IASLC

2020 North America Conference on Lung Cancer

OCTOBER 16-17, 2020 | WORLDWIDE VIRTUAL EVENT

ABSTRACTS

www.IASLC.org

IASLC 2020 North America Conference on Lung Cancer
OCTOBER 16-17, 2020 | WORLDWIDE VIRTUAL EVENT
VIRTUAL CONFERENCE

OA03.02

Nivolumab (NIVO) + ipilimumab (IPI) + 2 Cycles of Platinum-Doublet Chemotherapy (Chemo) vs. 4 Cycles Chemo as First-Line (1L) Treatment) for Stage IV/Recurrent Non-Small Cell Lung Cancer (NSCLC): CheckMate 9LA

Martin Reck[1], Tudor-Eliade Ciuleanu[2], Manuel Cobo Dols[3], Michael Schenker[4], Bogdan Zurawski[5], Juliana Menezes[6], Eduardo Richardet[7], Jaafar Bennouna[8], Enriqueta Felip[9], Oscar Juan Vidal[10], Aurelia Alexandru[11], Hiroshi Sakai[12], Arnaud Scherpereel[13], Shun Lu[14], Tom John[15], **David Paul Carbone[16]**, Stephanie Meadows-Shropshire[17], Jinchun Yan[17], Luis G. Paz-Ares[18]

[1]Department of Thoracic Oncology, Airway Research Center North, German Center for Lung Research, LungClinic, Grosshansdorf, Germany, [2]Institutul Oncologic Prof. Ion Chiricuta and UMF Iuliu Hatieganu, Cluj-Napoca, Romania, [3]Unidad Intercentro HRU Málaga y VV. IBIMA, Málaga, Spain, [4]SF. Nectarie Oncology Center, Craiova, Romania , [5]Ambulatorium Chemioterapii, Bydgoszcz, Poland, [6]Hospital Nossa Senhora Da Conceição, Porto Alegre, Brazil, [7]Instituto Oncológico De Córdoba, Córdoba, Argentina, [8]Thoracic Oncology Unit, University Hospital of Nantes, Nantes, France, [9]Vall d'Hebron University Hospital, Barcelona, Spain, [10]Hospital Universitario La Fe, Valencia, Spain, [11]Institute of Oncology "Prof. Alexandru Trestioreanu" Bucha, Bucharest, Romania, [12]Saitama Cancer Center, Saitama, Japan, [13]Regional University Hospital Center of Lille, Hospital Calmette, Lille, France, [14]Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai JiaoTong University, Shanghai, China, [15]Austin Hospital, Heidelberg, Australia, [16]The Ohio State University Comprehensive Cancer Center, Columbus, USA, [17]Bristol Myers Squib, Princeton, USA, [18]Hospital Universitario 12 de Octubre, CNIO, Universidad Complutense & CiberOnc, Madrid, Spain

Oral Abstract Session 1, October 16, 2020, 15:20 - 17:00

Background: NIVO + IPI was shown to improve overall survival (OS) and durability of response vs chemo in 1L advanced NSCLC in CheckMate 227 Part 1, regardless of PD-L1 expression. We hypothesized that a limited course of chemo combined with NIVO + IPI could provide rapid disease control while building on the durable OS benefit seen with dual PD-1 and CTLA-4 inhibition. CheckMate 9LA (NCT03215706) is a phase 3 randomized study evaluating NIVO + IPI + 2 cycles chemo vs chemo in 1L stage IV/recurrent NSCLC. **Methods:** Adults with treatment-naive, histologically confirmed stage IV/recurrent NSCLC, ECOG performance status 0–1, and no known sensitizing EGFR/ALK alterations were randomized 1:1 to NIVO 360 mg Q3W + IPI 1 mg/kg Q6W + chemo (2 cycles) (n = 361) or chemo (4 cycles) alone (n = 358), stratified by PD-L1 (< 1% vs ≥1%), sex, and histology (squamous vs non-squamous). Chemo was based on histology. Pts with non-squamous NSCLC in the chemo-only arm could receive optional pemetrexed maintenance. Pts were treated with immunotherapy until disease progression, unacceptable toxicity, or for 2 y. The primary endpoint was OS; the interim analysis using Lan–DeMets alpha spending function with O'Brien–Fleming boundary was planned at ~80% information fraction (ie, after observing ~322 total events). Secondary endpoints included progression-free survival (PFS) and objective response rate (ORR) by blinded independent central review, and efficacy by PD-L1 subgroups. Exploratory endpoints included safety/tolerability. **Results:** Baseline characteristics were balanced across ar At a preplanned interim analysis (minimum follow-up 8.1 mo), OS was significantly prolonged with NIVO + IPI + chemo vs chemo (HR 0.69, 96.71% CI: 0.55–0.87; P = 0.0006); statistically significant improvements in PFS and ORR were seen. With longer follow-up (minimum 12.7 mo), NIVO + IPI + chemo vs chemo continued to provide longer OS; median 15.6 vs 10.9 mo (HR 0.66, 95% CI: 0.55–0.80); 1-y OS rates were 63 vs 47%. Clinical benefit was consistent across all efficacy measures in key subgroups including by PD-L1 and histology. Grade 3–4 treatment-related adverse events were reported in 47 vs 38% of pts in the NIVO + IPI + chemo vs chemo arms, respectively. **Conclusions:** CheckMate 9LA met its primary endpoint: a statistically significant improvement in OS was observed with NIVO + NSCLC-optimized IPI + a limited course of chemo vs chemo (4 cycles) in 1L advanced NSCLC. No new safety signals were reported.

OA03.03

Nivolumab (NIVO) + ipilimumab (IPI) Versus Platinum-Doublet Chemotherapy (Chemo) as First-Line (1L) Treatment for Advanced Non-Small Cell Lung Cancer (aNSCLC): 3-year Update from CheckMate 227 Part 1

Suresh S. Ramalingam[1], Tudor Eliade Ciuleanu[2], Adam Pluzanski[3], Jong-Seok Lee[4], Michael Schenker[5], Reyes Bernabe Caro[6], Ki Hyeong Lee[7], Bogdan Zurawski[8], Clarisse Audigier-Valette[9], Mariano Provencio[10], Helena Linardou[11], Sang-We Kim[12], Hossein Borghaei[13], Matthew David Hellmann[14], Kenneth John O'Byrne[15], Luis G. Paz-Ares[16], Martin Reck[17], Faith Ellen Nathan[18], **Julie R. Brahmer[19]**

[1]Winship Cancer Institute, Emory University, Atlanta, USA, [2]Institutul Oncologic Orif Dr Ion Chiricuta and UNF Iulia Hatieganu, Cluj Napoca, Romania, [3]Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland, [4]Seoul National University Bundang Hospital, Seongnam, Republic of Korea, [5]SF. Nectarie Oncology Center, Craiova, Romania, [6]Hospital Universitario Virgen Del Rocio, Instituto de Biomedicina de Sevilla, Sevilla, Spain, [7]Chungbuk National University Hospital, Cheongju, Republic of Korea, [8]Ambulatorium Chemioterapii, Bydgoszcz, Poland, [9]Hôpital Sainte Musse, Toulon, France, [10]Hosp. Univ. Puerta De Hierro, Madrid, Spain, [11]Metropolitan Hospital, Neo Faliro, Greece, [12]Asan Medical Center, Seoul, Republic of Korea, [13]Fox Chase Cancer Center, Philadelphia, USA, [14]Memorial Sloan Kettering Cancer Center, New York, USA, [15]Princess Alexandra Hospital, Brisbane, Queensland, Australia, [16]Hospital Universitario 12 de Octubre, CNIO, Universidad Complutense & CiberOnc, Madrid, Spain, [17]Lung Clinic Grosshansdorf, Airway Research Center North, German Center for Lung Research, Grosshansdorf, Germany, [18]Bristol Myers Squibb, Princeton, USA, [19]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, USA

Oral Abstract Session 1, October 16, 2020, 15:20 - 17:00

Background: In CheckMate 227 Part 1 (NCT02477826), 1L NIVO+IPI significantly improved overall survival (OS) vs chemo in patients with aNSCLC and tumor PD-L1 ≥1% (primary analysis) or <1% (descriptive analysis). We report data with 3-year minimum follow-up. **Methods:** Patients with stage IV/recurrent NSCLC and PD-L1 ≥1% (n=1189) were randomized to NIVO (3 mg/kg Q2W)+IPI (1 mg/kg Q6W), NIVO (240 mg Q2W), or chemo. Patients with PD-L1 <1% (n=550) were randomized to NIVO+IPI, NIVO (360 mg Q3W)+chemo, or chemo. Primary endpoint was OS with NIVO+IPI vs chemo in patients with PD-L1 ≥1%. An exploratory analysis was OS by response status (CR/PR, SD, progressive disease [PD]) at 6 months. **Results:** After median follow-up of 43.1 months, patients with PD-L1 ≥1% had continued OS benefit from NIVO+IPI vs chemo (HR: 0.79; 95% CI, 0.67–0.93); 3-year OS rates were 33% (NIVO+IPI), 29% (NIVO), and 22% (chemo). At 3 years, 18%, 12%, and 4% of patients with PD-L1 ≥1% treated with NIVO+IPI, NIVO, and chemo, respectively, remained progression-free; 38%, 32%, and 4% of confirmed responders remained in response at 3 years. In patients with PD-L1 <1%, OS HR for NIVO+IPI vs chemo was 0.64 (95% CI, 0.51–0.81); 3-year OS rates were 34% (NIVO+IPI), 20% (NIVO+chemo), and 15% (chemo); 13%, 8%, and 2% of patients remained progression-free; 34%, 15%, and 0% of confirmed responders remained in response. Effect of CR/PR, SD, or PD at 6 months on subsequent OS in patients with PD-L1 ≥1% is shown (Table). Any-Grade/Grade 3–4 treatment-related AEs were observed in 77%/33% and 82%/36% of all patients treated with NIVO+IPI and chemo, respectively. **Conclusions:** NIVO+IPI provided durable and long-term OS benefit vs chemo in 1L aNSCLC. Patients with PD-L1 ≥1% and had CR/PR at 6 months had marked OS benefit with NIVO+IPI. No new safety signals were identified for NIVO+IPI.

Table. Exploratory Landmark Analysis of OS by Response Status at 6 Months in Patients With PD-L1 ≥1%* (NIVO+IPI vs Chemo)

Patients alive at 6 months	Response status at 6 months, %	Post-landmark 1-year OS rate, %	Post-landmark 2-year OS rate, %	Post-landmark 3-year OS rate, %
NIVO+IPI (n = 295) vs Chemo (n = 306)	CR or PR, 39 vs 25	90 vs 73	76 vs 51	70 vs 39
	SD, 14 vs 18	69 vs 54	45 vs 38	34 vs 33
	PD, 46 vs 58	44 vs 47	22 vs 25	19 vs 17

* Results in PD-L1 <1% patients will be presented.

OA03.04

Tislelizumab Plus Chemotherapy vs Chemotherapy Alone as First-line Treatment for Advanced Squamous Non-Small Cell Lung Cancer

Jie Wang[1], S. Lu[2, 3], C. Hu[4], Y. Sun[5], K. Yang[6], M. Chen[7], J. Zhao[8], G. Yu[9], X. Zhou[10], G. Feng[11], Y. Pan[12], Y. Yu[13], J. Zhang[14], L. Liang[14], X. Lin[14], J. Cui[15]

[1]National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, [2]Shanghai Chest Hospital, Shanghai, China, [3]Shanghai Chest Hospita, Jiao Tong University, China, [4]The Second Hospital of Central South University, Changsha, China, [5]Jinan Central Hospital, Jinan, China, [6]Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Hubei, China, [7]The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [8]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education, Beijing), Department of Thoracic Medical Oncology, Peking University Cancer Hospital & Institute, Beijing, China, [9]Weifang People's Hospital, Weifang, China, [10]The First Affiliated Hospital to AMU (Southwest Hosptial), Luzhou, China, [11]The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, China, [12]Anhui Provincial Hospital, Hefei, China, [13]The Harbin Medical Cancer Hospital, The 3rd Department of Thoracic Oncology, Harbin, China, [14]BeiGene (Beijing) Co., Ltd., Beijing, China, [15]The First Hospital of Jilin University, Changchun, China

Oral Abstract Session 1, October 16, 2020, 15:20 - 17:00

PD-1/L1 inhibitors have provided new treatment approaches for patients with advanced NSCLC; however, resistance or low PD-L1 expression may limit clinical benefit. Tislelizumab, an anti-PD-1 monoclonal antibody, was engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. Tislelizumab, alone and with chemotherapy, demonstrated antitumor activity and was generally well tolerated in patients with advanced NSCLC, irrespective of PD-L1 expression. This open-label phase 3 study (NCT03594747) evaluated the efficacy and safety/tolerability of tislelizumab plus chemotherapy as first-line treatment in Chinese patients with histologically confirmed stage IIIB/IV squamous NSCLC. Patients (randomized 1:1:1) received IV Q3W: tislelizumab (200 mg, D1) plus paclitaxel (175 mg/m2, D1) and arboplatin (AUC 5, D1) (Arm A); tislelizumab plus nab-paclitaxel (100 mg/m2; D1, 8, and 15) and carboplatin (AUC 5, D1) (Arm B); or paclitaxel (175 mg/m2, D1) and carboplatin (AUC 5, D1) (Arm C). Patients were stratified by disease stage (IIIB vs IV) and tumor cell PD-L1 expression (<1% vs 1-49% vs ≥50%) as assessed using the VENTANA PD-L1 (SP263) Assay. Chemotherapy was administered for 4-6 cycles at investigator's discretion; crossover to tislelizumab monotherapy was allowed for patients in Arm C. The primary endpoint was PFS by Independent Review Committee per RECIST v1.1; secondary endpoints included ORR, DoR per RECIST v1.1, OS, and safety/tolerability. Across the 360 patients, PFS was significantly improved and higher ORR/DoR was observed with combination treatment (A and B) versus chemotherapy (C); there was no apparent relationship between PD-L1 expression and PFS or ORR (Table). Across all arms, median OS was not reached. Median number of treatment cycles was comparable across all arms and discontinuation of any treatment due to AEs was reported in 12.5%, 29.7%, and 15.4% of patients in Arms A, B, and C, respectively. The most common grade ≥3 AE was decreased neutrophil count, in line with known hematological toxicity of chemotherapy. Treatment-related AEs leading to death occurred in six patients (n=1 [A]; n=2 [B]; n=3 [C]); none were solely attributed to tislelizumab. First-line tislelizumab plus paclitaxel/carboplatin or nab-paclitaxel/carboplatin significantly improved PFS for patients with squamous NSCLC and demonstrated higher ORR than chemotherapy alone, irrespective of PD-L1 expression. The safety profile was comparable with those of tislelizumab, chemotherapy, and underlying NSCLC; no new safety signals were identified with the addition of tislelizumab to chemotherapy.

ITT Population (N=360)	***Arm A* (n=120)**	***Arm B* (n=119)**	***Arm C* (n=121)**
Median PFS, mo (95% CI)	**7.6 (6.0-9.8)**	**7.6 (5.8-11.0)**	**5.5 (4.2-5.7)**
HR[a] (95% CI)	0.52 (0.4-0.7)	0.48 (0.3-0.7)	NA
P-value[b]	0.0001	<0.0001	
ORR, % (95% CI)	**72.5 (63.6, 80.3)**	**74.8 (66.0, 82.3)**	**49.6 (40.4, 58.8)**
Median DoR, (95% CI)	**8.2 (5.0, NE)**	**8.6 (6.3, NE)**	**4.2 (2.8, 4.9)**
PD-L1 ≥50% TC (N=125)	***Arm A* (n=42)**	***Arm B* (n=42)**	***Arm C* (n=41)**
Median PFS, mo (95% CI)	**7.6 (5.6, 9.8)**	**7.6 (5.6, NE)**	**5.5 (4.1, 7.0)**
HR[c] (95% CI)	0.501 (0.282, 0.891)	0.425 (0.232, 0.776)	NA
ORR, % (95% CI)	**78.6 (63.2, 89.7)**	**88.1 (74.4, 96.0)**	**53.7 (37.4, 69.3)**
PD-L1 1-49% TC (N=91)	***Arm A* (n=30)**	***Arm B* (n=30)**	***Arm C* (n=31)**
Median PFS, mo (95% CI)	**7.6 (5.5, NE)**	**NE (5.6, NE)**	**4.2 (2.8, 6.5)**
HR[c] (95% CI)	0.439 (0.221, 0.870)	0.311 (0.145, 0.664)	NA
ORR, % (95% CI)	**70.0 (50.6, 85.3)**	**66.7 (47.2, 82.7)**	**41.9 (24.5, 60.9)**
PD-L1 <1% TC (N=144)	***Arm A* (n=48)**	***Arm B* (n=47)**	***Arm C* (n=49)**
Median PFS, mo (95% CI)	**7.6 (5.5, NE)**	**7.4 (5.6, 9.7)**	**5.5 (4.2, 7.0)**
HR[c] (95% CI)	0.636 (0.368, 1.101)	0.692 (0.406, 1.178)	NA
ORR, % (95% CI)	**68.8 (53.7, 81.3)**	**68.1 (52.9, 80.9)**	**51.0 (36.3, 65.6)**

Abbreviations: CI, confidence interval; DoR, duration of response; HR, hazard ratio; ITT, intention-to-treat; mo, months; NA, not available; NE, not evaluable; ORR, objective response rate; PFS, progression-free survival; TC, tumor cell.

[a]Stratified; [b]One-sided log-rank test; [c]Non-stratified.

OA03.07

Pembrolizumab for Advanced Mesothelioma: Results from the Phase 2 KEYNOTE-158 Study

Timothy A. Yap[1], Kazuhiko Nakagawa[2], Nobukazu Fujimoto[3], Kozo Kuribayashi[4], Tormod Guren[5], Luana Calabrò[6], Ronnie Shapira Frommer[7], Bo Gao[8], Steven Kao[9], Ignacio Matos[10], David Planchard[11], Arkendu Chatterjee[12], Fan Jin[12], Kevin Norwood[12], Hedy L. Kindler[13]

[1]Royal Marsden Hospital, London, United Kingdom, [2]Department of Medical Oncology, Kindai University Hospital, Osaka, Japan, [3]Okayama Rosai Hospital, Okayama, Japan, [4]Hyogo College of Medicine, Hyogo, Japan, [5]Department of Oncology, Oslo University Hospital, Oslo, Norway, [6]Medical Oncology and Immunotherapy, Center for Immuno-Oncology, Department of Oncology, University Hospital of Siena, Siena, Italy, [7]Chaim Sheba Medical Center, Ramat Gan, Israel, [8]Blacktown Hospital, Blacktown, Australia, [9]Chris O'Brien Lifehouse, Camperdown, Australia, [10]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain, [11]Department of Medical Oncology, Thoracic Unit, Gustave Roussy, Villejuif, France, [12]Merck & Co., Inc., Kenilworth, USA, [13]University of Chicago, Chicago, USA

Oral Abstract Session 1, October 16, 2020, 15:20 - 17:00

Background: Pembrolizumab showed preliminary clinical benefit in patients with PD-L1–positive malignant pleural mesothelioma (MPM) in the KEYNOTE-028 study. Here we report the results for patients with MPM regardless of PD-L1 expression enrolled in KEYNOTE-158 (ClinicalTrials.gov, NCT02628067), a phase 2 multicohort study of pembrolizumab in rare cancers. **Methods:** Patients enrolled in this cohort were ≥18 years with advanced MPM and failure of, progression on, or intolerance to standard therapy; measurable disease per RECIST version 1.1; ECOG PS ≤1; and tumor samples evaluable for biomarkers (including PD-L1 expression). PD-L1 positivity was defined as a PD-L1 combined positive score ≥1 using the PD-L1 IHC 22C3 pharmDx assay. Pembrolizumab 200 mg Q3W was administered for 35 cycles or until disease progression/intolerable toxicity. The primary endpoint was ORR. Secondary endpoints were duration of response (DOR), PFS, OS, and safety. Tumor imaging was performed every 9 weeks for 1 year and every 12 weeks thereafter. Response was assessed per RECIST version 1.1 by independent central radiologic review. **Results:** As of June 27, 2019, 118 patients were enrolled. Median time from first dose to data cutoff was 38.5 (range, 34.3–40.5) months. 5 patients (4%) had completed 35 cycles of pembrolizumab and 113 had discontinued, most commonly due to progressive disease (88 patients [75%]; 72 radiographic, 16 clinical) and AEs (19 patients [16%]). 61 patients (52%) had received ≥2 prior therapies. Tumors were PD-L1–positive in 77 patients (65%), PD-L1–negative in 31 patients (26%), and nonevaluable in 10 patients (9%). ORR was 8% (10/118 [all partial responses]; 95% CI, 4–15) overall, 8% (6/77; 95% CI, 3–16) in patients with PD-L1–positive tumors, and 13% (4/31; 95% CI, 4–30) in patients with PD-L1–negative tumors. Median DOR was 14.3 (range, 4.0–33.9+) months in all patients. Median PFS was 2.1 (95% CI, 2.1–3.9) months in all patients. Median OS was 10.0 (95% CI, 7.6–13.4) months overall, with an estimated OS rate at 12 months of 45%. Treatment-related AEs occurred in 82 patients (69%), 20 (17%) of whom had grade 3–5 events (most frequent: rash, n=15; fatigue, n=14); 1 patient died due to a treatment-related AE (apnea). **Conclusion:** Pembrolizumab showed durable responses (ORR, 8%; median DOR, 14.3 months; 12-month OS, 45%) in previously treated patients with advanced MPM regardless of PD-L1 expression. Toxicity was consistent with previous studies evaluating pembrolizumab monotherapy.

OA03.08

Trilaciclib Reduces the Need for Growth Factors and Red Blood Cell Transfusions to Manage Chemotherapy-Induced Myelosuppression

Gunta Purkalne[13], **Renata Ferrarotto[1]**, Ian Anderson[2], Balazs Medgyasszay[3], Maria Rosario García-Campelo[4], William Edenfield[5], Trevor Feinstein[6], Jennifer Johnson[7], Sujith Kalmadi[8], Philip Lammers[9], Gunta Purkalne[13], Alfredo Sanchez Hernandez[10], Yili Pritchett[11], Rajesh K. Malik[11], Shannon R. Morris[11], Tibor Csőszi[12]
[1]University of Texas MD Anderson Cancer Center, Houston, United States, [2]St Joseph Heritage Healthcare, Santa Rosa, United States, [3]Veszprém County Lung Medicine Institute, Veszprém, Hungary, [4]Hospital Teresa Herrera, A Coruña, Spain, [5]Prisma Health Cancer Institute, Greenville, United States, [6]Piedmont Cancer Institute, Atlanta, United States, [7]Thomas Jefferson University Hospital, Philadelphia, United States, [8]Ironwood Cancer & Research Center, Chandler, United States, [9]Meharry Medical College, Nashville, United States, [10]Hospital Provincial de Castellon, Castelló, Spain, [11]G1 Therapeutics, Inc., Research Triangle Park, United States, [12]Hetenyi Geza Korhaz, Szolnok, Hungary, [13]Pauls Stradins Clinical University Hospital, Riga, Latvia

Oral Abstract Session 1, October 16, 2020, 15:20 - 17:00

Background: Supportive care interventions for chemotherapy-induced myelosuppression, including granulocyte colony-stimulating factors (G-CSF), erythropoiesis-stimulating agents (ESA), and red blood cell (RBC) transfusions, add to the physical and economic burden of cancer patients. Trilaciclib is a transient intravenous CDK4/6 inhibitor that protects hematopoietic stem and progenitor cells and immune system function from chemotherapy-induced damage (myelopreservation). Here, the relationship between supportive care interventions and the myelopreservation benefits of trilaciclib was explored.**Methods:** Data were pooled from three randomized, double-blind, placebo-controlled, phase 2 clinical studies of trilaciclib administered prior to chemotherapy in patients with extensive-stage small cell lung cancer (NCT02499770; NCT03041311; NCT02514447). Duration of severe (grade 4) neutropenia (DSN) and occurrence of SN and RBC transfusions were analyzed across cycles 1–4 of treatment, and concordance and association between grade 3/4 decreased hemoglobin levels (anemia), RBC transfusions on/after week 5, and ESA administration was determined. **Results:** Overall, among patients receiving trilaciclib or placebo prior to chemotherapy, use of G-CSF, ESA, or RBC transfusions on/after week 5 was 28.5% versus 56.3% ($P < 0.0001$), 3.3% versus 11.8% ($P = 0.0254$), and 14.6% versus 26.1% ($P = 0.0252$), respectively. Across cycles 1–4, trilaciclib reduced DSN and the percentage of patients with SN, irrespective of G-CSF administration, and fewer patients receiving trilaciclib needed RBC transfusions (Table). RBC transfusions and ESA were mostly reserved for patients with grade 3/4 anemia; however, while most patients with grade 3/4 anemia received RBC transfusions, grade 3/4 anemia did not frequently result in ESA administration (Table). **Conclusions:** Administering trilaciclib prior to chemotherapy significantly reduces utilization of supportive care interventions. Chemotherapy-induced SN is reduced with trilaciclib, irrespective of G-CSF administration. Grade 3/4 anemia was more highly correlated with RBC transfusions than ESA administration, supporting the clinical relevance of RBC transfusions on/after week 5 as an endpoint to assess the multilineage benefits of trilaciclib.

	Trilaciclib prior to chemotherapy (n = 123)		Placebo prior to chemotherapy (n = 119)	
G-CSF administration	**Yes**	**No**	**Yes**	**No**
Mean DSN, days (SD)				
Cycle 1	0 (1.0)	0 (1.9)	7 (5.5)	4 (4.8)
Cycle 2	1 (1.6)	0 (0.7)	2 (5.2)	1 (3.0)
Cycle 3	0 (1.9)	0 (0.4)	1 (2.3)	2 (5.8)
Cycle 4	0 (0.0)	0 (0.0)	1 (3.4)	1 (1.9)
Patients with SN, n/n (%)				
Cycle 1	2/12 (16.7)	6/108 (5.6)	20/25 (80.0)	38/94 (41.3)
Cycle 2	2/17 (11.8)	2/92 (2.2)	10/39 (25.6)	11/68 (16.2)
Cycle 3	1/17 (5.9)	2/79 (2.5)	7/44 (15.9)	8/54 (14.8)
Cycle 4	0/18 (0.0)	0/68 (0.0)	3/40 (7.5)	4/51 (7.8)
Patients with RBC transfusion, n/n (%)				
Cycle 1	9/123 (7.3)		10/119 (8.4)	
Cycle 2	7/109 (6.4)		11/107 (10.3)	
Cycle 3	8/96 (8.3)		14/98 (14.3)	
Cycle 4	5/86 (5.8)		13/91 (14.3)	
Grade 3/4 anemia	**Yes**	**No**	**Yes**	**No**
Patients with RBC transfusion on/after week 5, n (%)	16 (13.0)	2 (1.6)	29 (24.4)	2 (1.7)
Patients without RBC transfusion on/after week 5, n (%)	9 (7.3)	96 (78.0)	9 (7.6)	79 (66.4)
Chi-square *P* value	<0.0001		<0.0001	
Cohen's kappa	0.6917		0.7764	
Patients with ESA administration, n (%)	3 (2.4)	1 (0.8)	12 (10.1)	2 (1.7)
Patients with no ESA administration, n (%)	22 (17.9)	97 (78.9)	26 (21.8)	79 (66.4)
Chi-square *P* value	0.0057		<0.0001	
Cohen's kappa	0.1598		0.3497	
ESA administration	**Yes**	**No**	**Yes**	**No**
Patients with RBC transfusion on/after week 5, n (%)	3 (12.0)	13 (52.0)	9 (23.7)	20 (52.6)
Patients without RBC transfusion on/after week 5, n (%)	0 (0.0)	9 (36.0)	3 (7.9)	6 (15.8)
Chi-square *P* value	0.1661		0.8969	
Cohen's kappa	0.1425		–0.0139	

DSN, duration of severe neutropenia; ESA, erythropoiesis-stimulating agent; G-CSF, granulocyte colony-stimulating factors; RBC, red blood cell; SD, standard deviation; SN, severe neutropenia.

OA05.02

Analysis of Resistance Mmechanisms to Pralsetinib in Patients with RET Fusion-Positive Non-Small Cell Lung Cancer (NSCLC) from the ARROW Study

Justin Gainor[1], Giuseppe Curigliano[2], Robert C. Doebele[3], Jessica J. Lin[1], S.-H. Ou[4], Stephen Miller[5], Christopher D. Turner[5], Vivek Subbiah[6]

[1]Massachusetts General Hospital, Boston,, United States, [2]European Institute of Oncology, IRCCS, University of Milano, Milan, Italy, [3]University of Colorado Cancer Center, Aurora,, United States, [4]University of California Irvine School of Medicine, Orange,, United States, [5]Blueprint Medicines Corporation, Cambridge,, United States, [6]The University of Texas MD Anderson Cancer Center, Houston,, United States

Oral Abstract Session 2, October 17, 2020, 07:50 - 09:35

Background: Chromosomal rearrangements involving the RET receptor tyrosine kinase are validated oncogenic drivers in 1–2% of patients with NSCLC. Pralsetinib is a selective RET tyrosine kinase inhibitor that has demonstrated clinical activity in patients with NSCLC harboring a RET fusion. Here, we report potential mechanisms of resistance in patients with NSCLC whose disease progressed on pralsetinib. **Methods:** Patients with RET fusion-positive NSCLC were included in the ongoing phase 1/2 ARROW study (NCT03037385). Patients were treated with pralsetinib at 60–600 mg once daily or 100–200 mg twice daily in phase 1 dose-escalation and at 400 mg once daily in phase 2 expansion. Paired plasma samples were collected at baseline and following radiologic disease progression according to RECIST v1.1. Plasma samples were analyzed by next generation sequencing using a 64-gene panel (PlasmaSelect™ 64, Personal Genome Diagnostics). **Results:** Paired baseline/progression plasma samples were available from 48 patients enrolled in the study. A RET fusion was detected in plasma at baseline in 36 (75%) of these patients. At disease progression, 6 (17%) of these 36 patients had no detectable fusion, and 21 (58%) had only the RET fusion originally observed. Acquired RET resistance mutations in the kinase domain were seen in 4 (11%) patients (G810C, L730V, G810S + L730V, G810C + T729_L730delinsL, n=1 for each). Potential off-target mechanisms of resistance were observed in 4 (11%) patients. Sample collection is ongoing. **Conclusions:** These preliminary results demonstrate a diversity of resistance mechanisms in patients with NSCLC treated with pralsetinib. However, in 75% of the cases no putative resistance mechanism was identified. In the remaining 25%, on-target acquired resistance due to mutations in RET and potential off-target mechanisms that have been observed with other tyrosine kinase inhibitors were seen at similar frequencies. Additional insights from tissue biopsies and further understanding of resistance mechanisms will help inform potential next-generation RET inhibitor profiles and appropriate combination strategies.

OA05.03

Tepotinib in Patients with Advanced NSCLC with MET Exon 14 (METex14) Skipping: Overall Efficacy Results from VISION Cohort A

Julien Mazieres[1], Paul Paik[2], Enriqueta Felip[3], Remi Veillon[4], Hiroshi Sakai[5], Alexis Cortot[6], Santiago Viteri[7], Marina Garassino[8], Jan Van Meerbeeck[9], Jo Raskin[9], Michael Thomas[10], Masahiro Morise[11], Byoung Chul Cho[12], Pierfranco Conte[13], Rolf Bruns[14], Tim Demuth[15], Karl Maria Schumacher[15], Xiuning Le[16]

[1]CHU de Toulouse, Institut Universitaire du Cancer, Toulouse, France, [2]Thoracic Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, USA, [3]Department of Oncology, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, [4]CHU Bordeaux, service des maladies respiratoires, Bordeaux, France, [5]Department of Thoracic Oncology, Saitama Cancer Center, Saitama, Japan, [6]Univ. Lille, CHU Lille, CNRS, Inserm, Institut Pasteur de Lille, UMR9020 – UMR-S 1277 - Canther, F-59000 Lille, France, [7]Dr Rosell Oncology Institute, Dexeus University Hospital, QuironSalud Group, Barcelona, Spain, [8]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, [9]Department of Pulmonology and Thoracic Oncology, Antwerp University Hospital (UZA), Edegem, Belgium, [10]Thoraxklinik, University Heidelberg and Translational Lung Research Center Heidelberg (TLRC-H), The German Center for Lung Research (DZL), Heidelberg, Germany, [11]Department of Respiratory Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan, [12]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea, [13]Department of Surgery, Oncology and Gastroenterology, University of Padova and Oncologia Medica 2, Istituto Oncologico Veneto, I.R.C.C.S., Padova, Italy, [14]Department of Biostatistics, Merck KGaA, Darmstadt, Germany, [15]Global Clinical Development, Merck KGaA, Darmstadt, Germany, [16]Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, USA

Oral Abstract Session 2, October 17, 2020, 07:50 - 09:35

Background: The multi-cohort Phase II VISION study investigates tepotinib in patients with NSCLC harboring MET alterations, and is the largest study of patients with METex14 skipping detected by liquid (L+) or tissue (T+) biopsy. Here, we report efficacy outcomes in the overall intention-to-treat population. **Methods:** Patients with advanced, EGFR/ALK wild-type, METex14 skipping NSCLC received oral tepotinib 500 mg once daily. Evaluable patients for objective response rate (ORR) had ≥2 post-baseline assessments or discontinuation for any reason. Primary endpoint: ORR by independent review committee (IRC). Secondary endpoints: investigator-assessed (INV) ORR, duration of response (DOR), progression-free survival (PFS), and safety. Subgroup analyses were preplanned. **Results:** As of 01 Jan 2020, Cohort A enrolled 152 patients: 52% male, median age 73 years (range 41–94), 43% non-smokers, 55% had received prior treatment for advanced/ metastatic disease. Overall ORR (95% CI) in evaluable patients (n=146; 95 L+, 84 T+) was 44.5% (36.3, 53.0) by IRC and 54.8% (46.4, 63.0) by INV. ORR was consistent across subgroups, supporting robustness of efficacy (table). Median DOR (95% CI) in L+ patients was 9.9 months (7.2, not estimable [ne]) by IRC and 14.0 months (7.2, ne) by INV, and in T+ patients was 12.4 months (9.7, ne) by IRC and 16.4 months (9.7, ne) by INV. Median PFS in L+ patients was 8.5 months (6.7, 10.9) by IRC and 8.5 months (5.8, 11.0) by INV, and in T+ patients was 11.0 months (7.8, 17.1) by IRC and 12.2 months (6.8, 19.6) by INV. Grade ≥3 treatment-related adverse events (TRAEs) were reported by 27.6% of patients; 17 (11.2%) discontinued due to TRAEs, mostly peripheral edema (4.6%). The safety profile was similar across subgroups. **Conclusion:** Tepotinib has durable clinical activity across subgroups and manageable toxicity in the largest study of patients with METex14 skipping NSCLC identified by L+ or T+. Previously presented at ESMO Congress 2020, "FNP:1283P", "Julien Mazieres et al." - Reused with permission

ORR, % (95% CI)	Independent review committee	Investigator-assessed
Liquid-biopsy group	47.4 (37.0, 57.9)	54.7 (44.2, 65.0)
Tissue-biopsy group	45.2 (34.3, 56.5)	58.3 (47.1, 69.0)
Gender		
Male	46.1 (34.5, 57.9)	52.6 (40.8, 64.2)
Female	42.9 (31.1, 55.3)	57.1 (44.7, 68.9)
Age		
<75 years	50.0 (38.6, 61.4)	56.3 (44.7, 67.3)
≥75 years	37.9 (26.2, 50.7)	53.0 (40.3, 65.4)
Race		
Caucasian	43.1 (33.4, 53.3)	52.0 (41.8, 62.0)
Asian	47.4 (31.0, 64.2)	60.5 (43.4, 76.0)
ECOG performance score		
0	59.5 (42.1, 75.2)	56.8 (39.5, 72.9)
1	39.4 (30.2, 49.3)	54.1 (44.3, 63.7)
Smoker		
Yes	51.3 (39.6, 63.0)	51.3 (39.6, 63.0)
No	35.5 (23.7, 48.7)	56.5 (43.3, 69.0)
Therapy line		
1	44.6 (32.3, 57.5)	52.3 (39.5, 64.9)
≥2	44.4 (33.4, 55.9)	56.8 (45.3, 67.8)
Prior platinum-based therapy		
Yes	48.6 (36.7, 60.7)	58.3 (46.1, 69.8)
No	42.3 (30.6, 54.6)	50.7 (38.6, 62.8)

OA05.04

Real-World Progression-Free Survival in Oncogenic Driver-Mutated Non-Small Cell Lung Cancer (NSCLC) Treated With Single-Agent Immunotherapy

Joseph Bodor[1], J. Bauman[1], E. Handorf[1], C. Zawislak[1], E. Ross[1], M. Clapper[1], J. Treat[1]
[1]*Fox Chase Cancer Center, Philadelphia, United States*

Oral Abstract Session 2, October 17, 2020, 07:50 - 09:35

Checkpoint inhibitors have dramatically changed the treatment landscape for advanced NSCLC, however only a fraction of patients (pts) benefit with durable responses. Tumors that possess oncogenic driver mutations may have increased resistance to PD-1/PDL-1 inhibitors based on subgroup data from clinical trials, though little research has been performed using large real-world patient cohorts, nor is it clear whether PD-L1 expression or smoking history is predictive of immunotherapy response in these pts. This retrospective study assessed realworld progression-free survival (rwPFS) in pts with driver-mutated advanced NSCLC and correlated endpoints with PD-L1 expression and smoking history. The nationwide Flatiron Health Electronic Health Record (EHR)-derived deidentified database was used to analyze data from pts with advanced NSCLC with tumors possessing an oncogenic driver mutation treated with single-agent immunotherapy (pembrolizumab, nivolumab, or atezolizumab). Median rwPFS (based on clinician documentation of clinical progression) in months (m) was determined for tumor molecular subtypes (EGFR, ALK, BRAF, and KRAS) and correlated to PD-L1 expression and smoking history. Kaplan-Meier curves characterized rwPFS and comparisons were assessed in the overall cohort and in driver-mutated subgroups using the log-rank test. 1,746 pts with driver-mutated tumors involving alterations in EGFR (n = 458), ALK (n = 65), BRAF (n = 146), and KRAS (n = 1077) received single-agent immunotherapy between 4/23/14 to 2/28/19. Median age was 69 years, 58% were female, and 19% had no smoking history. Median rwPFS varied significantly by tumor mutation subtypes ($p < 0.001$) with KRAS- (3.3 m, 95% CI 3.0, 3.6) and BRAF-mutated (3.6 m, 95% CI 2.6, 4.7) tumors having longer rwPFS than EGFR- (2.5 m, 95% CI 2.3, 2.6) and ALK-mutated tumors (2.3 m, 95% CI 1.6, 3.1). Percent progression-free at 12 m was 21% for KRAS-, 21% for BRAF-, 8% for EGFR-, and 11% for ALK-mutated tumors. In a subset of 795 patients, PD-L1 expression data were available. Only in KRAS-mutated tumors did rwPFS vary significantly by PD-L1 expression with PD-L1 positive (> 1%) tumors having longer rwPFS than PD-L1 negative tumors (4.2 m vs. 3.0 m, $p < 0.001$). PD-L1 expression was not associated with rwPFS in EGFR-, ALK-, or BRAF-mutated tumors. However, a history of smoking was associated with longer rwPFS as compared to no smoking history in EGFR- (2.6 m vs. 2.3 m, $p < 0.05$) and ALKmutated tumors (3.0 m vs. 2.1 m, $p < 0.05$). In this study, of one of the largest cohorts of pts with driver-mutated NSCLC to date, rwPFS with single-agent checkpoint inhibitors varied significantly between oncogenic mutation subtypes. PD-L1 expression may not be a useful biomarker of immunotherapy response in EGFR-, ALK-, and BRAF-mutated tumors. Moreover, rwPFS was relatively short for EGFR- and ALK-mutated tumors and patients with these molecular subtypes of NSCLC may derive little benefit from single-agent immunotherapy. Continued study in these sub-populations of immuno-chemo +/- VEGF inhibitor therapy combinations that may overcome resistance to PD-1/PD-L1 inhibitors is needed.

