity of blood-based tests. When blood-based biomarker results are negative, there is a need for confirmatory tissue-testing to maximize the biomarker detection rate. While targeted therapy rates were similar across cohorts, not all biomarker-positive patients received matched targeted therapy in LOT1.

PP01.37:
Quality of Life in Non-Small Cell Lung Cancer Patients with Brain/CNS Metastases–Real-World Evidence

Miss Hollie Bailey[1], Mr Cameron Forshaw[1], Ms Sanjana Chandrasekar[2], Ms Chew Hooi Wong[3], Mr. Matthew Last[1], Miss Helen Burlison[1], Ms Grace Foley[4], Ms Laura Iadeluca[5], Mr. Stan Krulewicz[6], Mr Robin Wiltshire[2], Ms Despina Thomaidou[7], Dr Kirsten Duncan[2]

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Background: Non-small cell lung cancer [NSCLC] is often associated with poor patient-reported quality of life [QoL] and prognosis, which are exacerbated in patients with metastasis. This study aims to describe real-world QoL in NSCLC patients with brain/central nervous system [CNS] metastases in Europe, Asia, the United States [US] and Brazil.

Methods: Real-world data were collected via the Adelphi NSCLC Disease Specific ProgrammeTM; a point-in-time survey of oncologists/pulmonologists and their NSCLC patients with brain/CNS metastases, conducted July-November 2020 in Europe [France, Germany, Italy, Spain, United Kingdom], Asia [Japan, Taiwan], US and Brazil. Physicians provided information on the next six consulting patients with advanced NSCLC (both patients with and without brain/CNS metastases). These same patients were invited to complete a voluntary questionnaire which included the EuroQol EQ-5D-5L utility score (US tariff), the EuroQol visual analogue scale [EQ-VAS] (utility score range: -0.573 to 1, EQ-VAS: 0-100; higher scores indicating better health status/QoL), and Functional Assessment of Cancer Therapy-General [FACT-G] (score range 0-108; higher scores indicating a higher QoL).

Results: Data were collected on 391 NSCLC patients with brain/CNS metastases, of those 122 completed the questionnaire providing QoL data. Patients' median (SD) age was 64 (11.3) years, 53% were male and 71% had an ECOG performance score of 0-1. At data collection, 57% of patients were on long-term sick leave, retired or unemployed; for 45% (n=32) of these patients this was due to their NSCLC. Overall, 34% of patients had at least one caregiver to help with their daily needs, of which the most common caregivers were partner/spouse (64%) followed by son/daughter over 18 years (41%). The mean (SD) EQ-5D-5L utility score and EQ-VAS were 0.69 (0.31) and 68.2 (17.94), which represented clinically meaningful differences from the respective population norms of 0.89 and 77.8. The mean (SD) FACT-G score was 64.0 (17.85) which was clinically meaningfully lower than the population norm of 79.0 in patients with varying types of cancer. According to treatment at time of data capture the lowest QoL was observed in those receiving chemotherapy with EQ-VAS score of 64.6 (20.59), EQ-5D-5L utility of 0.66 (0.33) and FACT-G OF 60.1 (19.87).

Conclusion: NSCLC patients with brain/CNS metastases experienced impairment in health-related QoL as quantified by validated instruments. These findings indicate a need to improve QoL for this subset of patients as a priority in the developing treatment landscape. Further research is needed into the factors associated with QoL impairment in this population.

PP01.38:
Biomarker Testing and Associated Treatment Patterns in Advanced Non-Small Cell Lung Cancer in the US

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Background: Biomarker testing in advanced non-small cell lung cancer(aNSCLC) is important to inform treatment decisions and management. However, data is limited on how biomarker testing effects treatment in the real-world. To address this, our real-world survey described biomarker testing at aNSCLC diagnosis and associated treatment patterns in the US.

Methods: Data were drawn from the Adelphi NSCLC Disease Specific Programme™, a point-in-time survey of oncologists/pulmonologists in the US, conducted July-November 2020. Physicians identified from publicly available lists were asked to take part. Physicians provided information on the next 6 consulting patients with aNSCLC. Data analysis was descriptive.

Results: Physicians (n=71) provided data on 470 patients with aNSCLC. At advanced diagnosis, 94% were tested for at least one biomarker (biomarkers included EGFR, ALK, ROS1, KRAS, BRAF, RET, MET, HER2, VEGF, TRK, CEACAM5, PD-L1 expression and tumor mutational burden(TMB)) and 26 (6%) were not tested for any biomarkers. Median age of patients tested was 67 years and 56% were males. Most patients tested and not tested had adenocarcinoma histology (75% and 69% respectively). Of patients tested and diagnosed at an advanced stage (n=421), 75% were tested via next generation sequencing(NGS). Although most patients were tested for at least one biomarker, many patients were not tested for their ALK (17%), ROS1 (23%), BRAF (31%), EGFR (11%), KRAS (29%) and/or PD-L1 (17%) status. At aNSCLC diagnosis patients tested positive for PD-L1 (54%, 212/392), EGFR (18%, 75/419), ALK (9%, 37/391), KRAS (9%, 30/336), ROS1 (2%, 8/364) or BRAF (2%, 6/332). Median duration from advanced diagnosis to initiation of first-line (1L) treatment ranged from 0.5 to 2.0 months across biomarkers. Of positive PD-L1 patients, 51% had an expression of 1-49%. Of the total cohort, 29% (134/470) received a combination of immunotherapy and chemotherapy at 1L, while 25% received chemotherapy alone and 17% immunotherapy alone. The most common 1L treatment for patients with ALK positive tumors (n=37) was ALK TKI monotherapy (46%), followed by chemotherapy alone (14%), and immunotherapy containing regimens (11%).

Conclusion: Despite the evolution of biomarker testing, this analysis shows biomarker testing remains sub-optimal in the US. Despite targeted therapies being standard of care in many biomarker driven tumors, patients were often treated with 1L immunotherapy containing regimens or chemotherapy alone. This research uncovers challenges in biomarker testing patients with aNSCLC for driver mutations (such as ALK, ROS1 and BRAF), as well as the treatments selected for these patients, which could be further improved.

PP01.39:
Infrastructure for Interobserver Variability Assessment of Pathologic Response (PR), in Surgical Resection Specimens Following Neoadjuvant Immune Check Point Inhibitor (ICI) Therapies in Early Stage NSCLC

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Background: Neoadjuvant therapies have unique advantages and opportunities in lung cancer but also present some challenges; including a lack of established guidance on how to process and evaluate resected lung cancer specimens in both clinical practice and clinical trials. The IASLC provided guidance for specimen processing and is now conducting this interobserver study for PR evaluation.

Methods: To determine interobserver variability for PR following neoadjuvant ICI therapy in NSCLC an entire infrastructure was required. This included a statistical plan, study identification, slide procurement from the studies, slide de-identification procedure, scoring pathologist identification, rotational plan for the slides, and an electronic scoring platform.

Results: A statistical plan determined that for most plausible ranges of variance, 90 patient samples provided reasonable power and should provide a good assessment of variability across raters. It is assumed that the variance of the measurements within a subject (across raters) will be smaller than the across-subject variance. MD Anderson Cancer Center (MDACC) was selected to serve as the central lab to receive the NSCLC H&E slides from 90 NSCLC patients, from 6 clinical trials: NEOSTAR, MDACC; LCMC3, Genentech; NADIM, Puerta de Hierro; MAC, Columbia University; TOP 1501, Duke University; and MEDI4736, Cornell University. An onsite lung pathologist assessed all slides, 10-15 per patient, for pathologic quality control and once confirmed, slides were de-identified and whole slides images scanned (Aperio™). Twelve expert pathologists were selected, 6 from the IASLC pathology committee and 6 from the included clinical trials, one per trial to determine the PR. A rotational structure was created so that each rater reviews 45 cases and each case is reviewed by six raters. MDACC developed an online tool (web-server secured password protected website) to capture each pathologist's PR score and centralize pathologic data. The system allows for sample ID assignment, histology quality control, randomization, distribution shipping and tracking.

Conclusion: In collaboration, the IASLC and MDACC have developed an operational workflow and web-served secured website to ensure the feasibility and success of a complex global interobserver study where 12 international pathologists evaluate PR for 90 cases from 6 clinical trials of early stage NSCLC patients treated with ICI.

PP01.40:
Target Lesion Response and Outcomes in Patients Treated with Brigatinib vs Crizotinib in ALTA-1L

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Background: In ALTA (NCT02094573), depth of target lesion response to brigatinib correlated with PFS and OS in patients with crizotinib-refractory advanced ALK+ NSCLC. We evaluated the association between maximum decrease in target lesions and PFS and OS in patients with ALK inhibitor-naive advanced ALK+ NSCLC from ALTA-1L (NCT02737501).

Methods: Patients were randomized 1:1 to brigatinib 180 mg qd (7-day lead-in at 90 mg; n=137) or crizotinib 250 mg bid (n=138). Patients with target lesion assessment by BIRC were grouped based on greatest decrease from baseline per RECIST v1.1: none–50%, 51%–75%, and 76%–100% shrinkage. Outcomes in the ≤50% target lesion shrinkage group served as the comparator for outcomes in the 51%–75% and 76%–100% groups.

Results: At study end (last patient contact: 29 Jan, 2021), 124/137 patients in the brigatinib arm and 125/138 patients in the crizotinib arm had ≥1 evaluable target lesion assessment; female (brigatinib/crizotinib), 51%/59%; median age, 57.5/60.0 years. Median follow-up was 40.8/15.7 months. In brigatinib/crizotinib arms, 76%–100% shrinkage was observed in 56%/34% of patients; 51%–75% shrinkage in 27%/30%; and ≤50% shrinkage in 16%/35%, respectively. Brigatinib was associated with significantly more patients with target lesion shrinkage >75% vs crizotinib (P=0.0005), and a Cochran–Armitage trend analysis demonstrated significantly deeper response across all groups for brigatinib vs crizotinib (P<0.0001). Patients treated with brigatinib or crizotinib with target lesion shrinkage >50% had lower risk of a PFS or an OS event than patients with ≤50% shrinkage (Table). In the brigatinib arm, patients with baseline brain metastases or prior chemotherapy exhibited tumor shrinkage trends consistent with the overall population.

Conclusions: In this exploratory post hoc analysis, brigatinib demonstrated significantly deeper target lesion response vs crizotinib. Patients with >75% shrinkage had significantly reduced risk of a PFS or OS event vs patients with ≤50% target lesion shrinkage.

Table.

Outcomes by Target Lesion Shrinkage						
	Brigatinib (n=124)[a]			Crizotinib (n=125)[a]		
	None–50%	51%–75%	76%–100%	None–50%	51%–75%	76%–100%
PFS,[b,c] mo						
Overall, n (%)	20 (16)	34 (27)	70 (56)	44 (35)	38 (30)	43 (34)
Events, n (%)	12 (60)	23 (68)	33 (47)	33 (75)	29 (76)	24 (56)
Median (95% CI)	3 (2–17)	11 (7–19)	44 (25–NE)	4 (4–9)	9 (7–13)	27 (13–NE)
HR (95% CI)	Reference	0.58 (0.29–1.18)	0.23 (0.12–0.46)	Reference	0.68 (0.41–1.12)	0.26 (0.15–0.45)
Baseline brain metastases, n (%)	5 (13)	9 (24)	24 (63)	16 (46)	10 (29)	9 (26)
Events, n (%)	2 (40)	7 (78)	15 (63)	11 (69)	8 (80)	7 (78)
Median (95% CI)	NE (1–NE)	13 (5–24)	27 (21–NE)	5 (2–9)	9 (2–12)	11 (4–NE)
HR (95% CI)	Reference	2.95 (0.60–14.53)	1.08 (0.25–4.72)	Reference	0.81 (0.32–2.03)	0.65 (0.25–1.68)
Prior CT, n (%)	10 (30)	5 (15)	18 (55)	17 (52)	8 (24)	8 (24)
Events, n (%)	5 (50)	3 (60)	11 (61)	12 (71)	7 (88)	6 (75)
Median (95% CI)	16 (2–NE)	9 (5–NE)	38 (18–NE)	9 (3–21)	12 (4–24)	17 (4–NE)
HR (95% CI)	Reference	1.62 (0.38–6.99)	0.64 (0.22–1.86)	Reference	0.95 (0.37–2.44)	0.60 (0.22–1.62)
OS,[b] mo						
Overall, n (%)	20 (16)	34 (27)	70 (56)	44 (35)	38 (30)	43 (34)
Events, n (%)	11 (55)	12 (35)	12 (17)	25 (57)	12 (32)	8 (19)
Median (95% CI)	28 (7–NE)	NE (35–NE)	NE (NE)	38 (19–NE)	NE (41–NE)	NE (NE)
HR (95% CI)	Reference	0.39 (0.17–0.89)	0.15 (0.07–0.35)	Reference	0.43 (0.21–0.85)	0.23 (0.10–0.50)
Baseline brain metastases, n (%)	5 (13)	9 (24)	24 (63)	16 (46)	10 (29)	9 (26)
Events, n (%)	2 (40)	3 (33)	5 (21)	7 (44)	6 (60)	4 (44)
Median (95% CI)	NE (1–NE)	NE (12–NE)	NE (NE)	NE (12–NE)	37 (14–NE)	NE (4–NE)
HR (95% CI)	Reference	0.92 (0.15–5.52)	0.47 (0.09–2.40)	Reference	1.37 (0.46–4.10)	0.91 (0.26–3.10)
Prior CT, n (%)	10 (30)	5 (15)	18 (55)	17 (52)	8 (24)	8 (24)
Events, n (%)	7 (70)	3 (60)	1 (6)	9 (53)	5 (63)	1 (13)
Median (95% CI)	22 (3–NE)	14 (7–NE)	NE (NE)	39 (13–NE)	39 (13–24)	NE (4–NE)
HR (95% CI)	Reference	0.86 (0.22–3.33)	0.05 (0.01–0.42)	Reference	1.01 (0.34–3.02)	0.18 (0.02–1.45)

CI, confidence interval; CT, chemotherapy; HR, hazard ratio; NE, not estimable; OS, overall survival; PFS, progression-free survival
[a] Evaluable patients; [b] Kaplan-Meier estimate; [c] Blinded, independent review committee (BIRC)-assessed

PP01.41:
Efficacy of Sotorasib Versus Standard Chemotherapy + Immunotherapy in KRAS G12C Mutated Lung Cancer: A Comparative Study Modeling Real-World Data

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Background: KRAS mutations are highly prevalent in Non-small-cell lung cancer (NSCLC). Ninety percent of such mutations involve codon 12 with the most common being G12C. Recently, Sotorasib has been approved as a targeted therapy for G12C NSCLC based on a phase 2 trial demonstrating a durable clinical benefit without major safety concerns. We conducted this study to compare the efficacy of Sotorasib to standard chemotherapy +/- immunotherapy (CIT) by modeling real-world data (RWD).

Methods: We used Sotorasib phase II trial progression-free survival (PFS) and overall survival (OS) to model the Sotorasib arm. We also used the published RWD from an observational retrospective KRAS G12C cohort using a US-based clinico-genomic database to create a comparator cohort and model the standard CIT arm. Kaplan-Meier curves were constructed. Descriptive statistics and X2 were calculated to describe characteristics and check for differences among the two cohorts. Log-rank test was used to compare the survival curves.

Results: The Sotorasib and CIT arms comprised 126 and 288 patients respectively. Median ages were 63 and 68 for Sotorasib and CIT respectively. There was no statistical difference between the two arms with respect to sex, race, and histology. Although the Sotorasib arm had more “any metastasis” (96.8% vs 86.1%, p=0.0007), brain metastases were not statistically different. The two arms were not statistically different with respect to lines of treatment. Sotorasib was found to have a statistically significant longer PFS compared to CIT (6.8 vs 4 months, p=0.011). Moreover, Sotorasib significantly improved OS when compared to CIT (12.5 vs 7 months, p<0.0001).

Conclusions: This is the first study to show that Sotorasib is associated with improved PFS and OS in KRAS G12C mutated lung cancer when compared to a RWD modeled cohort which received chemotherapy +/- immunotherapy.

PP01.42:
Efficacy of Adagrasib Versus Standard Chemotherapy +/- Immunotherapy in KRAS G12C Mutated Lung Cancer: A Comparative Study Modeling Real-World Data

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Background: KRAS mutations are highly prevalent in Non-Small-Cell Lung Cancer (NSCLC). Ninety percent of such mutations involve codon 12 with the most common being G12C. Adagrasib is currently being considered for approval as a targeted therapy for G12C NSCLC based on a phase 2 trial demonstrating a durable clinical benefit without major safety concerns. We conducted this study to compare the efficacy of Adagrasib to standard chemotherapy +/- immunotherapy (CIT) by modeling real-world data (RWD).