OA05.07
Lung Cancer Screening Modifies Smoking Behavior

Monica Reyes[1], Jaileene Perez-Morales[1], Vani Simmons[2], Matthew Schabath[1]
[1]*Department of Cancer Epidemiology, H. Lee Moffitt Cancer Center & Research Institute, Tampa, United States,* [2]*Department of Health Outcomes and Behavior, H. Lee Moffitt Cancer Center & Research Institute, Tampa, United States*

Oral Abstract Session 2, October 17, 2020, 07:50 - 09:35

Background: Multiple randomized clinical trials have demonstrated that screening high-risk smokers with low-dose computed tomography (LDCT) is associated with a significant reduction in lung cancer mortality. However, it's unclear whether disclosure of screening results has an impact on changes in smoking behavior. As such, using baseline and follow-up data from National Lung Screening Trial (NLST), we conducted a post hoc analysis to determine if smoking behavior changed after participants received the results of their LDCT screen. **Methods:** Baseline and follow-up demographic, clinical, and smoking-related data was obtained on a subset of participants (N=6,802) in the LDCT-arm of the NLST. Follow-up smoking data was analyzed after participants received the results of their LDCT screen (positive screen result vs. negative screen result) at three different intervals: baseline (T0), year 1 (T1), and year 2 (T2). Smoking status was defined as current or former and the Fagerstrom Test for Nicotine Dependence (FTND) score was used to assess low, moderate, or high nicotine dependency at baseline. Logistic regression analyses were performed to analyze the association between screening results and smoking status at follow-up. The data were stratified by smoking status prior to the screen and baseline nicotine dependency. Demographics were assessed as other potential effect modifiers. **Results:** Among current smokers at baseline who were highly nicotine dependent, we found an inverse association (OR=0.60; 95% CI 0.48-0.75) suggesting current smokers were quitting smoking after receiving their screening results. At the T1 screening interval, a similar association was found for current smokers who were highly nicotine dependent, but the point estimate was not statistically significant (OR=0.85; 95% CI 0.61-1.20). Interestingly, highly nicotine dependent current smokers at the T2 screening interval appeared to be reinitiating smoking (OR=1.45; 95% CI 0.75-2.78) after receiving their screening results. The former smokers at baseline who were highly nicotine dependent appeared to be reinitiating smoking (OR=1.39; 95% CI 0.86-2.24) after receiving their T0 screening results and this trend continued at the T1 (OR=1.11; 95% CI 0.76-1.63) and T2 (OR=1.45; 95% CI 0.89-2.38) screening intervals. There was evidence that pack-years smoked, sex, race, ethnicity, education, and marital status influenced changes in smoking behavior after the T2 screening interval. **Conclusion:** This is one of the first analyses to investigate longitudinal changes in smoking behavior following the results of lung cancer screening. Our findings highlight the potential value of assessing nicotine dependency to predict smoking behavior in the lung cancer screening setting.

OA05.08

Trends of Incidence and Burden of Metastatic Disease at Diagnosis of Lung Cancer after Implementation of Low Dose CT Screening in the United States

Manoj P Rai[2], P. Bedi[1], B. Ansari[3], S. Siddappa Malleshappa[4], P. Neupane[3], C. Huang[3], J. Zhang[3], K. Mehta[3]
[1]UPMC East, Pittsburgh, United States, [2]Asante Rogue Regional Medical Center, Medford, United States, [3]University of Kansas Medical Center, Kansas City, United States, [4]Bay State Medical Center, Springfield, United States

Oral Abstract Session 2, October 17, 2020, 07:50 - 09:35

The incidence of lung cancer has been declining in the United States (US) from 2007 to 2014. However, the impact of the implementation of low dose CT screening (LDCT) in high-risk population in 2015, on the incidence of lung cancer and on the proportion of patients with metastatic disease at the time of diagnosis in that population is unknown. We conducted a cross-sectional study using Surveillance, Epidemiology, and End Results data to identify trends of incidence of lung cancer and the proportion of patients with metastatic disease at the time of diagnoses across 4 periods from 2007 to 2016. Period 1 and period 2 occurred before the publication of the National Lung Cancer Screening Trial (NLST) to establish baseline trends (2007- 2009 and 2010- 2011 respectively). Period 3 and period 4 were after the publication of NLST (2012-2014) and LDCT implementation (2015-2016) respectively. The population of interest was between the age of 55-79 years. The study included 471,300 patients with newly diagnosed lung cancer with age of 55-79 years (mean age 68.2 [6.7] years, 52.5% male, 83.3% white, 11.1% black and 5.4% Hispanic). The age-adjusted incidence of lung cancer steadily declined from 243.9 per 100k population in period 1 to 203.2 per 100k population in period 4. The proportion of patients with metastatic disease at the time of diagnoses was stable before the publication of NLST (0.04% increase from period 1 to period 2, p=0.8) and remained stable after the publication of NLST until the implementation of LDCT (0.28% decrease from period 2 to period 3, p=0.2). Compared with this baseline trend, implementation of LDCT was significantly associated with a decrease in the proportion of patients with metastatic disease at the time of diagnoses (3.29% decrease from period 3 to period 4: difference in change, -3.33%, P < 0.01). These results were consistent in sex (male or female) and ethnic (Hispanic or non-Hispanic) subgroups. After the implementation of LDCT screening, the proportion of lung cancer patients with metastatic disease at the time of diagnosis has declined in the US without any impact on trends of incidence of lung cancer among the population with age of 55-79 years.

OA05.09

Volume Doubling Time and Radiomic Features Predict Tumor Behavior of Screen-Detected Lung Cancers in the National Lung Screening Trial (NLST)

Jaileene Perez-Morales[1], Ilke Tunali[2,3], Hong Lu[2], Wei Mu[2], Yoganand Balagurunathan[4], Robert Gillies[2], Matthew Schabath[1,5]

[1]Department of Cancer Epidemiology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, United States, [2]Department of Cancer Physiology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, United States, [3]Institute of Biomedical Engineering, Bogazici University, Istanbul, Turkey, [4]Department of Bioinformatics and Biostatistics, H. Lee Moffitt Cancer Center and Research Institute, Tampa, United States, [5]Department of Thoracic Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, United States

Oral Abstract Session 2, October 17, 2020, 07:50 - 09:35

Background: Utilizing non-invasive biomarkers, such as CT radiomics, could have translational implications by characterizing tumor behavior lung cancers diagnosed in the lung cancer screening setting. This goal of this study was to utilize radiomics features and volume doubling time (VDT) to generate parsimonious models to predict lung cancer outcomes in the lung cancer screening setting. **Methods:** Patient data and LDCT images were acquired from incidentally-detected lung cancer patients from the NLST. VDT was calculated as the difference between two LDCT scans ~1 year apart. Peritumoral (N=109) and intratumoral (N=155) radiomic features were extracted from LDCT images and correlated, unstable, and non-reproducible features were removed prior to analysis. Overall survival (OS) was the main endpoint. Classification and Regression Tree (CART) analyses were used to identify the most predictive models to discriminate between classes of tumor behaviors using stable peritumoral and intratumoral features, and VDT as the inputs. **Results:** For all patients, when the VDT data and radiomic features were combined, decision tree analysis stratified patients into four risk-groups (low-, intermediate-, high-, and very-high risk) based on VDT and two radiomic features (compactness and average co-occurrence). Patients in the very-high risk group had extremely poor survival outcomes (HR= 11.96; 21.4% 5-year OS) versus the low-risk group (HR= 1.00; 82.4% 5-year OS; C-index=0.7310). Among early-stage lung cancers, the decision tree analysis identified a novel volume doubling time (VDT= 234 days) to discriminate (C-index= 0.6589) between aggressive lung cancers (HR = 4.13; 39.9% 5-year OS) versus indolent/low-risk cancers (HR= 1.00; 80.8% 5-year OS). When the VDT and radiomic data were combined for early-stage patients, high-risk patients had poor survival outcomes (HR= 15.20; 33.3% 5-year OS) versus the low-risk group (HR= 1.00; 90.6% 5-year OS; C-index = 0.7218). The multivariable model using 10-fold cross-validation achieved high prediction performance (C-index=0.84). **Conclusion:** Utilizing VDT and radiomic features, decision tree analysis identified subsets of screen-detected lung cancers associated with very poor survival outcomes suggesting such patients may more aggressive treatment, such as adjuvant therapies, and more aggressive surveillance/follow-up.

VIRTUAL POSTERS

Oral Featured Posters

OFP01.01

Liquid Biopsy to Detect MET Alterations in Patients with Advanced NSCLC: Biomarker Analysis from the VISION Study

Xiuning Le[1], Dariusz Kowalski[2], Byoung Chul Cho[3], Pierfranco Conte[4], Enriqueta Felip[5], Marina Garassino[6], Santiago Viteri[7], Gee-Chen Chang[8], John Richart[9], Luiz Paz-Ares[10], Dilafruz Juraeva[11], Josef Straub[12], Christopher Stroh[13], Paul Paik[14]

[1]Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, USA, [2]Department of Lung Cancer and Thoracic Oncology, Maria Sklodowska-Curie Institute of Oncology, Warsaw, Poland, [3]Department of Internal Medicine, Yonsei University, Seoul, Republic of Korea, [4]Department of Surgery, Oncology and Gastroenterology, University of Padova and Oncologia Medica 2, Istituto Oncologico Veneto, I.R.C.C.S., Padova, Italy, [5]Department of Oncology, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, [6]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, [7]Dr Rosell Oncology Institute, Dexeus University Hospital, QuironSalud Group, Barcelona, Spain, [8]Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, [9]Department of Internal Medicine, Saint Louis University School of Medicine, Saint Louis, USA, [10]Medical Oncology Department, Hospital Universitario Doce de Octubre, Madrid, Spain, [11]Translational Medicine, Department of Oncology Bioinformatics, Merck KGaA, Darmstadt, Germany, [12]Translational Medicine, Department of Clinical Biomarkers and Companion Diagnostics, Merck KGaA, Darmstadt, Germany, [13]Translational Innovation Platform, Oncology, Merck KGaA, Darmstadt, Germany, [14]Thoracic Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, USA

Background: In the ongoing, single-arm, Phase II VISION study (NCT02864992), tepotinib (a highly selective MET inhibitor) showed durable clinical activity in NSCLC patients with MET exon 14 skipping. Here, we report the biomarker profile of patients screened with liquid biopsy for inclusion in the study. **Methods:** Patients with advanced NSCLC and previously confirmed EGFR/ALK wild-type status were prospectively screened for MET alterations using plasma samples collected during pre-screening/screening. Plasma circulating tumor DNA sequencing was performed centrally using a 73-gene next-generation sequencing panel (Guardant360®). **Results:** Of 6,034 patients screened, 813 patients had results pending at data cut-off and, of 5,221 patients tested, sequencing failed in 41 patients. The success rate of liquid biopsy was consistent across centers. Of 5,180 patients analyzed, 694 patients (13.4%) had no mutation detected. Despite the intent of screening EGFR/ALK wild-type patients, 327 patients (6.3%) had EGFR mutations and 49 (0.9%) had ALK/ROS fusions. 188 patients (3.6%) had MET exon 14 skipping (table) and 256 patients (4.9%) had MET amplification without MET exon 14 skipping. The median age of MET exon 14 patients was 72 years, 46% were male, 46% were never smokers, and 64% had adenocarcinoma histology. In MET exon 14 patients, the most frequent driver co-alterations were amplification in MET (13.8%), EGFR (8.0%), CDK4 (6.4%), BRAF (5.3%) and CDK6 (4.8%), and mutations in GNAS (5.3%). In MET amplification patients, the most frequently occurring driver co-alterations were CDK6 (63.3%), BRAF (50.0%), EGFR (38.7%), MYC (22.3%), and CCNE1 (21.5%) amplifications. Overall, TP53 mutations were detected in 56.4% of MET exon 14 patients and 80.9% of MET amplification patients. **Conclusion:** MET exon 14 skipping can be successfully detected through non-invasive liquid biopsy analysis using next-generation sequencing. The rate of MET exon 14 skipping and the genomic profile and demographics of patients were similar to previously reported data. This abstract and presentation was previously presented at AACR 2020. Le et al. Cancer Res 2020; DOI: 10.1158/1538-7445.AM2020-3385

Table: Characterization of *MET* exon 14 skipping (n=188)	
Type of *MET* exon 14 skipping alteration	n (%)
Insertions/deletions (indels)	93 (49.5)
Acceptor site	54 (28.7)
Donor site	36 (19.1)
Whole exon 14 deletion	3 (1.6)
Single nucleotide variation (SNV)	95 (50.5)
Donor site	93 (49.5)
Acceptor site	2 (1.1)
Location of *MET* exon 14 skipping alteration	
Donor site	129 (68.6)
Acceptor site	56 (29.8)
Whole exon 14 deletion	3 (1.6)

OFP01.02

KEYNOTE-021 Cohort G Long-Term Follow-up: First-Line (1L) Pemetrexed and Carboplatin (PC) with or without Pembrolizumab for Advanced Nonsquamous NSCLC

Mark M. Awad[1], Shirish M. Gadgeel[2], Hossein Borghaei[3], Amita Patnaik[4], James Chih-Hsin Yang[5], Steven F. Powell[6], Ryan D. Gentzler[7], Renato G. Martins[8], James P. Stevenson[9], Mehmet Altan[10], Shadia I. Jalal[11], Amit Panwalkar[12], Matthew Gubens[13], Lecia V. Sequist[14], Sanatan Saraf[15], Bin Zhao[15], Bilal Piperdi[15], Corey J. Langer[16]

[1]Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute, Boston, United States, [2]Thoracic Oncology, Karmanos Cancer Institute/Wayne State University, Detroit, United States, [3]Hematology and Oncology, Fox Chase Cancer Center, Philadelphia, United States, [4]Clinical Research, START Center for Cancer Care, San Antonio, United States, [5]Department of Oncology, National Taiwan University Hospital, Taipei, Republic of China, [6]Oncology, Sanford Health, Sioux Falls, United States, [7]Hematology/Oncology, University of Virginia, Charlottesville, United States, [8]Medicine, University of Washington, Seattle, United States, [9]Taussig Cancer Institute, Cleveland Clinic, Cleveland, United States, [10]Thoracic/Head and Neck Oncology, The University of Texas MD Anderson Cancer Center, Houston, United States, [11]Indiana University School of Medicine, Indianapolis, United States, [12]Hematology/Oncology, Sanford Roger Maris Cancer Center, Fargo, United States, [13]Medical Oncology, University of California San Francisco, San Francisco, United States, [14]Hematology/Oncology, Massachusetts General Hospital, Boston, United States, [15]Merck & Co., Inc., Kenilworth, United States, [16]Department of Medicine, Abramson Cancer Center, University of Pennsylvania, Philadelphia, United States

Background: Pembrolizumab + PC demonstrated clinically meaningful improvements in ORR, PFS, and OS vs PC alone as 1L therapy for advanced nonsquamous NSCLC in prior analyses of KEYNOTE-021 (NCT02039674) cohort G, at median follow-up of 10.6 and 23.9 months. We report outcomes with 31.0 months median follow-up. **Methods:** Patients with previously untreated, stage IIIB/IV nonsquamous NSCLC without sensitizing EGFR/ALK alteration were randomized 1:1 (stratification: PD-L1 tumor proportion score <1% vs ≥1%) to carboplatin AUC 5+pemetrexed 500 mg/m² Q3W (4 cycles) ± pembrolizumab 200 mg Q3W (up to 35 cycles). Maintenance pemetrexed was permitted. Eligible patients with radiologic progression on PC could cross over to pembrolizumab. Response was assessed by blinded, independent central review (RECIST v1.1). **Results:** Median follow-up (time from randomization to data cutoff [19Aug2019]) was 48.3 (range, 42.8–55.6) mo. ORR was improved with pembrolizumab + PC vs PC (Table). 5 patients with SD/PR at prior analysis (median follow-up, 23.9 mo) achieved CR (pembrolizumab + PC, n = 4; PC, n = 1). OS and PFS HRs favored pembrolizumab + PC (Table). 43 (68%) patients in the PC arm crossed over to PD-(L)1 therapy, 28 of whom received pembrolizumab in the on-study crossover. In the on-study crossover, median OS and PFS (from first pembrolizumab dose) were 16.9 (95% CI, 6.3–29.6) mo and 3.9 (95% CI, 1.9–8.3) mo, respectively. Grade 3–5 treatment-related AEs occurred in 23 (39.0%) and 19 (30.6%) patients in the pembrolizumab + PC and PC groups, respectively. Data on patients who completed 35 cycles of pembrolizumab + PC will be presented. **Conclusions:** Pembrolizumab + PC reduced the risk of death by ~30% vs PC despite crossover to PD-(L)1 therapy in the majority of patients randomized to PC. No new toxicities were identified. These results support 1L pembrolizumab + PC in patients with advanced nonsquamous NSCLC without EGFR/ALK alteration.

Table. Efficacy Results

	Pembrolizumab + PC (N = 60)	PC (N = 63)
ORR, n (%)	35 (58.3)	21 (33.3)
Difference, % (95% CI)	24.9 (7.3–41.1)	
Median DOR, mo (range)	36.3 (1.4+ to 49.3+)	22.8 (2.8+ to 47.2+)
Median PFS, mo (95% CI)	24.5 (9.7–36.3)	9.9 (6.2–15.2)
HR (95% CI)	0.54 (0.35–0.83)	
3-y PFS rate, % (95% CI)	37.4 (24.2–50.5)	16.3 (7.4–28.2)
Median OS, mo (95% CI)	34.5 (24.0–not reached)	21.1 (14.9–35.6)
HR (95% CI)	0.71 (0.45–1.12)	
3-y OS rate, % (95% CI)	49.7 (36.5–61.6)	37.1 (25.3–48.9)

DOR, duration of response; ORR, objective response rate; OS, overall survival; PC, pemetrexed and carboplatin; PFS, progression-free survival.

OFP01.03

Systemic and Intracranial Efficacy of Brigatinib vs.Crizotinib: Updated Results from the ALTA-1L Trial

Sanjay Popat[1], Hye Ryun Kim[2], Myung-Ju Ahn[3], James CH Yang[4], Ji-Youn Han[5], Maximilian Hochmair[6], Ki Hyeong Lee[7], Angelo Delmonte[8], Maria Rosario Garcia Campelo[9], Dong-Wan Kim[10], Frank Griesinger[11], Enriqueta Felip[12], Raffaele Califano[13], Alexander Spira[14], Scott Gettinger[15], Marcello Tiseo[16], Huamao Lin[17], Yuyin Liu[17], Pingkuan Zhang[17], D Ross Camidge[18]

[1]Royal Marsden Hospital, London, United Kingdom, [2]Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea, [3]Samsung Medical Center, Seoul, South Korea, [4]National Taiwan University Hospital, Taipei, Taiwan, [5]National Cancer Center, Goyang, South Korea, [6]Department of Respiratory and Critical Care Medicine, Karl Landsteiner Institute of Lung Research and Pulmonary Oncology, Krankenhaus Nord, Vienna, Austria, [7]Chungbuk National University Hospital, Cheongju, South Korea, [8]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy, [9]Complejo Hospitalario Universitario A Coruna, Coruna, Spain, [10]Seoul National University Hospital, Seoul, South Korea, [11]Pius-Hospital Oldenburg, University of Oldenburg, Oldenburg, Germany, [12]Vall d'Hebron University Hospital, Barcelona, Spain, [13]Department of Medical Oncology, The Christie NHS Foundation Trust and Division of Cancer Sciences, University of Manchester, Manchester, United Kingdom, [14]Virginia Cancer Specialists and US Oncology Research, The Woodlands, United States, [15]Yale Cancer Center, New Haven, United States, [16]University Hospital of Parma, Parma, Italy, [17]Millennium Pharmaceuticals, Inc., Cambridge, MA, USA, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, United States, [18]University of Colorado Cancer Center, Aurora, United States

Background: At ALTA-1L (NCT02737501) first interim analysis (IA1), brigatinib demonstrated superior BIRC-assessed PFS and iPFS vs crizotinib. We report IA2 results, planned at ~75% of 198 expected PFS events. **Methods:** Patients with TKI-naive advanced ALK+ NSCLC were randomized 1:1 to brigatinib 180 mg qd (7-day lead-in at 90 mg) or crizotinib 250 mg bid. Endpoints: Primary, BIRC-assessed PFS (RECIST v1.1); secondary included confirmed ORR and iORR, and iPFS (BIRC). **Results:** 275 patients were randomized (brigatinib/crizotinib, n=137/138); median age, 58/60 years; prior chemotherapy, 26%/27%; baseline brain metastases (BIRC), 34%/36%; brain radiotherapy, 13%/14% (WBRT/SRS balanced across arms). At data cutoff (28 June 2019, median follow-up [brigatinib/crizotinib], 24.9/15.2 months, 150 PFS events): BIRC-assessed PFS HR, 0.49 (95% CI, 0.35–0.68, log-rank P<0.0001); brigatinib mPFS, 24.0 months (95% CI, 18.5–NE) vs crizotinib 11.0 months (9.2–12.9). Investigator-assessed PFS HR was 0.43 (95% CI, 0.31–0.61, median 29.4 vs 9.2 months). OS was immature (total events: 33/37, brigatinib/crizotinib). In patients with baseline brain metastases, PFS HR was 0.25; data were less mature in brigatinib patients without brain metastases. Additional results in Table. Radiological overall disease progression occurred in (brigatinib vs crizotinib) 54 (39%) vs 74 (54%) patients (BIRC) and 50 (36%) vs 84 (61%) (investigator); of these, brain was first site of progression more frequently with crizotinib vs brigatinib: 31 (42%) vs 17 (31%) patients (BIRC); 22 (26%) vs 7 (14%) (investigator). Most common TEAEs grade ≥3: brigatinib: increased CPK (24.3%) and lipase (14.0%), hypertension (11.8%); crizotinib: increased ALT (10.2%), AST (6.6%), lipase (6.6%). Brigatinib significantly delayed median time to deterioration vs crizotinib for global health score/QoL (log-rank P=0.0485), emotional and social functioning, fatigue, nausea and vomiting, appetite loss, constipation. **Conclusions:** Brigatinib demonstrated superior systemic and intracranial efficacy vs crizotinib in all patients with TKI-naive ALK+ NSCLC and in patients with baseline brain metastases.

BIRC-Assessed Efficacy	Brigatinib	Crizotinib	*P* Value
All patients (ITT), n	137	138	
Confirmed ORR, %	74 (66–81[a])	62 (53–70[a])	0.0342[b]
Median DoR[c], mo	NE (19–NE[a])	14 (9–21[a])	
PFS events, n (%)	63 (46)	87 (63)	
Median PFS, mo	24.0 (18.5–NE[a])	11.0 (9.2–12.9[a])	
2-yr PFS, %	48 (39–57[a])	26 (18–35[a])	
PFS HR	0.49 (0.35–0.68[a])		<0.0001[d]
iPFS events, n (%)	40 (29)	51 (37)	
Median iPFS, mo	32 (30–NE[a])	24 (13–NE[a])	
2-yr iPFS, %	65 (55–73[a])	50 (38–60[a])	
iPFS HR	0.45 (0.29–0.69[a])		0.0001[d]
Any baseline brain metastases, n	40[e]	41[e]	
PFS events, n (%)	20 (50)	30 (73)	
Median PFS, mo	24.0 (18.4–NE[a])	5.6 (3.8–9.4[a])	
2-yr PFS, %	43 (25–59[a])	10 (2–25[a])	
PFS HR	0.25 (0.14–0.46[a])		<0.0001[d]
	47[f]	49[f]	
iPFS events, n (%)	21 (45)	32 (65)	
Median iPFS, mo	24.0 (12.9–NE[a])	5.6 (3.7–7.5[a])	
2-yr iPFS, %	48 (30–63[a])	15 (5–32[a])	
iPFS HR	0.31 (0.17–0.56[a])		<0.0001[d]
Confirmed iORR, %	66 (51–79[a])	16 (7–30[a])	<0.0001[b]
No baseline brain metastases[e], n	97	97	
PFS events, n (%)	43 (44)	57 (59)	
Median PFS, mo	24.0 (15.7–NE[a])	13.0 (9.5–21.1[a])	
2-yr PFS, %	50 (39–61[a])	32 (22–43[a])	
PFS HR	0.65 (0.44–0.97[a])		0.0298[d]
Measurable brain metastases, n	18	23	
Confirmed iORR, %	78 (52–94[a])	26 (10–48[a])	0.0014[b]
Median iDOR[c], mo	NE (6–NE[a])	9 (4–9[a])	

BIRC, blinded independent review committee; DoR, duration of response; HR, hazard ratio; iDoR, intracranial duration of response; iORR, intracranial objective response rate; iPFS, intracranial progression-free survival; ITT, intent-to-treat; NE, not estimable; ORR, objective response rate; PFS, progression-free survival

[a]95% CI; [b]Cochran-Mantel-Haenszel test; [c]Confirmed responders; [d]Log-rank; [e]Per investigator assessment; [f]Per BIRC assessment

OFP01.04

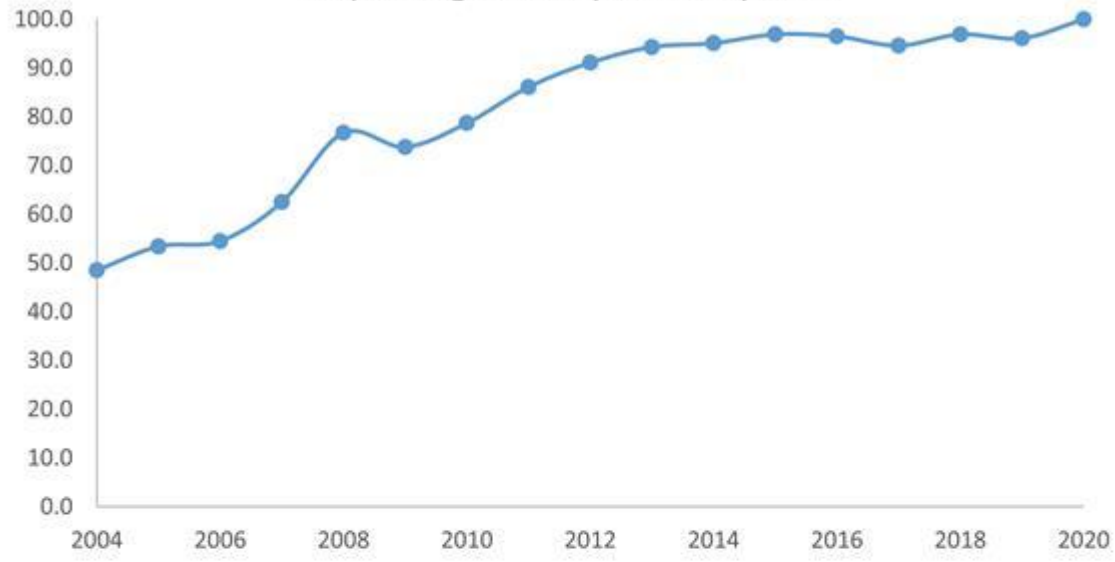
Improving Quality of Pathology Reports for Resected Non-Small Cell Lung Cancer (NSCLC) in the Mid-South US

Matthew Smeltzer[1], Yu-Sheng Lee[1], Nicholas Faris[2], Carrie Fehnel[2], Cheryl Houston-Harris[2], Meghan Meadows-Taylor[2], Meredith Ray[1], Amin Mahul[3], John Fullenwider[4], Sherry Okun[5], David Spencer[6], Elizabeth Sales[7], Raymond Osarogiagbon[2]

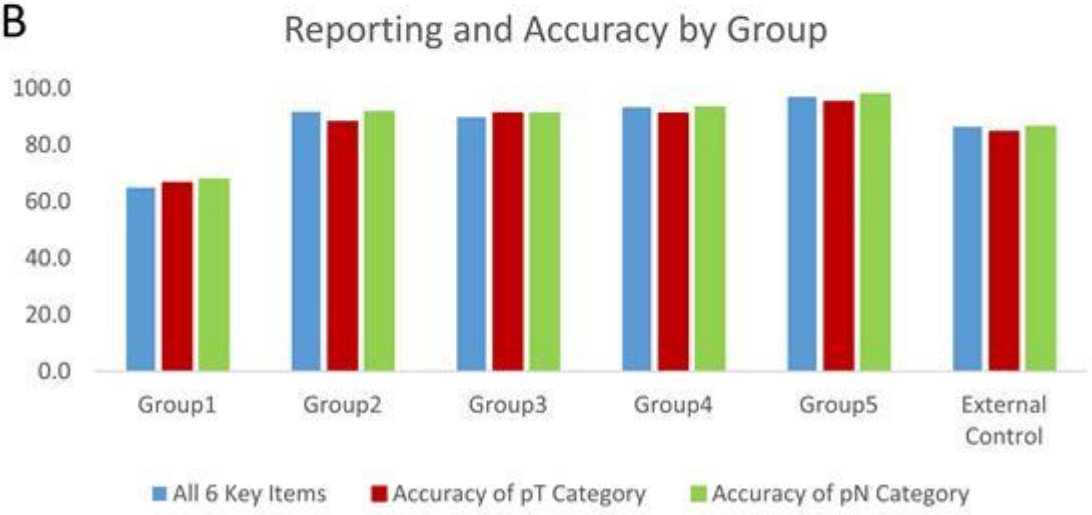
[1]University of Memphis, Memphis, United States, [2]Multidisciplinary Thoracic Oncology Program, Baptist Cancer Center, Memphis, United States, [3]Methodist LeBonheur Health System, Memphis, United States, [4] JPB Pathology , Oxford, United States, [5]Tupelo Pathology Group, PA, Tupelo, United States, [6]Trumbull Labs, Memphis, United States, [7]Doctors' Anatomic Pathology Services, P.A., Jonesboro, United States

Background: Complete and accurate pathologic reports are vital to postoperative prognostication and management. We evaluated the impact of three quality improvement interventions on the accuracy and comprehensiveness of post-resection NSCLC pathology reports across a diverse group of hospitals. **Methods:** The population-based mid-south quality of surgical resection cohort includes >95% of all curative-intent surgical resections for NSCLC in a defined geographic region of the US with high lung cancer incidence and mortality from 2004-2020. We evaluated pathology reports for completeness and accuracy before and after quality improvement initiatives including, 1: educational intervention, 2: synoptic reporting, and 3: a lymph node specimen collection kit. We identified six crucial items for a pathology report (specimen type, tumor size, histology, margin status, T-category, N-category), and compared reporting across six groups: pre-intervention control, post-intervention external control, and post-intervention with four combinations of interventions (Figure 1B). Statistical analysis included chi-square tests and logistic regression with odds ratios adjusted for pathologist and surgeon (aOR). **Results:** We evaluated 4,758 post-resection pathology reports. Overall, there was a yearly trend of improvement in reporting all 6 key items from 2004-2020 (Figure 1A). The post-intervention odds of reporting all 6 key items were 3.8 times higher than pre-intervention (aOR: 3.84 (95% CI: 2.83, 5.21), p<0.0001). There were significantly higher odds of accurate pT- and pN-category reporting post-intervention compared to pre-intervention (aOR: 2.26 (95% CI:1.71, 2.99); aOR: 3.14 (95% CI: 2.30, 4.29); both p<0.0001). Within the intervention groups (2-4), the odds of reporting all 6 key items, accurate pT category, and accurate pN category increased with the level of intervention (Figure 1B). The external control group suggested some temporal improvements but lagged behind the four intervention groups (Figure 1B). **Conclusions:** Gaps in the quality of pathologic reportage can be identified, quantified, and corrected with rationally designed interventions that are well-implemented.