Methods: We used Adagrasib phase II trial progression-free survival (PFS) and overall survival (OS) to model the Adagrasib arm. We also used the published RWD from an observational retrospective KRAS G12C cohort using a US-based clinico-genomic database to create a comparator cohort and model the standard CIT arm. Kaplan-Meier curves were constructed. Descriptive statistics and X2 were calculated to describe characteristics and check for differences among the two cohorts. Log-rank test was used to compare the survival curves.

Results: The Adagrasib and CIT arms comprised 116 and 288 patients respectively. Median ages were 64 and 68 for Adagrasib and CIT respectively. There was no statistical difference between the two arms with respect to sex, race, and histology. Although the Adagrasib arm had more “any metastasis” (95.7% vs 86.1%, p=0.004), brain metastases were not statistically different. The two arms were not statistically different with respect to lines of treatment. Adagrasib was found to have a statistically significant longer PFS compared to CIT (6.5 vs 4 months, p=0.004). Moreover, Adagrasib significantly improved OS when compared to CIT (12.6 vs 7 months, p<0.0001).

Conclusions: This is the first study to show that Adagrasib is associated with improved PFS and OS in KRAS G12C mutated lung cancer when compared to a RWD modeled cohort which received chemotherapy +/- immunotherapy.

PP01.43:
A Retrospective Single-Center Analysis of Patients with Atypical EGFRm NSCLC Treated with First-Line EGFR-TKIs

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Background: 7-23% of EGFR mutations are atypical, defined as non-exon 19 deletion/exon 21 L858R point mutations.[1] A recent novel classification system using a structure-function approach further defined four EGFR mutation subgroups with different EGFR-TKI sensitivities.[2] This study aimed to characterize patients with atypical EGFR-mutant (EGFRm) NSCLC treated at MD Anderson Cancer Center, and their clinical outcomes with treatment.

Methods: Records of patients treated from January 2014 - January 2020 were analyzed. Inclusion criteria included histologically confirmed advanced NSCLC not amenable for curative therapy, with atypical EGFR alterations in exons 18-21. Primary objectives: atypical EGFR mutation distribution, and clinical outcomes (time-on-treatment [ToT]) with EGFR-TKIs. Secondary objectives included patient demographics, OS, and afatinib-associated AEs.

Results: Patients (N=72) with atypical EGFRm NSCLC were treated with first-line afatinib (n=22 [most common EGFR mutations: G719X, n=13; E709X, n=7; S768I, n=6]), erlotinib/gefitinib (n=32), or osimertinib (n=18). Median ToT was longest with afatinib (14.0 months), compared to erlotinib/gefitinib (8.3 months) and osimertinib (6.9 months; p=0.034; log rank test; Figure). No significant differences in OS were observed (afatinib, 22.7 months; erlotinib/gefitinib, 31.2 months; osimertinib, not reached; p=0.89). Median ToT in patients with EGFR PACC mutations[2] was 14.9 (n=17), 9.2 (n=12), and 5.3 (n=6) months (p=0.15), respectively (acknowledging small sample sizes). Of the 21 afatinib-treated patients with adequate clinical information, starting doses were 40 mg (n=14, 66.7%) 30 mg (n=6, 28.6%) and 20 mg (n=1, 4.8%). Most patients (n=14, 66.7%) had ≥1 treatment-related AE (TRAE), most commonly diarrhea (n=12, 57.1%) and rash (n=5, 23.8%); one patient discontinued treatment due to diarrhea.

Conclusion: Most patients treated with afatinib had G719X mutations, followed by E709X and S768I. ToT was significantly longer in patients treated with afatinib versus other EGFR-TKIs. Observed TRAEs were consistent with afatinib's established safety profile. Based on this small, single-center data set, afatinib represents a valid treatment option in patients with atypical EGFRm NSCLC.

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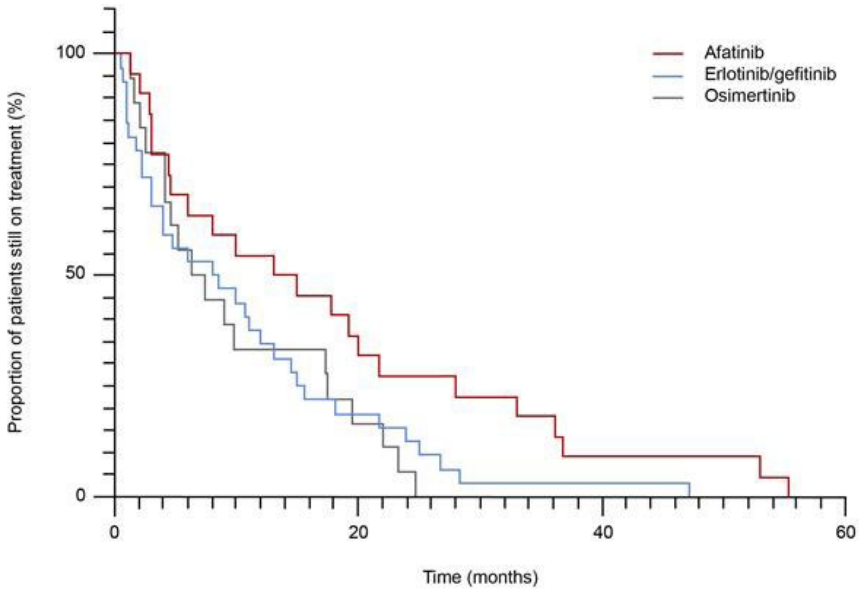

PP01.44:
Long-Term Survival and Outcomes by Race from the Phase I/II trial of Carboplatin, Nab-paclitaxel, and Pembrolizumab for Advanced NSCLC: HCRN LUN13-175

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Background: Combination chemotherapy and immunotherapy regimens have significantly improved survival for patients with previously untreated advanced non-small cell lung cancer (NSCLC). In phase III trials combining chemotherapy and immunotherapy, 3-year OS has been reported at 30% (Keynote 407), 31% (Keynote 189), and 27% (Checkmate 9LA). We conducted a phase I/II trial of pembrolizumab with nab-paclitaxel and carboplatin in all-histology NSCLC. Previous FDA-approved phase III trials using chemotherapy and immunotherapy combinations enrolled only 1% Black/African American patients. Here we report long-term outcomes and outcomes by race.

Methods: Adult patients with previously untreated, stage IIIB/IV NSCLC (all histology) with an ECOS PS of 0-1, any PD-L1 expression, and no EGFR mutations or ALK translocations, received carboplatin AUC 6 day 1, nab-paclitaxel 100 mg/m2 days 1, 8, 15, and pembrolizumab 200 mg day 1 q21 days for 4 cycles followed by maintenance pembrolizumab q3w. Co-primary endpoints were progression-free survival (PFS) and overall response rate (ORR). Exploratory analysis was conducted to report outcomes by race.

Results: 46 evaluable patients enrolled, 14 on phase I and 32 in phase II, from June 2015–July 2018 with a median duration of follow-up of 2.95 years. Median time from enrollment to data lock was 3.5 years. Median age was 65 years, 48% were female, 76% Caucasian, 13% African American (AA), 46% adenocarcinoma, 94% current/former smokers, 9% brain metastases. PD-L1 expression (TPS) by <1%, 1-49%, and ≥ 50% cutoffs was 44%, 28%, and 28%, respectively. In the ITT population, the ORR was 35%, median PFS was 5.6 months (CI, 4.6-8.2), and median OS was 15 mo (CI 12-28). There were no statistical differences in PFS or OS by PD-L1 status. The 2-, 3- and 4-yr landmark OS rates were 32.9%, 23.8%, and 23.8%, respectively. Black/AA patients had an ORR of 50%, median PFS of 5 mo, median OS of 18 mo, and a 3-year OS rate of 33%.

Conclusion: Long-term survival outcomes with carboplatin, nab-paclitaxel and pembrolizumab are similar to outcomes reported in phase III trials with immunotherapy + chemotherapy for first-line treatment of advanced NSCLC. This trial enrolled a higher proportion of African American patients (13% AA) than phase III trials submitted to the FDA (1% AA) and showed that outcomes in this patient population are similar to those of the overall trial population.

PP01.45:
Implementation Challenges and Disparities in Molecular Testing for Patients with NSCLC at a Safety-Net Hospital

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Background: The advent of next-generation sequencing (NGS), including both tissue assays and circulating tumor DNA (ct-DNA), has been pivotal in improving outcomes for patients with non-small cell lung cancer (NSCLC). Although molecular testing is standard of care for advanced NSCLC, barriers still exist in its implementation.

Methods: One hundred fifty-seven patients with stage IV NSCLC from our institution were reviewed over the period January 2015 through January 2022. Patients were analyzed in two time cohorts: January 2015 through March 2018 (pre-guideline group) and April 2018 through January 2022 (post-guideline group), based on the publication of updated molecular testing guidelines from International Association for the Study of Lung Cancer (IASLC), Association for Molecular Pathology (AMP), and College of American Pathologists (CAP) in March of 2018. Molecular testing was categorized into "none," meaning no molecular testing was performed; "limited," referring to testing only for EGFR and BRAF mutations, ALK rearrangements, ROS1 fusions; and "next-generation sequencing," which includes NGS via either tissue or ct-DNA liquid biopsy. For those patients who did not undergo NGS tissue testing, charts were reviewed and categorized by reason for lack of testing.

Results: The rate of tissue NGS increased from 9% to 39% for all patients (n = 157). The rate of liquid NGS increased from 1% to 41% for all patients, but for the subgroup of squamous cell carcinoma patients this rate increased only from 0% to 7%. NGS overall increased from 9% to 57%. No racial disparities in completion of NGS were observed. Barriers to NGS included lack of physician ordering (79%) and for tissue NGS, insufficient tissue on biopsy (15%). Of patients who did not have tissue biopsy ordered, few (4%) underwent liquid biopsy. In contrast, 77% of those with insufficient tissue on biopsy ultimately went on to receive liquid biopsy.

Conclusion: While NGS adoption has expanded over the past 7 years, it is still not being performed for many patients. In those with squamous cell carcinoma particularly, NGS is rarely utilized. While other groups in multi-institution studies have found racial disparities in molecular testing for NSCLC, we did not find such disparities within our institution. Liquid NGS remains under-utilized, particularly in patients for whom tissue NGS is not initially ordered. A potential solution to the lack of physician ordering of NGS may be the reflexive ordering of NGS for patients with advanced NSCLC and efforts to increase awareness regarding the utility of NGS testing.

PP01.46:
Unfiltered Patient Insights: Experiences of Patients With ALK+ or EGFR Exon20 Insertion+ Non-Small Cell Lung Cancer

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Background: Although many studies evaluating efficacy of investigational non-small cell lung cancer (NSCLC) therapies exist, few studies focus on the holistic experiences of people with cancer. We conducted interviews with patients and their care partners to understand the multifactorial (ie, behavioral, psychosocial, cognitive, interactional, and linguistic aspects) experiences of people with ALK+ NSCLC (ALK+) or EGFR Exon20 insertion+ NSCLC (Exon20i).

Methods: We interviewed 11 patients (7 ALK+; 4 Exon20i) and 8 patient care partners (2 ALK+; 6 Exon20i) who responded to a request to be interviewed; interviews place March-April, 2020 (ALK+) or October, 2020 (Exon20i).

Results: Patients in both groups experienced shock and disbelief upon their NSCLC diagnosis. Initially, patients in both groups were not made aware of next-generation sequencing (NGS) to test for oncogenic mutations, which may have delayed targeted therapy. Furthermore, patients often did not receive NGS until ordered by a specialist or at an academic care center. Upon learning about their specific mutations, patients with ALK+ saw themselves as members of a "fortunate few" due to availability of targeted daily oral therapy and accepted treatment side effects as part of their "new normal"; however, many patients with ALK+ also described "living in limbo", waiting for potential bad news of disease progression to disrupt their new normal. By contrast, patients with Exon20i experienced hopelessness due to limited treatment options and frustration with clinical trial experiences; patients with Exon20i found treatment side effects difficult to manage and reported that expectations regarding medication side effects were not properly set, even in clinical trials. Patients in both groups found information provided by their doctors regarding their condition and treatments to be inadequate. Instead, they relied heavily on patient advocacy groups for information regarding treatment side effects, clinical trials, and other information about their disease. All patients felt empowered by patient advocacy groups.

Conclusions: The experiences of patients with ALK+ differed starkly from those with Exon20i due to the availability of targeted therapies and the information communicated regarding their prognosis. Greater health care provider knowledge of and access to NGS, such as those found at academic care centers, may improve quality of life and treatment outcomes for patients who would otherwise delay targeted therapy. Since the conclusion of this study, there are newly approved treatments for Exon20i, which may improve these patients' experiences. Upfront education, in lay terms, regarding prognosis, ongoing clinical trials, and patient advocacy groups may improve holistic patient experiences.

PP01.47:
HERTHENA-Lung02: A Randomized Phase 3 Study of Patritumab Deruxtecan vs Platinum-Based Chemotherapy in Locally Advanced or Metastatic EGFR-Mutated NSCLC After Progression with a Third-Generation EGFR TKI

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Background: Standard therapies for patients (pts) with epidermal growth factor receptor–mutated (EGFRm) non-small cell lung cancer (NSCLC) that has progressed after treatment with third-generation (3rd-gen) EGFR tyrosine kinase inhibitors (TKIs) offer only limited benefit. Human epidermal growth factor receptor 3 (HER3) is often expressed in primary NSCLC tumors, and HER3 expression is commonly observed in patients with EGFR mutations. HER3-DXd is a novel antibody-drug conjugate composed of a human anti-HER3 monoclonal antibody (patritumab) linked to a topoisomerase I inhibitor payload via a tetrapeptide-based cleavable linker. HER3-DXd demonstrated efficacy and safety in a phase 1 study in pts with EGFRm NSCLC that progressed following an EGFR TKI and platinum-based chemotherapy (PBC) (U31402-A-U102; NCT03260491).

Trial Design: HERTHENA-Lung02 (NCT05338970) is a global, open-label, randomized, phase 3 trial evaluating the efficacy and safety of HER3-DXd vs PBC in pts (≈560) with metastatic or locally advanced nonsquamous NSCLC with an EGFR-activating mutation (exon 19 deletion or L858R) who have received 1 or 2 lines of EGFR TKI treatment including a 3rd-gen EGFR TKI and had disease progression following treatment with a 3rd-gen EGFR TKI. Pts are randomized 1:1 to receive either HER3-DXd 5.6 mg/kg every 3 weeks or 4 cycles of PBC containing pemetrexed (can be continued as maintenance) with cisplatin or carboplatin. Pts are stratified by prior 3rd-gen EGFR TKI treatment (osimertinib vs other), line of prior 3rd-gen EGFR TKI use (first vs second line), region (Asia vs rest of world), and presence of stable brain metastases (yes vs no). The primary endpoint is progression-free survival (PFS) per blinded independent central review (BICR per RECIST v1.1). The key secondary endpoint is overall survival. Other secondary endpoints include investigator-assessed PFS, objective response rate, duration of response, clinical benefit rate, disease control rate, time to response (all assessed by investigator and BICR per RECIST v1.1), safety, and patient-reported outcomes. Enrollment began May 2022 and is ongoing, with sites in the US, Canada, EU, Asia, and Australia. This trial in progress was previously presented at ESMO 2022.

PP01.48:
Efficacy and Safety of Patritumab Deruxtecan (HER3-DXd) in Locally Advanced/ Metastatic Non-Small Cell Lung Cancer (NSCLC) without EGFR-Activating Mutations

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Background: Patients with advanced NSCLC without EGFR-activating mutations (EGFRm) have limited treatment options after failure of molecularly targeted therapies or platinum-based chemotherapy (PBC) with or without immunotherapy (IO). HER3-DXd is an antibody drug conjugate consisting of a fully human anti-HER3 mAb attached to a topoisomerase I inhibitor payload via a tetrapeptide-based cleavable linker. Here we present updated results, previously presented at ASCO 2022, in patients without tumor EGFRm who progressed after PBC ± IO treatment.

Methods: This ongoing phase 1 study included a dose-expansion cohort of patients with advanced NSCLC without EGFRm who received prior PBC ± IO (NCT03260491). Stable brain metastases, tumor non-EGFR oncogenic alterations, and prior targeted therapy were permitted. Primary endpoint was confirmed ORR by blinded independent central review (BICR) per RECIST v1.1; secondary endpoints included DOR, PFS, and safety.