A



B



Group 1: Pre-Intervention; Group 2: Education Only; Group 3: Education + Synoptic Reporting; Group 4: Education + Kit Use; Group 5: Education + Synoptic Reporting + Kit Use; Group 6: Post-Intervention External Control (2009-2020)

OFP01.05

Circulating Ensembles of Tumor Associated Cells Facilitate Efficient Triaging of Asymptomatic Individuals for Low Dose Computed Tomography

Dadasaheb Akolkar[1], Darshana Patil[1], Sewanti Limaye[2], Pradip Fulmali[1], Pooja Fulmali[1], Archana Adhav[1], Sachin Apurwa[1], Sushant Pawar[1], Shoeb Patel[1], Rohit Chougule[1], Vishal Ranjan[1], Pradyumna Shejwalkar[1], Shabista Khan[1], Raja Dhasarathan[1], Vineet Datta[1], Stefan Schuster[1], Prashant Kumar[1], Cynthe Sims[1], Pradip Devhare[1], Ajay Srinivasan[1], Rajan Datar[1]

[1]Datar Cancer Genetics, Nashik, India, [2] Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Mumbai 400053, India

Background: Screening of Individuals for Lung cancer is presently based on radiological evaluation for presence of suspicious thoracic nodules by Low Dose Computed Tomography (LDCT). LDCT is not only associated with risks of exposure to radiation but is also not confirmatory and often necessitates an invasive biopsy in suspicious cases. We present a non-invasive approach for triaging of asymptomatic individuals prior to screening investigations such as LDCT. This approach is based on detection of Circulating Ensembles of Tumor Associated Cells (C-ETACs) which are clusters of malignant cells derived from a tumor mass. **Methods:** We collected peripheral blood from 10625 asymptomatic individuals (6627 females and 3398 males) with no prior diagnosis of cancer and no clinical symptoms indicative of cancer. All individuals underwent LDCT scans following blood collection. Peripheral blood mononuclear cells (PBMCs) were isolated from blood samples and treated with an epigenetically activating medium which induces cell death in normal (non-malignant) hematolymphoid cells as well as epithelial cells in peripheral blood, but selectively confers survival privilege on apoptosis resistant tumor-derived Circulating Tumor Cells (CTCs)and their clusters (C-ETACs). Two-way association studies were performed to correlate detection of C-ETACs and LDCT findings (Lung RADS score). **Results:** Among the 10625 individuals, samples from 467 were positive for C-ETACs while 10158 were negative for C-ETACs. Among the 10625 individuals, 8422 had no abnormal findings on LDCT (LungRADS = 1), 1833 had borderline risk of malignancy (Lung RADS = S / 2), 283 had marginally elevated risk of malignancy (Lung RADS = 2S / 3), while 78 individuals had elevated risk of malignancy (Lung RADS = 3S / 4A / 4B / 4x). Detection of C-ETACs was associated with 5-fold increase in risk of malignancy based on Lung RADS (3.2% vs 0.6%). Conversely, 19.2% of all individuals with elevated risk of malignancy were positive for C-ETACs as compared with 4.1% - 5.3% individuals with no suspicious findings or borderline risk of malignancy suggesting 4.5-fold increased risk. **Conclusion:** The findings suggest a positive association between detection of C-ETACs and incidence of significant findings in LDCT indicative of higher risk of malignancy. Non-invasive evaluation of asymptomatic individuals for presence of C-ETACs can facilitate efficient triaging prior to LDCT, thus significantly expediting diagnosis and treatment.

OFP01.06

Improving Rural Disparity in Lung Cancer Outcomes Starting With An Academic-Community Network Model of LDCT Screening

Charles Shelton[1], Lysle Ailstock[1,2], Bryan Jordan[2,3], Matthew Sean Peach[3]
[1]*Vidant Medical - The Outer Banks Hospital, Nags Head, United States,* [2]*Eastern Radiology Associates, Greenville, USA,* [3]*East Carolina University*

Background: Outcomes in Lung Cancer (LC) are unfavorable rurally. Rural hospitals service high-risk populations with disparities often tied to lower levels of education, higher tobacco use, and later stages. Furthermore, these smaller hospitals often lack specialty resources. We are network of community hospitals serving a mostly non-metropolitan population of 1.4 million. Most are <100 bed facilities lacking specialists, including two remote critical access hospitals (CAH). We have shared ownership with an academic hospital of 954 beds, serving as central hub. In rural North Carolina, we began a collaborative community-based screening program using an academic-community network model to primarily increase screening rates rurally with LDCT, and secondarily increase early detection. **Methods:** A central academic facility (1) served as specialty hub for pulmonary care. Patients underwent primary screening at community hospitals based on 2013 USPSTF criteria with shared decision-making, and smoking cessation counseling. Ultra-low dose non-contrasted CT done at 1.25mm intervals annually; further evaluation as recommended based on standardized Lung RADS interpretations by radiologist, and referals of all abnormalities left to primary care discretion. Patients enrolled in American College of Radiology LC Screening Registry (LCSR) for data analysis. **Results:** Five years of data analyzed. Each facility saw significant growth in the numbers of screening exams annually, with CAH showing greatest increase over time. Community rural hospitals accounted for 73.5% of all scans done within network, including larger academic hub. Twenty percent of all scans within the network came from 1 CAH. Cumulative smoking and median age were comparable to national values. The percentage of abnormal screens (Lung RADS 3 or 4) averaged 15 percent as a system over 5 years. Data from CAH showed two-thirds of all LC discovered by LDCT screening were early stage, consistent with previous national trials and overall cancer rate of 1 per 50 scans. Rates of tobacco cessation also increased over time. **Conclusion:** LC screening is feasible at small hospitals using a network hub and spoked wheel model. Our cancer detection rate over 5 years with LDCT is 5 times higher than the reported ACR LCSR averages, but in line with NLST and Nelson trials. This suggests some centers do not update their registry data to reflect recently diagnosed cancers, which negatively skews national data. Networking with a center of excellence is crucial in this endeavor to increase screening rurally. The majority of cancers detected were early stage. With new guidelines, we anticipate these results will continue.

OFP01.07
Delayed ALK Testing Results in the US - Analysis with a Large Real World Oncology Database

Eric Bernicker[1], Y. Xiao[2], A. Abraham[3], S. Redpath[4], J. Engstrom-Melnyk[5], D. Croix[4], B. Yang[2], R. Shah[2], T. Allen[6]
[1]houston Methodist Hospital, Houston, United States, [2]Roche Diagnostics, Belmont, United States, [3]Genesis Research, Hoboken, United States, [4]Roche Diagnostics, Indianopolis, United States, [5]Astra-Zeneca, Gaithersburg, United States, [6]The University of Mississippi Medical Center, Jackson, United States

Timely assessment of driver mutation status in advanced non-small cell lung carcinoma (aNSCLC) patients is critical for selecting optimal therapy for each patient and potentially avoiding harm. However, patients as well as physicians are often hesitant to wait on beginning systemic therapy until genomic information is back. In order to understand the length of time it takes to receive ALK mutational status and factors related to delays, a retrospective study of the nationwide Flatiron Health electronic record derived de-identified databases was undertaken. The first post aNSCLC diagnosis ALK tests (n=14,657) were analyzed from 14,197 patients who were 18 years of age or older and had aNSCLC diagnosis between 1 Jan 2015-31 May 2019. Patients may have multiple ALK tests at the same day (e.g. FISH and NGS tests). Time from aNSCLC diagnosis to ALK sample received date was used as a surrogate of test order time. Testing order was considered delayed if it took more than 20 days. Overall, the median ALK test order time was 15 days with 36.4% delayed orders. Orders for FISH had the shortest median order time and fewer delayed tests (12, 29.9%) vs IHC (18, 42.2%) or NGS (21, 50.4%) and in house labs had shorter order time (11, 29.3%) compared to send-out laboratories (16, 37.5%). Results from multivariable logistic regression showed that non-FISH testing, send-out laboratories, testing prior to 2018, non-adenocarcinoma histology, and smoking history were associated with delayed ALK test orders. Turnaround time (TAT) was defined as time from receiving ALK test samples to receiving test results, and it was considered delayed if it took more than 10 days. The overall median TAT was 9 days with 40.3% of tests having delayed results; these varied by test type, sample type, and order type. Immunohistochemistry (10, 48.3%) and NGS (12, 66.8%) had longer TAT and more delayed tests than FISH (8, 29.3%). Tissue was the predominant specimen and results were reported in 9 days (41.4% delayed), while test results using blood specimens were reported in 8 days (32.3% delayed). Single order tests were returned more quickly (8, 36.0%) than combination orders (10, 53.2%) with one or more additional biomarkers (PD-L1, EGFR, BRAF, KRAS, ROS1). Results from multivariable logistic regression showed that non-FISH testing, tissue sample, and combination order were associated with delayed ALK reporting. With 94% of aNSCLC patients in this analysis data set coming from community practices, this analysis provides a snapshot of the real world ALK testing order and reporting time in the U.S. Test type along with other factors were identified as having an impact on delayed ALK test order and reporting. Additional investigation is needed to develop pathways to expedite biomarker testing. Ideally, the ordering physician would have results within 10 days of ordering the test. Opportunities to tighten timelines from diagnosis to test order to reporting exist and would significantly improve patient opportunities to receive targeted therapies or avoid potentially unhelpful immunotherapy. The use of liquid biopsies to access results faster need to be studied further.

OFP01.08

Tolerability, Low-Fat Meal Effect, and Relative Bioavailability (BA) of Oral EGFR Inhibitor TAK-788 in Healthy Volunteers

Steven Zhang[1], S. Jin[1], C. Griffin[1], Z. Feng[1], J. Lin[1], R. Brake[1], K. Venkatakrishnan[1], N. Gupta[1]
[1]*Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, United States*

TAK-788 is an investigational oral tyrosine kinase inhibitor (TKI) targeting EGFR. The TAK-788 clinical development program to treat non-small cell lung cancer (NSCLC) with EGFR exon 20 insertions is ongoing. We report the results of a phase 1, open-label, single rising dose (SRD) study, followed by a study evaluating the effects of a low-fat meal on the pharmacokinetics (PK) of TAK-788, and an evaluation of relative BA between 2 drug-in-capsule formulations in healthy adult volunteers. The study (NCT03482453) was composed of 3 parts: (1) Randomized, doubleblind, placebo-controlled, SRD study of TAK-788 with Capsule-B; (2) The effects of a low-fat meal (≤350 calories and ≤15% calories from fat) on TAK-788 PK with Capsule-A; (3) Relative BA of 4×40 mg size 1 Capsule-B (test) versus 8×20 mg size 2 Capsule-A (reference). In Part 1, 5 cohorts of 8 healthy volunteers each were randomized: 6 volunteers received a single oral dose ranging from 20 to 160 mg (recommended phase 2 dose) of TAK-788 and 2 volunteers received placebo under fasting conditions in each cohort. Parts 2 and 3 were evaluated in a 2-way crossover design with a 7-day washout period. The initial dose in Part 2 was selected as 120 mg (n=6) and subsequently the 160 mg (n=10) dose was tested. In Part 3, 12 volunteers were randomly assigned to 2 crossover sequences and administered a single dose of 160 mg TAK-788 in Capsule-A or Capsule-B on Days 1 and 8 under fasting conditions. In Part 1, no grade >2 TEAE was observed. In Parts 2 and 3, all TEAEs were grade ≤2 except for one grade 3 event of lipase increased. The most common TEAEs by preferred term (≥2 subjects overall) were nausea (12.5%), diarrhea (10.0%), headache (7.5%), and abdominal pain upper (5.0%) in Part 1 and headache (31.3%), nausea (31.3%), abdominal pain upper (18.8%), soft feces (12.5%), and flatulence (12.5%) in Part 2. No TEAE occurred in ≥2 volunteers in Part 3. In Part 2 at the 120 mg dose, the least square geometric mean ratios (90% CI) of TAK-788 Cmax and AUC∞ comparing TAK-788 oral administration with a low-fat meal to those under fasting conditions were 0.881 (0.711, 1.09) and 1.02 (0.898, 1.15), respectively. At 160 mg, these ratios (90% CI) were 0.964 (0.836, 1.11) and 0.951 (0.874, 1.03), respectively. In Part 3, the geometric mean ratios of TAK-788 Cmax and AUC∞ comparing Capsule-B to Capsule-A were 0.932 and 0.960, respectively. The 90% CIs of geometric mean ratios for both TAK-788 Cmax and AUC∞ were 0.846, 1.03 and 0.886, 1.04, falling within the bioequivalence range of 0.80 to 1.25. TAK-788 was well tolerated at single oral doses from 20 to 160 mg in healthy volunteers. A low-fat meal did not affect TAK-788 systemic exposure. Therefore, TAK-788 can be administered with or without a low-fat meal for patients' convenience with TAK-788 daily dosing. Capsules A and B used during the clinical development program have been demonstrated to be bioequivalent.

OFP01.09

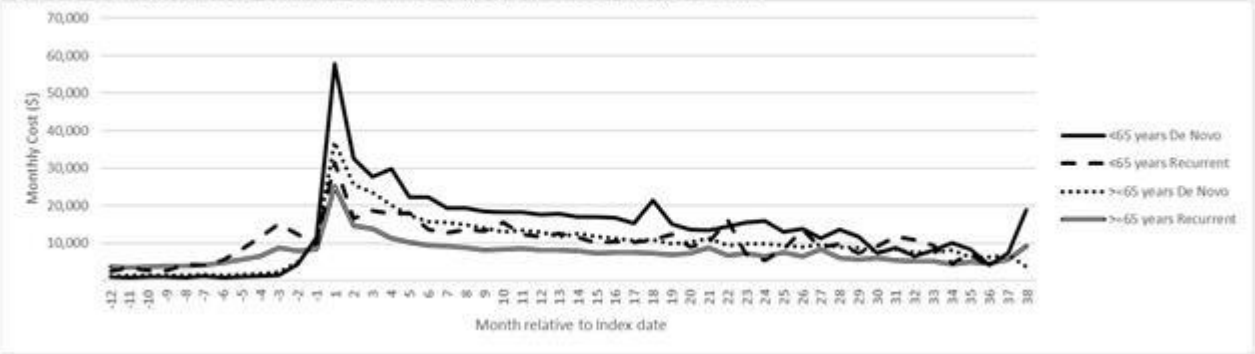
Economic Burden of Metastatic Non-Small Cell Lung Cancer (mNSCLC) in a Large United States (US) Claims Database

Engels Chou[1], Apar K. Ganti[2], Kenan Katranji[3], Ion Cotarla[1], Chandrakant Sharma[3], Benjamin Miao[3], Manu Garg[3], **Brian Seal[1]**

[1]AstraZeneca, Gaithersburg, United States, [2]VA Nebraska Western Iowa Health Care System and University of Nebraska Medical Center, Omaha, United States, [3]ZS Associates, Bethesda, United States

Background: Metastatic non-small cell lung cancer (mNSCLC) is associated with a high healthcare burden. **Methods:** This retrospective cohort analysis of a US claims database identified patients with mNSCLC (November 2016 - September 2019). Patients were ≥18 years at first date of metastasis (index). Metastasis was determined by diagnosis codes and/or mNSCLC treatment. Patients had to have >1 primary lung/secondary metastatic diagnosis codes (≥30 days apart) after index, continuous enrollment ≥12 months pre-index (baseline) and ≥3 months post-index (follow-up), and were not enrolled in clinical trials. Healthcare utilization/costs were summarized by age (<65 [commercial] vs ≥65 [Medicare Advantage] years) and NSCLC history (prior NSCLC [recurrent] vs newly diagnosed [de novo]). **Results:** The mNSCLC cohort (n=10,075) had 51% female and with mean [SD] age, 73 [9] years. Most were ≥65 years (87%) and de novo mNSCLC (64.5%). Forty percent had distant metastases in ≥3 sites, most commonly lung (42%), lymph node (38%), bone (35%), and brain (23%). PET and brain MRI were more common in de novo (62% and 61%, respectively) than recurrent (45% and 34%) mNSCLC. Total cost/patient/month (mean [SD]) was $18,565 (15,861), and highest around index; cost was primarily driven by inpatient-hospitalizations. Regardless of age, total monthly costs were higher for de novo vs recurrent mNSCLC (Figure 1). After index, a second cost peak was observed near end-of-life. End-of-life costs/patient/month were double for age <65 vs ≥65: $31,137 (25,745) vs $15,160 (18,578). The major drivers of end-of-life cost were inpatient-hospitalizations (~58% ICU), followed by IV drug administration. Inpatient-hospitalization costs near end-of-life costs were $15,481 (18,779) for <65 and $7,577 (12,962) for ≥65 years. **Conclusions:** Total cost of mNSCLC was highest around index; the major driver was inpatient-hospitalization. A second peak in cost was observed near end-of-life, more pronounced among younger patients, and driven by inpatient-hospitalization followed by drug administration.

Figure 1. Monthly total cost in patients with mNSCLC by age and NSCLC history over time



POSTERS

Community Practice Posters

CP01.01

Utilization of Cancer Immunotherapy Prior to Biomarker Test Results Among Patients with Advanced Non-Small Cell Lung Cancer in US Community Settings

Aaron Mansfield[1], Sarika Ogale[2], Tu My To[2], Danny Sheinson[2], William Wong[2], Ravindra Gupta[2], Chia-Wei Lin[2]
[1]Division of Medical Oncology, Mayo Clinic, Rochester, United States, [2]Genentech, Inc., South San Francisco, United States

Background: For patients with advanced non-small cell lung cancer (aNSCLC) and positive driver mutations (DM)s, NCCN guidelines recommend first-line targeted therapy. Cancer immunotherapies (CIT)s are recommended for patients with ≥ 1% PD-L1 expression and no DM. Our study aimed to describe current aNSCLC testing and treatment patterns in US community settings. **Methods:** Adult (≥ 18 years old) patients with non-squamous aNSCLC who were diagnosed between 10/1/2016-8/31/2019, had ≥ 1 visit within 90 days of advanced diagnosis, and received care in community practices were obtained from Flatiron Health EHR-derived de-identified database. PD-L1 and DM (EGFR, ALK, ROS1, and BRAF) test result date within 90 days of advanced diagnosis were used to identify the presence of biomarker tests. Treatment patterns were described pre and post the first positive DM test results and focused on patients who initiated CITs prior to DM results. **Results:** A total of 12212 patients with aNSCLC were analyzed. Overall, 72% had evidence of testing both DMs and PD-L1 while 13% and 4% were tested only for DMs or only PD-L1, respectively. Among DM positive patients (n= 1945), 19% initiated treatment (7% CITs, 7% chemo, 5% targeted) prior to receiving their positive test results. Only 26% (n= 35/135) of those who had started CITs prior to positive DM result switched to a targeted therapy after receiving a positive result (median (IQR) time to switch from positive DM result: 1.6 (0.8-5.2) months), while most of these patients had no evidence of new treatment (58%, n= 78/135; median (IQR) follow-up time from positive DM result: 3.6 (1.3-10.2) months). More than half of the patients with EGFR+ or ALK+ aNSCLC who started CITs before DM result have no evidence of receiving targeted therapy even after their positive result date. **Conclusions:** In this study, 19% of patients with DMs positive aNSCLC had started treatment before DM test results were available. Despite overwhelming clinical evidence supporting the benefits of targeted therapy specific to DMs, most patients who started CITs prior to test results stayed on CITs, rather than switching to a targeted therapy, after the identification of a targetable mutation. It is possible that symptomatic burden precluded waiting for test results, highlighting the need for more expedient testing strategies. Given the short follow-up time for some patients, some of these patients may transition to targeted therapy at a later time, however, there is also the possibility of lost treatment opportunity.

CP01.02

Improving Care for Patients With Stage III/IV NSCLC: Learnings for Multidisciplinary Teams From the ACCC National Quality Survey

Ravi Salgia[1], **Leigh Boehmer[2]**, Catherine Celestin[3], Hong Yu[3], David Spigel[4]
[1]Beckman Research Institute of City of Hope, Comprehensive Cancer Center and National Medical Center, Duarte, USA, [2]Association of Community Cancer Centers, Rockville, USA, [3]AstraZeneca, Gaithersburg, USA, [4]Sarah Cannon Research Institute, Nashville, USA

Background: Refinement of the multidisciplinary team (MDT) approach continues to offer significant potential for improving the quality of non-small cell lung cancer (NSCLC) care and adherence to guideline recommended protocols. This opportunity arises, in part, from insufficient characterization of MDT practice patterns and barriers to optimal care provision within U.S. cancer progra The Association of Community Cancer Centers (ACCC) conducted a national survey to improve understanding on the diagnosis and management of patients with stage III/IV NSCLC across different practice settings, with the aim of informing the design and execution of process-improvement plans to address identified barriers. **Methods:** ACCC convened an expert steering committee of multidisciplinary specialists, including oncologists, thoracic surgeons, pathologists, pulmonologists, and representation from patient advocacy, for a comprehensive, double blind, web-based survey (January–April 2019) to obtain insights on cancer care delivery for patients with NSCLC in a diverse set of U.S. community cancer progra **Results:** Overall, 639 responses affiliated to 160 unique cancer programs across 44 U.S. states were suitable for analysis. In total, 41% (n=261) of respondents indicated that their cancer program lacked a thoracic multidisciplinary clinic. Nurse navigators (P=0.03) and radiation oncologists (P=0.04) were significantly more likely to engage in shared decision-making practices than other disciplines. The average time to first therapeutic intervention in newly diagnosed patients was 4 weeks (range: 1–10 weeks; n=298). A significant negative correlation between frequency of tumor board meetings and time to complete disease staging (P=0.03) was observed. The key barriers to delivering high-quality NSCLC care are listed (Table). **Conclusion:** Multiple opportunities exist to improve the delivery and quality of care for patients with stage III/IV NSCLC, including reducing barriers to effective care coordination and patient education, screening, diagnosis and biomarker testing, and adherence to evolving standards of care.

Table: Key Barriers to Delivering Quality NSCLC Care

Care Coordination	Screening	Diagnosis
Insufficient quantity of biopsy material	Lack of primary care provider referral	Cost
Coverage and reimbursement	Lack of community awareness	Poor handling of biopsy samples
Turn-around time	Cost	Scheduling challenges and/or limited access to biopsy procedures

CP01.03
COVID 19's Pandemic 's Effect on a Community Lung Cancer Screening Program

Michael Gieske[1], **Goetz Kloecker[1]**, Megan Lockwood[1], Jessica Kerns[1], Royce Calhoun[1]
[1]St Elizabeth Health Care, Edgewood, United States

Background: COVID-19's pandemic spread in the US in early 2020 led to a drastic change in health care delivery. In April 2020 consensus statement on LC screening advised deferring enrollment in LC screening and modified the evaluation of nodules. This single institution has had an active LC screening program before COVID, which enrolled more than 300 patients per month before COVID and completed more than 11,000 screens over the last six years. Kentucky is the state with the highest LC mortality rate in the US and one of the highest smoking rates in the country. Government directed social distancing was put in place 3/14/2020. **Methods:** LC Screening Registry data 2015-2020 for St Elizabeth Healthcare (SEH) was accessed. The lung cancer screening volumes listed until May 2020 were recorded and graphically illustrated using polynomial trendlines and well as monthly point by point lines. John Hopkin's COVID Status Report on Kentucky's and SEH surrounding counties confirmed cases, fatality rate and number of tested patients. **Results:** By June 2020, Kentucky (pop 4.6m) had 13.630 confirmed COVID cases, 524 deaths and a 3.84% fatality rate with 317,161 tests performed. SEH's surrounding counties, (pop 370k) had 386 cases per 100k population and a 4.5 % county fatality rate with 71 deaths. The county with the highest rate in the county at the time was Cook county, IL, (pop 5,2m) with 1,711 cases per 100k population and 4,500 deaths due to COVID. 379 LC screens were performed at SEH in February 2020. 212 in March and 13 LC screens in April, 114 in May. The lung cancer rate in the screened population has been 1.81% over the course of six years. **Conclusion:** The consensus statement on LC screening during COVID advised a delay in LC screening, work up and treatment, even for high probability nodules and stage 1 lung cancers. A delay of LC screens in this community setting by 6 months would delay the diagnosis and treatment of 36 lung cancer cases. The course of the COVID pandemic is presently uncertain. Considering the fact that COVID will affect health care for the foreseeable future, it would be helpful to modify the recommendations based on the area's prevalence of COVID and prevalence of lung cancer.

CP01.04

Biomarker Testing Among Users of Online Lung Cancer Resources - Can Online Communities Make a Clinical Impact?

Margot Tishberg[1], **Shayna Yeates[1]**, Kaitlyn McNamara[1], Sara Hayes[1]
[1]Health Union Llc, Philadelphia, United States

Background: Comprehensive biomarker testing is vital to ensure detection of actionable mutations and appropriate treatment for lung cancer. However, research shows a lack of awareness among patients and few receiving biomarker testing. We aim to determine whether a link exists between involvement in online lung cancer resources, including community-based resources and online communities, in which patients can read and share experiences, and the receipt of biomarker testing. **Methods:** An online survey was conducted among lung cancer patients (n=867) to better understand patients' experiences. Survey questions included diagnosis, HCP interaction, treatment, resources, and quality of life measures. Responses were evaluated using descriptive statistics and comparisons tests. **Results:** Of 867 lung cancer patients, 29% received biomarker testing while 71% have not or were unsure. Patients using online community-based resources to learn about and manage lung cancer were more likely to have had biomarker testing than those not using these resources. These resources include social media (40% v 24%, p<.0005), online forums and message boards (41% v 26%, p<.0005), online support groups (45% v 23%, p<.0005), lung cancer blogs (38% v 25%, p<.0005), and lung cancer-specific websites (35% v 21%, p<.0005). **Conclusions:** Despite biomarker testing rates remaining low, a higher rate of patients leveraging online lung cancer resources, including community-based resources, received biomarker testing than those not using these resources, demonstrating the potential positive clinical influence and value of these resources. Broader awareness is needed about biomarker testing to ensure both patients who do and do not utilize online resources are aware and benefitting from biomarker testing.

CP01.05

Relapse Rate and Associated Healthcare Resource Utilization in Stage IIA-IIIB Adjuvant NSCLC Patients Treated in a US Oncology Community Network

Beilei Cai[1], Nicole Fulcher[2], Marley Boyd[2], Alexander Spira[3]
[1]Novartis Pharmaceuticals, East Hanover, United States, [2]McKesson Life Sciences, The Woodlands, United States, [3]The US Oncology Network, McKesson Life Sciences, Fairfax, United States

Background: Despite adjuvant systemic therapy in patients with completely resected non-small-cell lung cancer (NSCLC), many will subsequently relapse. This study evaluated real-world relapse rates and healthcare resource utilization in Stage IIA-IIIB NSCLC patients receiving adjuvant therapy after complete resection. **Methods:** This retrospective descriptive study included Stage IIA-IIIB NSCLC patients with complete resection (R0), receiving any adjuvant therapy within the US Oncology Network during 06/2008–04/2017, with follow-up through 04/2019. Data were captured using structured fields and chart review of iKnowMed electronic health records. Rate of relapse and time to relapse (TTR) were characterized descriptively. Relapse-free survival (RFS) and overall survival (OS) were estimated from the date of surgery using Kaplan-Meier method. Per patient per month (PPPM) emergency department (ED) visits and hospitalizations before and after relapse were compared. **Results:** The study identified 456 patients; median age was 66 years, 50% were male. A majority of patients (67%) had non-squamous histology, 67% were former/current smokers, and at the time of surgery 64% had Stage II and 25% Stage III (1.5% Stage IIIB) disease. In patients with relapse (45.2%), the median follow-up was 31.7 months, and the median time to relapse was 13.7 months (95% CI: 11.9 to 16.7 months). Median RFS for overall population was 42.9 months (95% CI 36.8 to 59.5 months). The median OS was 82.4 months in the overall population and was significantly shorter in the relapsed patients than those without relapse (41.6 months vs. median not reached, $p<0.0001$). Patients with relapse had significantly more ED visits (PPPM visits, mean[SD]: 0.10 [0.24] vs 0.03 [0.08], $p<0.0001$) and hospitalizations (PPPM hospitalizations, mean[SD]: 0.20 [0.43] vs 0.05 [0.10], $p<0.0001$) following relapse than they had before relapse. **Conclusions:** Patients with stage II-IIIB NSCLC receiving adjuvant therapy after complete resection have high relapse rates, reduced survival and significantly increased healthcare resource use when relapse occurred. Efforts to reduce relapse in early stage NSCLC patients could reduce healthcare utilization and generate substantial cost savings.

CP01.06

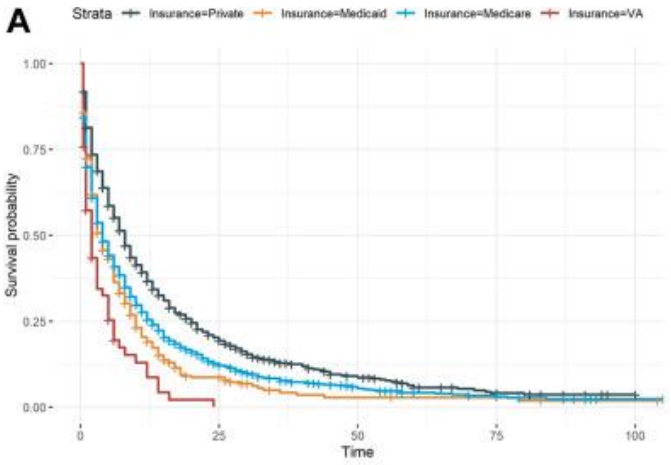
Veterans Affairs Insurance Disparities for Metastatic Lung Cancer in the Hawaiian Islands

John Lin, Shirley Li, Todd Pezzi, Abdallah Mohamed, Clifton Fuller, Aileen Chen, Bruce Minsky, David Schwartz, Brenda Hernandez, **Stephen Chun**[1]

[1]*MD Anderson, Houston, United States*

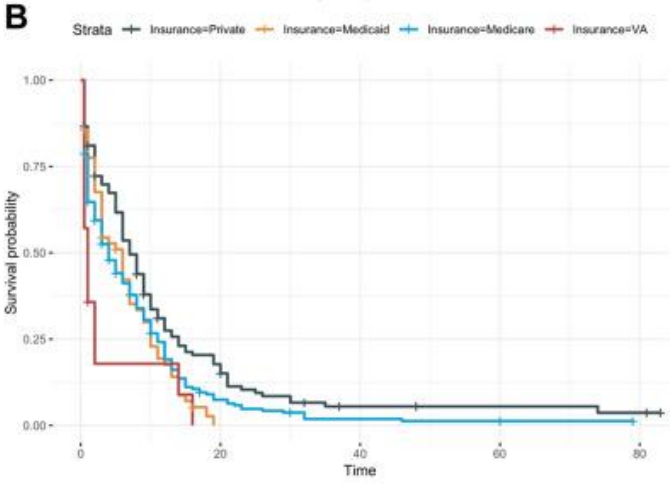
Background: The highest concentration of military personnel in the United States is located in Hawaii where occupational exposures, such as to asbestos in the Pacific Fleet shipyards, predispose them to thoracic malignancies. For this reason, Veterans Affairs (VA) insurance outcomes for lung cancer in Hawaii are of interest. **Methods:** All cases of lung cancer in the Hawaii Tumor Registry from 2000 to 2015 were evaluated. The selection criterion included evidence of extensive-stage SCLC (ES-SCLC) or metastatic NSCLC. Overall survival was compared using the Kaplan-Meier log-rank method. Univariate analysis and multivariable analysis (MVA) were carried out to understand the variables associated with overall survival. **Results:** There were 434 cases of ES-SCLC and 2139 cases of metastatic NSCLC identified. VA insurance (median survival [MS], 2 mo), Medicaid (MS, 4 mo), and Medicare (MS, 4 mo) had worse survival (log-rank $p < 0.001$) than private insurance (MS, 8 mo). In ES-SCLC, VA insurance (hazard ratio [HR], 2.74; 95% confidence interval [CI]: 1.50–5.01; $p = 0.001$) and Medicaid (HR, 1.46; 95% CI: 1.04–2.03; $p = 0.027$) had significantly worse survival compared with private insurance on MVA. VA insurance (HR, 1.84; 95% CI: 1.34–2.53; $p < 0.001$) and Medicaid (HR, 1.40; 95% CI: 1.20–1.63; $p < 0.001$) also had worse survival compared with private insurance in metastatic NSCLC on MVA. **Conclusion**: VA insurance coverage was associated with dismal survival for metastatic lung cancer that was effectively similar to hospice or supportive care, compelling further investigation to identify reasons for this disparity.