Results: At the 28 January 2022 data cutoff (DCO), 47 patients were treated with HER3-DXd 5.6 mg/kg IV Q3W; 21 patients had an identified driver genomic alteration (4 KRAS and 1 NRAS mutations; 4 EGFR Ex20ins; 3 ROS1, 1 RET, and 2 ALK fusions; and 6 other). Median age was 62 years (range, 29-79 years); 17% had squamous NSCLC. Median follow-up was 19.7 months (range, 13.8-29.2 months). Median number of prior anticancer regimens in the advanced setting was 3 (range, 1-8). At DCO, median treatment duration on study was 4.2 months (range, 0.7-19.8 months); treatment was ongoing in 5 patients (10.6%).

Among patients with identified driver genomic alterations, the confirmed ORR by BICR was 28.6% (6/21 patients; 95% CI, 11.3%-52.2%; 6 PRs, 10 SD), including 3 of 5 patients with KRAS/NRAS mutations and 2 of 2 with ALK fusions. Median DOR was 9.4 months (95% CI, 4.2-NE months) and median PFS was 10.8 months (95% CI, 2.8-16.0 months). Among patients without identified driver genomic alterations, 26.9% (7/26) had a confirmed response by BICR.

The most common grade ≥3 treatment-emergent adverse events (TEAEs) were neutropenia (26%), fatigue (17%), and thrombocytopenia (15%). Drug-related interstitial lung disease by central adjudication occurred in 5 patients (10.6%; 0 grade ≥3). Five patients (10.6%) had TEAEs associated with treatment discontinuation. No drug-related deaths occurred.

Conclusions: These data extend previous findings in patients with EGFRm NSCLC and demonstrate promising clinical activity in patients with NSCLC harboring genomic alterations other than EGFRm and in those without identified driver genomic alterations. The overall safety profile was similar to that previously reported in patients with EGFRm NSCLC.

PP01.49:
Analysis of Outcomes by Race in Patients with Advanced NSCLC

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Northwestern University, United States

Background: Black patients have a higher mortality rate in NSCLC. Black patients diagnosed with lung cancer face worse outcomes compared to white Americans because they are less likely to be diagnosed with early-stage disease, less likely to receive surgical treatment, and more likely to not receive any treatment. There are other factors that have been posited as contributing, including higher rates of smoking resulting in fewer targetable mutations, or the presence of more comorbid conditions. In our study, we compared outcomes in Black and White patients with advanced NSCLC diagnosed at Northwestern.

Methods: We queried the Enterprise Data Warehouse for all patients with a new diagnosis of NSCLC between January 1, 2019 and December 31, 2020 at Northwestern Memorial Hospital (NMH) and two affiliate hospitals. This yielded a total of 864 patients. We then limited to patients with initial biopsy at NM and confirmed stage IV disease. Charlson Comorbidity Index (CCI), a validated tool used to predict one-year mortality based on specific comorbid conditions, was determined for each patient. 2-sample test for equality of proportions was done to evaluate for statistical significance.

Results: 143 white patients (W) and 22 Black patients (B) were identified. Most (17/22, 77%) Black patients underwent diagnostic evaluation at the urban academic center. Women made up 63% of B and 56% of W patients. The median age of diagnosis W 70.1 years; B 66.9 years. Active or former smoking W 18.9%; B 13.6%. Average CCI score was B 9.04; W 9.35. Rates of targetable mutations seen for first-line standard of care therapy were B 31.6% (6/19); W 20.8% (27/130) (p =0.4). 68.2% (15/22) of Black patients and 77.6% (111/143) of White patients received first-line targeted therapy (p = 0.2). The median overall survival was 10.68 months for Black patients and 11.24 months for White patients.

Conclusions: Black patients at Northwestern had equivalent outcomes to White patients. Black patients were overwhelmingly diagnosed at the downtown Chicago hospital, NMH. They had comparable demographics to White patients, specifically, age at diagnosis, smoking history, and number of comorbid conditions compared through CCI score. Black patients had a higher, though not statistically significant, rate of actionable mutations. This work highlights the vital role urban, academic medical centers play in the care of Black patients, raising the question of whether inequitable access to care is driving the national outcomes disparity.

PP01.50:
EMERGE-201: Phase 2 Basket Study of Lurbinectedin Monotherapy in Advanced or Metastatic Solid Tumors

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Background: Lurbinectedin (Zepzelca®), a selective inhibitor of oncogenic transcription, received accelerated approval from the US Food and Drug Administration on June 15, 2020, as monotherapy (3.2 mg/m^2 by 1-hour IV infusion every 3 weeks) for the treatment of adults with metastatic small-cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy. Approval was based on overall response rate (ORR; 35.2%) and median duration of response (5.3 months) in a phase 2 study. In addition to SCLC, antitumor activity with lurbinectedin as monotherapy or in combination with additional therapeutic agents has been observed in other advanced solid tumors. The EMERGE-201 study will evaluate the efficacy and safety of lurbinectedin monotherapy in adults with advanced (metastatic and/or unresectable) large-cell neuroendocrine tumor (LCNET) of the lung, as well as in other advanced (metastatic and/or unresectable) solid tumors with high unmet medical needs, including urothelial cancer (UC) and homologous recombination–deficient (HRD) tumor-agnostic malignancies.

Methods: EMERGE-201 is a multicenter, open-label, phase 2 basket study (NCT05126433) currently enrolling patients in the United States. Key eligibility criteria include age ≥18 years; diagnosis of advanced (metastatic and/or unresectable) UC, LCNET of the lung, or HRD tumor-agnostic malignancies; ECOG PS of 0 to 1; life expectancy ≥3 months; measurable disease by RECIST v1.1; and no prior lurbinectedin or trabectedin treatment. For UC and LCNET cohorts, cancer must have progressed on a platinum-containing regimen. For the HRD malignancies cohort, patients were not eligible if they had >3 prior lines of chemotherapy or prior PARP inhibitor usage, or if they did not have a mutational analysis assessment.

Patients will receive lurbinectedin monotherapy (3.2 mg/m^2 by 1-hour IV infusion every 3 weeks) until confirmed disease progression, withdrawal of consent, lost to follow-up, unacceptable toxicity, or study termination, whichever occurs first. Review of safety and efficacy will be performed on an ongoing basis. For each cohort, futility assessments will be conducted, and if appropriate, the cohorts will be expanded for interim efficacy and final analyses.

The primary study endpoint is investigator-assessed ORR; patients will be assessed for response (per RECIST v1.1) every 6 weeks through Week 36 and every 12 weeks thereafter. Secondary endpoints include investigator-assessed progression-free survival, time-to-response, duration of response, disease control rate (per RECIST v1.1), overall survival, and evaluation of adverse events and serious adverse events (per NCI CTCAE v5.0; until 30 days after end of treatment). Exploratory objectives include translational and biomarker analyses and lurbinectedin pharmacokinetics.

PP01.51:
Cost-Efficiency and Budget-Neutral Expanded Access Modeling of Toripalimab over Pembrolizumab in Advanced NSCLC

Dr. Karen MacDonald[1], Dr. Paul Walden[2], Dr. Robert Geller[2], Dr. Ivo Abraham[1,3]

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Background: In the CHOICE-01 phase 3 randomized trial, toripalimab+chemo (nab-paclitaxel+carboplatin [nPC] in squamous [s] and pemetrexed+platinum [PP] in non-squamous [ns]) significantly improved PFS compared to placebo+chemo (8.3 vs 5.6 months; HR=0.58, 95%CI=0.442-0.769) in previously untreated advanced non-small cell lung cancer (NSCLC). The KEYNOTE-407 (squamous) and KEYNOTE-189 (non-squamous) phase 3 randomized trials in previously untreated metastatic NSCLC also showed significant improvement of PFS compared to placebo+chemo. We conducted two ex ante simulation analyses to compare the cost-efficiency of the toripalimab regimens versus pembrolizumab in sNSCLC and nsNSCLC, and estimate the budget-neutral expanded access potential to additional treatment with toripalimab from accrued cost-savings.

Methods: Two simulation models from the US payer perspective in panels of 16,587 sNSCLC and 33,700 nsNSCLC patients were developed using Microsoft® Excel. Inputs included: 4Q2021 average selling price for pembrolizumab, nPC, and PP; toripalimab cost set to 70% of pembrolizumab; administration costs per CMS Outpatient Prospective Payment System; one year anti-PD-1 treatment with nPC/PP in first 4 cycles; and panel treatment rates for toripalimab ranging from 10%—100%. The number needed to treat (NNT) with toripalimab+nPC instead of pembrolizumab+nPC to provide toripalimab+nPC to 1 additional patient on a budget-neutral basis was also estimated (replicated for toripalimab+PP).

Results: Per-patient savings of toripalimab+nPC over pembrolizumab+nPC in sNSCLC were $3094/cycle; in nsNSCLC, per-patient savings of toripalimab+PP vs pembrolizumab+PP were $3089/cycle. Over 1 year of treatment, savings in sNSCLC were $55,624/patient; in nsNSCLC $55,604/patient. In a panel of 16,587 sNSCLC patients, savings over 1 year ranged from $92.3M at 10% treatment rate to $922.6M at 100%; at 50% treatment rate, savings were $461.3M. In a panel of 33,700 nsNSCLC patients, 1-year savings ranged from $187.4M (10%) to $1.9B (100%); at 50% treatment rate, savings were $936.9M. Panel savings over 1 year could be reallocated to provide a full year of treatment with toripalimab+nPC to between 543 (10%) and 5433 (100%) additional sNSCLC patients; in nsNSCLC, savings could provide between 714 (10%) and 7143 (100%) patients with a full year of toripalimab+PP. The number of patients needed to treat with toripalimab+nPC in order to provide 1 additional patient with 1 year of toripalimab+nPC is 3.05; the NNT with toripalimab+PP is 4.72.

Conclusions: Potential savings afforded by use of toripalimab in NSCLC may be substantial. Those savings could be reallocated to provide additional patients with efficacious and lower-cost PD-1 inhibitor therapy on a budget-neutral basis, adding value to payors and increasing access to treatment.

PP01.52:
Budget Impact Analysis of Toripalimab Versus Pembrolizumab in Previously Untreated Advanced Squamous NSCLC

Matthias Calamia[1], Dr. Robert Geller[2], Dr. Paul Walden[2], Dr. Karen MacDonald[1], Dr. Ivo Abraham[1,3]

[1]Matrix45, Tucson, United States, [2]Coherus BioSciences Inc., Redwood City, United States, [3]University of Arizona, Tucson, United States

Background: The CHOICE-01 phase 3 randomized trial in previously untreated advanced non-small cell lung cancer (NSCLC) compared toripalimab or placebo plus chemotherapy (nab-paclitaxel+carboplatin [nPC] in squamous [s] and pemetrexed+platinum in non-squamous NSCLC). Toripalimab+chemo significantly improved PFS compared to placebo+chemo (8.3 vs 5.6 months; HR=0.58, 95%CI=0.442-0.769). In the KEYNOTE-407 phase 3 randomized trial in previously untreated metastatic sNSCLC, pembroluzimab+taxane+carboplatin showed significant improvement of PFS compared to placebo+taxane+carboplatin (8.0 vs 5.1 months; HR 0.57, 95%CI=0.47-0.69). We conducted a budget impact analysis of adding the toripalimab+nPC (T+nPC) regimen to the treatment mix in sNSCLC.

Methods: An indirect treatment comparison of CHOICE-01 and KEYNOTE-407 being impossible, we developed an ex ante budget impact model assuming, as in previous analyses, a simulated regimen of pembrolizumab with the same nPC chemotherapy (P+nPC) as toripalimab from the budget holder perspective using accrual budgeting that compared a treatment mix "without" (P+nPC only) and "with" T+nPC (P+nPC and T+nPC) in an eligible incident 2022 US population of 24,794 sNSCLC patients, adjusted annually for population growth. The model assumed a 5-year time horizon and a P+nPC/T+nPC market share split of 90%/10% in 2022 growing by 10% annually to 50%/50% in 2026. The eligible population was adjusted for discontinuation, death, or progression per 24-month trial data and medication use was adjusted accordingly to estimate fully treated patient equivalents. Grade 3+ adverse events (AEs) were per the respective trial data. Cost inputs included those for drugs (average sales price for P+nPC), drug administration, and grade 3/4 AE management, with toripalimab priced ex ante at 70% of pembrolizumab.

Results: In the "without" scenario, the 5-year costs for the P+nPC regimen were $15,085,424,410 for treatment and $426,730,663 for AE management, for a total of $15,512,155,074. In the "with" scenario, the 5-year total costs for P+nPC declined to $10,352,473,913 for treatment and $295,308,140 for AE management, for a total of $10,647,782,054. The 5-year total costs for toripalimab+nPC were estimated at $3,574,925,001 for treatment and $272,763,129 for AE management, for a 5-year gross budget impact of $3,847,688,130. The 5-year net budget impact of adding the toripalimab regimen to the treatment mix totaled $1,016,684,890 in savings.

Conclusion: The 5-year budget efficiencies that can be achieved by treating 10-50% of the eligible incident US sNSCLC population with the toripalimab regimen in annually increasing increments of 10% market share at the price point of 70% of the pembrolizumab ASP are estimated to be $1.02 billion in savings.

PP01.53:
Pathologic Response Assessment Tool – Architecting a Cloud-Based Tool to Streamline Logistics for Shipping, Tracking, Scoring, and Reporting.

Mr. Juan Posadas Ruiz[1], Angela Walker[1], Ms. Helen Zhu[1], Ms Neus Bota-Rabassedas[1], Shani Wijeratne[1], Casey Connolly[2], Dr Murry Wynes[2], Dr. Beatriz Sanchez-Espiridion[1], Dr. Sanja Dacic[3], Dr. Ignacio Wistuba[1], Mr. Jack Lee[1]

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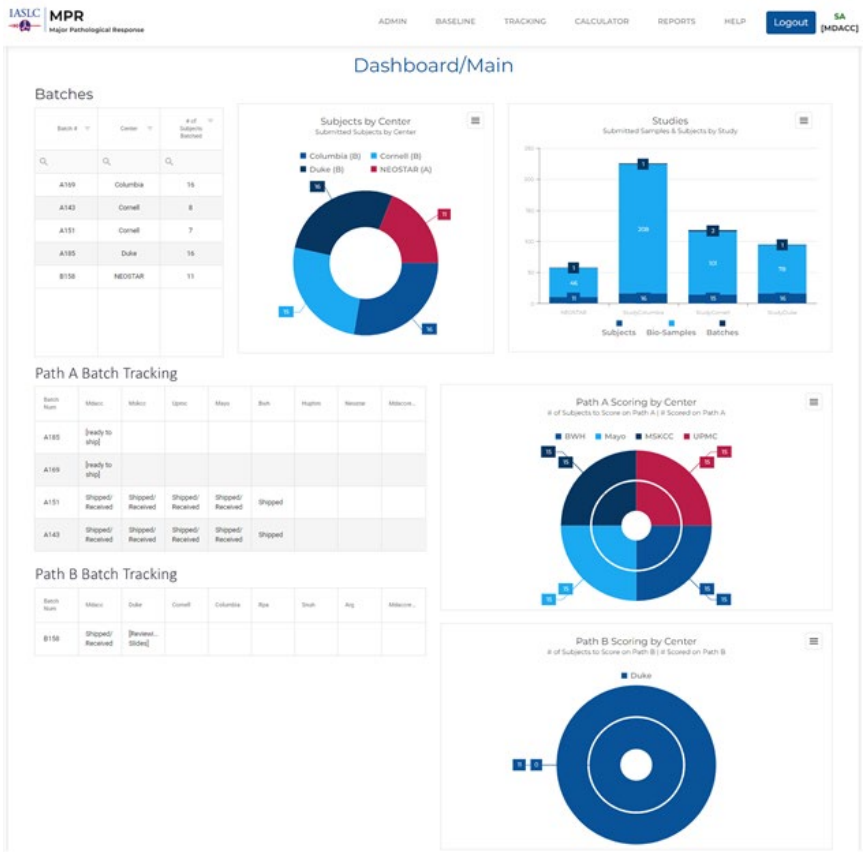
Background: Immune checkpoint inhibitor (ICI) therapies given in the neoadjuvant setting have been approved for early-stage NSCLC. Pathologic response (PR) in the surgical specimen could be an early clinical indicator of better outcome. However, there is a need to standardize PR assessment. Therefore, IASLC and MDACC have collaborated to conduct an inter-observer PR assessment study using specimens from NSCLC patients treated with ICI based regimens in 6 different clinical trials. In order to collect and store the PR scores from the global pathologists an online tool (cloud-based secured password protected website) had to be created.