A



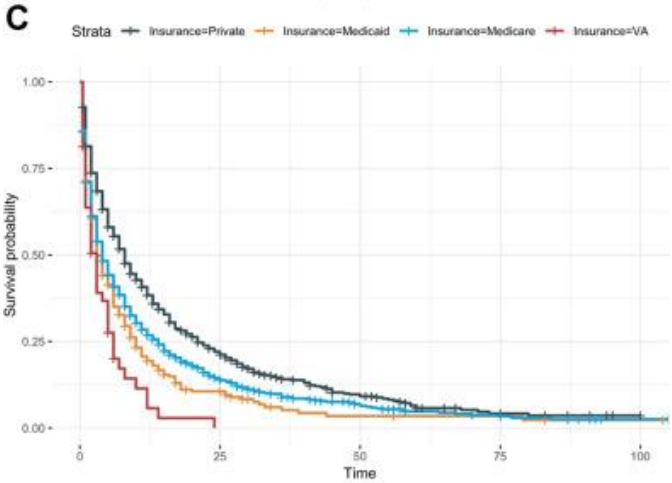
(Months)

B



(Months)

C



(Months)

Immunotherapy Posters

IM01.01

4-Year Survival in Randomised Phase II (POPLAR) and Phase III (OAK) Studies of Atezolizumab vs. Docetaxel in 2L+ NSCLC

Julien Mazieres[1], A. Rittmeyer[2], S.M. Gadgeel[3], T. Hida[4], D. Gandara[5], D. Cortinovis[6], F. Barlesi[7], W. Yu[8], C. Matheny[8], M. Ballinger[8], K. Park[9]

[1]Toulouse University Hospital, Toulouse, France, [2]Lungenfachklinik Immenhausen, Immenhausen, Germany, [3]Comprehensive Cancer Center, University of Michigan, Ann Arbor, United States, [4]Aichi Cancer Center Hospital, Nagoya, Japan, [5]UC Davis Comprehensive Cancer Center, Sacramento, United States, [6]SC Oncologia Medica, SS Lung Unit Asst Ospedale San Gerardo, Monza, Italy, [7]Aix-Marseille University, CNRS, INSERM, CRCM, APHM, Marseille, France, [8]Genentech, Inc., South San Francisco, United States, [9]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Atezolizumab (anti–PD-L1) showed overall survival (OS) benefit over docetaxel in the Phase II (POPLAR; N=287) and Phase III (OAK; N=1225) studies in patients with advanced NSCLC. 4-year survival analysis from both studies is reported. In both studies, patients were randomised 1:1 to receive atezolizumab (1200 mg) or docetaxel (75 mg/m2) intravenously every 3 weeks; PD-L1 expression was assessed by the Ventana SP142 assay on tumour cells (TC) and tumourinfiltrating immune cells (IC); landmark OS was estimated using the Kaplan-Meier method. The minimum follow-up was 53 (POPLAR) and 45 (OAK) months, representing an additional 17 and 19 months of follow-up, respectively, from prior reports. 4-year survival rates with atezolizumab vs docetaxel were 14.8% vs 8.1% and 15.5% vs 8.7% in POPLAR and OAK, respectively. The long-term OS benefit of atezolizumab vs docetaxel was seen across histology and PD-L1 expression subgroups. Of patients in the atezolizumab arms who lived ≥4 years in POPLAR (N=15) and OAK (N=43), 40% and 23% were in the PD-L1–high (TC3 or IC3) subgroup, 33% and 37% were in the PD-L1–negative (TC0 and IC0) subgroup, and 87% and 88% had non-squamous histology, respectively. Among 4-year survivors in the docetaxel arms, 2/4 (50%) and 17/26 (65%) received subsequent immunotherapy in POPLAR and OAK, respectively, vs 3/15 (20%) and 10/43 (23%) in the atezolizumab ar Fewer Grade 3-4 treatment-related adverse events and adverse events leading to treatment withdrawal occurred in the atezolizumab vs docetaxel arms in both studies. 4-year OS rates favoured atezolizumab vs docetaxel across histology and PD-L1 expression subgroups in both studies. The PD-L1–high (TC3 or IC3) subgroups continued to derive the greatest OS benefit with atezolizumab vs docetaxel; however, the PD-L1–negative (TC0 and IC0) subgroups also sustained an improved long-term OS benefit with atezolizumab vs docetaxel. Most patients in the docetaxel arms received subsequent immunotherapy. Atezolizumab treatment was well tolerated, and safety was consistent with prior reports. Previously presented at ESMO Congress 2020, FNP: 1907, Julien Mazieres et al. - Reused with permission

Table. 4-year landmark OS rates in POPLAR and OAK

Population	4-year OS rate, %							
	POPLAR				OAK			
	N	Atezo %	Doc %	Δ% (95% CI)	N	Atezo %	Doc %	Δ% (95% CI)
ITT	287	14.8	8.1	6.7 (−1.1, 14.4)	1225	15.5	8.7	6.8 (2.8, 10.8)
PD-L1 expression subgroups								
TC3 or IC3	47	33.3	14.9	18.4 (−5.8, 42.7)	174	27.8	9.8	18.1 (6.1, 30.0)
TC2/3 or IC2/3	105	19.1	7.9	11.2 (−2.2, 24.6)	350	19.9	11.9	8.0 (−0.6, 16.7)
TC1/2/3 or IC1/2/3	195	14.6	8.5	6.2 (−3.2, 15.5)	684	16.8	11.8	5.0 (−0.8, 10.8)
TC0 and IC0	92	15.2	6.8	8.4 (−5.6, 55.4)	531	13.9	5.1	8.7 (3.3, 14.2)
Histology subgroups								
Non-squamous	190	18.6	10.0	8.6 (−1.7, 19.0)	904	17.9	10.1	7.7 (2.8, 12.7)
Squamous	97	7.0	NE	NE	321	8.5	4.8	3.7 (−2.4, 9.9)

Atezo, atezolizumab; doc, docetaxel; NE, not estimable.

P values not presented due to small sample sizes.

Medical Oncology Posters

MO01.01

Durvalumab for Patients with Stage III EGFR-Mutated Non-Small Cell Lung Cancer Receiving Definitive Chemoradiotherapy

Jacqueline V. Aredo[1], Jessica A. Hellyer[2], Joel W. Neal[2], Sukhmani K. Padda[2], Caroline E. McCoach[3], Jonathan W. Riess[4], Elwyn C. Cabebe[5], Billy W. Loo[6], Maximilian Diehn[6], Heather A. Wakelee[2]
[1]Stanford University School Of Medicine, Stanford, United States, [2]Stanford Cancer Institute, Stanford University School of Medicine, Stanford, United States, [3]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, San Francisco, United States, [4]UC Davis Comprehensive Cancer Center, Sacramento, United States, [5]Stanford Cancer Center South Bay, San Jose, United States, [6]Department of Radiation Oncology, Stanford Cancer Institute, Stanford, United States

Background: Following the results of the PACIFIC trial, durvalumab was FDA-approved as consolidation immunotherapy for patients with stage III non-small cell lung cancer (NSCLC) who completed definitive chemoradiotherapy (CRT). However, the PACIFIC trial subset analysis of outcomes in patients with EGFR-mutated NSCLC was inconclusive due to small sample size. Furthermore, recent studies indicate that patients who receive EGFR tyrosine kinase inhibitors (TKIs), such as osimertinib, after immunotherapy have an increased risk of immune-related adverse events (irAEs). These data raise concerns about the safety of durvalumab in patients who have recurrence during or shortly after consolidation treatment. Here, we present our real-world experience of patients with stage III EGFR-mutated NSCLC who received CRT with or without durvalumab. **Methods:** We conducted a multi-institutional retrospective analysis on a series of patients with unresectable stage III EGFR-mutated NSCLC who completed CRT from 01/2017 to 07/2020. Factors related to durvalumab treatment were analyzed descriptively. Kaplan-Meier curves were generated to evaluate progression-free survival (PFS) between patients who completed consolidation durvalumab versus those who did not from the date of radiotherapy completion. **Results:** Overall, 20 patients with EGFR-mutated NSCLC (10 L858R, 7 exon19del, 3 other) completed platinum-based CRT and were included in the cohort. Among these patients, 11 (55.0%) initiated durvalumab a median 18 days (range 2-178) after radiotherapy completion. Patients received a median 5.5 cycles (range 1-27) of durvalumab with two (18.2%) patients completing 12 months of treatment. Three patients (27.3%) discontinued durvalumab due to interval progression and five (45.5%) discontinued due to grade ≥3 irAEs (2 pneumonitis, 1 colitis, 1 hepatitis, 1 myocarditis). Treatment-related adverse events (all grade) occurred in all 10 patients receiving durvalumab with available documentation. Five patients initiated EGFR TKIs (4 osimertinib, 1 erlotinib) due to disease progression after a median 66 days (range 15-199) from the last dose of durvalumab without any incident serious irAEs (median follow up 7.5 months). Median PFS was 10.8 months in patients receiving durvalumab and not reached in patients who completed CRT without durvalumab (HR 1.61, 95% CI 0.41-6.30; log-rank P=0.49). Overall survival data were immature at data cutoff. **Conclusion:** In this cohort, patients with EGFR-mutated NSCLC experienced a high frequency of irAEs and disease progression preventing completion of consolidation durvalumab over 12 months. Initiating EGFR TKIs after durvalumab was not associated with incident serious irAEs, though a majority of patients had a >1 month washout between therapies. Further analysis with a larger cohort is warranted.

MO01.02

Cost-Effectiveness Analysis of Nivolumab Plus Ipilimumab in the First-Line Treatment of Metastatic Non-Small Cell Lung Cancer in the United States

Malin Berling[1], Mohammad A. Chaudhary[3], Yong Yuan[3], Nebibe Varol[4], Peter Dale[2], Eleonora Testa[1], Johan Klint[1], Adam Lee[4], Solomon J. Lubinga[3], John R Penrod[3]
[1]PAREXEL International, Stockholm, Sweden, [2]Parexel International, London, United Kingdom, [3]Bristol-Myers Squibb, Princeton, United States, [4]Bristol-Myers Squibb Pharmaceutical Ltd, Uxbridge, United Kingdom

Background: The objective of this study was to evaluate the cost-effectiveness of nivolumab in combination with ipilimumab (NIVO+IPI) versus platinum doublet chemotherapy (PDC) for the first-line (1L) treatment of stage IV or recurrent non-small cell lung cancer (NSCLC) in the United States (US) from a payer perspective. **Methods:** A partitioned survival model with three health states (progression-free, progressed disease and death) was developed from a US perspective. The efficacy, safety and utility inputs were derived from the Phase III CheckMate 227 Part 1 trial (3-year minimum follow-up). Overall survival and progression-free survival were estimated using parametric models selected based on goodness-of-fit statistics and validation with external sources. Duration of treatment Kaplan-Meier curves were used for treatment cost calculations in both treatment ar Drug list prices, resources used and costs of administration, disease management, adverse events, and subsequent treatment were derived from publicly available sources reflecting 2019 costs. Time to death utility weights were estimated from CheckMate 227 Part 1 based on US tariffs and applied in the base case, whilst the use of treatment specific progression-based utility was tested in the scenario analysis. The base case applied a 20-year time horizon and an annual discount rate of 3% for costs and outcomes. Outcomes were life years (LY), quality adjusted LY (QALY), total cost, and incremental cost effectiveness ratios. Model uncertainty was assessed through univariate and probabilistic sensitivity analyses. **Results:** NIVO+IPI resulted in increased LYs (3.53 vs. 2.00), QALYs (2.89 vs 1.55) and total costs ($256,414 vs $117,217) compared with PDC. The incremental cost per LY gained was $90,766 and the incremental cost per QALY gained was $104,385. Applying treatment specific progression-based utility the incremental cost per QALY gained increased to $114,695. The univariate sensitivity analysis indicated the discount rate applied to QALY as the most influential parameter on the results, followed by patients' average body weight and discount rate applied to cost, both directly influencing the drug acquisition cost. Probabilistic sensitivity analysis generated results consistent with the base case, showing NIVO+IPI to have a probability of 99.5% to be cost-effective at a willingness to pay (WTP) threshold of $150.000 per QALY. **Conclusion:** NIVO+IPI is associated with increased survival and higher costs compared with PDC in the 1L treatment of stage IV or recurrent NSCLC in the US. Estimated incremental cost-utility ratio is within what is considered acceptable value for money in the US, particularly in the metastatic cancer setting.

MO01.03

Biomarker Testing Patterns and Treatment Outcomes in Patients With Advanced Non-Small Cell Lung Cancer and MET Exon 14 Skipping Mutations

Megan Coakley, Fatemeh Asad Zadeh Vosta Kolaei[1], **Beilei Cai[1]**, Hemanth Kanakamedala[2], Julia Kim[2], Vitalii Doban[1], Shiyu Zhang[1], Michael Shi[1]
[1]Novartis Pharmaceuticals Corp, East Hanover, United States, [2]Genesis Research, Hoboken, United States

Background: MET exon 14 skipping mutation (METex14) occurs in ~3% of patients with non-small cell lung cancer (NSCLC) and is a poor prognostic factor. Prior to capmatinib, the first FDA-approved therapy targeting METex14, chemotherapy and immuno-oncology (IO) therapy were commonly used to treat patients with METex14 NSCLC. Because treatment decisions also depend upon biomarker testing results, this study examines biomarker testing patterns and clinical outcomes of chemotherapy and IO in patients with advanced NSCLC (aNSCLC) and METex14. **Methods:** A descriptive retrospective study was conducted using the Flatiron Health–Foundation Medicine Clinico-Genomic Database (CGDB). Adult aNSCLC patients with METex14 confirmed by next-generation sequencing (NGS) testing who received ≥1 line of systemic therapy were included in the biomarker testing pattern analysis. The duration from specimen collection (as testing order date was unavailable) to reported results was assessed for METex14 and PD-L1 tested patients. Duration was only reported for specimens collected in 2019, the most recent year for which data were available, to minimize potential overestimation due to tissue archiving. Clinical outcomes were assessed in patients initiating IO monotherapy or chemotherapy as first-line (1L) and second-line (2L) therapy. Real-world progression-free survival (RW-PFS) was estimated using Kaplan-Meier analysis. **Results:** Among 91 patients eligible for inclusion in the biomarker testing pattern analysis and confirmed positive for METex14 by NGS testing, 62% received PD-L1 testing, and 60% and 77% received NGS and PD-L1 testing within 3 months post aNSCLC diagnosis, respectively. Among 9 patients who were assessed for both METex14 and PD-L1 with specimen collection dates in 2019, the median duration between specimen collection and reporting for NGS was 7 days longer than that for PD-L1. Median RW-PFS was 5.7 months [95% CI, 4.6-7.1] and 2.4 months [95% CI, 1.4-3.2] in patients on 1L chemotherapy (n=59) and 1L IO monotherapy (n=18), with 3-month RW-PFS rates of 78% and 33%, respectively. Median RW-PFS was 3.5 months [95% CI, 1.9-11.1] and 4.7 months [95% CI, 2.8-12.9] in patients on 2L chemotherapy (n=16) and 2L IO monotherapy (n=23), with 3-month RW-PFS rates of 54% and 67%, respectively. **Conclusions:** Among patients with METex14 aNSCLC in the real-world setting, IO monotherapy was associated with limited RW-PFS, and similar results were observed with chemotherapy. In this study, the difference in median duration between specimen collection and reporting of NGS and PD-L1 results was 7 days. Future real-world studies are needed to assess the effectiveness of different regimens in the METex14 population.

MO01.04

Management of Selected Adverse Events With Capmatinib: Institutional Experiences From the GEOMETRY Mono-1 Trial

Kelly Goodwin[1], Blanca Ledezma[2], Rebecca Heist[1], Edward Garon[2]
[1]Massachusetts General Hospital, Boston, United States, [2]Ronald Reagan UCLA Medical Center, Santa Monica, United States

Background: Capmatinib is approved in the United States and Japan for adults with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to MET exon 14 skipping (METex14), based on results from the Phase II GEOMETRY mono-1 trial (NCT02414139). The most common adverse reactions (≥20%) were peripheral edema, nausea, fatigue, vomiting, dyspnea, and decreased appetite. Here, we describe the management of peripheral edema, nausea, and vomiting experienced by patients receiving capmatinib across two institutions in the United States. **Methods:** In GEOMETRY mono-1, patients received capmatinib tablets at a dose of 400 mg twice daily. Dose reductions in 100-mg steps to a minimum dose of 200 mg twice daily were required for adverse events of grade ≥3. Grade 3 adverse events of nausea or peripheral edema required withholding capmatinib until resolved to grade ≤1, then dose reducing one level. Grade 2 vomiting required withholding capmatinib until resolved to grade ≤1; grade ≥3 and recurrent grade 2 required withholding capmatinib until resolution to grade ≤2 and grade ≤1, respectively, and dose reducing one level. **Results:** Across two institutions, patients received capmatinib 400 mg twice daily as a first-line or second-line therapy for the treatment of NSCLC with METex14 as part of the GEOMETRY mono-1 study. Patients taking capmatinib commonly experienced mild (grade 1) peripheral edema. Peripheral edema was generally managed with compression stockings, elevation of affected limbs, and/or diuretics. At one institution, patients were referred to a lymphedema clinic; these patients were managed with lymphatic massage, prescription-grade compression stockings, and/or stretching exercises. Stretching exercises and compression stockings (20-30 mm Hg) improved grade 1 bilateral lower edema without discontinuation of capmatinib treatment. In general, bilateral lower edema resolved with discontinuation of capmatinib. Patients sometimes experienced nausea and vomiting when taking capmatinib while fasted. Methods for treating nausea or vomiting included as-needed antiemetics and premedication with a phenothiazine or 5-HT3 antagonist. Some patients reported reduced nausea when capmatinib was taken after eating, and others experienced reduced vomiting after reducing capmatinib dosage to 300 mg twice daily. **Conclusions:** Across two institutions, patients treated with capmatinib who experienced peripheral edema, nausea, and vomiting were generally managed successfully. In some cases, compression stockings improved peripheral edema. In our experience, taking capmatinib with food reduced nausea and vomiting.

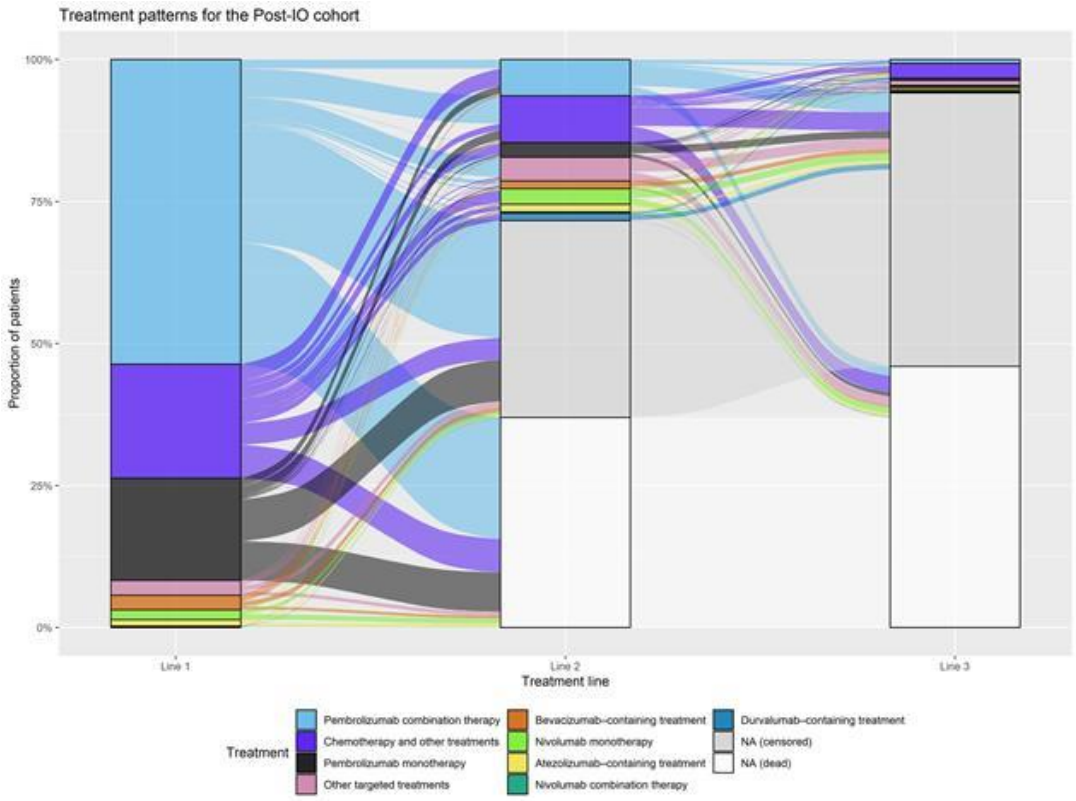
MO01.05

Treatment Patterns in Patients with Advanced Non-Small Cell Lung Cancer (NSCLC) in the Era of Immunotherapy (IO)

David Stenehjem[1], Solomon Lubinga[2], Keith A. Betts[3], Wenxi Tang[3], Mads Jenkins[3], Yong Yuan[2], John Hartman[2], Sumati Rao[2], Jenny Lam[2], David Waterhouse[4]

[1]University of Minnesota, Minneapolis, USA, [2]Bristol Myers Squibb, Lawrenceville, USA, [3]Analysis Group, Los Angeles, USA, [4]OHC Cincinnati, Cincinnati, USA

Background: Chemotherapy (CT) was previously the standard first-line (1L) therapy for metastatic NSCLC, but alternative treatments, including IO, are now available. This retrospective study describes real-world treatment patterns and evaluates factors associated with treatment choice of 1L CT in patients with NSCLC in the IO era. Methods: Adults (≥18 years) with an initial diagnosis of stage IV NSCLC who initiated 1L treatment after August 2018 (when 1L IO + CT received full FDA approval) and had ≥2 visits were identified in the Flatiron database. Patients with EGFR-/ALK-positive tumors, and those with unknown mutation status who received 1L TKIs were excluded. Baseline characteristics and treatment patterns for three lines of therapy were described for four treatment groups (CT, IO+CT, IO monotherapy, other). Multivariate logistic regressions were used to evaluate factors associated with treatment choice. **Results:** A total of 2,588 patients were included. The median age was 70 years, and a majority had non-squamous histology (72%). In the 1L, 520 (20%) received CT, 1408 (54%) IO+CT, 527 (20%) IO monotherapy, and 133 (5%) other therapies. 734 patients received 2L treatment: 214 (29%) CT, 182 (25%) IO+CT, 195 (27%) IO monotherapy, and 143 (19%) other. 152 patients received 3L treatment: 69 (45%) CT, 27 (18%) IO+CT, 27 (18%) IO monotherapy, and 29 (19%) other. Treatment sequences are shown in the Sankey diagram. A multivariate logistic regression found that squamous histology (versus non-squamous histology, OR: 2.50, p<0.001), PD-L1<1% (versus 50-100% OR: 3.44, p<0.001) and PD-L1 1-49% (versus 50-100% OR: 2.20, p<0.001) were associated with higher odds of 1L CT use. **Conclusions:** Approximately 20% of patients with stage IV NSCLC still receive 1L CT. These patients tend to have squamous histology and low levels of PD-L1 expression. Sponsorship: This study was sponsored by Bristol Myers Squibb.



MO01.06

Real-World Outcomes of Immunotherapy-Based Regimens in First-Line Advanced Non-Small Cell Lung Cancer

David Waterhouse[1], Jenny Lam[2], Keith A. Betts[3], Lei Yin[3], Sophie Gao[3], Yong Yuan[2], John Hartman[2], Sumati Rao[2], Solomon Lubinga[2], **David Stenehjem[4]**

[1]OHC Cincinnati, Cincinnati, USA, [2]Bristol Myers Squibb, Lawrenceville, USA, [3]Analysis Group, Los Angeles, USA, [4]University of Minnesota, Minneapolis, USA

Background: Immunotherapy (IO) as first-line (1L) treatment has improved outcomes in patients with advanced non-small cell lung cancer (aNSCLC) in clinical trials. This study describes real-world (RW) outcomes among patients with squamous (SQ) and non-squamous cell (NSQ) aNSCLC receiving either 1L IO monotherapy or 1L single-agent IO in combination with chemotherapy (IO+CT). **Methods:** This descriptive, non-comparative study used the Flatiron database to identify patients (age ≥18 years) with confirmed advanced NSCLC (stage III−IV) and ≥2 documented visits who received 1L IO agents alone or with CT on or after January 1, 2016, the first year of 1L IO FDA approval. Patients with EGFR-/ALK-positive tumors and patients with unknown histology were excluded. Baseline patient characteristics were described and overall survival (OS), RW progression-free survival (rwPFS) and duration of therapy were estimated by Kaplan-Meier methods. **Results:** The analysis included 6,227 patients: 2,693 (43%) received IO and 3,534 (57%) received IO+CT. In the IO cohort, 1,943 and 750 patients had NSQ and SQ aNSCLC, and in the IO+CT cohort, 2,947 and 587 patients had NSQ and SQ aNSCLC, respectively. Median age (years) at start of therapy was 73 (IO) and 69 (IO+CT). Key results are reported in the table below. **Conclusions:** There remains room to improve survival of patients receiving 1L IO monotherapy and single-agent IO + CT therapies in the RW. While NSQ patients with higher PD-L1 levels had better OS, this trend was not as evident for SQ patients. ECOG performance status has a strong association with survival in patients receiving 1L IO therapy. Sponsorship: This study was sponsored by Bristol Myers Squibb.

Table. Survival outcomes for patients with SQ and NSQ aNSCLC receiving IO or IO+CT

	IO		IO+CT	
	NSQ (N=1,943)	SQ (N=750)	NSQ (N=2,947)	SQ (N=587)
Median duration of therapy (months)	4.9	3.9	5.8	6.3
% of patients on-treatment rate at 12 months	29.0	24.5	28.7	32.0
% of patients on-treatment rate at 24 months	16.2	10.5	17.2	NA[a]
12-month OS rate (% of patients)	53.0	46.7	49.7	45.2
24-month OS rate (% of patients)	38.5	24.4	31.0	NA[a]
Median OS (months)[b]				
Overall	13.8	10.4	11.9	11.1
PD-L1 <1%	12.4	11.0	10.1	9.5
PD-L1 ≥1–49%	12.0	9.1	11.7	11.1
PD-L1 50–100%	14.9	10.9	18.8	11.1
Median OS by ECOG (months)[c]				
0 and 1	18.4	13.0	14.3	13.6
2+	5.1	4.8	6.2	9.3
12-month rwPFS rate (% of patients)	30.1	23.2	23.9	20.5
24-month rwPFS rate (% of patients)	17.6	9.5	11.9	NA[a]
Median rwPFS (months)[b]				
Overall	4.6	3.8	5.4	5.8
PD-L1 <1%	5.5	3.7	4.7	5.4
PD-L1 ≥1–49%	2.8	2.9	5.4	6.2
PD-L1 50–100%	5.1	4.8	7.6	5.8
Median rwPFS by ECOG (months)[c]				
0 and 1	6.1	5.4	5.6	5.8
2+	2.7	2.8	3.8	5.0

[a]There were only 2 patients with follow-up at 24 months.
[b]PD-L1 distribution for the IO monotherapy cohort (NSQ+SQ): PD-L1<1%: 5%; PD-L1 1-49%: 12%; PD-L1 50-100%: 71%; Unknown PD-L1: 12%. PD-L1 distribution for the IO + CT cohort (NSQ+SQ): PD-L1<1%: 29%; PD-L1 1-49%: 28%; PD-L1 50-100%: 19%; Unknown PD-L1: 24%.
[c]ECOG distribution for the IO monotherapy cohort (NSQ+SQ): ECOG 0-1: 52%; ECOG 2+: 23%; Unknown ECOG: 25%. ECOG distribution for the IO + CT cohort (NSQ+SQ): ECOG 0-1: 63%; ECOG 2+: 16%; Unknown ECOG: 21%.

MO01.07

Incidence of Aggressive End of Life Measures in a Retrospective Cohort of High-Risk Patients with Advanced Lung Cancer Receiving Immunotherapy

Ankur Singh[1], Jeffrey Lantz[1], Nathan Roberts[1], Greg Russell[1], Daniel Margalski[1], Vanya Aggarwal[1], Kavya Kannan[1], Andy Dothard[1], Thomas Lycan[1]
[1]*Wake Forest Baptist Health, Winston Salem, United States*

Background: Early integration of palliative care has been shown to improve the quality of life and decrease aggressive end-of-life measures for patients with cancer. However, data is limited in patients receiving immunotherapy who experience treatment-related complications. **Methods:** This single-center retrospective cohort study examined the effect of palliative care evaluation among all lung cancer patients who received at least one dose of immune checkpoint inhibitor between 6/1/18 and 2/1/20 (n=210) and who were subsequently hospitalized and started on steroids (n=97). We evaluated the rates of ICU admissions, intubation, CPR, hospice referrals and code status changes. **Results:** In our high-risk cohort of 97 patients, median follow-up was 23 months with progression in 54 patients (56%) at median 11 months (IQR 6-26) and death in 67 patients (69%) at median 14mo (IQR 9-29). Primary outcomes are described in Table 1. Thirty-one patients (32%) were referred and 25 (26%) were seen by palliative care. Patients who initially presented with cancer as an incidental, asymptomatic finding were less likely to be referred to palliative care (OR 0.07, 95% CI 0.01-0.55). Patients who were first seen by palliative care as an outpatient (n=9) were seen earlier in their disease course at median 146 days (IQR 104-469) compared to those who were first seen while hospitalized (n=15) at median 610 days (IQR 287-944, p 0.03). **Conclusion:** Involvement of palliative care was associated with a lower rate of ICU admission and increased rate of referral to hospice for end of life care. Code status changes were not associated with palliative care consultation. Intubation and CPR were uncommon events even in this high-risk cohort. Prospective evaluation is needed for validation of these findings.

	Previously seen by Palliative Care (n=25)	Not previously seen by Palliative Care (n=72)	p-value	Odds Ratio (seen vs. not seen) [95% CI]
Code status change	9	39*	0.11	0.45 [0.18, 1.15]
ICU admission	3	36**	0.0008	0.14 [0.04, 0.50]
Intubation	1	8	0.44	0.33 [0.04, 2.5]
CPR	1	1	0.45	3.03 [0.18, 50]
Hospice referral	18	34***	0.038	2.86 [1.06, 7.69]

* 6 patients changed code status prior to being seen by Palliative Care
** 5 patients were admitted to the ICU prior to being seen by Palliative Care
*** 3 patients were referred to hospice prior to being seen by Palliative Care

MO01.08

Phase 2 Basket Trial of Lurbinectedin in Second-line SCLC: Characteristics and Outcomes in Treatment Responders

Vivek Subbiah[1], Luis Paz-Ares[2], Benjamin Besse[3], Victor Moreno[4], Solange Peters[5], Maria Angeles Sala[6], José Antonio López-Vilariño[7], Cristian Fernández[7], Carmen Kahatt[7], Ali Zeaiter[7], Khalil Zaman[5], Jean-Pierre Delord[8], Maite Martínez[9], Antonio Antón[10], Ahmad Awada[11], Rebecca Kristeleit[12], Maria Eugenia Olmedo[13], María Jesús Rubio[14], John Sarantopoulos[15], Manolo D'Arcangelo[16], Armando Santoro[17], José M Trigo[18], Jacob Sands[19]

[1]The University of Texas MD Anderson Cancer Center, Houston, USA, [2]Hospital Universitario Doce de Octubre, Madrid, Spain, [3]Gustave Roussy Cancer Campus, Villejuif, France, [4]START Madrid-FJD, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain, [5]University Hospital CHUV, Lausanne, Switzerland, [6]Hospital Universitario de Basurto, Bilbao, Spain, [7]PharmaMar, Colmenar Viejo, Spain, [8]Institut Claudius Regaud, IUCT-Oncopole, Toulouse, France, [9]Complejo Hospitalario de Navarra, Pamplona, Spain, [10]Hospital Universitario Miguel Servet, Zaragoza, Spain, [11]Institut Jules Bordet, Université Libre De Bruxelles, Brussels, Belgium, [12]UCL Cancer Institute, London, United Kingdom, [13]Hospital Universitario Ramón y Cajal, Madrid, Spain, [14]Hospital Universitario Reina Sofía, Cordoba, Spain, [15]Institute for Drug Development, Mays Cancer Center at University of Texas Health San Antonio MD Anderson Cancer Center, San Antonio, USA, [16]Ospedale Santa Maria delle Croci, Ravenna, Italy, [17]Humanitas Clinical and Research Center IRCCS, Humanitas University, Rozzano, Italy, [18]Hospital Universitario Virgen de la Victoria, Málaga, Spain, [19]Dana-Farber Cancer Institute, Boston, USA

Background: Lurbinectedin (Zepzelca™) is a novel anticancer agent that selectively inhibits oncogenic transcription, induces DNA double-strand breaks leading to apoptosis, and modulates the tumor microenvironment. Lurbinectedin is approved by the FDA for adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy based on a single-arm, open-label, phase 2 basket trial. We report the baseline characteristics and outcomes in the subset of SCLC patients who responded to lurbinectedin. **Methods:** Patients with SCLC previously treated with a platinum-based chemotherapy received lurbinectedin 3.2 mg/m² infusion once every 3 weeks. The primary endpoint was overall response rate by investigator assessment (IA). **Results:** Of the 105 patients treated, 37 (35%) were responders by IA. Among responders, the median age was 63 years (range: 49, 79), 65% were male, 57% had an ECOG performance status of 1 and 43% of 0, 73% had a chemotherapy-free interval (CTFI) ≥90 days, 51% had extensive-stage disease at diagnosis, median number of disease sites was 3 (range: 1, 6), and 8% had received 2 prior therapy lines. Outcomes in responders overall and by CTFI subgroups are shown in the Table. Among responders overall, the median time from randomization to response was 5.4 weeks, and the median duration of response was 5.3 months. Median overall survival (OS) among responders was 12.6 months, and among those with CTFI <90 days and ≥90 days was 10.9 months and 15.8 months, respectively (Table). Grade ≥3 adverse events (AEs) were reported for 24 responders (65%), serious AEs for 9 (24%), and AEs leading to treatment discontinuation for only 1 responder (3%). **Conclusion:** In patients with relapsed SCLC who responded to lurbinectedin, time from randomization to response was similar regardless of prior resistance or sensitivity to platinum-based chemotherapy, and clinically meaningful duration of response and survival were noted in both subgroups of responders.

Table. Outcomes in Patients Assessed as Responders by IA

		CTFI subgroups	
	Overall (n = 37)	**<90 days (n = 10)**	**≥90 days (n = 27)**
Median time from randomization to response (range), weeks	5.4 (5.0, 11.7)	5.6 (5.0, 11.7)	5.4 (5.0, 11.1)
Median duration of response (95% CI), months	5.3 (4.1, 6.4)	4.7 (2.6, 5.6)	6.2 (3.5, 7.3)
Median OS (95% CI), months	12.6 (10.8, 15.8)	10.9 (6.3, 14.0)	15.8 (10.2, NR)
OS at 12 months, %	54.3%	40.0%	60.0 %

IA, investigator assessment; CTFI, chemotherapy-free interval; CI, confidence interval; OS, overall survival; NR, not reached.