Methods: Based on the physical logistics, we adapted and streamlined the web application to make it easy to use, reproducible, and private to each evaluator. Leveraging Cloud technologies (Microsoft Azure) we were able to implement a content delivery network (CDN) as a global solution for rapid delivery of high bandwidth content at a low cost. Our data-driven model allows changes to take effect immediately such as re-routing samples. Additionally, we integrated an email service that sends notifications based on roles.

Results: The Web tool has a secure two-factor authentication and encryption and that simplifies distribution, tracking, scoring, and reporting of PR assessment at a very granular level. This PR tool allows pathologist to enter tumor and stroma percentages, area sizes, and the percentage of mean viable tumor per slide, then it calculates total values for all specimens. All information is centralized in this tool, that can be easily accessible authorized personnel. Contains built-in dashboards, reporting, and visualization functionality (see figure below) for easy tracking. Each reviewer can export their results to excel and view a report of their scores.

Conclusion: A user friendly, scalable, affordable, and institution-independent solution has been implemented, enabling reviewers to score bio-samples for PR assessment for future research and clinical applications



PP01.54:
ImmunoBlood: A Prospective Study Evaluating the Development of Anti-Checkpoint Inhibitor Antibodies in Patients with Advanced Non-Small Cell Lung Cancer Treated with Immunotherapy

Dr. Corrado Orciuolo[1], Rosalinda Sorrentino[2], Chiara Colarusso[2], Serena Ceddia[1], Gabriele Minuti[1], Laura Conti[1], Chiara Mandoj[1], Silvia Carpano[1], Laura Canali[1], Cecilia Fucci[1], Martina Brandi[1], Francesca Fusco[1], Maristella Giammaruco[1], Blerina Resuli[1], Lorenza Landi[1], Federico Cappuzzo[1]

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Background: Immunotherapy has radically changed the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC). PD-L1 expression is generally associated with efficacy of immunotherapy, with PD-L1 overexpressing (PD-L1 >50%) NSCLC patients deriving the greatest benefit. However, a consistent proportion of positive cases do not respond to treatment, while some PD-L1 negative patients gain a significant survival benefit. Mechanisms underlying these different outcomes remain largely unknown. The development of antibodies directed against immune checkpoint inhibitors (ICIs) could affect sensitivity and tolerability to treatment. Aim of the present study was to investigate whether patients receiving ICIs develop antidrug antibodies and if this event impact on drug efficacy and/or toxicity.

Methods: Patients with advanced NSCLC candidate for immunotherapy were included. Serial blood samples were collected at baseline and every cycle until disease progression. Levels of antidrug antibodies (ADA) assessed in plasma using enzyme immunoassay (ELISA) were correlated with response, duration of response, progression-free survival (PFS), overall survival (OS).

Results: From May 2021 to February 2022, a total of 50 patients were enrolled, median age was 67.5 years (43 - 83), twenty-five of patients (50%) were men. The majority had adenocarcinoma histology (78%), ECOG PS 0, history of smoke with a median of 44.5 pack/years and received immunotherapy in front-line. Eleven patients received single agent ICIs (pembrolizumab = 7, nivolumab = 2, atezolizumab = 2), 3 patients ICIs combination (nivolumab – ipilimumab =2, atezolizumab – bevacizumab = 1), and 36 patients platinum-based chemotherapy plus ICI (35 = pembrolizumab; 1= nivolumab). Overall, 108 blood samples at different timepoints were collected and analyzed; among them, 83 were from patients treated with chemo-immunotherapy, 22 from patients treated with single agent immunotherapy and 3 for patients receiving nivolumab-ipilimumab combination. No ADA were detected in plasma samples at baseline and in early timepoints, in patients treated with immunotherapy as single agent as well in patients treated with the combination of chemo-immunotherapy.

Conclusions: Development of ADA was not an early event during immunotherapy and chemo-immunotherapy. Analysis on additional biomarkers including LDH, IgG1, IgG4, complement proteins, histamine, cytokines as CXCL8, CXCL4, TGF-beta, IFN-alpha are ongoing. Updates results will be presented at the meeting.

PP01.55:
Real-World Treatment Sequencing and Impact on Outcomes in ALK-Positive (ALK+) Non–Small Cell Lung Cancer (NSCLC)

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Background: ALK TKIs are the standard of care for advanced ALK+ NSCLC, but optimal treatment sequencing beyond 2 ALK TKIs has not been established. We evaluated time-to-treatment discontinuation (TTD) and overall survival (OS) with third-line (3L) ALK TKI versus non-ALK TKI therapy in patients treated with 2 prior ALK TKIs.

Methods: Real-world data (US Flatiron Health OncoEMR database [January 2015 - March 2022]) were used to evaluate outcomes in patients with advanced ALK+ NSCLC. Eligible patients had first- (1L) and second-line (2L) ALK TKI therapy, followed by 3L ALK TKI (Group A) or non-ALK TKI treatment (chemotherapy, chemotherapy in combination with immune checkpoint inhibitors and/or anti-VEGF; Group B). A Cox proportional hazard model adjusting for age, gender, ECOG performance status, smoking, presence of baseline brain metastases, and time from advanced diagnosis to start of therapy line was used to calculate HRs for TTD and OS from start of 1L, 2L, and 3L.

Results: 128 patients were included (A/B: 85/43); baseline median age: 60/61 years; female: 49%/61%; smoking=yes: 42%/49%; baseline brain metastases (1L/2L/3L): A, 15%/22%/33%; B, 23%/26%/33%; median follow-up (1L/2L/3L): A, 37/24/9; B, 21/12/4 months. Baseline ECOG ≥2 at 3L (A/B): 14%/26%; median time from advanced diagnosis to 3L: 24.5/16.5 months. Group A had longer median TTD (HR [95% CI], 1L: 0.62 [0.41-0.93]; 2L: 0.50 [0.33-0.75]; 3L: 0.61 [0.37-0.997]) and OS (HR [95% CI], 1L: 0.32 [0.19-0.54]; 2L: 0.40 [0.24-0.66]; 3L: 0.57 [0.33-0.98]) compared with B. Additional outcomes provided in Table.

Conclusion: Patients with ALK+ NSCLC who were treated with prior ALK TKIs for a longer period appeared to benefit from 3L ALK TKI treatment. Patients receiving 3L non–ALK-directed therapy appeared to have suboptimal response to prior TKIs.

Table. Summary of Treatment Sequence and Clinical Outcomes in Patients With *ALK*+ NSCLC by Treatment Line

Parameters	Group A n=85	Group B n=43
Treatments ≥15% (%)		
First line	crizotinib (64)	crizotinib (61)
	alectinib (32)	alectinib (35)
Second line	alectinib (36)	alectinib (30)
	ceritinib (24)	lorlatinib (30)
	lorlatinib (15)	ceritinib (19)
Third line	lorlatinib (41)	IO (30)
	alectinib (33)	chemotherapy (28)
	brigatinib (15)	chemotherapy + IO (21)
Median TTD from start of treatment line, months (95% CI)[a]		
First-line ALK TKI therapy	8.9 (7.2–11.2)	6.6 (4.7–8.4)
HR (95% CI); *P* value	0.62 (0.41–0.93); 0.020	
Second-line ALK TKI therapy	9.2 (5.7–11.3)	4.1 (3.0–6.6)
HR (95% CI); *P* value	0.50 (0.33–0.75); <0.001	
Third-line therapy		
ALK TKI	6.2 (3.9–9.4)	–
Non-ALK TKI	–	2.4 (1.4–3.7)
HR (95% CI); *P* value	0.61 (0.37–0.997); 0.049	
Median OS from start of treatment line, months (95% CI)[a]		
First-line ALK TKI therapy	49.6 (37.4–72.1)	21.8 (15.7–33.6)
HR (95% CI); *P* value	0.32 (0.19–0.54); <0.001	
Second-line ALK TKI therapy	38.5 (23.4–61.1)	13.6 (10.4–22.1)
HR (95% CI); *P* value	0.40 (0.24–0.66); <0.001	
Third-line therapy		
ALK TKI	17.6 (13.0–24.9)	–
Non-ALK TKI	–	6.5 (3.9–8.0)
HR (95% CI); *P* value	0.57 (0.33–0.98); 0.042	

[a] Cox proportional hazard model.
CI, confidence interval; HR, hazard ratio; IO, immuno-oncology; OS, overall survival; TTD, time to discontinuation.

PP01.56: Peripheral T-Cell Receptor Repertoire Dynamics in Patients with Small Cell Lung Cancer

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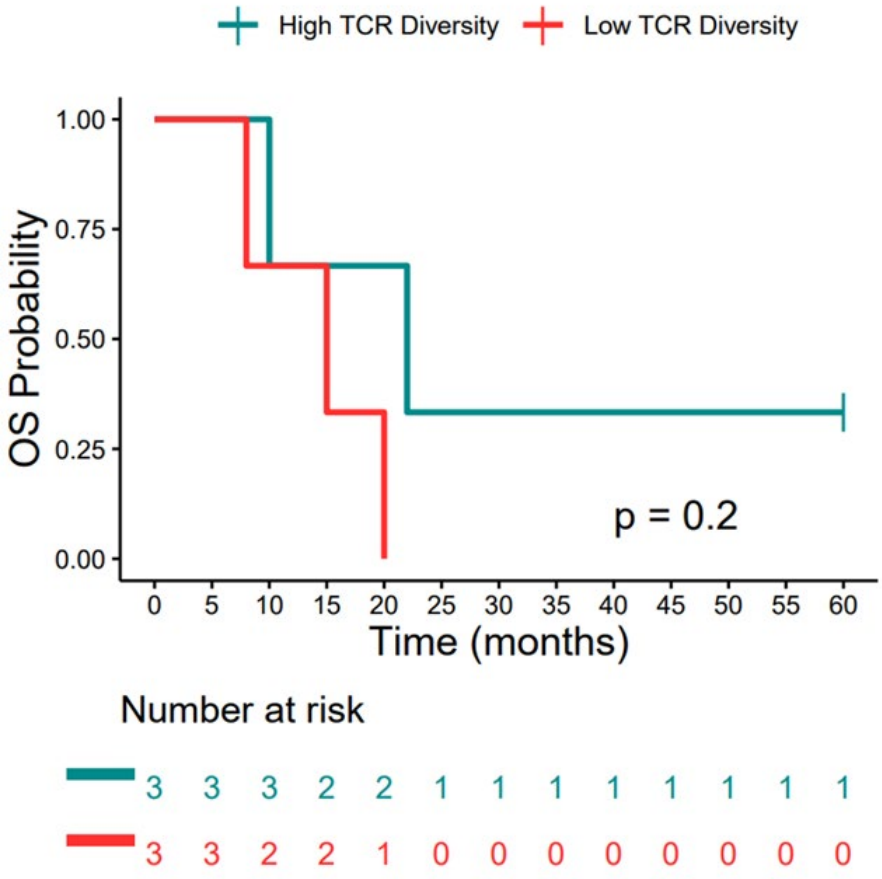
Introduction: Identifying a circulating biomarker predictive of immune checkpoint inhibitor (ICI) benefit in patients with small cell lung cancer (SCLC) remains an unmet need. Characteristics of peripheral and intratumoral T-cell receptor (TCR) repertoires have been shown to predict clinical outcomes in non-small cell lung cancer (NSCLC). Identifying a knowledge gap, we sought to characterize circulating TCR repertoires and their relationship with clinical outcomes in SCLC.

Methods: SCLC patients with limited (n= 4) and extensive (n = 10) stage disease were prospectively enrolled for blood collection and chart review. Targeted next-generation sequencing of TCR beta and alpha chains of peripheral blood samples was performed. Unique TCR clonotypes were defined by identical CDR3, V gene, and J gene nucleotide sequences of the beta chain and subsequently used to calculate TCR diversity indices.

Results: Patients with stable versus progressive and limited versus extensive stage disease did not demonstrate significant differences in V gene usage. Kaplan-Meier curve and log-rank analysis did not identify a statistical difference in progression-free survival (PFS, p= 0.900) or overall survival (OS, p= 0.200) between high and low on-treatment TCR diversity groups, although the high diversity group exhibited a trend toward increased OS.

Conclusions: We report the first study investigating peripheral TCR repertoire diversity in SCLC. With a limited sample size, no statistically significant associations between peripheral TCR diversity and clinical outcomes were observed, though further study is warranted.



PP01.57:
Evaluation of the Metabolism of the Biogenic Amines on the Neuroendocrine Differentiation of A549 Adenocarcinoma Cells.

Dr. Irasema Mendieta[1], Ph.D. Gilberto Pérez-Sánchez[2], Ph.D. Lenin Pavón-Romero[2], Ph.D. Guadalupe García-Alcocer1, Ph.D. Laura Cristina Berumen[1]

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Background: One of the major causes of death by cancer is lung cancer, and the additional presence of neuroendocrine phenotype has been correlated to a worsened outcome in patients due to an increased number of peripheral tumor cells, drug-resistant tumors, and a higher percentage of metastasis. The process where one somatic cell type changes into another cell type without passing through the pluripotent state to generate functional cells is called transdifferentiation. This transdifferentiation has been described in vitro and in vivo for many cancer cell types; such as prostate, pancreas, liver and lung; in vitro, the induction has been observed by the exposure to different stimuli (i.e. cAMP analogs, IL-6, ionizing radiation, among others). The characteristics of the in vitro transdifferentiated cells with neuroendocrine phenotype are the low proliferation rate, dense chromatin, neurite-like projections, and the presence of secretory granules with neuroendocrine markers expression. Furthermore, the development of mature granules involves calcium influx, acidification, prohormone processing, and the uptake of amines (i.e. serotonin, 5-HT) through vesicular monoamine transporters. In particular, the significant increase of 5-HT and decrease of Dopamine (DA) in A549 neuroendocrine transdifferentiated (A549NED) cells was previously reported by our group suggesting the presence of mature secretory granules in transdifferentiated cells. For that matter, the purpose of this study was to determine the metabolites of the biogenic amines 5-HT (5HIIA) and DA (DOPAC and HVA) secreted by A549NED cells to understand the influence of this metabolism on the autocrine or paracrine signaling of the tumor microenvironment.

Methods: A human lung cancer cell line A549 was induced to neuroendocrine transdifferentiation (NED) with two [cAMP] increasing agents (IBMX, FSK, and the combination of both agents) to observe the changes in the pattern of biogenic amines production (5HIIA, DOPAC and HVA) by HPLC.

Results and conclusion: The transdifferentiated cell line (A549NED) acquired a differential pattern of the biogenic amines metabolites consistent with the production of biogenic amines reported previously (less DA and increased 5-HT after NED), an increased DOPAC and HVA production, and decreased 5HIIA production after NED. The results together suggest an important metabolic bioaminergic switch of the neuroendocrine cells, these findings contribute to a previous proposal that biogenic amines (among other immunomodulators) have an important role in the bidirectional communication within the tumor microenvironment.

Acknowledgments: This work was partially supported by grants CONACYT CB2017-2018- A1-S-25275 Ph.D. grant 400028 and FOFI-UAQ FCQ201820.

PP01.58:
Multi City Opportunistic Screening of Lung Nodules Amidst COVID-19

Mr. Souvik Mandal[1], Dr. Saigopal Sathyamurthy[1], Dr Arunkumar Govindarajan[2], Mrs Era Dwivedi[3], Mr Vikas Challa[1], Mr Prakash Vanapalli[1], Mr Ram Prakash[1], Mr. Ankit Modi[1], Mr. Rohit Chouhan[1], Mr. Preetham Putha[1], Mr. Arpit Kothari[3], Mr Bharghava Reddy[1]

[1]Qure.ai, Mumbai, India, [2]Aarthi Scans Private Limited, Chennai, India, [3]BodyScans Private Limited, Indore, India

Background: Early diagnosis of lung cancer can substantially reduce cancer related deaths. Missed nodules have been reported in literature, as is the benefits of incidental nodule detection and management. The use of AI in flagging incidental nodules was explored on CT scans taken for COVID and this has been submitted to CHEST, and RSNA during various stages of the processing with respect to sites.

Methods: 2502 scans taken during the second and third wave of COVID at two specialist radiology chain (5 sites) were processed by qCT Lung, an AI capable of detecting and characterizing nodules. Radiologist report of the cases flagged by qCT were searched for findings suggestive of cancer. Cases for which nodule was not reported were re-read by an independent radiologist with AI assistance on online portal. They were asked to either confirm or reject the flag, rate the nodule for malignancy potential if confirmed or provide alternate finding if rejected (See Figure).