MO01.09

Phase 2 Basket Trial of Lurbinectedin in Small-Cell Lung Cancer (SCLC): Analysis of Efficacy by Baseline Characteristics

Jacob Sands[1], Luis Paz-Ares[2], Benjamin Besse[3], Solange Peters[4], Maria Angeles Sala[5], José Antonio López-Vilariño[6], Cristian Fernández[6], Carmen Kahatt[6], Ali Zeaiter[6], Antonio Nieto[6], Mariano Siguero[6], Khalil Zaman[4], Jennifer Arrondeau[7], Jean-Pierre Delord[8], Maite Martínez[9], Antonio Antón[10], Ahmad Awada[11], Rebecca Kristeleit[12], Maria Eugenia Olmedo[13], María Jesús Rubio[14], John Sarantopoulos[15], Joaquín Mosquera-Martinez[16], Manolo D'Arcangelo[17], Armando Santoro[18], José M Trigo[19], Vivek Subbiah[20], Jennifer Arrondeau[7]

[1]Dana-Farber Cancer Institute, Boston, USA, [2]Hospital Universitario Doce de Octubre, Madrid, Spain, [3]Gustave Roussy Cancer Campus, Villejuif, France, [4]University Hospital CHUV, Switzerland, [5]Hospital Universitario de Basurto, Bilbao, Spain, [6]PharmaMar, Colmenar Viejo, Spain, [7]Hôpital Cochin, Paris, France, [8]Institut Claudius Regaud, IUCT-Oncopole, Toulouse, France, [9]Complejo Hospitalario de Navarra, Pamplona, Spain, [10]Hospital Universitario Miguel Servet, Zaragoza, Spain, [11]Institut Jules Bordet, Université Libre De Bruxelles, Brussels, Belgium, [12]UCL Cancer Institute, London, United Kingdom, [13]Hospital Universitario Ramón y Cajal, Madrid, Spain, [14]Hospital Universitario Reina Sofía, Cordoba, Spain, [15]Institute for Drug Development, Mays Cancer Center at University of Texas Health San Antonio MD Anderson Cancer Center, San Antonio, USA, [16]Complexo Hospitalario Universitario A Coruña, A Coruña, Spain, [17]Ospedale Santa Maria delle Croci, Ravenna, Italy, [18]Humanitas Clinical and Research Center IRCCS, Humanitas University, Rozzano, Italy, [19]Hospital Universitario Virgen de la Victoria, Málaga, Spain, [20]The University of Texas MD Anderson Cancer Center, Houston, USA

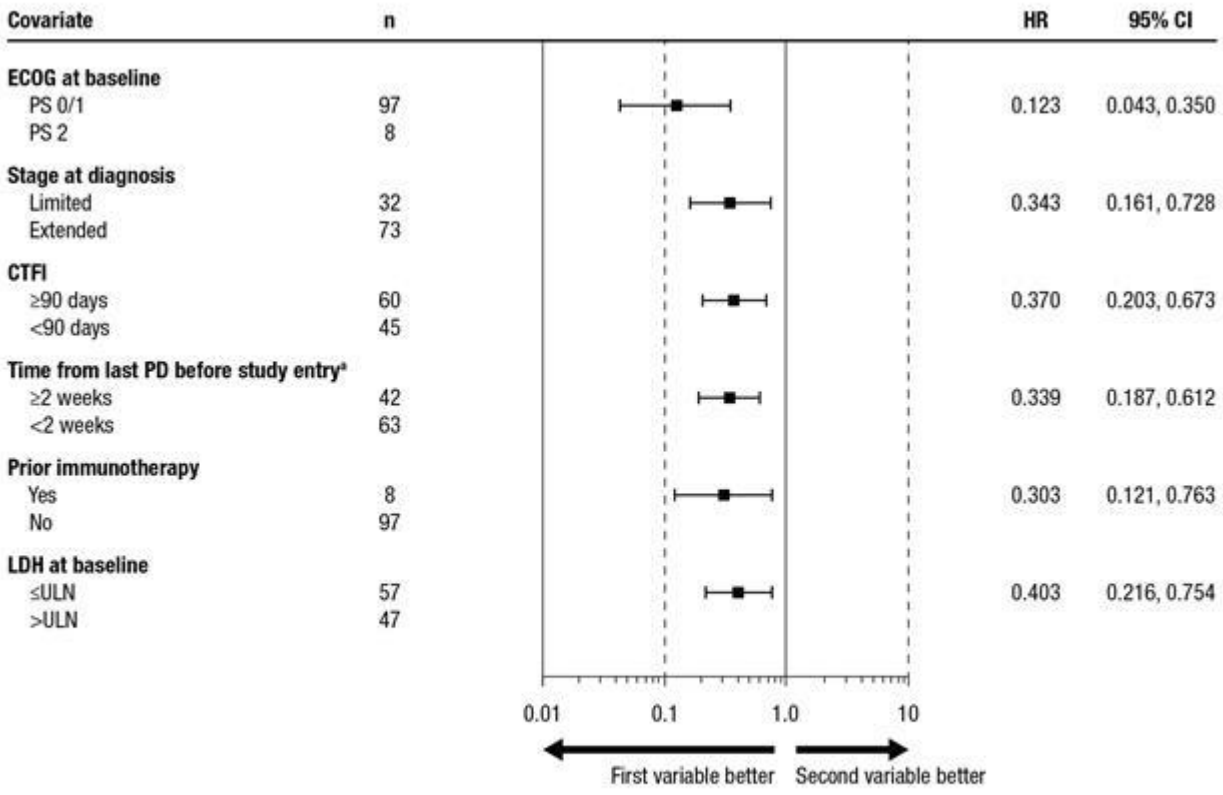
Background: Lurbinectedin (Zepzelca™) is FDA approved for adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy based on results of a phase 2 basket trial. In that trial, lurbinectedin was associated with an overall response rate (ORR) of 35.2% and median overall survival (OS) of 9.3 months. We present efficacy outcomes by baseline patient characteristics. **Methods:** Patients previously treated with platinum-based chemotherapy received lurbinectedin 3.2 mg/m² infusion once every 3 weeks. ORR was calculated by baseline characteristic subgroups. A stepwise Cox regression model for OS with baseline characteristics covariates was performed. **Results:** 105 patients were treated with lurbinectedin. ORR was similar across baseline characteristics, including age (Table). In a separate multivariable analysis, parameters of prior immunotherapy, ECOG performance status of 0/1, limited-stage disease at diagnosis, chemotherapy-free interval ≥90 days, ≥2 weeks since progressive disease before study entry, and lactate dehydrogenase ≤ULN were associated with improved OS (Figure). Common grade 3/4 adverse events included neutropenia (46%), leukopenia (29%), anemia (9%), and thrombocytopenia (7%). **Conclusion:** Response to lurbinectedin appeared consistent regardless of baseline patient characteristics. Of note, prior immunotherapy was associated with improved OS (hazard ratio = 0.303). However, small sample sizes preclude firm conclusions at this time.

Table. ORR by Baseline Characteristics

		ORR (by IA)	
Covariate	**n**	**n (%)**	**95% CI**
Age			
<65 years	68	25 (36.8)	25.4, 49.3
≥65 years	37	12 (32.4)	18.0, 49.8
Gender			
Female	42	13 (31.0)	17.6, 47.1
Male	63	24 (38.1)	26.1, 51.2
Prior lines of therapy			
1	98	34 (34.7)	25.4, 45.0
≥2	7	3 (42.9)	9.9, 81.6
BSA			
≤1.8 m^2	55	19 (34.5)	22.2, 48.6
>1.8 m^2	50	18 (36.0)	22.9, 50.8

ORR, overall response rate; IA, investigator assessment; CI, confidence interval; BSA, body surface area.

Figure. Multivariable Cox Regression for OS



OS, overall survival; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; PS, performance status; CTFI, chemotherapy-free interval; PD, progressive disease; LDH, lactate dehydrogenase; ULN, upper limit of normal.
[a]Refers to the time interval from determination of progressive disease on the last prior treatment regimen until entry into the phase 2 basket trial.

MO01.10

Activity of Lurbinectedin in Second-line SCLC Patients Who Are Candidates for Platinum Rechallenge

Vivek Subbiah[1], Luis Paz-Ares[2], Benjamin Besse[3], Khalil Zaman[4], Maria Angeles Sala[5], José Antonio López-Vilariño[6], Cristian Fernández[6], Carmen Kahatt[6], Mariano Siguero[6], Ali Zeaiter[6], Jennifer Arrondeau[7], Jean-Pierre Delord[8], Maite Martínez[9], Antonio Antón[10], José M Trigo[11], Luciano Wannesson[12]

[1]The University of Texas MD Anderson Cancer Center, Houston, United States, [2]Hospital Universitario Doce de Octubre, Madrid, Spain, [3]Gustave Roussy Cancer Campus, Villejuif, France, [4]University Hospital CHUV, Lausanne, Switzerland, [5]Hospital Universitario de Basurto, Bilbao, Spain, [6]PharmaMar, Colmenar Viejo, Spain, [7]Hôpital Cochin, Paris, France, [8]Institut Claudius Regaud, IUCT-Oncopole, Toulouse, France, [9]Complejo Hospitalario de Navarra, Pamplona, Spain, [10]Hospital Universitario Miguel Servet, Zaragoza, Spain, [11]Hospital Universitario Virgen de la Victoria, Málaga, Spain, [12]Ospedale San Giovanni, Bellinzona, Switzerland

Background: Lurbinectedin (Zepzelca™) is a novel anticancer agent that selectively inhibits oncogenic transcription, induces DNA double-strand breaks leading to apoptosis, and modulates the tumor microenvironment. FDA approval for lurbinectedin in metastatic small-cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy was recently granted based on the results of a phase 2 basket trial. Lurbinectedin is a preferred regimen for patients with chemotherapy-free interval (CTFI) <6 months in the NCCN guidelines and a recommended regimen for CTFI >6 months. **Methods:** In the SCLC cohort of the basket trial, 60 patients with CTFI ≥90 days (20 with CTFI ≥180 days) received one prior platinum-containing line and were treated with lurbinectedin 3.2 mg/m² as a 1-hour intravenous infusion on once every 3 weeks. **Results:** Median age was 59 years (range: 44, 78); 57% were males; ECOG PS 0/1/2 was 45%/ 50%/5%; 32% had liver metastases; 5% had brain metastases; 58% had extensive disease at diagnosis; 8% had received prior immunotherapy; and 85% had a best response to prior platinum-based chemotherapy of complete response or partial response. Median CTFI was 4.7 months (range: 2.9, 16.1). Median number of cycles of lurbinectedin was 6 (range: 1, 24). Response and overall survival by CTFI are shown in the Table. The main adverse events were hematologic (grade 3/4 neutropenia: 25%; grade 3/4 anemia: 10%) and grade 3 fatigue (10%). One patient had febrile neutropenia (2%). Further systemic treatment was administered in 73% of patients after lurbinectedin discontinuation (55% received platinum-based chemotherapy and 20.5% received immunotherapy). **Conclusion:** Lurbinectedin appears to be an effective treatment for patients with platinum-sensitive relapsed SCLC with CTFI ≥90 days and CTFI ≥180 days (post hoc analysis), with acceptable safety and tolerability. These results suggest lurbinectedin may represent a valuable alternative to platinum rechallenge.

Table. ORR and OS by CTFI

	CTFI ≥90 days (n = 60)		CTFI ≥180 days (n = 20)	
	IA	IRC	IA	IRC
ORR (95% CI), % (confirmed responses)	45.0 (32.1, 58.4)	43.3 (30.6, 56.8)	60.0 (36.1, 80.9)	50.0 (27.2, 72.8)
Disease control rate at 8 weeks (95% CI), %	81.7 (69.6, 90.5)	73.3 (60.3, 83.9)	95.0 (75.1, 99.9)	80.0 (56.3, 94.3)
Median duration of response (95% CI), months	6.2 (3.5, 7.3)	5.3 (4.9, 7.0)	5.5 (2.9, 11.2)	5.5 (2.8, 8.5)
Median OS (95% CI), months	11.9 (9.7, 16.2)		16.2 (9.6, NR)	
OS at 12 months (95% CI), %	48.3 (32.5, 64.1)		60.9 (35.7, 86.2)	

ORR: overall response rate; OS: overall survival; CTFI: chemotherapy-free interval; IA: investigator assessment; IRC: Independent Review Committee; CI: confidence interval; NR: not reached.

MO01.11

The Relative Survival Impact of Thorough Staging and Appropriate Treatment in Non-Small-Cell Lung Cancer (NSCLC).

Meghan Taylor[1], Matthew Smeltzer[2], Meredith Ray[2], Nicholas Faris[1], Carrie Fehnel[1], Olawale Akinbobola[1], Bianca Jackson[1], Courtney Foust[1], Laura McHugh[1], Raymond S. Signore[1], Roy Fox[3], Jeffrey Wright[4], Robert Optican[5], Keith Tonkin[5], Edward T. Robbins[1], Raymond Osarogiagbon[1]

[1]Multidisciplinary Thoracic Oncology Program, Baptist Cancer Center, Memphis, United States, [2]Division of Epidemiology, Biostatistics, and Environmental Health, School of Public Health, University of Memphis, Memphis, United States, [3]Mid-South Pulmonary Specialists, Memphis, United States, [4]Memphis Lung Physicians Foundation, Memphis, United States, [5]MidSouth Imaging/Therapeutics, Memphis, United States

Background: Quality care for non-small cell lung cancer (NSCLC) patients depends on both thorough staging and guideline-concordant treatment. We evaluated the relative survival impact of thorough staging and appropriate treatment in a community-based cohort. **Methods:** Prospective observational cohort of NSCLC patients diagnosed from 2014-2019 treated at the Baptist Cancer Center, Memphis, TN. Invasive staging (IS) included any minimally-invasive staging or mediastinoscopy (including those the same day as surgery). Stage-appropriate treatment (SAT) was defined as concordance with National Comprehensive Cancer Network treatment guidelines. Patients were grouped as to whether they received IS only, SAT only, both, or neither. Overall survival (measured from the date of diagnosis) was evaluated with Kaplan-Meier curves and multivariable Cox proportional hazards models. Sensitivity analyses excluded subjects with poor performance status (PS). **Results:** The 1217 patients were 49% female; 67% white. The stage I/II/III/IV distribution was 33%/10%/26%/31%. 55% of patients received both IS+SAT, 14% received IS but no SAT, 21% received SAT only, and 10% received neither. These 4 groups of patients did not differ significantly by age, sex, insurance, or race. Patients receiving both SAT and IS as well as SAT only had the fewest co-morbidities (p=0.003) and better PS (p=0.0005). Patients who received SAT had significantly better survival than those who did not (log-rank p<0.0001). After adjusting for age, sex, race, insurance, number of comorbidities, and histology, patients receiving both IS and SAT had a 48% reduction in the risk of death compared to those receiving neither (HR= 0.52 (0.41, 0.68)). Patients receiving only SAT (HR= 0.55 (0.41, 0.75)) had significantly better survival than those receiving neither, while those receiving only IS did not significantly differ from neither (HR= 0.90 (0.66, 1.23)). Results remained comparable even after excluding patients with poor PS. **Conclusions:** NSCLC survival depends more on appropriate treatment delivery than thorough staging.

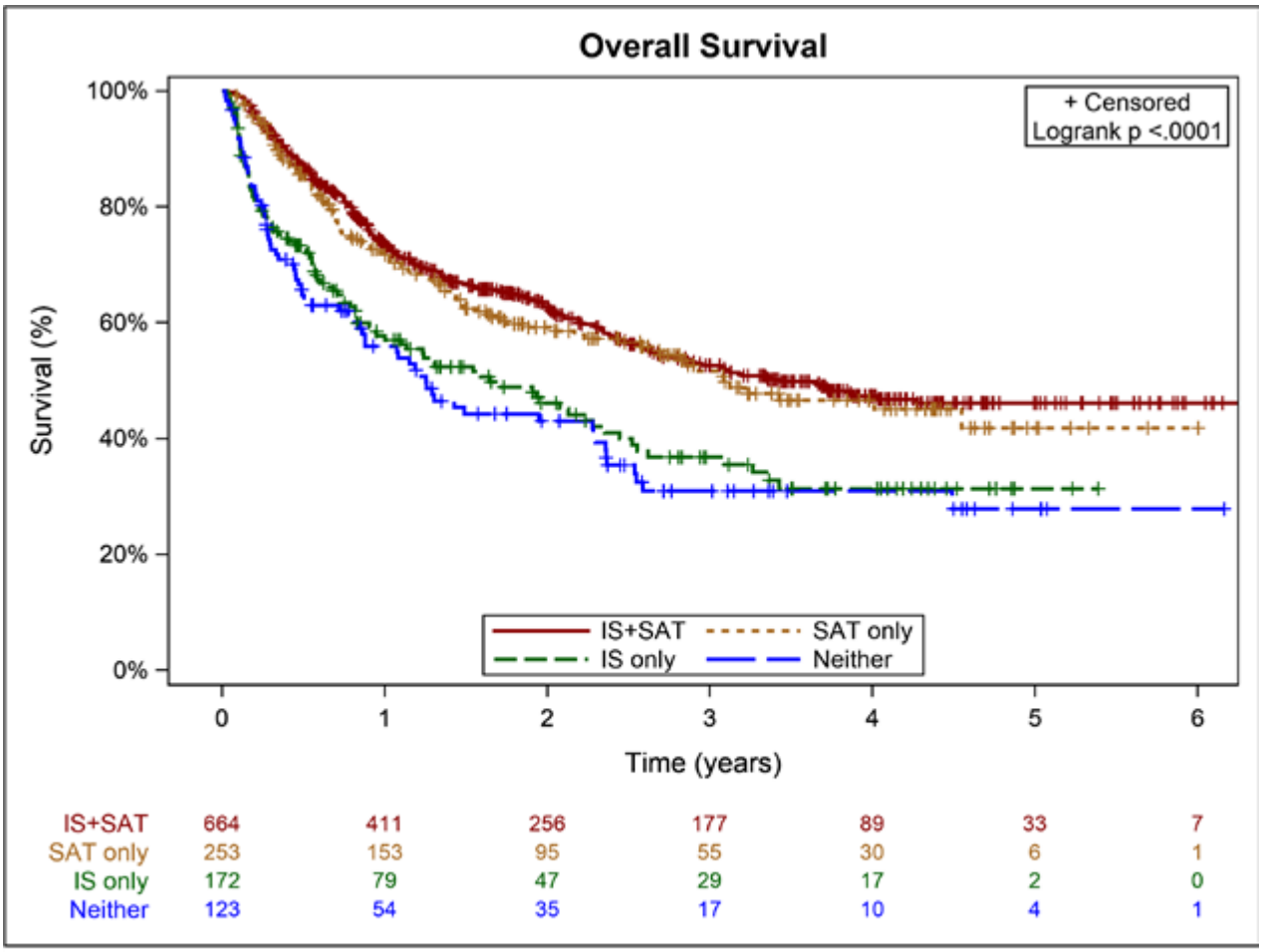


Figure 1. Kaplan-Meier survival curves for patients who received both invasive staging and stage appropriate (guideline-concordant) treatment (IS+SAT), invasive staging only (IS), stage appropriate treatment only (SAT), or neither.

MO01.12

Association of Opioid Use with Survival in Non-Small Cell Lung Cancer Patients Treated with Immune Checkpoint Inhibitor Therapy

Joseph Mock[1], Emmett Wynter[2], Philip Young[2], Alexander Sytov[3], Omar Elghawy[3], Ryan Gentzler[1], Wendy Novicoff[4], Linda Martin[5], Richard Hall[1]

[1]University of Virginia Department of Medicine, Division of Hematology/Oncology, Charlottesville, United States, [2]University of Virginia Department of Medicine, Charlottesville, United States, [3]University of Virginia School of Medicine, Charlottesville, United States, [4]University of Virginia School of Medicine, Department of Public Health Sciences, Charlottesville, United States, [5]University of Virginia Department of Surgery, Division of Thoracic Surgery, Charlottesville, United States

Background: Immune checkpoint inhibitors (CPIs) have been shown to improve overall survival and disease-free survival in patients with non-small cell lung cancer (NSCLC), but as many as 50% of patients do not respond to therapy. Identifying the patient and clinical characteristics that influence treatment response remains vital to further advancement. Opioids, through a variety of mechanisms, have been reported to blunt both the innate and adaptive immune syste Given the ubiquitous use of opioids to treat cancer-related pain, further investigation of their influence on immunotherapy is warranted. This study examined the impact of opioid use on overall survival (OS) and duration on therapy (DOT) in patients with advanced NSCLC treated with CPIs. **Methods:** A single-center, retrospective, cohort study of 208 patients with stage IV NSCLC treated with CPIs between February 4, 2015 and January 1, 2020 was performed. Patient demographics, treatments received, duration on therapy, opioid prescriptions, and clinical outcomes were collected. Opioid utilization was determined by tabulating all opioid prescriptions written during the patients' CPI therapy (including 2 weeks prior). A morphine equivalent daily dose (MEDD) for duration of CPI therapy was calculated for each patient to classify high opioid use (MEDD > 50) and low opioid use (MEDD < 50). A multivariate regression model was developed to compare OS and DOT between high and low opioid use. **Results:** Among 208 patients identified, 114 (55%) were male with median age of 65 years (range: 37-92). Thirty-seven (18%) patients had high opioid use. Patients classified as low opioid use had a median OS of 14.5 months (95% CI: 11.7-16.3) compared to 3.8 months (95% CI: 3.0-4.8) for high opioid use, p=0.001. Median DOT for low opioid use was 7.4 months (95% CI: 6.2-8.8) compared to 1.8 months (95% CI: 1.1-2.3) for high opioid use, p=0.001. The multivariate analysis demonstrated that OS was negatively associated with increasing age (p=0.050), male gender (p=0.034), ECOG > 2 (p=0.009), and high opioid use (p=0.001). Duration on therapy was negatively associated with increasing age (p=0.028) and high opioid use (p=0.001) and positively associated with PD-L1 expression > 50% (p=0.012). **Conclusion:** Our data suggest high opioid use is associated with decreased duration on therapy and worse overall survival in stage IV NCSLC patients treated with CPIs. Further study is needed to investigate underlying mechanisms.

MO01.13

Molecular Risk Stratification is Independent of EGFR Mutation Status in Identifying Early Stage Non-Squamous Non-Small Cell Lung Cancer Patients at Risk for Recurrence and Likely to Benefit from Adjuvant Chemotherapy

Gavitt Woodard[1], Johannes Kratz[2], Greg Haro[2], Matthew Gubens[2], Collin Blakely[2], Kirk Jones[2], Michael Mann[2], David Jablons[2]

[1]Yale, New Haven, United States, [2]University of California, San Francisco, San Francisco, United States

Background: Mutation analysis and targeted therapy are standards of care in late stage non-small cell lung cancer (NSCLC). Prospective data from a cohort of 100 patients suggested that a rigorously validated, clinically certified gene expression profile may improve unacceptably low long-term survival in stage I-IIA NSCLC by identifying patients likely to benefit from adjuvant intervention. Despite exploration of EGFR-targeted TKIs in the adjuvant setting, mutation status has not been found to provide prognostic information to support adjuvant intervention in early stage disease. We compared EGFR mutation data to molecular risk stratification in a prospective, early stage cohort. **Methods:** An expanded cohort of 250 consecutive stage I-IIA non-squamous NSCLC patients underwent prospective molecular risk-stratification by the 14-gene prognostic assay; driver mutation next generation sequencing (NGS) was available in a subset of 150 patients. Platinum doublet adjuvant chemotherapy (AC) was recommended for molecular high-risk (HR) patients (defined as high or intermediate risk score) without consideration of driver mutations. Kaplan-Meier analysis and log-rank tests were used to evaluate differences in freedom from recurrence (FFR) and disease-free survival (DFS). **Results:** At a median follow up of 29 months, prospective efficacy of the 14-gene assay was confirmed in this expanded cohort, with estimated FFR of 94.6% and 72.4% in molecular low risk (LR) and untreated HR patients, respectively ($P<0.001$). Importantly, HR patients undergoing AC had FFR of 97.0%. In 168 stage IA patients, for whom there is no guideline recommendation for adjuvant therapy, similar FFR of 97.4%, 73.2% and 100% was seen in LR, untreated HR and treated HR, respectively. In the NGS cohort, EGFR mutation was observed in 56 patients (37.3%). Unlike molecular risk stratification, there was no significant association between EGFR status and recurrence. Although LR was more prevalent among EGFR+ patients (64% vs. 53% in the overall population, $P=0.04$), more than a third of EGFR+ patients were HR. Furthermore, molecular risk continued to predict both survival as well as response to AC within the EGFR+ population, with DFS of 90.1%, 61.2% and 100% among LR, untreated HR and treated HR, respectively. **Conclusion:** This prospective study indicates the utility of the 14-gene assay independent of EGFR mutation. Prognostication based on EGFR status may overlook up to 36% of patients likely to benefit from adjuvant intervention, whereas basing expensive, morbid, long-term TKI therapy on EGFR status without molecular stratification could overtreat as many as 65% of patients likely to be free of residual disease.

MO01.14

Real-World Effectiveness and Safety of Afatinib Following Immunotherapy (IO) in the Treatment of Metastatic, Squamous Cell/Mixed Histology Carcinoma of the Lung: A Multi-Site Retrospective Chart Review Trial in the US

Edward S. Kim[1], Janakiraman Subramanian[2,3], Jonathan Kish[4], Agnieszka Cseh[5], Wenbo Tang[6], Elizabeth Terlizzi[6]
[1]Department of Solid Tumor Oncology, Levine Cancer Institute, Atrium Health, Charlotte, USA, [2]Division of Oncology, Saint Luke's Cancer Institute, Kansas City, USA, [3]Center for Precision Oncology, Saint Luke's Cancer Institute, Kansas City, USA, [4]Cardinal Health, Dublin, USA, [5]Medical Affairs, Boehringer Ingelheim International GmbH, Ingelheim, Germany, [6]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, USA

Background: Pembrolizumab+chemotherapy is approved for first-line treatment of metastatic squamous NSCLC; afatinib is approved after platinum-based chemotherapy. To date, no prospective trials have investigated afatinib following first-line IO+chemotherapy for metastatic squamous NSCLC. This real-world trial characterized the profiles and outcomes of patients who progressed on first-line IO+platinum-based chemotherapy and received afatinib as second-line therapy. **Methods:** In this retrospective, non-interventional, multi-site cohort trial, US-based community oncologists identified patients, and data were extracted from electronic health records. Patients had advanced or metastatic squamous/mixed histology NSCLC treated with first-line pembrolizumab+platinum-based chemotherapy, followed by second-line afatinib (Cohort 1) or chemotherapy (Cohort 2). Primary outcomes included description of patient demographics and clinical characteristics, incidence of severe immune-related adverse events (irAEs), and time on treatment (TOT). **Results:** Two hundred patients were included: Cohort 1 (n=99); Cohort 2 (n=101). Patient disposition and demographics are shown in Table 1; numbers of patients with EGFRm+ tumors/squamous cell histology differed between Cohorts 1 and 2 (39/65% and 5/97%, respectively). In Cohort 1, six patients (6%) had Grade 3/4 irAEs (pneumonitis, n=3; colitis, n=2; hepatitis, n=1); all had a prior Grade 3/4 irAE during first-line therapy (two had the same irAE, Table 1), all had squamous cell histology, and one was EGFRm+. No patients in Cohort 2 had a Grade 3/4 irAE. Median TOT in Cohort 1 overall was 7.3 months, in squamous/mixed histology was 5.8/8.1 months, and in EGFRm+/EGFRm- was 7.4/5.9 months, respectively. Median TOT in Cohort 2 was 4.2 months. **Conclusion:** These real-world data suggest that second-line afatinib is generally well tolerated and effective in patients with metastatic squamous carcinoma of the lung; they provide rationale for further evaluation of second-line afatinib treatment following first-line pembrolizumab+platinum-based chemotherapy in this patient group. A high proportion of EGFRm+ patients received first-line IO rather than an EGFR TKI, highlighting the importance of testing.

	Second-line afatinib; Cohort 1 N=99 (%)	Second-line chemotherapy*; Cohort 2 N=101 (%)
Patient disposition at data cut-off, n (%)		
Still receiving second-line therapy	53 (53.5)	41 (40.6)
Discontinued second-line, no further therapy	9 (9.1)	9 (8.9)
Initiated third-line therapy	4 (4.0)	5 (5.0)
Died	33 (33.3)	46 (45.5)
Patient demographics		
Histology, n (%)		
Squamous cell	64 (64.6)	98 (97.0)
Mixed histology	35 (35.4)	3 (3.0)
*EGFR*m+, n (%)	39 (39.4)	5 (5.0)
Age†, years (range)	68.0 (61.0–73.0)	66.0 (61.0–70.0)
Male, n (%)	56 (56.6)	67 (66.3)
Smoking status, n (%)		
Ex	71 (71.7)	82 (81.2)
Current	16 (16.2)	19 (18.8)
Stage at diagnoses, n (%)		
IIIB	7 (7.1)	3 (3.0)
IV	79 (79.8)	90 (89.1)
Ethnicity, n (%)		
White	59 (59.6)	73 (72.3)
Asian	6 (6.1)	1 (1.0)
Black/African American	30 (30.3)	23 (22.8)
Other	4 (4.0)	4 (4.0)
ECOG PS, n (%)		
0–1	45 (45.5)	50 (49.5)
≥2	54 (54.5)	51 (50.5)
Duration of first-line therapy, months (95% CI)	7.8 (6.6, 9.1)	8.2 (7.0, 8.7)
Severe irAEs during second-line therapy‡,§, n (%)	6 (6.1)	0 (0.0)
Immune-mediated colitis	2 (2.0)	0 (0.0)
Immune-mediated hepatitis	1 (1.0)	0 (0.0)
Immune-mediated pneumonitis	3 (3.0)	0 (0.0)
TOT, months (95% CI)	7.3 (5.2, 8.1)	4.2 (3.9, 4.9)

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*m+, *EGFR* mutation positive; irAEs, immune-related adverse events; TOT, time on treatment

*Most common second-line chemotherapy: docetaxel/ramucirumab, gemcitabine, and docetaxel; †at initiation of second-line therapy; ‡an additional patient had an indeterminate severe irAE; §two patients had a diagnosis of the same irAE during first-line therapy: one patient with immune-related hepatitis, and one patient with immune-related pneumonitis

MO01.15
Nitric Oxide Lung Cancer Active Vaccination

Hila Confino[1], Shay Yarkoni[1], Matan Goldshtein[1], Elya Dekel[1], Omer Lerner[1], Shani Puyesky[1], Steve Lisi[2], Rinat Kalaora[1], Pam Golden[2], Amir Avniel[1], Ido Wolf[3]
[1]Beyond Air Ltd., Rehovot, Israel, [2]Beyond Air inc., New York, USA, [3]Oncology Division, Sourasky Medical Center, Tel Aviv, Israel

Background: Metastases are responsible for a major portion of the morbidity and mortality of cancer, accounting for approximately 90% of all cancer-related deaths. In situ destruction of the tumor mass has been reported to provide the immune system with an antigen source for the induction of antitumor immunity, which can destroy distant metastases. One of the proposed mechanisms involves the induction of antigen presenting cells that may result in the stimulation of adaptive immunity. Our research group is developing an innovative gaseous Nitric Oxide (gNO) based tumor ablation method. NO is a short-lived free radical which, at high doses, possesses anticancer properties. Moreover, NO has been proven to activate the immune system against tumors. Previous in vivo results showed that all gNO-treated colon tumor-bearing (CT26 model) mice (n=6) were resistant to a secondary CT26 cell inoculation. In the current study, high dose gNO has been used to destroy lung cancer cells in vitro and ablate solid tumors in mice. The immune response stimulated following this treatment in mice was tested in vivo. **Methods:** (I) The mouse lung cancer cell line, LLC1, was exposed to gNO at 10,000-50,000 ppm for 10 seconds – 15 minutes in vitro. Cell viability was examined at 24 hrs by XTT-based cell proliferation and apoptosis-necrosis (Annexin V – Propidium Iodide) assays. (II) LLC1 lung tumor-bearing mice were treated with 50,000 ppm gNO intratumorally. A metastasis model was induced in all gas-treated tumor bearing mice up to 7 days post treatment by challenging the mice with a second cancer cell inoculation (challenge assay). Naïve mice, inoculated with the same cancer cells, served as an internal control. **Results:** According to both XTT and apoptosis-necrosis assays, less than 10% of LLC1 cells remained viable when exposed to 15,000 ppm NO for 3 minutes ($p<0.05$). After this time point cells were not viable. At 24 hours after 15,000 ppm NO exposure, 88% of LLC1 cells treated with gNO for 3 minutes were at late apoptosis. According to the in vivo data, both gNO-treated lung tumor-bearing mice (n=2) were resistant to a second LLC1 lung cancer cell inoculation as compared to 100% tumor take in the control group (n=3, $p = 0.03$). **Conclusion:** These results demonstrate the possibility for a novel treatment for lung cancer. Our innovative gNO based treatment may serve to treat lung tumors locally and their distant metastases systemically via the stimulation of an anti-tumor immune response.

MO01.16

Sociodemographic and Contextual Factors Associated with Biomarker Testing for Patients with Non-Small Cell Lung Cancer in Community Practice

Louise Henderson[1], Danielle Durham[1], Marjory Charlot[1], Allison Throneburg[1], Lindsay Lane[1], Pasangi Perera[1], Danielle Samulski[1], Patricia Rivera[1]
[1]*University Of North Carolina, Chapel Hill, United States*

Background: Discovery of driver oncogenes and development of targeted therapies has improved survival and shepherded in the era of precision medicine in non-small cell lung cancer (NSCLC). Professional society guidelines recommend molecular biomarker testing in all patients with non-squamous and select patients with squamous advanced stage NSCLC. We examined the use of biomarker testing and evaluated geographic access to testing to identify potential gaps in care. **Methods:** We included 389 patients ages 18 and older diagnosed with stage IV NSCLC in 2018 in 41 North Carolina hospitals. We abstracted data on patient socio-demographics, cancer characteristics and biomarkers (EGFR, KRAS, ALK, ROS1, BRAF, HER2), from pathology reports. Using the patient's residence, we calculated travel time to location where the biopsy was performed. We also incorporated contextual factors related to socioeconomics and demographics available from US Census Data. We compared the frequency of testing by age group, race, sex, patient residence (rural vs. urban), hospital location (rural vs. urban), travel time, and area level factors of median income, unemployment rate, diversity index, poverty level, linguistic isolation, and internet access. We used multivariable logistic regression to determine predictors of testing by histology (non-squamous vs. squamous) and report adjusted odds ratios (OR) and 95% confidence intervals (95%CIs). **Results:** In our cohort, 80.2% (312/389) had non-squamous and 19.8% (77/389) had squamous cell histology. Overall, 64.4% of patients with non-squamous NSCLC (201/312) underwent biomarker testing and 35.6% were untested. In contrast, 32.5% of patients with squamous cell (25/77) had biomarker testing performed, which is not in line with guidelines. Biomarker testing rates for non-squamous cell were similar across patient and contextual factors in unadjusted and adjusted analyses. Among patients with squamous cell, rates of testing were 53.3% in black patients versus 27.4% in white patients (p-value=0.0544) and 45.2% in those living in rural vs. 23.9% in those living in urban areas (p-value=0.0508). Among patients with squamous histology, testing was more common among patients living in rural versus urban areas (aOR=3.7, 95%CI:1.1-12.7), adjusting for age, race, gender and hospital location. The next iteration of the analyses will further adjust for patient smoking status and biopsy specimen size. **Conclusion:** Biomarker testing remains underutilized across subgroups of the population with non-squamous histology, and potentially overutilized in squamous histology. Additional investigation into the use of biomarker testing in patients with squamous histology is warranted. Future work should evaluate hospital-specific testing protocols to understand discrepancies with guideline recommendations.

MO01.17

Real-World Characteristics and Outcomes of Advanced NSCLC Patients with Exon 19 or 21 EGFR Mutations

Katherine Winfree[1], Cliff Molife[1], Patrick Peterson[1], Yongmei Chen[1], Carla Visseren[1], Julie Beyrer[1], Mark Leusch[1], Anastasios Dimou[2]

[1]Eli Lilly and Company, Indianapolis, United States, [2]Mayo Clinic, Rochester, United States

Background: Patients with exon 21 mutations may derive a more modest benefit with EGFR tyrosine kinase inhibitor (TKI) monotherapy than patients with exon 19 mutations. This study describes baseline patient characteristics and estimates clinical outcomes for patients with exon 19 or 21 mutations in routine practice in the real-world. **Methods:** This retrospective study used US Flatiron Health EHR-derived de-identified data to analyze advanced NSCLC patients having tumors with an EGFR Exon 19 or 21 mutation who underwent FoundationOne® tumor sequencing and were treated as part of routine care between January 2014 - September 2019. Real-world progression-free survival (rwPFS), rwPFS2, and overall survival (OS) were indexed to start of first-line (1L) treatment and estimated using Kaplan-Meier method. Real-world tumor response (rwTR) was calculated. Cox models were used to estimate hazard ratios (HRs) and to evaluate and identify patient characteristics prognostic of outcome. **Results:** Of the 244 1L-treated patients , those with exon 21 mutations were older (mean 70.5 vs 66.4 years), more likely to have smoking history (52.4% vs 41.1%), less likely to be white race (49.5% vs 68.1%) and less likely to have bone metastases (50.5% vs 60.3%) than those with exon 19 mutations; other baseline characteristics appeared similar. Select outcomes are shown in Table. rwTR rates were 74% and 79% respectively for Exon 19 and 21 groups. Observed trends in outcomes by exon status are consistent for TKI monotherapy treatment and across all TKI generations. Multivariable analyses adjusting for identified prognostic factors resulted in similar outcomes. **Conclusions:** In real-world clinical practice, patients with an EGFR exon 19 mutation have a prognostic advantage over Exon 21 with statistically better rwPFS and rwPFS2. Further research is needed to examine the unmet need and optimal treatment options for these exon 21 patients.

	Exon 19 (N=141)	Exon 21 (N=103)
rwPFS		
Median months (95% CI)	10.6 (9.4-14.0)	8.1 (7.3-10.9)
HR (95%CI), p-value	1.72 (1.17-2.52), 0.006	
1-year PFS rate % (95% CI)	45 (35-55)	27 (15-40)
TKI monotherapy	n=114	n=64
Median months (95% CI)	11.8 (9.4-15.3)	10.8 (6.2-12.0)
HR (95%CI), p-value	1.62 (1.03-2.56), 0.036	
Other therapy	n=27	n=39
Median months (95% CI)	7.8 (4.2-18.1)	7.8 (4.9-10.4)
HR (95%CI), p-value	1.56 (0.73-3.32), 0.241	
rwPFS2		
Median months (95% CI)	23.1 (14.3-46.1)	14.0 (12.1-18.6)
HR (95% CI), p-value	2.11 (1.02-4.34), 0.042	
OS		
Median months (95% CI)	37.4 (25.1-49.7)	25.1 (18.8-32.2)
HR (95% CI), p-value	1.47 (0.96-2.25), 0.074	
1-year OS rate % (95% CI)	79 (70-86)	71 (59-79)

MO01.18

An indirect Comparison of Pembrolizumab+Chemo vs Ipilimumab+Nivolumab as First-Line Therapies in Patients with PD-L1 TPS≥1% Metastatic NSCLC

Balazs Halmos[1], Thomas Burke[2], Chrysostomos Kalyvas[3], Ralph Insinga[2], Kristel Vandormael[3], Andrew Frederickson[4], Bilal Piperdi[5]

[1]Department of Oncology, Montefiore/Albert Einstein Cancer Center, Bronx, USA, [2]Center for Observational & Real World Evidence (CORE), Merck & Co., Inc., Kenilworth, USA, [3]Biostatistics and Research Decision Sciences, MSD Europe, Inc, Brussels, Belgium, [4]precisionHEOR, Oakland, USA, [5]Oncology Clinical Development, Merck & Co., Inc, Kenilworth, USA

Background: Multiple anti-PD-1/PD-L1 first-line treatment options are approved for advanced non-small cell lung cancer (NSCLC), including pembrolizumab+chemotherapy studied in KEYNOTE 021G (KN021G), KEYNOTE-189 (KN189) and KEYNOTE-407 (KN407) and nivolumab+ipilimumab studied in CheckMate 227 Part 1A. A comprehensive understanding of the potential differences between these treatment options is required to inform clinical decision making. In the absence of head-to-head trial data, this analysis indirectly compared the effectiveness of pembrolizumab+chemotherapy versus nivolumab+ipilimumab for the first-line treatment of metastatic NSCLC patients with a PD-L1 tumor proportion score (TPS) ≥1%. **Methods:** A matching-adjusted indirect comparison (MAIC) was conducted using pooled individual patient data (IPD) from the intention-to-treat (ITT) population of KN021G, KN189 and KN407 restricted to patients with stage IV disease (N=816; database cut-off dates: 8/19/2019, 5/20/2019, and 5/9/2019, respectively) and published aggregated data of nivolumab+ipilimumab from the CheckMate 227 Part 1A (N=793; database cut-off date: 7/2/2019). Since platinum-doublet chemotherapy was the comparator in all trials it was used as the anchor for the MAIC. Study designs were similar for all three trials. To adjust for cross-trial differences in baseline characteristics, data from KN021G/KN189/KN407 were re-weighted to match the baseline characteristics of CheckMate 227 Part 1A (including age, sex, region, smoking status, ECOG status, histology, metastasis, PD-L1 expression). Outcomes of interest included overall survival (OS), progression-free survival (PFS) and objective response rate (ORR). Assessment of PFS and ORR was based on blinded independent review. Base case analyses were restricted to the patient population with PD-L1 TPS≥1%, with sub-group analyses in TPS≥50% and 1–49% sub-groups. **Results:** The effective sample size of the KN021G/KN189/KN407 population after adjusting for cross trial differences was 456. The estimated HR (95% CIs) of pembrolizumab+chemotherapy versus nivolumab+ipilimumab was 0.80 (0.59, 1.09) and 0.53 (0.41, 0.68) for OS and PFS, respectively, which favored pembrolizumab+chemotherapy. For ORR, the estimated risk ratio (95% CI) was 1.78 (1.32, 2.39) for pembrolizumab+chemotherapy versus nivolumab+ipilimumab and the risk difference was 25% (15, 36). After matching, the landmark 1-year OS rate was 70.95% versus 62.40% for pembrolizumab+chemotherapy and nivolumab+ipilimumab, respectively, and the 2-year OS rate was 49.22% versus 39.79%, respectively. Findings were consistent across PD-L1 TPS 1–49% and TPS≥50% sub-groups. **Conclusion:** These MAIC results show that the pembrolizumab+histology-specific platinum-doublet chemotherapy option leads to a greater clinical benefit than nivolumab+ipilimumab in patients with PD-L1≥1% and in different PD-L1 TPS sub-groups. Given the lack of head-to-head studies, these analyses may inform clinical and formulary decision making for prioritizing treatments.

MO01.19

An Indirect Comparison of Pembrolizumab Monotherapy Versus Ipilimumab+Nivolumab for First-Line Metastatic NSCLC with PD-L1 TPS≥1%

Balazs Halmos[1], Thomas Burke[2], Chrysostomos Kalyvas[3], Ralph Insinga[2], Kristel Vandormael[3], Andrew Frederickson[4], Bilal Piperdi[5]

[1]Department of Oncology, Montefiore/Albert Einstein Cancer Center, Bronx, USA, [2]Center for Observational & Real World Evidence (CORE), Merck & Co., Inc., Kenilworth, USA, [3]Biostatistics and Research Decision Sciences, MSD Europe, Inc., Brussels, Belgium, [4]precisionHEOR, Oakland, USA, [5]Oncology Clinical Development, Merck & Co., Inc, Kenilworth, USA

Background: Recently, multiple immunotherapy-based treatment choices have emerged for the management of advanced non-small cell lung cancer (NSCLC). Pembrolizumab monotherapy, based on KEYNOTE-024 (KN024) and KEYNOTE-042 (KN042), and nivolumab+ipilimumab, based on CheckMate 227 Part 1A, are approved for patients with metastatic NSCLC with PD-L1 tumor proportion score (TPS) ≥1%. In the absence of head-to-head trial data, the comparative effectiveness of pembrolizumab monotherapy versus nivolumab+ipilimumab for the first-line treatment of metastatic NSCLC patients with PD-L1 TPS≥1% can be assessed only by using indirect treatment comparisons.
Methods: A matching-adjusted indirect comparison (MAIC) of pembrolizumab monotherapy compared to nivolumab+ipilimumab was conducted using pooled individual patient data (IPD) from KN024 and KN042 restricted to patients with stage IV disease (N=1,428; database cut-off dates: 2/15/2019 and 9/4/2018, respectively) and published aggregated data from CheckMate 227 Part 1A (N=793; database cut-off date: 7/2/2019). Since platinum-doublet chemotherapy was the comparator in all trials it was used as the anchor for the MAIC. Study designs were similar for all three trials. To adjust for cross-trial differences in baseline characteristics, data from the intention-to-treat (ITT) population of KN024/KN042 with TPS>1% were re-weighted to match the baseline characteristics of CheckMate 227 Part 1A (including age, sex, region, smoking status, ECOG performance status, histology, metastasis, PD-L1 expression). Outcomes of interest included overall survival (OS), progression-free survival (PFS) and objective response rate (ORR). Assessments of PFS and ORR were based on blinded independent review in each trial. Base case analyses were conducted in the patient population with TPS≥1%, with sub-group analyses in TPS≥50% and 1–49% sub-groups.
Results: The effective sample size of the KN024/KN042 population after adjusting for cross-trial differences was 993. The estimated HR (95% CIs) of pembrolizumab monotherapy versus nivolumab+ipilimumab after matching was 1.07 (0.82, 1.39) and 1.16 (0.93, 1.45) for OS and PFS, respectively. For ORR, the estimated risk ratio (95% CI) and the risk difference (95% CI) was 0.93 (0.71, 1.22) and -3% (-11, 6), respectively. After matching, the landmark 1-year OS rate was 58.32% versus 62.40% for pembrolizumab monotherapy and nivolumab+ipilimumab, respectively, and the 2-year OS rate was 39.65% versus 39.79%, respectively. Sub-group analysis in PD-L1 TPS≥50% and TPS1–49% populations showed an OS HR equal to 1.05 (0.78, 1.42) and 0.96 (0.65, 1.40), respectively. **Conclusion:** MAIC results demonstrated comparable effectiveness in PFS, OS, and ORR between pembrolizumab monotherapy and nivolumab+ipilimumab as first-line therapy for metastatic NSCLC with PD-L1 TPS>1% and in different TPS sub-groups.

MO01.20

Pembrolizumab+Chemo versus Atezolizumab+Chemo+/-Bevacizumab for First-Line Nonsquamous NSCLC: A Matching-Adjusted Indirect Comparison

Balazs Halmos[1], Thomas Burke[2], Chrysostomos Kalyvas[3], Kristel Vandormael[3], Andrew Frederickson[4], Bilal Piperdi[5]
[1]Department of Oncology, Montefiore/Albert Einstein Cancer Center, Bronx, USA, [2]Center for Observational & Real World Evidence (CORE), Merck & Co., Inc., Kenilworth, USA, [3]Biostatistics and Research Decision Sciences, MSD Europe, Inc, Brussels, Belgium, [4]precisionHEOR, Oakland, USA, [5]Oncology Clinical Development, Merck & Co., Inc, Kenilworth, USA

Background: Combination of chemotherapy and immunotherapy is widely used for treatment of advanced non-small cell lung cancer (NSCLC) without epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) aberrations. Pembrolizumab+chemotherapy, studied in KEYNOTE-021 Cohort G (KN021G) and KEYNOTE-189 (KN189), and atezolizumab+chemotherapy and atezolizumab+chemotherapy+bevacizumab, studied in IMpower 130 and IMpower 150, are all regulatory-approved regimens for nonsquamous NSCLC. Optimal choice with regards to the effectiveness between these regimens is not well-defined in the absence of head-to-head trial data. This study indirectly compared the effectiveness of pembrolizumab+chemotherapy versus atezolizumab+chemotherapy+/-bevacizumab for previously untreated non-squamous NSCLC patients without EGFR and ALK aberrations. **Methods:** A matching-adjusted indirect comparison (MAIC) was conducted using individual patient data (IPD) from KN021G (pembrolizumab+carboplatin+pemetrexed; N=59) and KN189 (pembrolizumab+pemetrexed+platinum chemotherapy; N=410) and published aggregated data from IMpower 130 (atezolizumab+carboplatin+nab-paclitaxel; N=451) and IMpower 150 (atezolizumab+carboplatin+paclitaxel+bevacizumab; N=356). Study designs and patient selection criteria were similar for all three trials. To adjust for cross-trial differences in baseline characteristics, data from patients randomized to pembrolizumab+chemotherapy in KN189/KN021G were re-weighted to match the baseline characteristics of patients randomized to atezolizumab+chemotherapy from IMpower 130 or atezolizumab+chemotherapy+bevacizumab in IMpower 150. Due to the lack of common comparators between trials, an unanchored comparison was performed. Outcomes of interest included overall survival (OS), blinded independent review-assessed progression-free survival (PFS) and objective response rate (ORR). OS and PFS follow-up were truncated to the trial with shorter follow-up. Sensitivity analyses were conducted without truncation of follow-up of OS and PFS. **Results:** After adjusting for cross-trial differences, the effective sample size of pembrolizumab+chemotherapy was 428 and 389 for the IMpower 130 and IMpower 150 comparisons, respectively. The estimated HRs (95% CIs) of pembrolizumab+chemotherapy versus atezolizumab+chemotherapy were 0.80 (0.67, 0.95) and 0.79 (0.67, 0.93) with regard to OS and PFS, respectively. For pembrolizumab+chemotherapy versus atezolizumab+chemotherapy+bevacizumab, the estimated HR (95% CIs) was 0.86 (0.72, 1.03) for OS and 0.81 (0.68, 0.96) for PFS. For ORR, the estimated risk ratio (95% CI) and the risk difference (95% CI) was 0.93 (0.81, 1.07) and -3% (-10.04, 3.14) for pembrolizumab+chemotherapy versus atezolizumab+chemotherapy, respectively, and 0.78 (0.67, 0.91) and -12% (-20, -5) for pembrolizumab+chemotherapy versus atezolizumab+chemotherapy+bevacizumab, respectively. Findings were consistent across sensitivity analyses for both outcomes. **Conclusion:** MAIC results showed a better OS and PFS effect with pembrolizumab+chemotherapy compared with atezolizumab+chemotherapy+/-bevacizumab. Given the lack of head-to-head studies comparing these regimens, results from these MAIC analyses may be useful to inform clinical practice and decision makers for prioritizing treatments.

MO01.21

Phase 2 GEOMETRY Mono-1 Study: Capmatinib in Patients with METex14-mutated Advanced Non-Small Cell Lung Cancer who Received Prior Immunotherapy

Rebecca S. Heist[1], J. Vansteenkiste[2], E. Smit[3], H. Groen[4], E Garon[5], T. Hida[6], M Nishio, K Kokowski, C Grohe[9], N Reguart[10], A Mansfield[11], A Robeva[12], S Ghebremariam[13], M Waldron-Lynch[14], M Akimov[15], N Nwana[16], M Giovannini[17], J Wolf[18]

[1]Massachusetts General Hospital, Harvard Medical School, Boston, USA, [2]University Hospitals Leuven - Campus Gasthuisberg, Leuven, Belgium, [3]Netherlands Cancer Institute, Amsterdam, Netherlands , [4]University of Groningen and University Medical Center Groningen, Netherlands , [5]David Geffen School of Medicine, UCLA/TRIO-US Network, Los Angeles, USA, [6]Aichi Cancer Center Hospital, Japan, [7]Cancer Institute Hospital, Japanese for Cancer Research, Japan, [8]Klinik für Pneumologie und Pneumologische Onkologie, Klinikum Bogenhausen, München, Germany, [9]Klinik für Pneumologie, Evangelische Lungenklinik ELK Berlin Chest Hospital, Germany, [10]Hospital Clinic de Barcelona, Spain, [11]Mayo Clinic, Rochester, USA, [12]GDO Trial Management - Oncology, Novartis Pharmaceuticals Corporation, East Hanover, USA, [13]Oncology Global Development – BDM, Novartis Pharmaceuticals Corporation, East Hanover, USA, [14]Global Drug Development - Oncology, Novartis Pharma AG, Switzerland, [15]Oncology Department, Novartis Pharma AG, Switzerland, [16]Translational Precision Oncology, Novartis Pharmaceuticals Corporation, East Hanover, USA, [17]Oncology Global Development, Novartis Pharmaceuticals Corporation, East Hanover, USA, [18]University Hospital Cologne, Germany

Background: MET exon 14 skipping mutations (METex14) are seen in 3-4% of patients with non-small cell lung cancer (METex14 NSCLC) and are associated with poor outcomes. In the phase 2 GEOMETRY mono-1 study, capmatinib was efficacious in patients with METex14 NSCLC who were treatment-naive (overall response rate [ORR] 68%) or received one/two lines of therapy (ORR 41%). We present a post-hoc analysis evaluating efficacy and safety of capmatinib in patients with METex14 NSCLC who received immunotherapy (IO) before study entry. **Methods:** Cohort 4 (pre-treated METex14 NSCLC) is included in this analysis. Efficacy (ORR and progression free survival [PFS]) on prior IO, determined by the investigator is reported. Efficacy (ORR, duration of response [DOR] and PFS by blinded independent review committee (BIRC) per RECIST 1.1) of capmatinib 400 mg BID are reported for patients with or without prior IO, as well as safety and biomarker status. **Results:** As of 28 October 2019, 69 patients with METex14 NSCLC were enrolled. Of these, 19 had prior IO (median age 71 years; women 63.2%; never smokers 63.2%) and 50 did not (median age 71.5 years; women 56%; never smokers 56%). Of 19 prior IO patients, 9 received IO first-line and 10 second-line, 18/19 received IO monotherapy. 14/19 patients did not respond to IO (8/19 had progressive disease as best overall response). Median PFS on prior IO was 3.29 months (95%CI 2.10-5.16). Efficacy of capmatinib was demonstrated in patients who received and who did not receive prior IO: ORR 57.9% (n=11/19; 95%CI 33.5-79.7) and 34% (n=17/50; 95%CI 21.2-48.8); median DOR 11.20 months (95%CI 3.35-NE) and 7.16 months (95%CI 4.17-11.14), respectively. Durable responses were observed in patients with lack of response/primary resistance to IO. Safety findings with capmatinib for prior IO patients were similar to patients without prior IO. No increased risk of interstitial lung disease/pneumonitis was observed. Average tumor mutation burden was <10 mut/mb in both groups. **Conclusions:** Efficacy data of IO in patients with METex14 NSCLC is limited. Capmatinib demonstrated efficacy irrespective of the prior treatment with IO, including in patients with lack of response/primary resistance to IO. Capmatinib was well tolerated in post IO patients.

MO01.22

Canakinumab as Adjuvant Therapy in Patients with Completely Resected Non-Small Cell Lung Cancer (NSCLC): CANOPY-A Trial

Alexander I. Spira[1], Andrea Ardizzoni[2], Fabrice Barlesi[3], Byoung Chul Cho[4], Pedro De Marchi[5], Yasushi Goto[6], Dariusz Kowalski[7], Shun Lu[8], Luis Paz-Ares[9], David R. Spigel[10], Michael Thomas[11], Mimi Leung[12], Jason Baum[13], Wen Zhou[12], Socorro Portella[12], James Chih-Hsin Yang[14], Edward B. Garon[15]

[1]US Oncology Research/Virginia Cancer Specialists, USA, [2]S., Orsola-Malpighi University Polyclinic, Italy, [3]Aix-Marseille University, France, [4]Yonsei University College of Medicine, Republic of Korea, [5]Hospital de Câncer de Barretos, Brazil, [6]National Cancer Center Hospital, Japan, [7]Oncology Centre - Institute M. Sklodowska- Curie, Poland, [8]Shanghai Chest Hospital, China, [9]University Hospital 12 de Octubre, Spain, [10]Sarah Cannon Research Institute, USA, [11]Internistische Onkologie der Thoraxtumoren, Thoraxklinik im Universitätsklinikum Heidelberg, Germany, [12]Novartis Pharmaceuticals Corporation, East Hanover,, USA, [13]Novartis Institutes for BioMedical Research, Cambridge,, USA, [14]Graduate Institute of Oncology, National Taiwan University College of Medicine, Taiwan, [15]David Geffen School of Medicine at UCLA/TRIO-US Network, Los Angeles,, USA

Background: In the CANTOS study, canakinumab (selective IL-1β inhibitor) treatment was associated with reduced incidence and mortality from NSCLC in patients with stable post-myocardial infarction with elevated high-sensitivity C-reactive protein (hs-CRP) levels. In CANOPY-A study, we investigate the therapeutic role of canakinumab in NSCLC.
Methods: The CANOPY-A study (NCT03447769) is evaluating the efficacy and safety of canakinumab as adjuvant therapy in adult patients with completely resected NSCLC. Patients with AJCC/UICC v.8 stages II–IIIA and IIIB (T > 5 cm, N2), any histology, completely resected (R0) NSCLC who completed adjuvant cisplatin-based chemotherapy (≥2 cycles) and radiotherapy (if applicable) are eligible. Patients must not have had prior neoadjuvant chemotherapy or radiotherapy. Patients (~1500) are randomized 1:1 to receive canakinumab (200 mg Q3W, SC) or placebo (Q3W, SC) for 18 cycles or until disease recurrence as determined by investigator, unacceptable toxicity, treatment discontinuation at the discretion of the investigator or patient, start of a new antineoplastic therapy, death, or loss to follow-up. Randomization is stratified by AJCC/UICC v.8 stage (IIA vs IIB vs IIIA vs IIIB with T > 5 cm, N2 disease), tumor histology (squamous vs non-squamous), and region (Western Europe and North America vs eastern Asia vs rest of the world). Primary objective was to determine disease-free survival (DFS) per local investigator assessment, and secondary objectives were overall survival (OS), lung cancer specific survival, safety, pharmacokinetics, immunogenicity, and patient reported outcomes. Adult patients with stage IIA–IIIA, IIIB (N2 disease only) NSCLC who are candidates for complete resection surgery (and therefore prospective candidates for the main study) will be asked to participate in a biomarker sub-study to understand how resection may impact biomarkers involved in the IL-1β inflammatory pathway and mutations present in blood. In the sub-study, the levels of hs-CRP, other cytokines, and additional biomarkers in blood will be assessed at pre- and post-surgery (endpoint: summary statistics of hs-CRP and other pharmacodynamics [PD] biomarkers). For patients who will enroll in the main study, possible associations between pre- and post-surgery biomarker levels with canakinumab efficacy will be assessed (endpoint: DFS and OS by hs-CRP and other PD biomarkers). The CANOPY-A study is currently enrolling. As of July 01, 2020, there are 332 study locations.

MO01.23

Canakinumab or Pembrolizumab as Monotherapy or in Combination as Neoadjuvant Therapy in Patients with Surgically Resected Non-Small Cell Lung Cancer (NSCLC): CANOPY-N Trial

Jay Lee[1], Pilar Garrido[2], Edward Kim[3], Cagatay Arslan[4], JL Pujol[5], Masahiro Tsuboi[6], Tuochuan Dong[7], Cecile Blin[8], Vanessa Rodrik-Outmezguine[7], Bijoyesh Mookerjee[7], Vanessa Passos[7], Tony Mok[9]
[1]University of California, Los Angeles, USA, [2]Hospital Ramon Y Caja, Madrid, Spain, [3]Levine Cancer Institute, USA, [4]Izmir Medical Park Hospital, Izmir and Bahcesehir University Medicine Faculty, Turkey, [5]Hospital Arnaud de Villeneuve, France, [6]Department of Thoracic Surgery, National Cancer Center Hospital East, Japan, [7]Novartis Pharmaceuticals Corporation, United States of America, [8]Novartis Pharma AG, Switzerland, [9]Chinese University of Hong Kong, Hong Kong

Background: Complete surgical resection is the standard treatment for patients with stage I-IIIA non-small cell lung cancer (NSCLC). 5-year survival rates range from 19-50%, with most patients dying from distant recurrence. Neoadjuvant or adjuvant chemotherapy improves overall survival by only 5% in patients with NSCLC, and new treatment options are needed. Preliminary data with PD-1 or PD-L1 inhibitors as neoadjuvant therapy has shown major pathologic responses (MPR) or pathologic complete responses (pCR) in patients with early stage NSCLC. CANTOS study demonstrated reduced incidence of NSCLC and decreased lung cancer-related mortality with canakinumab (an IL-1β inhibitor) versus placebo, in a dose-dependent manner for patients with atherosclerosis. In preclinical NSCLC humanized models, treatment with canakinumab with or without an anti PD-1 inhibitor demonstrated anti-tumor activity. Combination of canakinumab and pembrolizumab is expected to enhance the efficacy of PD-1 inhibition by inhibiting dysregulated inflammation in tumor microenvironment. Based on available evidence, CANOPY-N study was designed to evaluate effect of canakinumab and pembrolizumab as monotherapy or in combination as neoadjuvant treatment for patients with resectable NSCLC. **Methods:** CANOPY-N (NCT03968419) is a phase II, randomized, open-label study evaluating effect of canakinumab or pembrolizumab monotherapy or in combination as neoadjuvant treatment in resectable NSCLC patients. Histologically confirmed stage IB-IIIA, treatment-naive, Eastern Cooperative Oncology Group performance status 0-1 NSCLC patients eligible for surgery and with a planned surgical resection in approximately 4-6 weeks (after 1 dose of study treatment), are eligible to participate. An archival (if obtained up to 6 months before 1 day of treatment) or new biopsy is required. Approximately 110 patients will be randomized in 2:2:1 ratio (stratified by histology [squamous/non-squamous]) to one of the treatment arms to receive a total of 2 doses (200 mg Q3w) of canakinumab alone (n = 44) or in combination with pembrolizumab (n = 44) or pembrolizumab alone (n = 22) with safety follow-up up to 130 days from last study drug dose. Primary endpoint is to determine MPR rate (≤10% of residual viable tumor cells at time of surgery). Secondary endpoints include determination of overall response rate, MPR rate based on local review, surgical feasibility rates, anti-drug antibodies incidence and pharmacokinetic parameters.

MO01.24

Presentation and Radiographic Characteristics of Leptomeningeal Disease (LMD) in Non-Small Cell Lung Cancer (NSCLC)

Cristina Merkhofer[1], Boryana Eastman[1], Isabella Densmore[1], Christina Baik[1], Lia Halasz[1], Tresa McGranahan[1]
[1]*University Of Washington, Seattle, United States*

Background: Studies suggest that patients with tumors harboring EGFR and ALK driver mutations experience increased incidence of LMD relative to those without these mutations. We sought to characterize the clinical experience and treatment strategies for patients with LMD and NSCLC depending on mutation status. **Methods:** We retrospectively reviewed the electronic medical records (EMR) to identify patients treated at the Seattle Cancer Care Alliance for LMD and NSCLC diagnosed between 3/28/2000 and 3/2/2020. Patient demographics, tumor and treatment characteristics, and dates of death or last follow-up were obtained from the E The radiographic subtype of LMD and presence of ventriculomegaly were determined by independent review of brain and spinal MRIs. **Results:** Of 29 eligible patients, 18 (62%) had EGFR mutations (EGFR+), 3 (10%) had ALK mutations (ALK+) and 8 (28%) had no EGFR/ALK mutation. At NSCLC diagnosis, 93% had stage III or IV disease. Most developed parenchymal brain metastases (78% in EGFR+, 100% in ALK+, 88% in no EGFR/ALK mutation). The median time to LMD development was 20 months in EGFR+, 33 months in ALK+, and 13 months in no EGFR/ALK mutation. The most common LMD symptoms were cranial neuropathy (67%) in EGFR+, vertigo/dizziness, cranial neuropathy and weakness (100%) in ALK+, and headache (88%) in no EGFR/ALK mutation. The most common LMD appearances on MRI were nodular alone (39% in EGFR+, 33% in ALK+, 38% in no EGFR/ALK mutation) or linear alone (28% in EGFR+, 33% in ALK+, 50% in no EGFR/ALK mutation). Spinal LMD was present in 1/3 of patients across mutation types. Percentages of ventriculomegaly at LMD diagnosis and development of hydrocephalus were: 50% and 44% in EGFR+, 0% and 67% in ALK+, 25% and 25% in no EGFR/ALK mutation, respectively. Most patients received systemic therapy (67-100%) and all EGFR+ patients received osimertinib. Radiation therapy to the central nervous system was given in 50% of EGFR+, 100% of ALK+, 63% of no EGFR/ALK mutation cases. Median overall survival from LMD diagnosis was: 4.7 months (95% CI: 2.8, 9.9 months) for EGFR+, 6.0 months (95% CI: 3.4, 25.5 months) for ALK+, and 2.6 months (95% CI: 0.8, 22.7 months) for no EGFR/ALK mutation. **Conclusion:** The clinical and radiographic presentation of LMD is varied across different mutation profiles. LMD in NSCLC continues to be associated with a limited prognosis, although somewhat improved among patients with EGFR+ or ALK+ disease.

MO01.26

Second Primary Lung Cancer with NTRK1 mutation after Initial Primary mEGFR Lung Cancer

Goetz Kloecker[1], Colleen Darnell[1]
[1]*St Elizabeth Health Care, Edgewood, United States*

Background: Second Primary Lung Cancers (SPLC) in LC survivors occur in at least 8%.[1] Following the ACCP criteria SPLCs are often difficult to distinguish from intrapulmonary metastases of the Initial Primary Lung Cancer (IPLC) .[2] Recent genomic studies on SPLCs demonstrate the utility to classify SPLC correctly.[3] However even genomic data may be misleading, since IPLCs and their metastases may not share the same genome due to IPLC's heterogeneity and the its mutational evolution. On the other hand SPLCs may share genomic characteristics with IPLCs due to sharing the host's germline and similar environmental exposure. We present a case of SPLCs with two distinct mutation profiles in IPLC and SPLC. **Methods:** NGS testing on IPLC and SPLC in a male smoker with metachronous contralateral SPLC of moderately differentiated adenocarcinoma histology in RUL and occipital metastasis. The SPLC, adenocarcinoma histology, stage 1 occurred 1 year after TKI targeted treatment for advanced mEGFR IPLC, which remains in remission. Results: 10/2018, NGS of IPLC reveals mEGFR, G863D, PDL1 80% and TMB 11 mb. 9/2019, NGS of the SPLC reveals NTRK1 mutation. EGFR WT 5/2020, NGS of SPLC at time of local PD also reveals NTRK1 mutation. EGFR WT. **Conclusion:** Genomic profiling can assist in distinguishing multiple primaries. Especially in cancers with sensitizing mutations and long term PFS, distinguishing metachronous secondary primaries from metastatic disease will prevent abandoning targeted therapies for the IPLC.

1. Han, S.S., et al., Risk Stratification for Second Primary Lung Cancer. Journal of Clinical Oncology, 2017. 35(25): p. 2893-2899.
2. Shen, K.R., et al., Special Treatment Issues in Lung Cancer. Chest, 2007. 132(3): p. 290S-305S.
3. Liu, Y., et al., Genomic heterogeneity of multiple synchronous lung cancer. Nature Communications, 2016. 7(1): p. 13200.

MO01.27

Three-Year Follow-up of Bintrafusp Alfa, a Bifunctional Fusion Protein Targeting TGF-β and PD-L1, as Second-Line (2L) Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC)

Luis Paz-Ares[1], Tae Min Kim[2], David Vicente[3], Enriqueta Felip[4], Dae Ho Lee[5], Ki Hyeong Lee[6], Chia-Chi Lin[7], Maria Jose Flor[8], Massimo Di Nicola[9], Rosa Maria Alvarez[10], Christoph Helwig[11], Laureen S. Ojalvo[12], James Gulley[13], Byoung Chul Cho[14]

[1]Hospital Universitario 12 de Octubre, Madrid, Spain, [2]Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea, [3]Hospital Universitario Virgen Macarena, Seville, Spain, [4]Vall d'Hebron University Hospital and Institute of Oncology (VHIO), UVic-UCC, IOB-Quiron, Barcelona, Spain, [5]Asan Medical Center, University of Ulsan College of Medicine Seoul, Seoul, Republic of Korea, [6]Chungbuk National University Hospital, Chungcheongbuk-Do, Republic of Korea, [7]National Taiwan University Hospital, Taipei, Taiwan, [8]Servicio de Oncología Médica, Hospital Universitario Virgen del Rocío, Seville, Spain, [9]Unit of Immunotherapy and Anticancer Innovative Therapeutics, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, [10]Gregorio Marañon Hospital, Madrid, Spain, [11]Merck KGaA, Darmstadt, Germany, [12]EMD Serono Research & Development Institute, Inc., Billerica, MA, USA; a business of Merck KGaA, Darmstadt, Germany, [13]Genitourinary Malignancies Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA [14]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea,

Background: Bintrafusp alfa is a first-in-class bifunctional fusion protein composed of the extracellular domain of the TGF-βRII receptor (a TGF-β "trap") fused to a human IgG1 mAb blocking PD-L1. Results from a global phase 1 study (NCT02517398) found an objective response rate (ORR) of 27.5%, median overall survival (OS) of 17.1 months, and a manageable safety profile in patients who received bintrafusp alfa 1200 mg every 2 weeks (Q2W) in the 2L setting at 2 years of follow-up. Here we present efficacy and safety data for 3 years of follow up. **Methods:** Patients with advanced NSCLC, unselected for PD-L1 expression, who had disease progression after platinum-based 1L treatment with no prior immunotherapy were randomized to receive bintrafusp alfa at the recommended phase 2 dose of 1200 mg (n=40) Q2W until disease progression, unacceptable toxicity, or trial withdrawal. The primary objective was best overall response per RECIST 1.1. Secondary and exploratory objectives included safety, duration of response (DOR), and OS. **Results:** As of March 31, 2020, 40 patients received bintrafusp alfa 1200 mg Q2W for a median of 16.9 (range, 2-160) weeks. The median follow-up was 153.3 weeks, and 16 patients were still alive; 2 patients had an ongoing response, and 1 patient remained on treatment. The median DOR was 18 months and 21.2% (n=2) of patients had responses lasting ≥24 months. The 12-, 24-, and 36-month OS rates were 66.2%, 39.7%, and 23.2%, respectively. By subgroups of PD-L1 expression, the median OS was 21.7 months in PD-L1 positive (≥1%) patients and not reached in patients with high PD-L1 expression (≥80% by 73-10 assay). The 36-month OS rate was 33.6% in PD-L1 positive patients and 66.7% in patients with high PD-L1 expression. No new safety signals were observed. **Conclusions:** After 3 years of follow-up, bintrafusp alfa at 1200 mg Q2W as 2L therapy continues to show durable responses and long-term survival with a manageable toxicity profile in patients with advanced NSCLC. A phase 3 study evaluating bintrafusp alfa vs pembrolizumab as 1L treatment for patients with advanced NSCLC with high PD-L1 expression is ongoing (NCT03631706). Previously presented at ESMO 2020, Abstract 1443, Paz-Ares L, et al. Reused with permission.

MO01.28

A Phase 1b/2, Open-Label Study of Bintrafusp Alfa with Chemotherapy in Patients with Stage IV Non-Small Cell Lung Cancer

Fabrice Barlesi[1], Sandrine Hiret[2], Christian Rolfo[3], **Italia Grenga[4]**, Andre Koenig[5], Yulia Vugmeyster[4], Leora Horn[6]
[1]Aix-Marseille University, CNRS, INSERM, CRCM, APHM, Marseille, France and Gustave Roussy Cancer Campus, Villejuif, France, [2]Institut de cancérologie de l'Ouest, Saint Herblain, France, [3]University of Maryland Marlene and Stewart Greenebaum Comprehensive Cancer Center, Baltimore, MD, USA, [4]EMD Serono Research & Development Institute, Inc., Billerica, MA, USA; a business of Merck KGaA, Darmstadt, Germany, [5]Merck KGaA, Darmstadt, Germany, [6]Vanderbilt University Medical Center, Nashville, TN, USA,

Background: The combinations of pembrolizumab plus chemotherapy (CT) and atezolizumab plus bevacizumab and CT have been approved for first-line therapy in patients with advanced non-small cell lung cancer (NSCLC) regardless of PD-L1 expression; however, there is still a significant unmet need for this patient population who may not respond to immune checkpoint treatment. Bintrafusp alfa is a first-in-class bifunctional fusion protein composed of the extracellular domain of the TGF-βRII receptor designed to function as a TGF-β "trap" fused to a human IgG1 mAb blocking PD-L1. Promising antitumor activity and a manageable safety profile were observed with bintrafusp alfa in multiple cohorts of a phase 1 study (NCT02517398) that enrolled patients with advanced, pretreated NSCLC who experienced disease progression either after platinum-based CT or anti–PD-(L)1 monotherapy. This study (NCT03840915) is evaluating the safety and efficacy of bintrafusp alfa in combination with CT in patients with stage IV NSCLC. **Methods:** This is a phase 1b/2, open-label, 4-cohort study evaluating bintrafusp alfa in combination with CT in patients with stage IV NSCLC. All patients will receive bintrafusp alfa 2400 mg every three weeks (Q3W) intravenously and either cisplatin or carboplatin + pemetrexed (cohort A), carboplatin + nab-paclitaxel or paclitaxel (cohort B), cisplatin or carboplatin + gemcitabine (cohort C), or docetaxel (cohort D) Q3W for 4 cycles, followed by bintrafusp alfa maintenance (monotherapy or combination with pemetrexed [cohort A]) for up to 31 cycles or until disease progression, unacceptable toxicity, or death. Patients must be adults with histologically confirmed diagnosis of stage IV nonsquamous or squamous NSCLC (only nonsquamous for cohort A), adequate organ function, ECOG PS ≤1, life expectancy ≥3 months, and measurable disease based on RECIST 1.1. Patients in cohorts A-C must not have received prior systemic therapy, and patients in cohort D must have disease progression on previous anti–PD-(L)1 therapy. Patients with tumors with actionable mutations (for which targeted therapy is locally approved), mixed SCLC and NSCLC, active CNS metastases, active autoimmune disease, known severe hypersensitivity, or interstitial lung disease are not eligible. The primary endpoint of this study is to assess the safety of bintrafusp alfa in combination with CT. Planned enrollment is 64 patients (32 patients in the safety phase, and 32 patients in cohort A for expansion phase).