Results: 1737 nodules were flagged in 673 (26.9%). 80 were noted in radiology report. Of the 593 scan re-read by radiologist, 115 (19.4%) was confirmed as having nodules. 233 nodules were found in these scans. The median size (longest diameter) of these nodules was 15 mm (range: 6 – 48) and 64.4% were solid. The most common cause of rejection was ground glass opacities.
94 of 115 scans had a rating of 1 or 2. 19 were called unsure and two was probably malignant.
Two cases were called cancer by both AI and radiology report.

Conclusion: Missed cancer is medico-legal problem. In this study it cannot be assumed that the radiologist missed 115 nodules. These radiologists might have spotted the nodule but not reported it because of their perceived risk and this is supported by second reader. However, 21 cases would have warranted follow-up.

PP01.59:
Performance of a Deep Learning Algorithm for the Early Detection of Malignant Lung Nodules

Manoj Tadepalli[2], Mr. Anish Chhaparwal[1], Sanya Chawla[2], Shreya Srivastava[2], Thang Dao[1], Mr. Anish Chhaparwal[2], Sai Naren[2], Dr. Saigopal Sathyamurthy[2], Sai Vinayak Mukkavilli[2], Mr. Preetham Putha[2], Bhargava Reddy[2], Luan Vo1, Prashant Warrier[2]

[1]Friends For International TB Relief (FIT), Viet Nam, 2Qure.ai, India

Background: Lung cancer is the second most common cause of cancer-related mortality in Vietnam. The identification and follow-on evaluation of lung nodules during routine chest X-ray (CXR) screening has the potential to improve the early detection of lung cancer and to reduce cancer-related mortality.

Methods: This study collected CXR images from a community-based tuberculosis screening program in Vietnam. The images were re-read by a study radiologist and qXR Nodule software (Qure.ai, India) to identify the presence of nodules. A two-by-two table of these two interpretation methods was then constructed and 125 CXR images were randomly sampled from each cell to form the final test library (n=500). These images were blindly re-read by a panel of three independent radiologists to annotate for the presence of nodules and to assign a malignancy score (ranging from 1=benign to 5=malignant) by majority vote. The test library was also blindly re-read by a Vietnamese radiologist from a tertiary lung hospital in Ho Chi Minh City and by qXR's Lung Nodule Malignancy Score (LNMS) software.

Results: From a total of 23,514 CXR images, the study radiologist identified 1,124 (4.9%) lung nodules, while the qXR Nodule software identified 5,516 (23.4%). These two CXR interpretation methods had a positive percent agreement of 81.5%. In the final test library (n=500), the panel of radiologists identified 173 (34.6%) nodules, with 35 (20.2%) being classified as possibly malignant (score≥4). Readers A and B showed high inter-reader reliability (Cohen's kappa [K] = 0.85), but there was a higher degree of variability between readers A and B vs C (K=0.54 and K=0.59, respectively). Nodule detection by the panel spanned all four cells of the two-by-two table. The Vietnamese radiologist achieved a 62.9% sensitivity and 97.1% specificity, using the panel results as the reference standard. At the optimal threshold cut-off value (e.g. the point closest to ROC 0,1), the qXR LNMS software achieved a 71.4% sensitivity and 97.7% specificity. When the LNMS cut-off threshold was selected to match the sensitivity of the Vietnamese radiologist, software specificity was identical to the Vietnamese radiologist.

Conclusion: qXR software for the detection of potentially malignant lung nodules performed better than an experienced radiologist from Vietnam in this retrospective evaluation. This study highlights the potential for an integrated tuberculosis and lung cancer screening program, which warrants a prospective evaluation.

PP01.60:
Double the Lung Cancer Early Detection Rates with Incidental Lung Nodule Program

Dr. Roger Su[1], **Dr. William Mayfield**[1]

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Background: Lung cancer remains the deadliest form of cancer in the U.S. It alone makes up almost 25% of all cancer deaths, more than the fatalities caused by colon, breast, and prostate cancer combined. At Wellstar, we realize the importance of early detection of lung cancer, therefore we started an Incidental Lung Nodule Program in 2020. This complements our successful Lung Cancer Screening Program, proactively reaching out to the populations we serve in our effort to identify lung cancer as early as possible.

Methods: The Lung Cancer Screening (LCS) Program of Wellstar Health System (WHS) was established in 2008 as part of the International Early Lung Cancer Action Project (IELCAP trial) and has been growing since. We detected more than 50 lung cancers in 2021. The Incidental Lung Nodule (ILN) Program was established in 2020 as a formal Quality Improvement Program to identify and assess incidental lung nodule findings across the entire health system and determine the relative incidence of un-detected lung cancer in a non-screening population.

This report will review the progress of the ILN program from its October 2020 inception to December 2021.

Results: Since October 2020, using Natural Language Processing applied to Radiology Reports, our Report Coordinators identified more than 64,000 patients with reported pulmonary findings in scans performed for other indications. More than 5,000 were enrolled in the ILN program for further imaging based on clinical findings. 300 were scheduled to be seen in the ILN clinic for evaluation. More than 50 EBUS/biopsy procedures were scheduled, and almost 40 cancer cases were diagnosed.

Conclusion: The result from the first 500 days of the ILN program demonstrated its ability to significantly increase the rate of lung cancer early detection. It is undoubtedly an important part of a comprehensive Early Detection Program and a crucial component of the overall lung cancer early detection strategy.

As opposed to a Lung Screening Program, an Incidental Nodule Program is founded upon images that the Health System already possesses, and functions as a Safety Net for those who have abnormalities but no formal mechanism for follow-up.

An Incidental Lung Nodule Program can exist without a Screening Program. It is another means by which a System can elevate an Early Lung Cancer Detection Program. Our experience demonstrates that an ILN program can detect nearly as many cancers annually as a Lung Screening Program.

PP01.61:
First-Line Treatment Patterns of Patients with Metastatic Non-Small Cell Lung Cancer (mNSCLC) with and without BRAF Mutations in the US

Ms. Maria Cecilia Vieira[1], Dr Kirsten Duncan[1], Ms. Wei-Chun Hsu[2], Mr. Ryan Ross[2], Mr. Darrin Benjumea[2], Ms. Anna Vlahiotis[1], Dr. Benjamin Li[1], Dr. Keith D. Wilner[3]

[1]Pfizer Inc., New York, United States, [2]Genesis Research, LLC., Hoboken, United States, [3]Pfizer Inc., San Diego, United States

Background: There are treatment options for patients with BRAF V600E mutated metastatic NSCLC (mNSCLC), such as dabrafenib/trametinib, a BRAF/MEK inhibitor combination. This study aimed to describe first-line (1L) treatment in patients with mNSCLC +/- BRAF mutations using recent real-world data.

Methods: US adults with mNSCLC diagnosed between 01/01/2015 and 09/30/2021 were identified in the Flatiron Health electronic health records database. Baseline demographics at mNSCLC diagnosis were described in 3 cohorts: BRAF V600 mutated (BRAF V600), BRAF non-V600 mutated (BRAF non-V600), and BRAF wild-type patients (BRAFwt). 1L treatments were assessed after approval of dabrafenib/trametinib in the US (06/2017).

Results: The study included 747 (7.4%) BRAF mutated (BRAFm, comprised of 234 V600 and 513 non-V600) and 9,288 (92.6%) BRAFwt patients. Of the 234 BRAF V600 patients, 231 (98.7%) were BRAF V600E. Patient's median age was 70 years old and approximately two-thirds were white. Median follow-up ranged from 9.9 to 11.2 months; shortest in the BRAFwt and longest in the BRAF V600 cohort. In the BRAF V600 cohort, most patients were female (57%), whereas in the BRAF non-V600 and BRAFwt cohorts, most patients were male (53% and 57%, respectively). History of smoking was less common in BRAF V600 (76%) compared to BRAF non-V600 (93%) and BRAFwt (92%) cohorts.

The figure demonstrates 1L treatment patterns in this cohort since 06/2017. Across all cohorts, immuno-oncology (IO)-based therapies were the most common (range: 39.2% to 52.5%).

Conclusion: Fewer than 8% of patients with mNSCLC were BRAFm, the majority of which were non-V600 mutations. BRAF V600 patients received various treatments in 1L, with less than 30% receiving a BRAF inhibitor-based therapy. IO-based regimens were more frequently used than chemotherapy-only regimens across all cohorts.

Table 1. Treatments and clinical outcomes

	First Line		Second Line	
Total Patients, N (%)[a]	12	100.0%	3	100.0%
Treatment regimen				
Pembrolizumab	4	33.3	1	33.3
Carboplatin + Pembrolizumab + Pemetrexed	4	33.3	0	0.0
Carboplatin + Paclitaxel	2	16.7	0	0.0
Carboplatin + Etoposide + Atezolizumab	1	8.3	0	0.0
Nivolumab	1	8.3	0	0.0
Docetaxel	0	0.0	1	33.3
Paclitaxel	0	0.0	1	33.3
Time to discontinuation				
N (%) of patients who discontinued	12	100%	3	100.0%
Median TDD, months (95% CI)	5.8	0.9 - 10.1	1.4	0.7 - NE
PFS, systemic				
N (%) of patients with progression or death	10	83.3%	3	100.0%
Median PFS, months (95% CI)	5.5	0.9 - 9.9	2.9	1.5 - NE
PFS, intracranial				
N (%) of patients with progression or death	8	66.7%	3	100.0%
Median PFS, months (95% CI)	9.3	2.1 - NE	2.9	1.9 - NE
OS				
N (%) of patients with death	10	83.3%	3	100.0%
Median OS, months (95% CI)	9.3	2.1 - 19.2	6.0	2.9 - NE

[a]Four of 16 patients did not receive any systemic therapies with reasons reported as follows: referred to hospice (n=2), continuation of previously started radiation therapy (n=1), and reason unknown (n=1).
CI = confidence interval; NE = non-estimable.

PP01.62:
Therapeutic Potential of Folate Conjugated Actinonin Encapsulated Human Serum Albumin Nanoformulation against Lung Adenocarcinoma Model.

Dr. Priyanca Ahlawat[1], Dr. Amanjit Bal1, Dr. Sadhna Sharma[1]

[1]Post Graduate Institute of Medical Education, Sector 12, Chandigarh, India, [2]Post Graduate Institute of Medical Education, Sector 12, Chandigarh, India, [3]Post Graduate Institute of Medical Education, Sector 12, Chandigarh, India

Background: The 'immune cold' K-ras and EGFR mutant lung adenocarcinoma (LUAD) requires novel targets and chemotherapeutics as these tumors are immunotherapy non-responsive. Moreover, the ligand shedding pathway mediated by ADAM17 ultimately initiates EGFR/ERK signaling responsible for neoplastic behavior. Interestingly, ADAM17 has been reported to be inhibited by actinonin , a hydroxamate which also inhibits the mitochondrial peptide deformylase which is essential for mitochondrial translation initiation. The mitochondrial translation inhibition induces cellular apoptosis in multiple cancer cell lines, lung and renal in vivo xenograft models. Disappointingly, actinonin is a broad spectrum metalloprotease inhibitor and its free form administration poses a threat to biological tissue homeostasis. This in turn makes it a double edged sword. Therefore, this study was designed to evaluate anti-proliferative efficacy of folate receptor targeted human serum albumin (HSA) nanoformulation of actinonin against murine LUAD.

Methods: Folate conjugated human serum albumin nanoparticles were developed using desolvation method and pharmacokinetic study was performed. The therapeutic evaluation was conducted in urethane induced tumor bearing BALB/c mice. Free actinonin (i.p) and nanoformulated actinonin (i.p) were administered five times and two time for a week respectively. The survival analysis, reduction in tumor number/volume, histopathological examination of tumor lesions, cytometric assays such as apoptotic/necrotic cell populations; reactive oxygen species level quantification; mitochondrial membrane potential estimation as well as gene expression analysis of EGFR, FRα, PDF and TS was performed. Mann-Whitney, Kruskal-Wallis and one way ANOVA tests were used to determine the level of significance by using SPSS software. The study was ethically approved (80/IAEC/502 and 99/IAEC/692).

Results: The nanoformulation of actinonin displayed nanoparticulate properties with sustained release serum kinetics. Cellular response like higher reactive oxygen species levels as contributors of cell death, compromised mitochondrial integrity as reflected by reduced number of heterogenous high potential displaying cell sub-population as well as increased apoptotic/necrotic cell populations clearly distinguished between the untreated and treated mice groups. Furthermore, the downregulated expression of tumor markers such as EGFR, FRα and target genes viz PDF, TS supported nanoformulated actinonin's therapeutic efficacy despite low dose frequency.

Conclusion: Urgently, the pandemic has reinstated the need for recognizing the translation of nanomedicines from bench to bedside. This was due to widespread healthcare system collapse and thus nanomedicines are recommended as they improve the patient compliance by reducing dose cycles and adverse effects which otherwise increases patient hospital visits. Hence, current work on actinonin nanoformulation precisely fits in this context.

PP01.63:
Real-World Assessment of Clinical Outcomes Associated with Immunotherapy (IO) and Chemotherapy in Non–Small Cell Lung Cancer (NSCLC) Patients with Brain Metastases and METexon14 Skipping Mutations Treated in US Community Centers

Dr. Beilei Cai[4], Dr. Shanna A. Arnold Egloff[2], Ravi K. Goyal[3], Dr. Beilei Cai[4], Nydia Caro[4], Michael Frost2, Siraje Mahmud[1], Valerie Derrien Ansquer[3], Keith L. Davis[3], Lorraine Brisbin[1], Monica Lisi[1], Andrew J. McKenzie[2], Dr. Steven Paulson[1]

[1]Texas Oncology, United States, [2]Sarah Cannon Research Institute, United States, [3]RTI Health Solutions, United States, [4]Novartis Pharmaceutical Corporation, United States

Background: In a post-hoc analysis of GEOMETRY Mono-1 trial, 54% of patients with brain metastases treated with capmatinib had an intracranial response. Despite these data, NSCLC patients with METexon14 skipping mutations and brain metastases (BM) continue to receive IO or chemotherapy in community centers. In this study, we assessed the clinical outcomes associated with non-targeted therapies in the real-world setting for this population.

Methods: A retrospective medical record review was performed at two large community-based cancer centers. Eligible patients were aged ≥18 years, had confirmed NSCLC with METexon14 skipping mutations, BM diagnosis (≥1 lesion ≥5 mm), and had ≥12 months follow-up after BM diagnosis (except death). Patients treated with METi were excluded. Modified RECIST and RANO-BM criteria were used for response assessments. Key outcomes were time-to-treatment discontinuation (TTD), intracranial and systemic real-world overall response rate (rwORR), disease control rate (rwDCR), progression-free survival (rwPFS), and overall survival (OS).

Results: A total of 16 patient charts were abstracted (median age at BM diagnosis: 78.5 years; female: 50%; stage IV at initial diagnosis: 68.8%; median number of intracranial lesions: 3 [range: 1-10]; smoking history: 62.5%). Of the total sample, 75% (n=12) initiated first-line (1L) therapy after BM diagnosis and 18.8% (n=3) received second-line (2L) therapy. Immunotherapy (IO)-containing regimen (83.3% [n=10]) was the most commonly used 1L therapy (Table 1). Median TTD and OS for 1L were 5.8 and 9.3 months, respectively; median systemic and intracranial rwPFS for 1L were 5.5 and 9.3 months, respectively, with rwORR of 41.7% (95%CI: 15.2-72.3) for both systemic and intracranial responses.

Conclusion: Among NSCLC patients with METexon14 mutations and BM, IO and chemotherapy regimens were associated with poor clinical outcomes. These findings provide an important reference point for providers when making treatment decisions for this patient population.

Table 1. Treatments and clinical outcomes

	First Line		Second Line	
Total Patients, N (%)[a]	12	100.0%	3	100.0%
Treatment regimen				
Pembrolizumab	4	33.3	1	33.3
Carboplatin + Pembrolizumab + Pemetrexed	4	33.3	0	0.0
Carboplatin + Paclitaxel	2	16.7	0	0.0
Carboplatin + Etoposide + Atezolizumab	1	8.3	0	0.0
Nivolumab	1	8.3	0	0.0
Docetaxel	0	0.0	1	33.3
Paclitaxel	0	0.0	1	33.3
Time to discontinuation				
N (%) of patients who discontinued	12	100%	3	100.0%
Median TDD, months (95% CI)	5.8	0.9 - 10.1	1.4	0.7 - NE
PFS, systemic				
N (%) of patients with progression or death	10	83.3%	3	100.0%
Median PFS, months (95% CI)	5.5	0.9 - 9.9	2.9	1.5 - NE
PFS, intracranial				
N (%) of patients with progression or death	8	66.7%	3	100.0%
Median PFS, months (95% CI)	9.3	2.1 - NE	2.9	1.9 - NE
OS				
N (%) of patients with death	10	83.3%	3	100.0%
Median OS, months (95% CI)	9.3	2.1 - 19.2	6.0	2.9 - NE

[a]Four of 16 patients did not receive any systemic therapies with reasons reported as follows: referred to hospice (n=2), continuation of previously started radiation therapy (n=1), and reason unknown (n=1).
CI = confidence interval; NE = non-estimable.