MO01.29

Randomized, Open-Label Study of Bintrafusp Alfa vs. Pembrolizumab as First-Line (1L) Treatment in Patients with PD-L1–Expressing Advanced Non-Small Cell Lung Cancer (NSCLC)

Myung-Ju Ahn[1], Fabrice Barlesi[2], Enriqueta Felip[3], Edward Garon[4], Claudio Marcelo Martin[5], **Everett Vokes[6]**, Andre Koenig[7], Isabelle Dussault[8], Laureen S. Ojalvo[8], Luis Paz-Ares[9]
[1]Samsung Medical Center, Seoul, Republic of Korea, [2]Aix-Marseille University, CNRS, INSERM, CRCM, APHM, Marseille, France, and Gustave Roussy Cancer Campus, Villejuif, France, [3]Vall d'Hebron University Hospital and Institute of Oncology (VHIO), UVic-UCC, IOB-Quiron, Barcelona, Spain, [4]Ronald Reagan UCLA Medical Center, Los Angeles, CA, USA, [5]Alexander Fleming Institute, Buenos Aires, Argentina, [6]University of Chicago Medicine and Biological Sciences, Chicago, IL, USA, [7]Merck KGaA, Darmstadt, Germany, [8]EMD Serono Research & Development Institute, Inc., Billerica, MA, USA; a business of Merck KGaA, Darmstadt, Germany, [9]Hospital Universitario 12 de Octubre, Madrid, Spain,

Background: TGF-β promotes tumor progression via immune suppression, induction of epithelial-mesenchymal transition, and angiogenesis. Bintrafusp alfa is a first-in-class bifunctional fusion protein composed of the extracellular domain of the TGF-βRII receptor (a TGF-β "trap") fused to a human IgG1 mAb blocking PD-L1. Preclinical data demonstrated that the bifunctional nature of bintrafusp alfa might allow for colocalized inhibition of two nonredundant immunosuppressive pathways (TGF-β and PD-L1) within the tumor microenvironment. In an expansion cohort of a global phase 1 study (NCT02517398), bintrafusp alfa showed encouraging efficacy and tolerability at the recommended phase 2 dose (RP2D) of 1200 mg intravenously (IV) every 2 weeks (Q2W) as second-line treatment in patients with NSCLC; the objective response rate was 85.7% in patients with high PD-L1 tumor expression. Observed data support the hypothesis that bintrafusp alfa may be superior to other PD-(L)1 inhibitors, including pembrolizumab, for the treatment of NSCLC. This study (NCT03631706) will evaluate bintrafusp alfa treatment in patients with advanced NSCLC in the 1L setting on the basis of its promising antitumor activity and manageable safety profile.
Methods: Here we present an adaptive, multicenter, phase 3, open-label, randomized, controlled trial comparing bintrafusp alfa vs pembrolizumab in the 1L treatment of patients with metastatic NSCLC with high PD-L1 expression levels. Patients in this study must have a histologically confirmed diagnosis of advanced NSCLC with high PD-L1 expression on tumor cells. ECOG performance status must be 0 or 1. Patients must not have received prior systemic treatment for advanced NSCLC, and those with tumors with actionable mutations (for which targeted therapy is locally approved) are not eligible. Patients will receive bintrafusp alfa 1200 mg Q2W or pembrolizumab 200 mg every 3 weeks as an IV infusion until confirmed disease progression, unacceptable toxicity, or trial withdrawal. This study has dual primary endpoints of progression-free survival and overall survival. Secondary endpoints include safety, objective response, and duration of response. Estimated enrollment is up to 584 patients.

MO01.30

Trial in Progress: A Phase 1b Study of Sotorasib, a KRAS (G12C) Inhibitor, in Combination with other Anticancer Therapies in Patients with Advanced Solid Tumors Harboring KRAS p.G12C Mutation (CodeBreaK101)

Marwan Fakih[1], Gregory Durm[2], Ramaswamy Govindan[3], **Gerald Falchook[4]**, Neelesh Soman[5], Haby Henary[5], David S. Hong[6]

[1]Department of Medical Oncology and Therapeutics Research, City of Hope Comprehensive Cancer Center, Duarte, USA, [2]Department of Medicine, Division of Hematology/Oncology, Indiana University School of Medicine, Indianapolis, USA, [3]Alvin J Siteman Cancer Center at Washington University School of Medicine, St Louis, USA, [4]Sarah Cannon Research Institute at HealthONE, Denver, USA, [5]Department of Clinical Research, Amgen Research, Amgen Inc., Thousand Oaks, USA, [6]Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, USA

Background: Kirsten rat sarcoma viral oncogene homolog (KRAS) p.G12C mutation has been identified as a driver oncogenic mutation in several solid tumors (eg, non-small cell lung cancer [NSCLC], colorectal cancer [CRC]). Development of therapies targeting KRAS (G12C) has been unsuccessful. Sotorasib is a specific and irreversible small molecule inhibitor of KRAS (G12C). A first-in-human clinical trial of sotorasib monotherapy in patients with KRAS p.G12C mutant solid tumors is currently ongoing. Sotorasib in combination with additional anticancer therapies may lead to enhanced antitumor efficacy. This study is a master protocol designed to evaluate multiple investigational regimens of sotorasib in patients with KRAS p.G12C mutant solid tumors. Here, we present two combination cohorts of sotorasib with a mitogen-activated protein kinase kinase (MEK) inhibitor and an investigational anti-programmed cell death protein-1 (PD-1) therapy, respectively. Additional combination cohorts will be presented at the meeting.
Methods: This is a phase 1b, open-label study evaluating sotorasib in combination with a MEK inhibitor or an investigational anti-PD-1 therapy in patients with KRAS p.G12C mutant solid tumors. The dose exploration phase (part 1; n=20) will evaluate the safety and tolerability of sotorasib in combination with the MEK inhibitor or anti-PD-1 therapy; this will be followed by a dose expansion phase (part 2; n=40) to verify the safety and tolerability profile of sotorasib combination therapies and assess antitumor efficacy. Key eligibility criteria include locally-advanced or metastatic malignancy with KRAS p.G12C mutation identified through molecular testing and at least one or multiple lines of prior systemic therapy (eg, ≥2 for advanced/metastatic colorectal cancer). Primary endpoints include dose-limiting toxicities, treatment-emergent or -related adverse events. Secondary endpoints include pharmacokinetic parameters of combination regimens, disease control rate, duration of response, progression-free survival, and duration of stable disease (measured by computed tomography or magnetic resonance imaging and assessed per RECIST 1.1). The study began enrolling patients in December 2019 and is ongoing. For more information, please contact Amgen Medical Information: medinfo@amgen.com (clinical trial information: CodeBreaK101, NCT04185883)

MO01.31

Durability of Clinical Benefit and Biomarkers in Patients with Advanced Non-Small Cell Lung Cancer (NSCLC) Treated with Sotorasib, a KRAS(G12C) Inhibitor

David S. Hong[1], Yung-Jue Bang[2], Fabrice Barlesi[3], **Gregory Durm[4]**, Gerald Falchook[5], Ramaswamy Govindan[6], Grace Dy[7], Keunchil Park[8], John Strickler[9], Timothy Burns[10], June Kim[11], Agnes Ang[11], J. Russell Lipford[11], Gataree Ngarmchamnanrith[11], Abraham Anderson[11], Bob T. Li[12]

[1]Department of Investigational Cancer Therapeutics, Phase I Clinical Trials Program, The University of Texas MD Anderson Cancer Center, Houston, USA, [2]Seoul National University College of Medicine, Seoul, South Korea, [3]Aix Marseille Universite, University, CNRS, INSERM, CRCM, Assistance Publique Hôpitaux de Marseille, Marseille, France, [4]Department of Medicine, Division of Hematology/Oncology, Indiana University School of Medicine, Indianapolis, USA, [5]Sarah Cannon Research Institute at HealthONE, Denver, USA, [6]Alvin J Siteman Cancer Center at Washington University School of Medicine, St Louis, USA, [7]Department of Medicine, Roswell Park Comprehensive Cancer Center, Buffalo, USA, [8]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, [9]Duke University Medical Center, Durham, USA, [10]Department of Medicine, Division of Hematology/Oncology, University of Pittsburgh Medical Center Hillman Cancer Center, Pittsburgh, USA, [11]Amgen Inc., Thousand Oaks, USA, [12]Memorial Sloan Kettering Cancer, Center, New York, USA

Background: The phase 1 trial of sotorasib, a KRAS(G12C) inhibitor, demonstrated a favorable safety profile and preliminary antitumor activity in patients with advanced solid tumors harboring KRAS p.G12C. Here, we present durability of clinical benefit and biomarker data in patients with NSCLC. **Methods:** Key eligibility criteria include KRAS p.G12C mutation and prior systemic anticancer treatment. Primary endpoint is safety; key secondary endpoints include objective response rate (ORR), disease control rate (DCR), duration of response (DOR), and progression-free survival (PFS). KRAS p.G12C mutant allele frequency (MAF) and PD-L1 level were examined. **Results:** As of July 17, 2019, 40 patients with NSCLC (22 female [55.0%], median age: 68.0 years [range: 49-77]) were enrolled. Data cutoff date was March 25, 2020. 31 (77.5%) and 19 patients (47.5%) received ≥ 2 and 3 prior lines of therapy, respectively. Median follow-up was 10.2 (range: 8.3–19.0) months (months). 3 patients (7.5%) had adverse events leading to discontinuation. There were no dose-limiting toxicities or fatal treatment-related adverse events. Median PFS for all patients was 6.9 (range: 1.2–13.9) months. ORR was 30% (95% CI, 16.56–46.53). DOR ranged from 1.6 (+) to 12.7 months, with 7 of 12 responders still in response at data cutoff. DCR was 92.5% (95% CI, 79.61–98.43). 18 patients (45.0%) had progressive disease. At data cutoff, 10 patients (25.0%) were on study without disease progression, and 9 patients (22.5%) died. 18 patients (45.0%) (5 partial response (PR), 12 stable disease (SD), 1 progressive disease (PD)) had KRAS p.G12C MAF data available. There was no significant association between KRAS p.G12C MAF and response (Wilcoxon P = 0.80 for PR vs SD). 11 patients (27.5%) had PD-L1 data available. The median PD-L1 tumor proportion score [TPS] was 3% (range: 1–5) in 2 patients with PR, 0% (range: 0–0) in 8 patients with SD, and 75% (range: 75–75) in the patient with PD (Wilcoxon P = 0.044 for PR vs. SD). **Conclusions:** In patients with heavily pretreated NSCLC, durable responses to sotorasib were seen, with the majority of patients achieving disease control leading to a median PFS of 6.9 months. The current limited dataset suggests that neither KRAS p.G12C MAF nor PD-L1 expression level predicts response to sotorasib.

MO01.32

CodeBreaK 200: A Phase 3 Multicenter Study of Sotorasib, a KRAS(G12C) Inhibitor, versus Docetaxel in Patients with Previously Treated Advanced Non-Small Cell Lung Cancer (NSCLC) Harboring KRAS p.G12C Mutation

Martin Reck[2], **Alexander Spira[3]**, Benjamin Besse[4], Jürgen Wolf[5], Ferdinandos Skoulidis[6], Hossein Borghaei[7], Koichi Goto[8], Keunchil Park[9], Frank Griesinger[10], Enriqueta Felip Font[11], Michael Boyer[12], Carlos Henrique Barrios[13], Glenwood Goss[14], Hui Yang[15], Cynthia Obiozor[15], Suresh Ramalingam[16]

[1]Amgen Inc., Thousand Oaks, United States, [2]LungenClinic, Airway Research Center North, German Center of Lung Research, Grosshansdorf, Germany, [3]Virginia Cancer Specialists, Fairfax, USA, [4]Department of Cancer Medicine, Gustave Roussy, France, [5]Department of Internal Medicine, Universitatsklinikum Koln, Cologne, Germany, [6]Department of Thoracic and Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, USA, [7]Department of Hematology/Oncology, Fox Chase Cancer Center, Philadelphia, USA, [8]Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan, [9]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, [10]University Department of Internal Medicine-Oncology, Pius-Hospital, University of Oldenburg, Oldenburg, Germany, [11]Thoracic Oncology and H&N Cancer Unit, Medical Oncology Department, Vall d'Hebron University Hospital, Barcelona, Spain, [12]Department of Medical Oncology, Chris O'Brien Lifehouse, Camperdown, Australia, [13]Oncology Research Center, Hospital Sao Lucas, PUCRS, Porto Alegre, Brazil, [14]The Ottawa Hospital Research Institute, Ottawa, Canada, [15]Amgen Inc., Thousand Oaks, USA, [16]Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, USA

Background: Kirsten rat sarcoma viral oncogene homolog (KRAS) p.G12C mutation is an oncogenic driver mutation that occurs in approximately 13% of NSCLC and is often associated with poor prognosis. Sotorasib is a first-in-class small molecule that specifically and irreversibly inhibits KRAS(G12C) by locking it in its inactive GDP-bound state. Results from the first-in-human trial of sotorasib (CodeBreak 100, NCT03600883) demonstrated a favorable safety profile and promising and durable antitumor activity in patients with KRAS p.G12C mutant advanced NSCLC. These findings supported the initiation of a phase 3 trial of sotorasib versus docetaxel. Trial design: CodeBreak 200 is a global, randomized, open label, study of sotorasib versus docetaxel in NSCLC patients with KRAS p.G12C mutation. Key eligibility criteria include age of ≥ 18 years, locally-advanced and unresectable or metastatic NSCLC, KRAS p.G12C mutation confirmed by central molecular testing, progression on at least 1 prior systemic therapy, past treatment with platinum-based doublet chemotherapy and checkpoint inhibitor given either as one line of therapy or as individual lines, and performance status ECOG 0/1. Patients with active brain metastases or significant cardiovascular disease were excluded. Sotorasib or docetaxel will be administered for 21-day cycles until progression, start of another anticancer therapy, unacceptable toxicity, withdrawal of consent, lost to follow up, or death, whichever occurs earliest. The primary endpoint is progression-free survival, as assessed by blinded independent central review per RECIST v1.1. Key secondary endpoints include overall survival, objective response rate as assessed per RECIST v1.1, and patient-reported outcomes as assessed by EORTC QLQ-LC13 and QLQ-C30. Approximately 650 patients will be enrolled in the study globally. (Clinical trial identification: NCT04303780)

MO01.33

CRESTONE – Clinical Study of REsponse to Seribantumab in Tumors with NEuregulin-1 (NRG1) Fusions – A Phase 2 Study of the anti-HER3 mAb for Advanced or Metastatic Solid Tumors (NCT04383210)

David Spigel[1], Saiama N. Waqar[2], Mark E. Burkard[3], Jessica J. Lin[4], Young Kwang Chae, Mark A. Socinski[6], Shirish Gadgeel[7], Karen L. Reckamp[8], Shawn M. Leland[9], Douglas Plessinger[9], Lori Kunkel[10], Jessica R. Bauman[11], Gregory Otterson[12], Balazs Halmos[13], Sai-Hong Ignatius Ou[14], Tejas Patil[15], Yasir Y. Elamin[16], Edward S. Kim[17]
[1]Sarah Cannon Research Institute, Nashville, United States, [2]Division of Oncology, Washington University School of Medicine, St. Louis, United States, [3]University of Wisconsin Carbone Cancer Center, Madison, United States, [4]Massachusetts General Hospital, Boston, United States, [5]Northwestern University, Chicago, United States, [6]AdventHealth Cancer Institute, Orlando, United States, [7]Henry Ford Cancer Institute/Henry Ford Health System , Detroit, United States, [8]Cedars-Sinai Cancer, Los Angeles, United States, [9]Elevation Oncology, Inc. , New York, United States, [10]LAK505, Santa Fe, United States, [11]Fox Chase Cancer Center, Philadelphia, United States, [12]James Comprehensive Cancer Center, Columbus, United States, [13]Montefiore Medical Center, New York, United States, [14]University of California - Irvine, Irvine, United States, [15]University of Colorado Cancer Center, Aurora, United States, [16]MD Anderson Cancer Center, Houston, United States, [17]Levine Cancer Institute, Atrium Health, Charlotte, United States

Background: NRG1 (Neuregulin-1) gene fusions are rare oncogenic drivers found in 0.2% of solid tumors, including lung, pancreatic, gallbladder, breast, ovarian, colorectal, neuroendocrine, and sarcomas. NRG1 is the predominant ligand of HER3 and to a lesser extent HER4. NRG1 fusion proteins retaining an active EGF-like domain drive tumorigenesis and proliferation through aberrant HER3 activation. Importantly, NRG1 fusions are often mutually exclusive with other known driver alterations. NRG1 fusions have been correlated with worse overall and disease-free survival and poor response to treatment with standard therapies including chemotherapy, PD-(L)1 checkpoint inhibitors and combinations of these agents. Inhibition of HER3 and its dimerization partners represents a rational and novel therapeutic approach for tumors harboring an NRG1 fusion supported by case studies of clinical responses to anti-HER3 antibodies or pan-ERBB (tyrosine kinase inhibitors) TKIs like afatinib. Seribantumab is a fully human IgG2 mAb against HER3 uniquely able to inhibit NRG1-dependent activation of HER3, HER3-HER2 dimerization, and downstream signaling through the PI3K/AKT and MAPK pathways. The clinical safety profile of seribantumab has been well characterized through prior monotherapy and combination studies in over 800 patients. **Methods:** CRESTONE is an open label, multicenter Phase 2 basket trial of seribantumab in adult patients with NRG1 fusion-positive locally advanced or metastatic solid tumors who have progressed on or are nonresponsive to available therapies. The trial will enroll at least 75 previously treated patients across three cohorts. Cohort 1 (N=55) will include patients who have not received prior treatment with any ERBB targeted therapy. Cohort 2 (up to N=10) will include patients who have progressed after prior treatment which includes ERBB targeted therapy. Cohort 3 (up to N=10) will include patients harboring NRG1 fusions without an EGF-like binding domain. NRG1 fusion status for enrollment will be determined through a local CLIA or similarly accredited molecular assay. NRG1 fusion status for patients in Cohort 1 will be centrally confirmed using an RNA-based NGS assay. This study will evaluate a novel dosing regimen of weekly induction, biweekly consolidation, and Q3W maintenance designed to rapidly achieve steady state levels, optimize exposure, and deliver maximal NRG1 inhibition. The primary endpoint is ORR per RECIST v1.1 by independent radiologic review. Secondary endpoints include duration of response (DoR), safety, PFS, OS, and overall clinical benefit rate. An interim analysis is planned following enrollment of 20 patients in Cohort 1. CRESTONE is open and accruing patients in the United States. Clinical trial information: NCT04383210.

MO01.34

Patients with Solid Tumors Harboring NRG1 Gene Fusions: A Real-World Feasibility Study

Ajeet Gajra[1], Andrew J. Klink[1], Jill Kaufman[1], JaLyna Laney[1], Agnieszka Cseh[2], Kristie Fernamberg[3], Barbara Moehring[3], **Sushma Jonna[4]**

[1]Speciality Solutions, Cardinal Health, Dublin, US, [2]Medical Affairs, Boehringer Ingelheim International GmbH, Ingelheim, Germany, [3]Oncology Clinical Development and Medical Affairs, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, US, [4]Division of Hematology/Oncology, University of Illinois at Chicago, UI Health , Chicago, US

Background: Afatinib has shown durable responses in patients with solid tumors harboring NRG1 gene fusions, including NSCLC. Key objectives of this feasibility assessment were to determine the number of patients with NRG1 gene fusion-positive solid tumors available for analyses, characterize their treatment with afatinib/other systemic therapies, and gain insights into treatment patterns and testing for a larger, retrospective, real-world study. **Methods:** US physicians in the Cardinal Health Oncology Provider Extended Network retrospectively abstracted data from adult patient medical records. Eligible patients had any solid tumor harboring an NRG1 gene fusion, received ≥1 line of systemic therapy (Jan 2017–Mar 2020), and had been followed up for ≥8 weeks. Patients were grouped according to whether they received afatinib (in any line), or only received other systemic therapies. Data were reviewed by Cardinal Health and summarized using descriptive statistics. Subgroup analysis of NSCLC patients will be presented at the meeting. **Results:** Twelve physicians (community practices, n=9; academic settings, n=3) identified 108 eligible patients (treated with afatinib, n=67; other therapies only, n=41). Patient and tumor characteristics, and treatment patterns are reported in the table. NRG1 gene fusion detection methodologies were as follows: mRNA sequencing (n=54; 50%); DNA sequencing (n=28; 26%); other (n=1; <1%); unknown (n=25; 23%). Testing was conducted most frequently prior to first-line therapy (n=64; 59%). The most common fusion partners were CD74 (n=19; 18%) and SDC4 (n=14; 13%); fusion partners were unknown for 22 (20%) patients. **Conclusions:** These data support previous findings that NRG1 gene fusions are detected across multiple tumor types, most commonly NSCLC. Moreover, median duration of therapy reflected evidence of afatinib activity in all treatment lines. These findings provide a rationale to perform a larger, retrospective, chart-based cohort study assessing treatment outcomes in patients with NRG1-positive tumors.

	Afatinib (n=67)	Other (n=41)
Median age, years	60	59
Primary tumor type, n (%)		
NSCLC	27 (40)	23 (56)
Pancreatic	11 (16)	3 (7)
Colorectal	7 (10)	3 (7)
Cholangiocarcinoma	7 (10)	3 (7)
Bladder	4 (6)	3 (7)
Breast	3 (4)	4 (10)
Ovarian	4 (6)	1 (2)
Renal	2 (3)	1 (2)
Thyroid	1 (1)	0
Other*	1 (1)	0
Line in which afatinib/other treatment was received†, n (%)		
1	17 (25)	41 (100)
2	35 (52)	14 (34)
3	14 (21)	3 (7)
4	4 (6)	0
Median treatment duration by line, weeks (min–max)		
1	36 (20–63)	32 (12–52)
2	30 (10–40)	34 (12–60)
3	18.5 (8–38)	12 (12–12)
4	16 (16–16)	n/a
Patients still receiving active therapy, n (%)	31 (46)	13 (32)
Reasons for afatinib/other treatment discontinuation (≥5%), n (%)		
Disease progression	18 (27)	9 (22)
Patient died	5 (7)	4 (10)
Toxicity/adverse event	4 (6)	4 (10)
Other	5 (7)	5 (12)

*Mucinous adenocarcinoma, primary cancer unknown; †n=3 patients received afatinib in two lines of therapy; patients are reported in each line in which afatinib was received.

MO01.35

Efficacy and Safety of Larotrectinib in Patients with Tropomyosin Receptor Kinase (TRK) Fusion Lung Cancer

Alexander Drilon[1], Victor Moreno[2], Jyoti Patel[3], Ulrik Lassen[4], Benjamin Solomon[5], Lee Rosen[6], Serge Leyvraz[7], Daniel S.W. Tan[8], John A. Reeves[9], Laura Dima[10], Nicoletta Brega[9], Shivaani Kummar[11], Anna F. Farago[12]
[1]Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, USA, [2]START MADRID-FJD, Hospital Fundación Jiménez Díaz, Madrid, Spain, [3]Northwestern University, Chicago, USA, [4]Rigshospitalet, Copenhagen, Denmark, [5]Avera Cancer Institute, Sioux Falls, USA, [6]UCLA, Los Angeles, USA, [7]Charité – Universitätsmedizin Berlin, Berlin, Germany, [8]National Cancer Center, Singapore, [9]Bayer HealthCare Pharmaceuticals, Inc., Whippany, USA, [10]Bayer Pharmaceuticals, Basel, Switzerland, [11]Oregon Health & Science University, Portland, USA, [12]Massachusetts General Hospital Cancer Center, Boston, USA

Background: Neurotrophic tyrosine receptor kinase (NTRK) gene fusions occur in a range of tumor types. Larotrectinib, a central nervous system (CNS)-active and highly selective FDA- and EMA-approved TRK inhibitor, demonstrated an objective response rate (ORR) of 79% and a median duration of response (DoR) of 35.2 months across multiple cancers (Hong et al. Lancet Oncol 2020). We report updated data on patients with lung cancer treated with larotrectinib. **Methods:** Patients with lung cancer harboring an NTRK gene fusion enrolled in two clinical trials were pooled for this analysis. Larotrectinib 100 mg twice daily was administered on a continuous 28-day schedule. Response was assessed by the investigator per RECIST v1.1. **Results:** As of July 15, 2019, 14 patients with metastatic TRK fusion lung cancer were enrolled: 13 with non-small cell lung cancer and 1 with small cell lung cancer. The median age was 52 years (range 25–76). Eleven patients had fusions involving NTRK1 and 3 patients had fusions involving NTRK3. Seven patients had baseline CNS metastases. Patients were heavily pre-treated with a median of three prior therapies (range 1–5); 9 patients had received ≥2 prior therapies. The ORR with larotrectinib was 71% (95% CI 42–92%): 1 patient had a complete response, 9 had partial responses, 3 had stable disease and 1 had progressive disease. The ORR in patients with CNS metastases was 57% (95% CI 18–90%). The overall DoR ranged from 1.9+ to 28.7+ months. The median progression-free survival (PFS) had not been reached (range 1.8–30.3+ months), with an estimated PFS rate at 12 months of 69%. Treatment duration ranged from 2.1 to 39.6+ months. Larotrectinib was well tolerated, with treatment-emergent adverse events being mainly Grade 1–2. **Conclusions:** In this updated analysis, larotrectinib was shown to be highly active in patients with advanced lung cancer harboring NTRK gene fusions, including those with CNS metastases. The drug has a favorable safety profile. These results support inclusion of NTRK gene fusions in routine molecular testing of patients with lung cancer. This work was previously presented at ESMO 2020, Drilon et al. Reused with permission. Clinical trial registration numbers: NCT02122913 and NCT02576431

MO01.36

Afatinib in Asian and Non-Asian Patients (pts) with EGFR Mutation-Positive (EGFRm+) NSCLC Harboring Major Uncommon Mutations

James Chih-Hsin Yang[1], Martin Schuler[2], Sanjay Popat[3,4], Satoru Miura[5], Simon Heeke[6], Antonio Passaro[7], Filippo de Marinis[7], Keunchil Park[8], Edward S. Kim[9]

[1]Department of Oncology, National Taiwan University Hospital, Taipei 10002, Taiwan, [2]West German Cancer Center, University Duisburg-Essen & German Cancer Consortium (DKTK), Partner Site University Hospital Essen, Essen, Germany, [3]Lung Unit, Royal Marsden National Health Service Foundation Trust, London, United Kingdom, [4]The Institute of Cancer Research, London, United Kingdom, [5]Department of Internal Medicine, Niigata Cancer Center Hospital, Niigata, Japan, [6]Department of Thoracic/Head and Neck Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, USA, [7]Division of Thoracic Oncology, European Institute of Oncology IRCCS, Milan, Italy, [8]Division of Hematology/Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, [9]Department of Solid Tumor Oncology, Levine Cancer Institute, Atrium Health, Charlotte, USA

Background: Uncommon EGFR mutations show heterogeneity in their EGFR TKI sensitivities.[1] Afatinib has shown broad inhibitory activity against uncommon mutations in vitro,[1] and clinical activity against major uncommon mutations (G719X/L861Q/S768I).[2] However, clinical data regarding the efficacy of afatinib against other uncommon EGFR mutations are lacking, particularly between ethnicities. **Methods:** This pooled analysis assessed afatinib activity in Asian/non-Asian, EGFR TKI-naïve pts with NSCLC and uncommon EGFR mutations, treated in RCTs and real-world studies. Uncommon mutations were classed as: de novo T790M; exon 20 insertions (Ins20); major uncommon mutations (G719X/L861Q/S768I); compound mutations (≥2 uncommon mutations); and other uncommon mutations. Key endpoints were overall response rate (ORR), duration of response (DoR), and time to treatment failure (TTF). **Results:** Of the 178/120 Asian/non-Asian pts with uncommon EGFR mutations, 62/35% had a major uncommon mutation (G719X only: 20/20%; L861Q only: 26/8%; S768I only: 3/4%), 16/39% had an Ins20 mutation. Clinical activity (Asian/non-Asian) was observed against major uncommon mutations (ORR: 66/59%; median DoR: 14.7/15.9 mos; G719X: 62/65%; L861Q: 60/50%; S768I: 80/25%), compound mutations (ORR: 81/100%; median DoR: 11.5/18.6 mos) and other uncommon mutations (ORR: 79/60%; median DoR: 9.0/10.7 mos). Some pts with Ins20 responded (21/23%). TTF was longest in pts with compound mutations, particularly non-Asian pts (median 18.5 mos). **Conclusion:** Afatinib is effective in pts with NSCLC with major uncommon and compound EGFR mutations, with broad activity against other uncommon EGFR mutations and some Ins20 mutations, unaffected by ethnicity. Asian pts appeared to have a high proportion of major uncommon mutations, known to be highly sensitive to afatinib.[2]

1. Kohsaka S, et al. Sci Transl Med 2017;9:eaan6566
2. Yang JC, et al. Lancet Oncol 2015;16:830–8

	Patients*, n (%)		ORR, %		TTF, mos (95% CI)	
	Asian (N=178)	Non-Asian (N=120)	Asian	Non-Asian	Asian	Non-Asian
Major uncommon (MU)†	110 (61.8)	42 (35.0)	66	59	11.5 (11.5, 13.8)	9.0 (4.6, 15.4)
G719X	36 (20.2)	24 (20.0)	62	65	11.5 (9.6, 17.1)	9.0 (3.2, 18.7)
L861Q	46 (25.8)	9 (7.5)	60	50	11.5 (11.1, 11.5)	5.7 (1.4, 10.7)
S768I	5 (2.8)	5 (4.2)	80	25	NR (2.6, NR)	15.6 (3.0, 20.7)
Compound	26 (14.6)	8 (6.7)	81	100	11.5 (8.2, 16.6)	18.5 (1.6, NR)
Ins20	29 (16.3)	47 (39.2)	21	23	4.5 (2.6, 5.4)	3.9 (2.8, 5.4)
Any *de novo* T790M	19 (10.7)	14 (11.7)	38	17	4.7 (1.2, 5.5)	2.9 (0.9, 6.7)
Other	17 (9.6)	13 (10.8)	79	60	7.2 (1.8, 11.9)	10.7 (2.0, 24.0)

*Patients may be included in >1 group; †Includes patients with MU + Del19/L858R compound mutations

MO01.38

Registrational Dataset from the Phase 1/2 ARROW Trial of Pralsetinib (BLU-667) in Patients with Advanced RET Fusion+ Non-Small-Cell Lung Cancer (NSCLC)

Justin F. Gainor[1], Giuseppe Curigliano[2], Dong-Wan Kim[3], Dae Ho Lee[4], Benjamin Besse[5], Christina S. Baik[6], Robert C. Doebele[7], Philippe Cassier[8], Gilberto Lopes[9], Daniel S.-W. Tan[10], Elena Garralda[11], Luis Paz-Ares[12], Byoung C. Cho[13], Shirish M. Gadgeel[14], Michael Thomas[15], Stephen V. Liu[16], Corinne Clifford[17], Hui Zhang[17], Christopher D. Turner[17], Vivek Subbiah[18]

[1]Massachusetts General Hospital, Boston,, United States, [2]European Institute of Oncology, IRCCS, University of Milano, Milan, Italy, [3]Seoul National University Hospital, Seoul, Republic of Korea, [4]University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea, [5]Gustave Roussy Université Paris Sud, Villejuif, France, [6]University of Washington School of Medicine, Main Hospital, Seattle,, United States, [7]University of Colorado Cancer Center, Aurora,, United States, [8]Centre Léon Bérard, Lyon, France, [9]Sylvester Comprehensive Cancer Center, University of Miami, Miami,, United States, [10]National Cancer Center Singapore, Singapore, Singapore, [11]Hospital Universitari Vall d'Hebron, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, [12]Hospital Universitario 12 de Octubre, Madrid, Spain, [13]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea, [14]Henry Ford Cancer Institute, Detroit,, United States, [15]Thoraxklinik at Heidelberg University Hospital, Heidelberg, Germany, [16]Georgetown University, Washington,, United States, [17]Blueprint Medicines Corporation, Cambridge,, United States, [18]The University of Texas MD Anderson Cancer Center, Houston,, United States

Background: Pralsetinib is an investigational, highly potent, selective RET inhibitor. We provide the registrational dataset for patients with RET fusion+ NSCLC with and without prior treatment from ARROW. **Methods:** ARROW (75 sites/11 countries; NCT03037385) consists of phase 1 dose escalation to establish recommended phase 2 dose (400 mg once daily [QD] orally) and phase 2 expansion cohorts defined by tumor type and/or RET alteration. Primary objectives were overall response rate (ORR; blinded independent central review per RECIST v1.1) and safety. Efficacy is shown for response-evaluable patients (REP) with RET fusion+ NSCLC who initiated 400 mg QD pralsetinib by July 11, 2019 and safety for all patients (all diagnoses) who initiated 400 mg QD. **Results:** As of November 18, 2019, 354 patients with advanced solid tumors had initiated 400 mg QD pralsetinib (median follow-up 8.8 months). Efficacy outcomes are shown (Table) for patients with metastatic RET fusion+ NSCLC (n=116; 72% KIF5B; 16% CCDC6; 12% other/fusion present but type unknown) with prior platinum treatment (n=80) or without prior systemic treatment (n=26). ORR was similar regardless of RET fusion partner, prior therapies, or central nervous system involvement. Overall there were 7 (6%) complete responses, 4 (5%) in prior platinum patients and 3 (12%) in treatment-naïve patients; median time to response overall was 1.8 months and median duration of response (DOR) was not reached (95% CI, 11.3–not reached). In the safety population (n=354; all tumor types), most treatment-related adverse events (TRAEs) were grade 1–2, and included increased aspartate aminotransferase (31%), anemia (22%), increased alanine aminotransferase (21%), constipation (21%) and hypertension (20%). 4% of patients in the safety population discontinued due to TRAEs. **Conclusions:** Pralsetinib has rapid, potent, and durable clinical activity in patients with advanced RET fusion+ NSCLC regardless of RET fusion genotype or prior therapies, and QD oral dosing is well-tolerated.