PP01.64:
A Safety and Efficacy Analysis Comparing Elderly vs Nonelderly Patients Treated with Consolidation Immunotherapy after Chemoradiation for stage III NSCLC from the BTCRC LUN 16-081 Clinical Trial

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Background: Lung cancer is the leading cause of cancer related deaths. The median age of those diagnosed with lung cancer continues to increase as the population overall ages. Consolidation immunotherapy after chemoradiation has become standard treatment for patients with stage III NSCLC. However, little has been reported regarding the safety and efficacy of this strategy in an elderly patient population.

Methods: Data was analyzed from a randomized phase II clinical trial in patients with non resectable stage III non-small cell lung cancer (NSCLC) who were randomized to Nivolumab (N) or Nivolumab/Ipilimumab (NI) after chemoradiation. We performed an ad-hoc analysis comparing elderly (> 65 years of age) vs nonelderly patients on each arm. Groups were compared using the Chi-square test and Wilcox test.

Results: A total of 105 patients were enrolled. 54 patients received N (480mg IV every 4 weeks for up to 6 cycles) and 51 patients received N (3mg/kg IV every 2 weeks) + I (1mg/kg IV every 6 weeks for up to 4 cycles).
Patients were matched for age, gender, ethnicity, ECOG performance status. Results are presented in Table 1.

Conclusion: Patients > 65 treated with consolidation N or NI after chemoradiation had similar rates of AE's and rates of hospitalization compared to their younger counterparts. 18 mo PFS and OS were also similar between the groups.

Arms	Nivolumab only (Arm A) 54 patients			Nivolumab+Ipilimumab (Arm B) 51 patients		
	Age <65	Age ≥65	p value	Age <65	Age ≥65	p value
Number of patients in each group	26	28		29	22	
Pneumonitis	9/26 (34.6%)	5/28 (17.9%)	0.16	9/29 (31.0%)	9/22 (40.9%)	0.46
Grade 5 adverse Event	1/26 (1.9%)	1/28 (3.8%)	0.41	0 (0%)	1/22 (4.5%)	0.43
Adverse event causing hospitalization	5/26 (19.2%)	3/28 (10.7%)	0.46	9/29 (31.0%)	11/22 ((50.0%)	0.16
18 mo Progression free survival probability %	55.5	72.8	0.14	75.1	58.0	0.43
18 mo Overall Survival probability %	80.2	85.4	0.36	92.7	76.8	0.023

PP01.65:
Treatment Patterns of Malignant Pleural Mesothelioma in a Resource Limited Setting: A "Real World" Study

Dr. Karina Morales Hernández[1], Dr. Santiago Zarroca Palacio[1], Dr Marco Antonio Hernández Castillo[1], Dra Yuly Remolina Bonilla[1], Dr Juan Jose Sánchez Hernández[1], Dra Amairany Vélez Martínez[1], Dra Geraldine Chaires Navarro[1], Dra Miriam Najar Rodríguez[1], Dr Angel Irigoyen Alvarez[1], Dr Nestor Lizcano Aguilar[1], Dr Eduardo Sánchez Roman[1], Dra Brenda Lorena Rubio Anguiano[1], Dra Dulce Angelica De Jesús Hernández[1], Dra Celene Peña Campos[1], Dr Raúl Rogelio Trejo Rosales[1]

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Background: Malignant pleural mesothelioma (MPM) is a rare and highly aggressive cancer, most of patients have a poor prognosis. Only a minority patients may benefit from surgical management. Majority of patients with MPM should be evaluated in a multidisciplinary setting including thoracic surgery, medical oncology, and radiation oncology.

Methods: We performed a retrospective, multicenter study in 4 referral centers throughout Mexico City and Monterrey, the most populated cities in Mexico. We identified patients with MPM diagnosed and treated between January 2010 and January 2020. Descriptive statistics and Kaplan-Meier method with log-rank were used for analysis. Cox regression was used for multivariate analysis.

Results: A total of 500 patients were included in this study and the median follow-up was 63.5 months, median age was 63 years (range 32-91 years), the most common histological subtype is epithelioid with 82% followed by sarcomatoid with 6.4%, bifasic 2.6% unknown 9% performance status scale 0-1, and ≥ 2 represented 66 % and 34%, of the cohort, respectively.

According to the treatment patterns implemented, surgery with curative intent was performed in 9% , 86.8% (N=434) received systemic treatment. Most patients were treated with platinum-based chemotherapy. The regimens implemented were pemetrexed-platinum (64.1 %) , gemcitabine-platinum (35.9 %) and pemetrexed, platinum and bevacizumab (1.4 %) . Patients treated with immunotherapy as part of a clinical trial accounted for 7.2%. On the other hand, 13.2% received palliative care only, due to their poor functional status. Pemetrexed maintenance therapy was received in 36 (7.2 %) patients. The median number of maintenance pemetrexed cycles received was 3 cycles (range 1-30 cycles). Non platinum based chemotherapy included vinorelbine monotherapy, gemcitabine monotherapy and docetaxel.

Median overall survival of the cohort was 12.3 months (IC 95% 11.1-13.5). Median OS was 23.1, 18, 17.4 and 6.4 months among patients treated with immunotherapy within clinical trial, platinum-based chemotherapy, non-platinum chemotherapy and exclusive best support care, respectively (p=0.0001). A total of 38.2 % and 12.6 % received second- and third-line chemotherapy, respectively.

Conclusion: In this retrospective study of patients with MPM, patients who received immunotherapy within clinical trials have mostly benefited as it has prolonged overall survival compared to the remaining groups. The 13.2 % of patients could not receive systemic treatment and this leads to a strong impact on prognosis.

PP01.66:
A Case of Metastatic HER2-Amplified Non-Small-Cell Lung Cancer (NSCLC) Treated with Trastuzumab Deruxtecan

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Background: Human epidermal growth factor receptor 2 (HER2) is among the growing list of targetable alterations emerging in NSCLC, occurring as distinct molecular subtypes with HER2 protein overexpression, HER2 gene amplification or HER2 mutations. In the phase 2 DESTINY-Lung01 trial, trastuzumab deruxtecan (T-DXd), an antibody-drug conjugate comprising of an anti-HER2 antibody and topoisomerase I inhibitor payload, showed durable efficacy in patients with metastatic HER2-mutant NSCLC. Activity of T-DXd was limited in patients with HER2-overexpressed NSCLC. We do not currently have any data evaluating the efficacy of T-DXd in metastatic HER2-amplified NSCLC. Here, we describe a case of metastatic HER2-amplified NSCLC treated with T-DXd who achieved a durable response to therapy.

Methods: Our patient is a 49-year-old female with a history of early-stage right breast cancer status post mastectomy in 2011, former tobacco use with seven pack years, and stage IB adenosquamous lung cancer of the right middle lobe (pT2aN0M0) status post lobectomy and mediastinal lymph node dissection by video-assisted thoracic surgery in September 2018. In October 2020, a CT chest revealed disease progression with multiple pulmonary nodules in the right lung. Next generation sequencing (NGS) on a core biopsy of a right upper lobe pulmonary mass in January 2021 showed a ERBB2 copy number gain, TP53 C242fs, CDK12 copy number gain, tumor mutational burden of 3.2 mut/Mb, and no other targetable alterations. She completed four cycles of carboplatin, pemetrexed and pembrolizumab followed by three cycles of maintenance pembrolizumab from April 2021 to September 2021. However, the patient progressed in October 2021, four months after completing induction therapy, with evidence of enlarging pulmonary nodules. She declined second-line chemotherapy and agreed to proceed with T-DXd after we obtained off-label approval.

Results: T-DXd was started in October 2021 at 6.4 mg/kg every three weeks. Due to persistent grade two nausea despite antiemetics, T-DXd was dose reduced to 5.4 mg/kg starting at cycle three with improvement in symptoms. Repeat CT scans 3 months after starting T-DXd demonstrated a remarkable overall response to T-DXd with more than a 50% decrease in the size of the pulmonary nodules when compared to pretreatment scans. Patient remains in partial response at the time of writing this abstract in June 2022.

Conclusion: T-DXd in patients with HER2-mutated and HER2-overexpressed NSCLC has shown promise based on results from the DESTINY-Lung01 trial. Future prospective studies are needed to evaluate the efficacy of T-DXd in selected patients with HER2-amplified NSCLC.

PP01.67:
Decentralized, Real-World Study of Afatinib in Patients with Advanced/Metastatic Solid Tumors with NRG1 Fusions

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Background: Oncogenic neuregulin 1 (NRG1) gene fusions occur in ~0.2% of solid tumors overall and in up to 31% of cases of invasive mucinous lung adenocarcinoma.^{1,2} Afatinib, an irreversible pan-ErbB tyrosine kinase inhibitor, represents a potential treatment for NRG1-fusion positive (NRG1+) tumors. However, the scarcity of molecular alterations such as NRG1 fusions can limit timely recruitment for clinical trials. Undertaking decentralized trials represents a novel approach to increasing the potential patient pool. This decentralized study (previously presented at ASCO 2022) aims to examine the safety and efficacy of afatinib in patients with NRG1+ solid tumors, for which no authorized targeted therapy exists.

Methods: This prospective, US-based study (NCT05107193) will include 40 evaluable patients. Participating molecular test providers will identify eligible fusions (see table) during routine diagnostic assays. When a patient with an NRG1 fusion is identified, participating test providers will notify the treating physician of the study as a treatment option for the patient. Patients' primary oncologists will then contact the trial sponsor to confirm patient eligibility. Patients with NRG1+ tumors identified by oncologists/academic centers will also be considered for enrollment once their fusion is verified by a participating testing laboratory. Once approved by the central Institutional Review Board, patients will receive afatinib on a single-patient protocol basis, until disease progression or treatment is no longer tolerated. Patient demographics, clinical characteristics, prior treatments, afatinib exposure, and clinical outcomes will be captured in an electronic Clinical Report Form. The recommended dosage according to the Prescribing Information is 40 mg afatinib orally once daily. Patients will be screened and enrolled into the study at their existing point-of-care setting. Inclusion/exclusion criteria, endpoints, and safety assessments are described in the table. The study is open for recruitment.

[1]Laskin et al. *Ann Oncol.* 2020;31(12):1693–1703; [2]Cadranel et al. *Oncologist*. 2021;26(1):7–16.

Table. Inclusion and exclusion criteria, endpoints and safety

Inclusion criteria	**Exclusion criteria**
Histologically or cytologically confirmed diagnosis of an advanced, unresectable and/or metastatic non-hematologic malignancy harboring an *NRG1* gene fusion. • *NRG1* break point must occur before exon 6 on chromosome 8 ensuring conservation of the EGF domain • All genes are allowed as the second gene in the fusion; however, the region of the second gene involved in the splicing must be coding	Treatment with a systemic anti-cancer therapy or investigational drug within 14 days or five half-lives (whichever is shorter) of the first treatment with the study medication.
Patient must have measurable or evaluable lesions (according to RECIST 1.1).	Known, actionable oncogenic driver mutation other than *NRG1* fusion where FDA-approved targeted therapy is available.
At least 18 years of age at the time of consent.	Prior treatment with an ErbB-targeted therapy.
	Any patient considered ineligible by the treating physician.
Primary endpoint	
• Confirmed OR by independent central review per RECIST 1.1, defined as best overall response of either complete response or partial response and analyzed as the proportion of patients with an OR	
Secondary endpoints	
• Duration of response, defined as the time from the first documented OR to progression or death • Time to OR • Disease control per investigator assessment	
Safety From signing the ICF onwards until the patient completes the NRG1 treatment plan, the following AEs must be reported: • All SAEs • All CTCAE grade 3, 4, and fatal AEs • All CTCAE grade 2 AEs involving vital organs • All AEs which lead to dose modification, drug discontinuation, or withdrawal from the program	

AEs, adverse events; CTCAE, Common Terminology Criteria for Adverse Events; EGF, epidermal growth factor; ErbB, erythroblastic leukemia viral oncogene; FDA, Food and Drug Administration; ICF, informed consent form; *NRG1*, *neuregulin-1*; OR, overall response; RECIST, Response Evaluation Criteria in Solid Tumors; SAEs, serious AEs.

PP01.68:
Registry Based Analysis of Radiation Modality on Survival with Definitive Chemoradiation for Stage III Non-Small Cell Lung Cancer (NSCLC)

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Background: For unresectable NSCLC, concurrent chemoradiation followed by consolidative durvalumab showed significant improvement in progression free survival and overall survival (OS). Previously, studies evaluating radiation dose escalation failed to show any survival benefit compared to standard radiation dose. Using the unique Bragg-peak property, proton beam therapy (PBT) has the theoretical advantage to minimize radiation related normal tissue toxicities and thereby, increase the therapeutic ratio. We conducted a hospital-based registry analysis to evaluate outcomes of photon based Intensity Modulated Radiation Therapy (IMRT) and PBT. Our hypothesis is that the use of PBT is associated with a higher 3 year OS compared to IMRT.

Methods: We queried the National Cancer Database (NCDB) registry for patients with first-primary AJCC 7th Ed. Stage III non-small cell histology lung cancer from 2007-2014, age≥18 years that received definitive chemotherapy and radiation therapy. Only patients with minimal co-morbidities were included based on the Charlson-Deyo score. Three-year OS was estimated using the Kaplan-Meier method with comparison between groups using log-rank testing. A 20:1 nearest-neighbor propensity score matching was performed on demographic and clinicopathologic covariates with generation of a Love plot for assessment of covariate balance. Cox proportional hazards regression was used to identify covariates associated with OS from matched data with correction for multiple comparisons. Modified Schoenfeld residuals were analyzed to test the proportional hazards assumption.

Results: A total of 4491 patients were identified meeting inclusion criteria, 56 (1.2%) receiving PBT and 4435 (98.8%) receiving IMRT. The median follow up was 21.5 months (1.74 - 140.2). The 3 year OS rates by Kaplan Meier method were 33.9% for IMRT versus 46.5% for PBT (p=0.001). On univariable analysis younger age, race, sex, clinical stage IIIB and receipt of PBT were favorable. On multivariable analysis including these covariates showed statistically significant association of OS with female sex (HR 0.74, p <0.001), african-american race (HR 0.82, p = 0.048), older age (HR 1.02, p<0.001), clinical stage IIIB (HR 1.22, p = 0.004), and receipt of PBT (HR 0.63, p =0.0009).

Conclusion: In stage III NSCLC, the use of proton radiation as part of definitive chemoradiation therapy was associated with improved 3 year OS after adjusting for demographic and treatment parameters as compared to photon IMRT. Continued prospective evaluation of the effect of proton therapy on survival and toxicity outcomes is warranted, as well as refinement of selection criteria for patients deriving the greatest benefit, including the future results of RTOG 1308.

PP01.69:
NSCLC with Testicular Metastasis: A Case Report

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Background: Lung cancer is the second most common cancer diagnosis and therefore it is extremely important to recognize and highlight unusual presentations and clinical courses. Testicular masses are usually associated with germ cell tumors or lymphomas. Here, we present a rare case of a patient with non-small cell lung cancer who developed testicular metastases.

Case Report: A 60 year old asymptomatic man with an approximately 30 pack year smoking history was found to have a 2cm irregular mass in the right lower lobe on routine lung cancer screening. CT-guided lung nodule core biopsy, imaging and a right lower lobectomy with lymph node dissection were performed. The final pathological staging was pT1cN1M0 (Stage IIB) poorly differentiated adenocarcinoma. Foundation medicine testing showed PD-L1 expression of 70%, MSI and TMB could not be determined and no actionable mutations were reported. He then received four cycles of adjuvant pemetrexed and cisplatin. A surveillance CT chest and subsequent PET/CT imaging 6 months later showed abdominal lymphadenopathy, new bilateral adrenal masses, and a large hypermetabolic mass in his left testis. On exam, the left testicle was tender to palpation and enlarged with firm nodules on the inferior portion, suspicious for epididymitis. Testicular ultrasound showed a large nonvascular, noncalcified infiltrating lesion. Tumor markers were notable for mildly elevated beta-HCG and normal AFP levels. There were no risk factors for germ cell tumor. Left radical orchiectomy yielded a 6cm metastatic adenocarcinoma consistent with his lung primary. Foundation medicine testing from the testicular mass showed PD-L1 TPS 1%, microsatellite stable, TMB 5 MUTS/MB, with no other changes compared to the lung specimen. He was therefore started on carboplatin, nab-paclitaxel, and atezolizumab.

Discussion: Non-small cell lung cancer is one of the most common and most deadly malignancies and commonly metastasizes to the brain, bones and adrenal glands. Lung adenocarcinoma metastatic to the testes is a very rare occurrence. While some patients report symptoms such as testicular pain, erythema or swelling, many are also asymptomatic. With the unique attribute of the testes as an immune-privileged site, the use of immunotherapy is of particular interest and has been suggested to have superior penetration than traditional chemotherapy. The significance of the PD-L1 TPS decrease from 70% in the primary lung tissue to 1% in the testicular metastasis is unclear at this time.

Conclusions: This case underscores the need to remain vigilant to uncommon presentations, even in common diseases

PP01.70:
Prevalence, Treatment Patterns, and Survival by Age in Patients Diagnosed with Metastatic Non-Small Cell Lung Cancer (mNSCLC) and Brain Metastases (BM) in the United States

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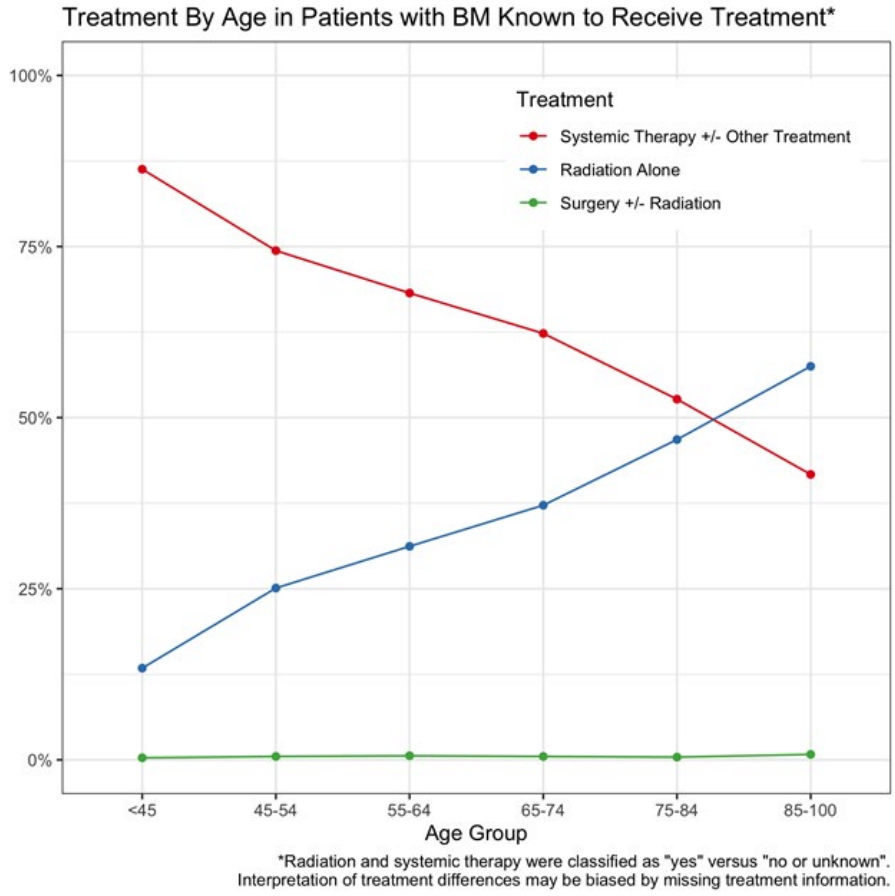
Background: BM are common in mNSCLC patients and may affect treatment patterns and survival. They are also associated with more debilitating disease.

Methods: Surveillance, Epidemiology, and End Results data (2016-2019) were used to identify adult patients with mNSCLC. We examined the prevalence of BM among newly diagnosed mNSCLC patients, along with treatment patterns by age group. A Cox proportional hazards model was used to examine the association between sites of metastasis (brain, bone, liver, etc.) and mortality controlling for patient characteristics, histology, and social determinants of health.

Results: Among 62,760 patients with mNSCLC, mean age was 69 years and 26% had BM at diagnosis. The prevalence of BM declined from 38% among patients aged <45 to 11% among patients aged 85-100. In an adjusted survival model using all mNSCLC patients, risk of death was 20% higher in patients with BM compared to those without BM (hazard ratio=1.20, 95% CI 1.18-1.23). The mNSCLC with BM population (n=16,508) had a mean age of 66 years, 51% were male, and 75% were White. In the 80% (n=13,287) of BM patients who were known to receive treatment, use of systemic therapy declined from 86% among patients aged <45 to 42% among those aged 85-100. Conversely, use of radiation alone increased from 13% to 58% (Figure). In patients with BM receiving systemic therapy, median survival was 13 months (95% CI: 12-14) for patients <65, and 9 months (95% CI 9-10) for patients ≥ 65. In patients selected to receive radiation alone, median survival was 2 months (95% CI 2-2) regardless of age.

Conclusion: BM are more common among younger mNSCLC patients and associated with increased mortality relative to those without BM. Consideration should be given to identifying the best treatment options to optimize survival and reduce the humanistic burden for patients across the age continuum.



PP01.71:
Survival Outcome of Pulmonary Sarcomatoid Carcinoma Treated with Immunotherapy: A Study of National Cancer Database

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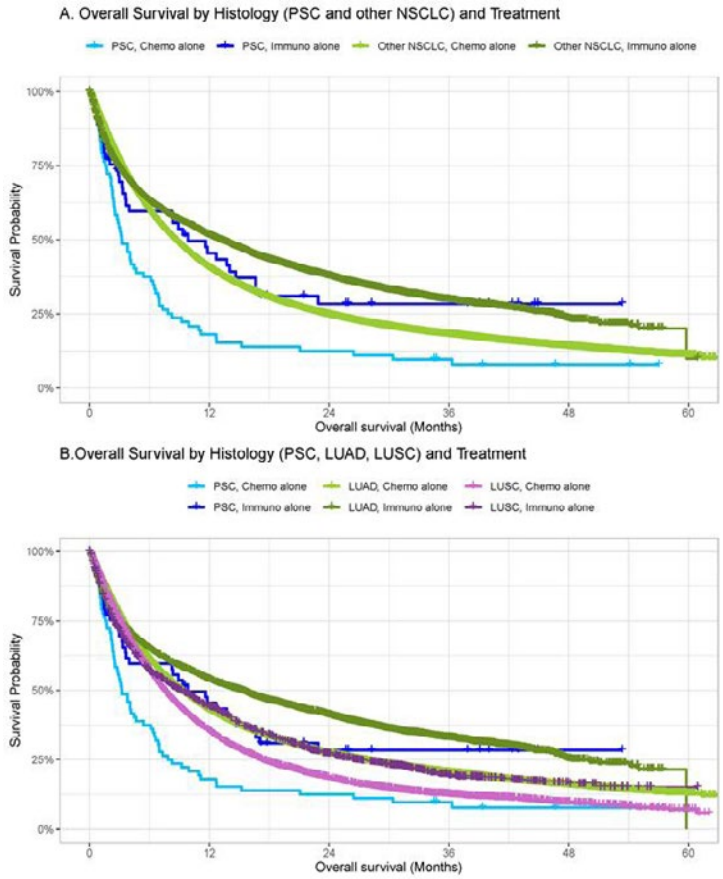
Background: Pulmonary sarcomatoid carcinoma (PSC) is a rare subtype of non-small cell lung cancer (NSCLC), with historically poor outcome. Excellent response of PSC to immunotherapy was reported, but its outcome compared to other NSCLCs is unknown in modern era.

Methods: National Cancer Database was queried for stage IV NSCLC diagnosed from 2016 to 2018. Patients who were treated with chemotherapy doublets only or immunotherapy only in the first course of treatment were included. Log-rank was used for survival analysis and adjusted by cox regression for age, gender, race, academic center, insurance, and comorbidity.

Results: A total of 27,012 patients were identified, including 126 PSCs and 26,886 NSCLCs. Pleomorphic (49%) was the most common PSC subtype. There was significant interaction between the survival effect of treatment and histology (p = 0.022). When treated with immunotherapy alone, no significant difference was found between PSC and other NSCLCs (median survival 9.9 vs. 12.9 months, logrank p = 0.47, HR 0.90, 95% CI 0.65 – 1.24). However, when treated with chemotherapy alone, PSC remained significantly associated with worse survival. Among PSC subtypes, spindle/giant cell (HR 0.21, 95% CI 0.10 – 0.45) PSCs were associated with survival benefit from immunotherapy compare to chemotherapy, but this was not observed in pleomorphic ones (HR 0.54, 95% CI 0.28 – 1.05, interaction p = 0.023).

Conclusions: Compared to other NSCLCs, PSC may not be associated with worse survival when treated with immunotherapy alone as it was when treated with chemotherapy. Distinct PSC subtype may respond differently to immunotherapy and may require more personalized treatment.



PP01.72:
Cell-free DNA for Treatment Response and Recurrence Monitoring in Advanced Stage Lung Cancer

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Background: Circulating cell free DNA (cfDNA) in lung cancer is used to identify sensitizing and resistance mutations. There may be other potential indications for cfDNA testing. This study reports the experience using cfDNA testing with three different platforms to monitor for treatment response and to assist in differentiating between radiation changes, progression, pseudoprogression, or lung infections/inflammation.

Methods: This is a single-center retrospective study that included a total of 11 patients (pts) with small cell lung cancer (SCLC) (n=2) and non-small cell lung cancer (NSCLC) (n=9). Three commercial platforms (Guardant360, Signatera, and Tempus) were utilized to identify somatic genomic alterations in cfDNA by high-output parallel sequencing of target genes. The number of cancers associated genes analyzed varied by platform and are as follows: Guardant360: 83, Tempus: 105, Signatera: 16. These genes were previously identified by whole exome sequencing of the primary tumor. The cfDNA were then evaluated in at least 1 or more time points.

Results: A total of 11 pts were evaluated. Guardant: 6 NSCLC, Signatera: 3 NSCLC, Tempus: 2 SCLC. One pt evaluated with Guardant360 platform, showed progression of disease based on cfDNA, correlated by imaging and clinical evolution. Two pts in Guardant360 group showed a reduction of variation allele fraction (VAF). These two pts also had a partial response on imaging. There were three pts who had Guardant360 assessment that showed concordant radiological response with decreased cfDNA VAF. Within the Signatera group, one of the pts had cfDNA VAF reduction, which was concordant with a radiological response, one case with initial complete response had no cfDNA and diagnosed with radiation pneumonitis, and one case showed an increased cfDNA VAF which was concordant with radiological progression. One of two SCLC pts in Tempus group presented with new lung nodules after chemoradiation, but no somatic mutations were detected on cfDNA. This ruled out progression and ultimately diagnosed with organizing pneumonia by tissue biopsy. The second case with SCLC showed a reduction of cfDNA VAF going along with disease response in the setting of unclear radiological findings due to superposed infection.

Conclusion: cfDNA VAF changes correlated with radiological resolution or progression which assisted with management and clinical decision for patients with advanced lung cancer. cfDNA monitoring was helpful in the setting of complete responses and withholding treatment due to immune-related side effects. cfDNA also provided clarity for recurrence of disease when radiological imaging did not provide clear evidence of treatment response.

PP01.73:
Time from Biopsy to Treatment Initiation at an Academic Hospital and Affiliate Hospitals: Overall Survival Analysis

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Background: In advanced NSCLC, the nature of NGS testing impacts time to treatment. In our system, Northwestern Medicine, NGS testing at Northwestern Memorial Hospital (NMH), the academic tertiary care hospital (AH), is done by an in-house reflex 200-gene panel for mutations and fusions sent at NSCLC diagnosis, while at satellite hospitals in community-based settings (CH), tissue is sent by an oncologist to private vendors for testing. We presented work at WCLC 2022 (EP04.01-008) assessing time to treatment in these two settings in 2019 and 2020, with median time from biopsy to treatment of 30 days at AH (35 in 2019, 26 in 2020) and 37 days at CH (38 in 2019, 37 in 2020). We now present overall survival data for these cohorts.

Methods: We queried the Northwestern Medicine Enterprise Data Warehouse for patients with new lung cancer diagnosis between January 1, 2019 and December 31, 2020 at NMH, CDH and Delnor, yielding 864 patients on initial screen. Inclusion criteria for analysis: de novo stage IV NSCLC + diagnostic biopsy at one of these three hospitals. 191 patients met inclusion criteria.

148 patients received systemic therapy, for whom overall survival (as of June 17, 2022) was calculated. Patients were excluded if they did not have available clinical data within the prior year. 145 patients met criteria for OS analysis.

Results: Median OS overall was 13 months; for those diagnosed in 2019 (n = 99), 11.03 months, and in 2020 (n = 46), 17.43 months (p = 0.2). Median OS at Northwestern (n = 69) was 14.9 months, and at CDH + Delnor (n = 76) 10.78 months (p = 0.11). At Northwestern, median OS for patients diagnosed in 2019 (n = 42) was 12.9 months, and in 2020 (n = 27) 17.47 months. At CDH + Delnor, median OS for those diagnosed in 2019 (n = 57) was 10.7 months, and in 2020 (n = 19) 15.53 months.

Conclusions: Overall survival trended longer in 2020 than 2019 at both sites, while prior data showed a decreased time to treatment in 2020 only at Northwestern. This suggests that factors beyond NGS testing are responsible for the higher OS, perhaps introduction of immunotherapy and novel targeted therapies. There remains a need to reduce time from biopsy to treatment, as 30 or 37 days represent a large part of median OS in patients with advanced lung cancer.

PP01.74:
Clinical Validation of a Promising New Amplicon-Based Liquid Biopsy Platform for Detection of Guideline Recommended Biomarkers in Metastatic NSCLC

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Background: Tissue profiling is the gold standard for guideline-recommended biomarker testing for treatment selection in non-squamous non-small cell lung cancer (NSCLC). However, such testing is not accomplishable in 15-40% of patients due to insufficient tissue. For such patients, liquid biopsy potentially offers a swift, comprehensive and non-invasive option for the testing of guideline-recommended biomarkers. For NSCLC, the 9 guideline-recommended biomarkers (G9) include specific somatic alterations in EGFR, ALK, ROS1, RET, BRAF V600E, MET, KRAS G12C, ERBB2/HER2 and NTRK1/2/3. LiquidHALLMARK is an amplicon-based next generation sequencing (NGS) liquid biopsy test, intended to detect alterations in 80 genes and 10 fusions in plasma.

Methods: LIQUIK-01 (LIQUId Biopsy for Detection of Actionable Genomic BiomarKers in Patients with Advanced Non-small Cell Lung Cancer; NCT04703153) was intended to prospectively evaluate the relative performance of liquid biopsies, including LiquidHALLMARK, with conventional tissue-profiling for metastatic non-squamous NSCLC. 200 treatment-naïve, newly diagnosed, histologically or cytologically confirmed metastatic non-squamous NSCLC subjects are being enrolled from 11 US and Singapore-based centers from April 2021. Interim analysis was conducted on June 1st 2022 as the cut-off date. Primary endpoints include non-inferiority of LiquidHALLMARK ctDNA testing (Lucence, Palo Alto, CA; Singapore) in comparison with tissue biopsy in the detection of G9 biomarkers; and a comparison of LiquidHALLMARK with Guardant360 (Guardant, Redwood City, CA), a hybrid-capture-based NGS test, for patients who had at least one G9 biomarker detected by tissue-genotyping.

Results: 45 patients enrolled by the cut-off date were analyzed. At least 1 G9 biomarker was identified in 26 patients (57.8%) by tissue-genotyping versus 22 patients (48.9%) identified by LiquidHALLMARK ctDNA testing. 27 G9 biomarkers were detected in 26 patients with any G9 biomarker detected on tissue-profiling. For the 26 patients with guideline-recommended biomarkers detected with tissue-genotyping, LiquidHALLMARK ctDNA testing detected 19/27 (70.4%) guideline-recommended biomarkers, while Guardant360 detected 18/27 (66.7%) guideline-recommended biomarkers. For 19 patients who tested tissue-negative or had insufficient tissue, 3 patients (15.8%) had G9 biomarkers detected by LiquidHALLMARK. Individual concordance between LiquidHALLMARK ctDNA and tissue-genotyping results was 95.2-100% across the G9 biomarkers.

Conclusion: Liquid biopsy has been very valuable in the identification of guideline-recommended biomarkers in metastatic non-squamous NSCLC. Our analysis revealed greater identification of guideline-recommended biomarkers with LiquidHALLMARK in comparison to Guardant360 thus far. Given the encouraging results, LIQUIK-01 recruitment, further investigations and analysis will continue.

PP01.75:
Neuro-Cognitive Effects of WBRT and HS-PCI in LS-SCLC

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Background: Small-cell lung cancer (SCLC) is an aggressive type of cancer associated with poor prognosis due to rapid growth and early distant metastasis, especially brain metastasis. Patients with limited stage (LS) achieve a median survival of 18 months and a 5-year survival rate of 15%. Several studies have shown prophylactic cranial irradiation (PCI) to be an independent prognostic factor. Hippocampal sparing (HS) PCI 25 Gy/10 fractions has minimum impact on neuro-cognitive function while Whole Brain RT (WBRT) 30Gy/10 fractions has maximum impact.

Methods: In this cohort study 10 patients of LS-SCLC were administered HS-PCI with IMRT, and same number of patients received WBRT during 2020. Baseline neuro-cognitive function was measured before administering radiation and final neuro-cognitive function was measured after median follow up of 18 months. Neuro-cognitive function was assessed by Montreal Cognitive Assessment (MoCA).

Results: At the end of 18 months, 7patients are alive in HS-PCI group and 6 in WBRT group with minor deterioration of neuro-cognitive function score compared to baseline measurement. For HS-PCI and WBRT groups mean pre-treatment MoCA score are 27/30 and 26/30. Mean post-treatment MoCA score for the groups are 25/30 and 23/30 respectively.

Conclusions: Both HS-PCI and WBRT are effective in LS-SCLC for preventing brain metastasis in long term. WBRT affects neuro-cognitive fiction more than HS-PCI. Hippocampal sparing as well as lower radiation dose in HS-PCI could be the major factors for this outcome.

PP01.76:
Lurbinectedin vs an External Control Arm in Patients with Small Cell Lung Cancer

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Background: Lurbinectedin received accelerated approval for metastatic small cell lung cancer (SCLC) patients with disease progression on or after platinum chemotherapy based on the results of a single-arm phase 2 study. This study compares overall response rate (ORR) and overall survival (OS) in the lurbinectedin trial to other treatments from a real-world external control arm. The data in this abstract was accepted as an e-abstract at ASCO 2022. All rights reserved.

Methods: The lurbinectedin trial arm (LTA) results were compared to outcomes from two real-world comparator arms (RWCA1 and RWCA2) sourced from ConcertAI electronic medical records (2010-2019). RWCA1 included patients with ECOG≤2 and those missing ECOG scores. RWCA2, a subset of RWCA1, included only patients with a known ECOG≤2. Propensity score weighting was used to balance measured confounders. ORR was assessed in two ways in the RWCAs due to the missingness of tumor response. ORR1 was assessed as the percentage of patients with a complete or partial response among all patients, and ORR2 was assessed among those with a recorded response or death within 90 days of treatment initiation. Cox regression was used to compare OS.

Results: This study included 105 patients in LTA, 121 in RWCA1, and 74 in RWCA2. ORR was approximately two-fold higher in the LTA compared to both RWCAs and across both definitions of ORR. The LTA had a higher proportion of patients with response to treatment with the differences in response rate ranging from 14.5% to 22.3%. Median survival time (months) was 9.3, 5.5, and 4.6 in the LTA, RWCA1, and RWCA2 respectively. Probability of survival was greater in LTA compared to RWCA1 and RWCA2 at 3 and 6 months.

Conclusion: Lurbinectedin demonstrated improved median OS and a higher response rate compared to other treatments in patients with relapsed/refractory SCLC.

	LTA (n=105)	RWCA1 (n=121)	RWCA2 (n=74)
Sum of weights*	105	102.48	96.61
Overall Response Rate (ORR)			
Complete Response	0 (0.0%)	3.3 (3.2%)	1.4 (1.4%)
Partial Response	37 (35.2%)	13.2 (12.9%)	11.1 (11.5%)
Stable Disease	35 (33.3%)	11.8 (11.5%)	7.6 (7.8%)
Progressive Disease	28 (26.7%)	31.8 (31.0%)	32.3 (33.4%)
Not Evaluable/Unknown	5 (4.8%)	22.5 (22.0%)	18.4 (19.1%)
No Response Recorded Among Those Who Died Within 3 Months of Treatment Start	N/A	19.8 (19.3%)	25.8 (26.7%)
ORR1	37 (35.2%)	16.5 (16.1%)	12.5 (12.9%)
Response Difference ORR1		19.1% (7.5%, 30.7%)	22.3% (11.0%, 33.6%)
ORR2	37 (35.2%)	16.5 (20.7%)	12.5 (16.0%)
Response Difference ORR2		14.5% (1.8%, 27.3%)	19.3% (7.0%, 31.5%)
Overall Survival			
Probability of Survival at 3 Months	87.2% (80.7%, 93.7%)	69.7% (59.8%, 79.6%)	58.4% (44.8%, 72.0%)
Probability of Survival at 6 Months	67.1% (57.6%, 76.7%)	44.3% (32.5%, 56.1%)	43.3% (29.4%, 57.2%)
Median Survival (months)	9.3	5.5	4.6
Hazard Ratio		0.89 (0.61, 1.30)	0.75 (0.48, 1.15)

*The sum of weights was calculated by adding the propensity score weights associated with each patient in each respective arm
ORR1 = percentage of patients with a complete or partial response among all patients
ORR2 = percentage of patients with a complete or partial response among those with a recorded response or death within 90 days of treatment initiation

PP01.77:
EMERGE 402: Real-world Characteristics and Safety of Lurbinectedin in Small-cell Lung Cancer (SCLC)

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Background: Lurbinectedin, a selective inhibitor of oncogenic transcription, received accelerated US FDA approval and conditional Health Canada approval as monotherapy (3.2 mg/m^2 IV every 3 weeks) for adults with metastatic (US) or stage III/metastatic (Canada) SCLC with disease progression on or after platinum-based chemotherapy. EMERGE 402 is assessing the effectiveness, safety, and QOL of patients with SCLC prescribed lurbinectedin in the real-world setting. An abstract presented at WCLC 2022 was from an earlier cut-off (01/24/2022).

Methods: EMERGE 402 is an ongoing prospective, observational, multicenter, phase 4 study enrolling patients with SCLC who progressed on or after ≥1 prior platinum-based chemotherapy regimen, with or without immunotherapy. Patients are assessed for enrollment after a physician prescribes lurbinectedin (per local prescribing information).

Results: Between 06/28/2021 and 05/16/2022, 42 patients were treated (Table). All patients received prior platinum-etoposide chemotherapy; 79% received prior immunotherapy; 45% had platinum-sensitive disease (chemotherapy-free interval ≥90 days: n=19 [45%]; ≥180 days: n=11 [26%]); 26% had CNS involvement. All patients received lurbinectedin monotherapy: 17 (40%) as second-line therapy and 25 (60%) as third/later-line therapy. Patients received a median of 3 (range: 1, 11) lurbinectedin cycles; treatment is ongoing for 17 (40%) patients. Dose delays and reductions were required by 3 (7%) and 6 (14%) patients, respectively. G-CSF was administered in 18 (43%) patients; 15 received G-CSF as primary prophylaxis. Treatment-related adverse events (AEs; any grade) were observed in 16 (38%) patients; events in ≥10% included anemia (17%), neutropenia (12%), and fatigue (10%). Serious AEs were reported in 10 (24%) patients.

Conclusions: EMERGE 402 continues to enroll patients to assess the effectiveness and safety of lurbinectedin among a broader SCLC population than the phase 2 study that supported approval of lurbinectedin monotherapy. The real-world safety profile of lurbinectedin was generally consistent with the phase 2 study, with no new safety signals.

Table. Demographic and Clinical Characteristics and Lurbinectedin Cycles of Patients Enrolled in EMERGE 402 (as of 05/16/2022)

	Total (N=42)
Line of lurbinectedin therapy, n (%)	
Second-line therapy	17 (40)
Third- or later-line therapy	25 (60)
Age	
Median (range), year	65.0 (44, 87)[a]
≥65 years, n (%)	21 (50)
Sex, n (%)	
Female	17 (40)
Male	25 (60)
Race, n (%)	
White	34 (81)
Black or African American	5 (12)
American Indian or Alaska Native	1 (2)
Declined to state	2 (5)
ECOG performance status at baseline, n (%)	
0	7 (17)
1	24 (57)
2	5 (12)
Missing	6 (14)
Stage at initial diagnosis, n (%)	
Extensive stage	29 (69)
Limited stage	13 (31)
CTFI, n (%)	
<30 days	6 (14)
≥30 to <90 days	7 (17)
≥90 to <180 days	8 (19)
≥180 days	11 (26)
Not reported	10 (24)
Prior therapy, n (%)	
Systemic therapy only	13 (31)
Systemic therapy and radiotherapy	29 (69)
First-line systemic therapy regimen, n (%)	
Platinum-etoposide chemotherapy only	17 (40)
Platinum-etoposide chemotherapy + immunotherapy	25 (60)
Sites of involvement other than lung, n (%)	
Liver	27 (64)
Distant nodes	15 (36)
Bones	13 (31)
Brain	11 (26)
Median (range) lurbinectedin cycles received[b]	
As second-line therapy	3 (1, 8)
As third- or later-line therapy	3 (1, 11)

ECOG, Eastern Cooperative Oncology Group; CTFI, chemotherapy-free interval.
[a]A data issue of a reported age of 7 years old was identified, but not corrected, at the time data extraction. To properly summarize age and age group of the treatment lines, that data point was set to missing.
[b]Treatment is ongoing for 17 (40%) patients.

PP01.78:
Brain Metastasis in Patients With KRAS Mutant Advanced NSCLC Receiving Docetaxel: Pooled Clinical Trial Data Analysis

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Background: Lung cancer is the leading cause of brain metastases (BMs). However, the risk of BM progression in KRASmut advanced NSCLC (aNSCLC) has not been well-described in clinical trial (CT) cohorts, which exclude patients with poor functional status or unstable, symptomatic BMs. This study used pooled CT data to evaluate the incidence and progression of BM in KRASmut aNSCLC CT participants (pts) treated with docetaxel (DOCE) containing regimens.

Methods: The Medidata Enterprise Data Store (MEDS) contains data from >26k completed CTs. Anonymized data was pooled from historical CTs for pts with previously treated KRASmut aNSCLC, treated with DOCE regimens, and naïve to MEK-TKI and DOCE before trial initiation. This analysis included pts with and without BMs at baseline who were required to have brain assessment (clinical or radiographic) before and after initiation of trial treatment(s)

Results: Of KRASmut aNSCLC pts, 90% (533/595) had no BMs, and 10% (62/595) had BMs at baseline. Of the 533 pts without baseline BMs, 8.4% (45/533) developed new BMs, and 89% (40/45) had CNS as first-site-of-progression. Of the 62 pts with baseline BMs, 17 (27.4%) had CNS progression, and 82% (14/17) as first-site-of-progression. CNS disease control rates (CNS-DCR) were similar between DOCE alone and DOCE + MEK-TKI cohorts. Median overall survival for pts with and without baseline BMs was 6.7 months (95% CI, 5.3-8.8) and 8.7 months (95% CI, 7.6-9.6), and the median progression-free survival was 3.6 months (95% CI, 2.6-4.2) and 5.6 months (95% CI, 5.2-6.1), respectively.

Conclusions: In highly selected CT populations of KRASmut aNSCLC, DOCE had a moderate CNS-DCR. However, a proportion of pts who only had baseline clinical assessment for BMs without follow-up brain imaging represented a significant limitation. The intracranial activity of existing and novel agents needs dedicated study in future CTs of KRASmut aNSCLC.

PP01.79:
ALK Positive, Inc - Patient Advocacy Accelerating Research and Clinical Trials Worldwide

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ALK Positive, Inc. a 501(c)(3) registered non-profit, partners with academia, industry, non-profit organizations to help bring promising treatments to patients faster, improving life expectancy, and quality of life, for ALK-positive cancer patients. Led and staffed by volunteers, most with advanced-stage ALK Positive cancer diagnoses, ALK Positive has raised over $6M USD in charitable donations, and has deployed and committed over $5M USD to advance research and clinical trial development. Key activities include:

Research Acceleration Committee: Collaborates with academic key opinion leaders and industry/biotech partners, helping to accelerate promising new treatments, which have the potential to further improve outcomes, to clinical stage.

Clinical Trials Committee: Collaborates with academic key opinion leaders and industry/biotech partners, to help shape clinical trial design and eligibility criteria, to help new treatments with potential to improve outcomes gain regulatory approval as rapidly as possible.

ALK Positive, Inc Longitudinal Outcomes Registry: An IRB-approved longitudinal study collecting patient-reported outcomes and data. Launched in 2022, this registry will record in-depth clinical, diagnostic, and disease progression information. Expected to chronicle the clinical journeys of hundreds of ALK positive cancer patients, these data will be made freely available to researchers.

ALK POWER Study: A collaborative IRB-approved study, by ALK Positive and a leading researcher. This study collects patient CT images to create artificial intelligence algorithms, with a goal of enabling faster and more accurate detection of ALK+ cancer, both at initial diagnosis and at progression, than currently obtainable.

University of Michigan's ALK-positive Cancer Initiative: The Judy Tam Foundation is funding a massive academic research project, dedicated to ALK-positive cancer research, and designed to advance precision medicine options for ALK-positive patients. ALK Positive is working with the University of Michigan research team, participating on its advisory board, and helping to recruit patients, KOLs, and industry to this study.

Advocacy: ALK Positive collaborates with ACS, ALCMI, Exact Sciences, Foundation Medicine, GO2 Foundation, Guardant 360, IASLC, LungCAN, LCRF, LUNGevity Foundation, NLCRT, The Oncogene Collaborative and more. Our collective efforts campaign for improved research funding, universal biomarker testing, more comprehensive insurance coverage of treatments and testing, and less community stigma.

ALK Research Library: A searchable library of over 1,000 publications and videos

ALK Clinical Trials Database: Restricted to clinical trials enrolling ALK-positive cancer patients.

ALK Positive Newsletter: An online newsletter with over 6,000 subscribers.

ALKtALK: Interactive online webinars featuring experts in their fields

ALK Positive Second Opinion Program: Provides patients with a free second opinion

ALK POSITIVE

PP01.80:
Long term Results of VATS Lobectomy for Early staged Non Small Cell Lung Cancer

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Background: Non Small Cell Lung Cancer (NSCLC) is frequently cancer and the leading cause death of cancer. Lobectomy and lymph node dissection is optimal surgical treatment method for early stage NSCLC. Video-assisted thoracoscopic surgery (VATS) approach is less trauma, quickly recovery, whereas those who advocate thoracotomy claim it as an oncologically superior procedure. The aims of study are evaluation the long term results of Video-Assisted Thoracoscopic Surgery for treating the patients who had early stage NSCLC.

Methods: All of patient with NSCLC in stage IA - IIB underwent lobectomy and lymph node dissection through VATS are collected. Operative datas, complications were assessed and survival was assessed by Kaplan–Meier and Cox proportional hazards analysis. Follow-up from 14 to 66 months.

Results: From 2016 to 2021, 112 patients with NSCLC stage IA - IIB underwent an attempt at VATS lobectomy and lymph node dissection. There are 72 male and 40 female, mean age is 56.3 ± 9.2 range 31 - 84. Lobectomy was performed in 106 cases and bilobectomy in 06 cases. The mean operating time is 150.7 ± 18 minutes. In 112 cases VATS, 7 cases (6.2%) were converted to thoracotomy. There are no death. One patient had bleeding need to reoperation for controlling bleeding, prolonged air-leak more than 5 day were 7 cases (6.2%). Hospitalization is 12.4 days. The 5-year OS rate was 67.8% and the 5-year DFS rate was 59.6%.

Conclusion: Video-assisted thoracoscopic surgery is effective and safe method for surgical treatment of early stage NSCLC. VATS lobectomy was associated with less complications and shorter length of hospital stay. The 5 years survival is not worse than conventional thoracotomy approach.

Keywords: VATS, lobectomy, Non Small Cell Lung Cancer (NSCLC), early staged NSCLC

Abstract Author Index

A

B

C

D

d

E

F

G

H

I

J

K

L

M

N

O

Ö

P

Q

R

S

T

U

V

W

X

Y

Z