	Overall (n=116[a])	Prior platinum treatment (n=80)	No prior systemic treatment (n=26)
ORR, % (95% CI)	65 (55–73)[b]	61 (50–72)[b]	73 (52–88)
DCR, % (95% CI)	93 (87–97)	95 (88–99)	88 (70–98)
Tumor size reduction, % of patients	96	95	100

[a]Including n=10 with prior non-platinum treatment. [b]Including n=2 with partial response pending confirmation

MO01.39

Liposomal Irinotecan in Adults with Small Cell Lung Cancer who Progressed on Platinum-Based Therapy: Subgroup Analyses by Platinum Sensitivity

David R. Spigel[1], Luis G. Paz-Ares[2], Yuanbin Chen[3], Maria Jove[4], Oscar Juan-Vidal[5], Patricia Rich[6], Theresa Hayes[7], Vanesa Gutiérrez Calderón[8], Reyes Bernabe Caro[9], Alejandro Navarro[10], Afshin Dowlati[11], Bin Zhang[12], Yan Moore[12], Tiffany Wang[12], Natalya Nazarenko[12], Jaba Kokhreidze[12], Santiago Ponce[2], Paul Bunn[13]
[1]Sarah Cannon Research Institute, Nashville, USA, [2]Hospital Universitario 12 de Octubre, Madrid, Spain, [3]Cancer & Hematology Centers of Western Michigan, Grand Rapids, USA, [4]Institut Català d'Oncologia, Hospital Duran i Reinals, Barcelona, Spain, [5]Hospital Universitari i Politècnic La Fe, Valencia, Spain, [6]Cancer Treatment Centers of America, Atlanta, USA, [7]South West Healthcare, Warrnambool, Australia, [8]Hospital Regional Universitario de Malaga, Malaga, Spain, [9]Hospital Universitario Virgen del Rocio, Seville, Spain, [10]Hospital Universitari Vall d'Hebron, Barcelona, Spain, [11]Case Western Reserve University, Cleveland, USA, [12]Ipsen, Boston, USA, [13]University of Colorado, Cancer Center and Department of Medicine, Denver, USA

Background: Most patients with extensive small cell lung cancer (SCLC) develop drug resistance to platinum-based first-line therapy or discontinue for other reasons, and second-line therapies are limited. RESILIENT (ClinicalTrials.gov identifier NCT03088813) is a two-part phase 2/3 study assessing the safety, tolerability and efficacy of second-line liposomal irinotecan monotherapy in adults with SCLC who progressed with platinum-based first-line therapy. Preliminary data from RESILIENT part 1 (cut off May 8 2019; ≥ 12 weeks follow-up) showed that liposomal irinotecan 70 mg/m2 free base every 2 weeks was generally well tolerated and had encouraging antitumor activity (Paz-Ares et al. WCLC 2019; OA03.03). Objective response rate (ORR; secondary endpoint) was 44% (11/25 patients). Here we report efficacy analyses in post hoc subgroups by platinum sensitivity. **Methods:** RESILIENT part 1 was an open-label, single-arm study comprising dose-finding and dose-expansion phases. Eligible patients were aged ≥ 18 years, with an Eastern Cooperative Oncology Group performance status score of 0/1 and adequate organ function; a single line of prior immunotherapy was permitted. Participants received liposomal irinotecan 70 mg/m2 or 85 mg/m2 free base every 2 weeks, with disease assessments every 6 weeks (Response Evaluation Criteria in Solid Tumors v1.1). Analyses were undertaken for the dose-finding phase recommended dose in subgroups of platinum-resistant/platinum-sensitive patients (with/without disease progression within 90 days from completion of first-line therapy). **Results:** During dose finding, 5 patients received liposomal irinotecan 85 mg/m2 (deemed not tolerable owing to dose-limiting toxicity) and 12 received 70 mg/m2 (deemed tolerable; recommended dose for dose-expansion phase in which 13 additional patients were included). Analyses included all 25 patients receiving the recommended dose (mean exposure, 13.95 weeks [median 14.86; standard deviation 7.222]). In the platinum-sensitive subgroup (33.3% men; median age 62.0 years), ORR was 53.3% (8/15 patients) and 12-week disease control rate (DCR12wks) was 60% (9/15 patients); in the platinum-resistant subgroup (50.0% men, median age 58.0 years) both ORR and DCR12wks were 30% (3/10 patients). Overall survival and progression-free survival (secondary endpoints) are not yet mature. **Conclusions:** ORR and DCR12wks were numerically higher in platinum-sensitive than in platinum-resistant patients with SCLC who had progressed with platinum-based first-line therapy before receiving second-line liposomal irinotecan 70 mg/m2 in this phase 2 study. RESILIENT part 2, an ongoing, phase 3, randomized controlled trial versus topotecan, will provide further data.

MO01.40

Trilaciclib has Myelopreservation Benefits in Patients with Small Cell Lung Cancer Treated with Chemotherapy, Irrespective of Age

Thaddeus Beck[1], Donald A. Richards[2], Richy Agajanian[3], David Berz[4], Hongbin Chen[5], Chukwuemeka Ikpeazu[6], Margarita Majem Tarruella[7], Didier Verhoeven[8], Yili Pritchett[9], Rajesh K. Malik[9], Joyce M. Antal[9], Maen Hussein[10]
[1]Highlands Oncology Group, Fayetteville, United States, [2]Texas Oncology-Tyler, Tyler, United States, [3]Innovative Clinical Research Institute (ICRI), Whittier, United States, [4]Beverly Hills Cancer Center, Beverly Hills, United States, [5]Roswell Park Comprehensive Cancer Center, Buffalo, United States, [6]Sylvester Comprehensive Cancer Center, Miami, United States, [7]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [8]AZ KLINA, University of Antwerp, Belgium, [9]G1 Therapeutics, Inc., Research Triangle Park, United States, [10]Florida Cancer Specialists, Leesburg, United States

Background: More than half of patients diagnosed with small cell lung cancer (SCLC) are aged ≥65 years. Elderly patients are particularly vulnerable to chemotherapy-induced myelosuppression (CIM) and its complications. Trilaciclib is a transient intravenous CDK4/6 inhibitor that protects hematopoietic stem and progenitor cells and immune system function from chemotherapy-induced damage (myelopreservation). This analysis investigated the myelopreservation effects of trilaciclib among patients aged <65 and ≥65 years. **Methods:** Data were pooled from three randomized, double-blind, placebo-controlled, phase 2 clinical studies of trilaciclib administered prior to chemotherapy in patients with extensive-stage SCLC (NCT02499770; NCT03041311; NCT02514447). Subgroup analyses of patients aged <65 and ≥65 years were performed to assess the effects of trilaciclib on duration of severe (grade 4) neutropenia (DSN) in cycle 1, occurrence of SN, occurrence of grade 3/4 decreased hemoglobin levels, and occurrence and number of red blood cell transfusions on/after week 5. Change from baseline and time to confirmed deterioration (TTCD) were analyzed for patient-reported outcome (PRO) endpoints included in the Functional Assessment of Cancer Therapy-Anemia questionnaire. **Results:** In both age groups, administration of trilaciclib reduced chemotherapy-induced SN and anemia, with a greater magnitude of effect among patients aged ≥65 years (Table). Myelopreservation benefits extended to improvements in PROs in younger (<65 years) and older (≥65 years) patients receiving trilaciclib. For each of the PRO endpoints, median TTCD for patients receiving trilaciclib was longer than for patients receiving placebo, with greater improvements seen in the older age group (Table). **Conclusions:** Data from this analysis indicate that the myelopreservation benefits of trilaciclib are observed regardless of a patient's age, with greater effects among older patients who may be more vulnerable to CIM. By both reducing CIM and improving symptoms and functional limitations associated with cancer and CIM, trilaciclib improves the experience for elderly patients receiving chemotherapy to treat SCLC.

	Age <65 years		Age ≥65 years	
	Trilaciclib (n = 66)	Placebo (n = 61)	Trilaciclib (n = 57)	Placebo (n = 58)
Myelopreservation				
Mean DSN in cycle 1, days (SD)	0 (1.7)	3 (4.5)	0 (2.1)	5 (5.6)
Patients with SN, n (%)	7 (10.6)	26 (42.6)	7 (12.3)	37 (63.8)
Patients with grade 3/4 decreased hemoglobin, n (%)	12 (18.2)	16 (26.2)	13 (22.8)	22 (37.9)
Patients with RBC transfusions on/after week 5, n (%)	8 (12.1)	11 (18.0)	10 (17.5)	20 (34.5)
Number of RBC transfusions, event rate (per week)	0.011	0.018	0.019	0.045
TTCD in patient-reported outcomes				
Physical wellbeing				
Events, n (%)	13 (19.7)	20 (32.8)	19 (33.3)	31 (53.5)
Median TTCD, months	NYR	NYR	7.20	3.38
HR (95% CI)	0.66 (0.322, 1.341)		0.62 (0.344, 1.130)	
Functional wellbeing				
Events, n (%)	15 (22.7)	22 (36.1)	16 (28.1)	33 (56.9)
Median TTCD, months	8.57	NYR	7.20	2.79
HR (95% CI)	0.57 (0.286, 1.117)		0.37 (0.196, 0.687)	
Fatigue subscale				
Events, n (%)	18 (27.3)	25 (41.0)	21 (36.8)	36 (62.1)
Median TTCD, months	NYR	6.51	6.21	1.48
HR (95% CI)	0.63 (0.335, 1.189)		0.49 (0.269, 0.882)	
Anemia trial outcome index				
Events, n (%)	13 (19.7)	21 (34.4)	20 (35.1)	34 (58.6)
Median TTCD, months	NYR	8.08	6.93	1.64
HR (95% CI)	0.59 (0.286, 1.208)		0.52 (0.289, 0.933)	
FACT-Anemia total				
Events, n (%)	12 (18.2)	22 (36.1)	19 (33.3)	36 (62.1)
Median TTCD, months	NYR	6.90	6.51	1.71
HR (95% CI)	0.54 (0.257, 1.115)		0.47 (0.260, 0.840)	

CI, confidence interval; DSN, duration of severe neutropenia; FACT, Functional Assessment of Cancer Therapy; HR, hazard ratio; NYR, not yet reached; RBC, red blood cell; SD, standard deviation; SN, severe neutropenia; TTCD, time to confirmed deterioration.

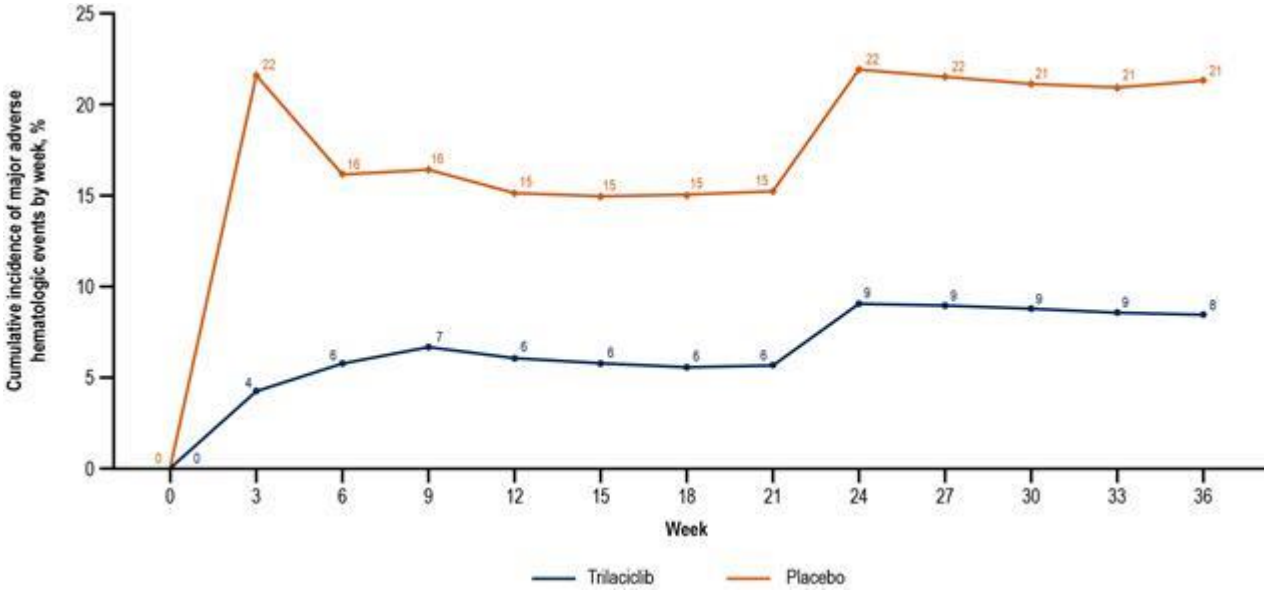
MO01.41

Using an Exploratory Composite Endpoint to Evaluate the Myelopreservation Benefits of Trilaciclib in Patients with Small Cell Lung Cancer

Janakiraman Subramanian[1], Jana Jaal[2], Iveta Kudaba[3], Krasimir Nikolov[4], Davorin Radosavljevic[5], Tibor Csőszi[6], Jie Xiao[7], Janet Horton[7], Rajesh K. Malik[7], Manuel Dómine Gómez[8]

[1]Saint Luke's Cancer Institute/University of Missouri , Kansas City, United States, [2]University of Tartu, Tartu, Estonia, [3]Riga East Clinical University-Latvian Oncology Center, Riga, Latvia, [4]Complex Oncology Center, Burgas, Bulgaria, [5]Institute for Oncology and Radiology of Serbia, Belgrade, Serbia, [6]Hetenyi Geza Korhaz, Szolnok, Hungary, [7]G1 Therapeutics, Inc., Research Triangle Park, United States, [8]Instituto de Investigacion Sanitaria-Fundación Jimenez Diaz (IIS-FJD), Madrid, Spain

Background: Myelosuppression is an acute, dose-limiting toxicity of chemotherapy regimens used in the treatment of extensive-stage small cell lung cancer (ES-SCLC). Trilaciclib is a transient intravenous CDK4/6 inhibitor that protects hematopoietic stem and progenitor cells and immune system function from chemotherapy-induced damage (myelopreservation). An exploratory composite endpoint of major adverse hematologic events (MAHE) was prospectively defined to assess the totality of benefit with trilaciclib across several clinically meaningful components of myelopreservation. **Methods:** The MAHE endpoint comprised five individual components: all-cause hospitalizations, all-cause chemotherapy dose reductions, febrile neutropenia, prolonged severe (grade 4) neutropenia (duration >5 days), and red blood cell transfusions on/after week 5. The cumulative incidence of MAHE and its individual components was assessed using pooled data from three randomized, double-blind, placebo-controlled, phase 2 clinical studies of trilaciclib administered prior to chemotherapy in patients with ES-SCLC (NCT02499770; NCT03041311; NCT02514447). **Results:** Compared with placebo, administration of trilaciclib prior to chemotherapy resulted in a statistically significant reduction in the cumulative incidence of MAHE (Table; Figure). **Conclusions:** Robust improvements in the exploratory MAHE composite endpoint further support the myelopreservation benefits of trilaciclib and its ability to improve the overall safety profile of chemotherapy regimens used to treat patients with ES-SCLC.



Event rate (per week)*	Trilaciclib prior to chemotherapy (n = 123)	Placebo prior to chemotherapy (n = 119)	Adjusted rate ratio (95% CI)†	*P* value
MAHE composite endpoint	0.054	0.139	0.355 (0.245, 0.513)	<0.0001
All-cause hospitalizations	0.024	0.028	0.786 (0.427, 1.448)	0.4403
All-cause chemotherapy dose reductions	0.028	0.093	0.263 (0.136, 0.507)	<0.0001
FN	0.002	0.008	0.278 (0.078, 0.991)	0.0485
Prolonged SN	0.020	0.171	0.097 (0.047, 0.202)	<0.0001
RBC transfusions on/after week 5	0.015	0.031	0.411 (0.230, 0.734)	0.0027

*Calculated as the total number of events divided by the total weeks of duration.
†Calculated using the negative binomial method, adjusting for duration of treatment in weeks. Three stratification factors: Eastern Cooperative Oncology Group performance status (0/1 vs 2), presence of brain metastases (yes/no), and study were included as fixed effects.
CI, confidence interval; FN, febrile neutropenia; MAHE, major adverse hematologic events; RBC, red blood cell; SN, severe (grade 4) neutropenia.

MO01.42

Myelopreservation with Trilaciclib Regardless of Risk of Chemotherapy-Induced Febrile Neutropenia and/or Anemia or Red Blood Cell Transfusions

Maen Hussein[1], Todd A. Gersten[2], Keith Lerro[3], Ivan Sinielnikov[4], Alexander Spira[5,6], Richy Agajanian[7], Antonio Calles[8], Sarada Gurubhagavatula[9], Gerli Kuusk[10], Eddie Thara[11], Oleksandr Vynnychenko[12], Yili Pritchett[13], Rajesh K. Malik[13], Shannon R. Morris[13], Marina Maglakelidze[14]

[1]Florida Cancer Specialists, Leesburg, United States, [2]Florida Cancer Specialists, West Palm Beach, United States, [3]Regional Medical Oncology Center, Wilson, United States, [4]Volyn Regional Oncology Center, Lutsk, Ukraine, [5]Virginia Cancer Specialists, Fairfax, United States, [6]US Oncology Research, The Woodlands, United States, [7]Innovative Clinical Research Institute (ICRI), Whittier, United States, [8]Hospital General Universitario Gregorio Marañon, Madrid, Spain, [9]Summit Medical Group PA, Florham Park, United States, [10]East Tallinn Central Hospital, Tallinn, Estonia, [11]Singing River Health System, Whittier, United States, [12]Sumy State University, Sumy, Ukraine, [13]G1 Therapeutics, Inc., Research Triangle Park, United States, [14]LLC Arensia Exploratory Medicine, Tbilisi, Georgia

Background: Febrile neutropenia (FN) and anemia are clinically important manifestations of chemotherapy-induced myelosuppression (CIM) that can negatively impact patient outcomes, and often incur significant costs. Trilaciclib is a transient intravenous CDK4/6 inhibitor that protects hematopoietic stem and progenitor cells and immune system function from chemotherapy-induced damage (myelopreservation). Data pooled from three randomized, double-blind, placebo-controlled, phase 2 clinical studies of trilaciclib administered prior to chemotherapy in patients with extensive-stage small cell lung cancer (NCT02499770; NCT03041311; NCT02514447) were analyzed to examine if patients at varying risk for FN or anemia/red blood cell (RBC) transfusions derived the same benefits from trilaciclib. **Methods:** Six baseline factors associated with an increased risk of FN (age, poor nutritional status, renal dysfunction, cardiovascular disease, multiple comorbid conditions, prior cytotoxic chemotherapy) and four factors for anemia/RBC transfusions (gender, Eastern Cooperative Oncology Group status, baseline hemoglobin, prior cytotoxic chemotherapy) were used to group patients into four FN risk categories (0, 1–2, 3–4, and 5–6 risk factors) and three anemia risk categories (0, 1–2, and 3–4 risk factors). Mean duration of severe (grade 4) neutropenia (DSN) in cycle 1 and occurrence of SN were analyzed by FN risk factors and categories, and occurrence of grade 3/4 decreased hemoglobin and RBC transfusions on/after week 5 were analyzed by anemia risk factors and categories. **Results:** Patient distribution across FN and anemia risk categories was comparable between the treatment groups. No patients fell into the category of 5–6 FN risk factors. Across the risk categories, effects on neutrophil- and RBC-related endpoints consistently favored trilaciclib versus placebo, and were aligned with the overall patient population (Table). **Conclusions:** Compared with placebo, the myelopreservation benefits of trilaciclib were observed regardless of underlying risks for FN and anemia/RBC transfusions, indicating that trilaciclib is effective at reducing CIM in all patient categories.

		FN risk category		
Trilaciclib vs placebo	**All patients**	**0**	**1–2**	**3–4**
Patients (trilaciclib vs placebo), n (%)	123 (50.8) vs 119 (49.2)	32 (26.0) vs 35 (29.4)	85 (69.1) vs 77 (64.7)	6 (4.9) vs 7 (5.9)
Mean DSN in cycle 1, days (SD)	0 (1.8) vs 4 (5.1)	0 (1.2) vs 2 (3.8)	1 (2.1) vs 5 (5.1)	0 (0.8) vs 9 (7.5)
Mean difference in DSN in cycle 1, days (95% CI)	−3.8 (−4.8, −2.8)	−2.0 (−3.4, −0.6)	−4.2 (−5.4, −3.0)	−8.4 (−15.3, −1.5)
Patients with SN, n (%)	14 (11.4) vs 63 (52.9)	2 (6.3) vs 11 (31.4)	11 (12.9) vs 46 (59.7)	1 (16.7) vs 6 (85.7)
RRR in SN with trilaciclib, % (95% CI)	79.4 (64.9, 88.0)	77.6 (9.0, 94.5)	79.1 (61.9, 88.5)	NE (NE, NE)
		Anemia risk category		
Trilaciclib vs placebo	**All patients**	**0**	**1–2**	**3–4**
Patients (trilaciclib vs placebo), n (%)	123 (50.8) vs 119 (49.2)	48 (39.0) vs 47 (39.5)	68 (55.3) vs 62 (52.1)	7 (5.7) vs 10 (8.4)
Patients with grade 3/4 decreased hemoglobin levels, n (%)	25 (20.3) vs 38 (31.9)	4 (8.3) vs 7 (14.9)	18 (26.5) vs 25 (40.3)	3 (42.9) vs 6 (60.0)
RRR in grade 3/4 decreased hemoglobin with trilaciclib, % (95% CI)	38.0 (5.1, 59.5)	NE (NE, NE)	43.4 (6.1, 65.9)	NE (NE, NE)
Patients with RBC transfusion on/after week 5, n (%)	18 (14.6) vs 31 (26.1)	1 (2.1) vs 6 (12.8)	14 (20.6) vs 19 (30.6)	3 (42.9) vs 6 (60.0)
RRR in RBC transfusions on/after week 5 with trilaciclib, % (95% CI)	43.1 (6.8, 65.3)	NE (NE, NE)	34.5 (−16.6, 63.1)	NE (NE, NE)

CI, confidence interval; DSN, duration of severe neutropenia; FN, febrile neutropenia; NE, not estimable (statistical model did not converge); RBC, red blood cell; RRR, relative risk reduction; SD, standard deviation; SN, severe neutropenia.

MO01.43

Examining the Impact of Tislelizumab Added to Platinum Doublet Chemotherapy on Health-Related Quality of Life in Patients with Non-Squamous NSCLC

Shun Lu[1], Yan Yu[2], Gisoo Barnes[3], Xiusong Qiu[4], Yuanyuan Bao[4], Jiang Li[3], **Boxiong Tang[3]**
[1]Shanghai Chest Hospital, Jiao Tong University; Shanghai Lung Cancer Center, Shanghai, China, [2]Affiliated Tumor Hospital of Harbin Medical University, Harbin, China, [3]BeiGene USA, Inc., San Mateo, United States, [4]BeiGene (Shanghai) Co., Ltd., Shanghai, China

Background: Platinum plus pemetrexed chemotherapy is one of the most widely accepted treatment options for patients with non-squamous non-small cell lung cancer (nSQ-NSCLC) without EGFR mutations or ALK rearrangements. This study is based on the clinical trial (NCT03663205) assessing the effects of the addition of tislelizumab to platinum doublet chemotherapy on the health-related quality of life (HRQoL) of patients with nSQ-NSCLC. **Methods:** Patients in this open-label, multicenter Phase 3 study were randomized to two arms: tislelizumab + platinum-pemetrexed (Arm T+PP) or platinum-pemetrexed alone (Arm PP). HRQoL was measured using EORTC-QLQ-C30 global health status (GHS/qol) and QLQ-LC13. Mean score changes from baseline to week 12 (cycle 5, combination therapy stage) and week 18 (cycle 7, maintenance stage) were compared between the two ar **Results:** A total of 334 nSQ-NSCLC patients were randomized (Arm T+PP: n=223; Arm PP; n=111). Patients were 74% male with a median age of 61 years (range 25 - 75). Baseline characteristics were comparable across the two treatment arms and were representative of the target patient population. GHS/QoL improved in Arm T+PP at cycle 5 [mean change (standard deviation) = 0.7(23.06)] and cycle 7 [2.8(19.57)] and declined in Arm PP at both timepoints [cycle 5: -3.8(15.53); cycle 7: -3.4(18.71)]. Furthermore, patients in Arm T+PP experienced larger reductions in coughing, chest pain, dyspnea, and arm/shoulder pain symptoms; whereas, Arm PP experienced numerically higher reductions in “pain in other parts”. Other symptoms remained similar between the two groups. (Table 1). **Conclusion:** The addition of tislelizumab to platinum-based chemotherapy was associated with improvements in nSQ-NSCLC patients’ HRQoL, especially in general health status and most importantly in disease specific symptoms of coughing, chest pain, and dyspnea.

Table 1. Mean Change from Baseline for the subscales of the QLQ-LC13.

QLQ-LC13 Subscale	Cycle	Arm T+PP mean change (SD)	Arm PP mean change (SD)
Alopecia	Cycle 5	5.7 (20.72)	5.5 (20.80)
	Cycle 7	6.2 (20.94)	5.6 (19.15)
Coughing	Cycle 5	-13.4 (29.10)	-5.5 (22.92)
	Cycle 7	-16.2 (27.24)	-5.6 (25.70)
Chest Pain	Cycle 5	-5.7 (22.78)	-3.2 (20.16)
	Cycle 7	-6.9 (22.62)	-2.5 (20.32)
Dysphagia	Cycle 5	0.2 (11.05)	0.5 (8.77)
	Cycle 7	-1.1 (11.85)	0.0 (9.16)
Dyspnea	Cycle 5	-1.5 (16.42)	2.0 (11.32)
	Cycle 7	-2.1 (16.32)	4.1 (13.53)
Hemoptysis	Cycle 5	-3.1 (13.05)	-4.1 (12.35)
	Cycle 7	-4.0 (12.76)	-3.7 (13.99)
Pain in Arm or Shoulder	Cycle 5	-7.3 (23.46)	-3.2 (19.38)
	Cycle 7	-8.2 (27.29)	-2.5 (24.10)
Pain in Other Parts	Cycle 5	-3.3 (24.55)	-5.0 (21.28)
	Cycle 7	-5.6 (26.31)	-7.4 (21.15)
Peripheral Neuropathy	Cycle 5	-1.5 (13.80)	2.3 (13.98)
	Cycle 7	-0.2 (15.20)	3.1 (14.86)
Sore Mouth	Cycle 5	0.8 (13.86)	3.2 (13.79)
	Cycle 7	2.0 (16.03)	5.6 (14.11)

MO01.44
Prognostic Factors in Extensive-Stage Small Cell Lung Cancer (SCLC)

Susana Baptista De Almeida[1], Marina Vitorino[1], Sara Gonçalves[1]
[1]*Hospital Prof. Doutor Fernando Fonseca, EPE, Amadora, Portugal*

SCLC accounts for 13% of lung cancer cases and is characterized by a rapid growth and early metastatic spread, with about 65% of patients (pts) diagnosed in extensive stage. Standard first-line chemotherapy (ChT) hasn't change over the last 4 decades. Despite high tumor response rates, most patients relapse within 6 months. Performance status (PS), gender, age, and body weight loss has traditionally been used to predict outcomes of pts with SCLC. The purpose of this analysis is to evaluate real world data of SCLC pts regarding survival outcomes and prognostic factors. Retrospective analysis of 84 pts diagnosed with SCLC, extensive stage, in our hospital between January 2014 and December 2019. Survival outcomes (OS and PFS) were determined, as well as the impact on survival of the following prognostic factors: age (< or >= 65 years), ECOG PS (<2 vs >=2), Body mass index (BMI; <25 vs >=25), neutrophil to lymphocyte ratio (NLR; < 3 vs >=3), presence of central nervous system metastasis, prophylactic cranial irradiation (PCI). Median population age was 63.5 years, 71,4% were male (n=60). At diagnosis, 13 patients (16%) had CNS metastases and 25 (30%) liver metastases. All pts received cis/carboplatin and etoposid as first-line ChT (median number of cycles 4) and 28 (33%) received second line ChT. Median OS was 6 months (C.I. 95% 4.1-7.9). Median OS was significantly longer in pts with: < 65 years (log-rank p=0,03; 7.0 months C.I. 95% 2.6-11.4 vs 4.0 months C.I. 95% 2.5-5.5); NLR<3 (log-rank p=0.029; 11 months CI. 95% 7.7-14.3 vs 4 months CI. 95% 1.6-6.4). No relationship was found between OS and ECOG PS, BMI and CNS metastases. Median PFS was 3 months (C.I. 95% 2.0-3.9). Median PFS was significantly longer in pts with: <65 years (log-rank p=0.01; 4 months C.I. 95% 2.8-5.2 vs 2 months C.I. 95% 1.2-2.8); BMI >=25 (log-rank p=0.02; 5 months C.I. 95% 2.2-7.8 vs 2 months C.I. 95% 1.0-3.0); ECOG PS <= 1 (log-rank p=0.045; 4 months (C.I. 95% 2.5-5.5) vs 2 months (95% C.I. 0.9-3.1); NLR < 3 (log-rank p=0.006). No relationship was found between CNS metastases and PFS. Median PFS in pts who did PCI was 8 months (C.I. 95% 6.8-9.2). The data we present here represents a real world setting population and identified the prognostic values of age, PFS, BMI and NLR. A prospective analysis is needed to obtain a consensus for prognostic factors in extensive-stage SCLC.

MO01.45

Health-Related Quality of Life (HRQoL) in Patients with NSCLC Harboring MET Exon 14 Skipping (METex14) Treated with Tepotinib

Marina Garassino[1], Xiuning Le[2], Dariusz Kowalski[3], Maria Migliorino[4], Helene Senellert[5], Jose Pradera[6], Radhika Walling[7], Terufumi Kato[8], Michael Thomas[9], Egbert Smit[10], Maya Gottfried[11], Christian Britschgi[12], Andreas Johne[13], Jürgen Scheele[13], Rolf Bruns[14], Helene Vioix[15], Boris Pfeiffer[15], Paul Paik[16]

[1]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, [2]Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, USA, [3]Department of Lung Cancer and Thoracic Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland, [4]Pulmonary Oncology Unit, San Camillo-Forlanini Hospital, Rome, Italy, [5]Department of Medical Oncology, Comprehensive Cancer Center, Institut de Cancérologie de l'Ouest, Saint-Herblain, France, [6]Hospital Universitario Nuestra Señora de Valme, Seville, Spain, [7]Community Regional Cancer Care, Community Health Network, Indianapolis, USA, [8]Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama, Japan, [9]Thoraxklinik, University Heidelberg and Translational Lung Research Center Heidelberg (TLRC-H), The German Center for Lung Research (DZL), Heidelberg, Germany, [10]Netherlands Cancer Institute, Amsterdam, The Netherlands, [11]Meir Medical Center, Tchernichovsky St 59, Kefar Sava, Israel, [12]Department of Medical Oncology and Hematology, Comprehensive Cancer Center Zurich, University Hospital Zurich, Zurich, Switzerland, [13]Global Clinical Development, Merck KGaA, Darmstadt, Germany, [14]Department of Biostatistics, Merck KGaA, Darmstadt, Germany, [15]Global Evidence and Value Development, Merck KGaA, Darmstadt, Germany, [16]Thoracic Oncology Service, Memorial Sloan Kettering Cancer Center, New York, USA

Background: The Phase II VISION study showed efficacy (ORR: by IRC, 46.5–50.0%; by investigator, 55.6–61.7%) of tepotinib in patients with advanced NSCLC with METex14 skipping, who are typically elderly with poor prognosis. HRQoL decline is high in elderly NSCLC patients, highlighting the importance of maintaining HRQoL. We report HRQoL, providing insight into the patient's perspective, complementing clinician-assessed symptom **Methods:** VISION Cohort A enrolled patients with EGFR/ALK wild-type NSCLC with METex14 skipping and ≤2 lines of prior therapy. Patients received oral tepotinib 500 mg once daily. HRQoL was measured using: EORTC Quality of Life Core 30 (QLQ-C30) and Quality of Life Lung Cancer 13 questionnaire (QLQ-LC13), EuroQol Five-Dimension Five-Level Scale (EQ-5D-5L) questionnaire and Visual Analog Scale (VAS), completed at baseline (BL) and every 6 weeks (predefined analysis at Week 12), scored from 0 to 100 (≥10 points change considered clinically meaningful). Time to deterioration (TTD) was defined as time from BL to first 10-point deterioration using Kaplan–Meier estimates; the proportion of patients without deterioration was estimated every 3 months. **Results:** As of 01 Jan 2020, 99 patients had ≥9 months' follow-up and were analyzed for HRQoL (median age 74 [41–94] years). QLQ-LC13 mean scores indicated meaningful improvement in cough (–12.1) and numerical improvements in dyspnea (–3.1) and chest pain (–4.0) at Week 12 that were maintained to Week ≥24. QLQ-C30 functional and symptom scales and EQ-5D-5L VAS scores were also stable. Median TTD and proportion of patients without deterioration is shown (table). **Conclusion:** In patients with advanced NSCLC with METex14 skipping, overall HRQoL was maintained during treatment with tepotinib, with meaningful improvement in cough and beneficial stabilization of dyspnea and chest pain. These HRQoL outcomes with the reported efficacy and safety profile support the use of tepotinib in elderly patients with METex14 skipping NSCLC. Previously presented at ESMO Congress 2020, "FNP:1347P", "Marina C. Garassino et al." - Reused with permission

		Median TTD; months (95% CI)	Patients without deterioration; % (95% CI)		
			3 months	6 months	9 months
QLQ-LC13 symptoms	Cough	19.3 (11.1, ne)	81 (69, 88)	78 (66, 86)	75 (62, 84)
	Dyspnea	5.6 (3.3, 11.1)	65 (53, 75)	45 (32, 56)	38 (26, 51)
	Chest pain	24.9 (11.1, ne)	86 (75, 92)	71 (58, 80)	66 (53, 77)
QLQ-C30 Global Health Score		15.2 (5.6, 33.2)	77 (65, 85)	61 (48, 72)	55 (41, 66)
EQ-5D-5L VAS		11.1 (5.8, 19.4)	78 (66, 86)	60 (47, 71)	52 (39, 64)

MO01.46

Tepotinib Activity in Brain Metastases (BM): Preclinical Models and Clinical Data from MET Exon 14 (METex14) Skipping NSCLC

Santiago Viteri[1], Julien Mazieres[2], Remi Veillon[3], Enriqueta Felip[4], Xiuning Le[5], Marina Garassino[6], Thomas Stanton[7], Masahiro Morise[8], Jong-Seok Lee[9], Shingo Matsumoto[10], Filippo De Marinis[11], Thomas Wehler[12], Anderson Clark[13], Manja Friese-Hamim[14], Christopher Stroh[14], Rolf Bruns[15], Gordon Otto[16], Paul Paik[17]

[1]Dr Rosell Oncology Institute, Dexeus University Hospital, QuironSalud Group, Barcelona, Spain, [2]CHU de Toulouse, Institut Universitaire du Cancer, Toulouse, France, [3]CHU Bordeaux, service des maladies respiratoires, Bordeaux, France, [4]Department of Oncology, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, [5]Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, USA, [6]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, [7]St Joseph Health Cancer Center, Santa Rosa, USA, [8]Department of Respiratory Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan, [9]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea, [10]Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwanoha, Kashiwa, Japan, [11]Division of Thoracic Oncology, European Institute of Oncology, IRCCS, Milan, Italy, [12]Department of Radio-Oncology, University Hospital Saarland, Homburg, Germany, [13]Translational Innovation Platform, Oncology, EMD Serono Research & Development Institute, Inc., Billerica, US, [14]Translational Innovation Platform, Oncology, Merck KGaA, Darmstadt, Germany, [15]Department of Biostatistics, Merck KGaA, Darmstadt, Germany, [16]Clinical Oncology Development, Merck KGaA, Darmstadt, Germany, [17]Thoracic Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, USA

Background: BM occur in 20–40% of NSCLC harboring METex14 skipping. We investigated the activity of the MET inhibitor tepotinib in BM in preclinical models and patients from the VISION study (NCT02864992). **Methods:** Penetration of the blood–brain barrier was assessed in Wistar rats (n=3) at 3.66 mg/kg/h intravenous tepotinib by determining the unbound brain (fu br)-to-plasma (fu pl) concentration or exposure ratio (Kp u,u). Efficacy was assessed in two lung cancer patient-derived xenografts (PDXs) from BM harboring high MET amplification (gain in copy number: LU5349 = 11, LU5406 = 24) grown in NOD-SCID mice. Subcutaneous PDXs (n=5/group) or PDXs orthotopically implanted into the brain (n=10/group) were treated with tepotinib 125 mg/kg or vehicle control orally once daily. Intracranial tumor growth was monitored by gadolinium-based MRI. In VISION Cohort A, patients with METex14 skipping NSCLC received tepotinib 500 mg once daily. Systemic objective response per RECIST v1.1 by independent review committee (IRC) was a preplanned analysis in patients with baseline BM identified by IRC (BM-IRC) or investigator assessment (BM-INV). **Results:** Preclinical data indicated high binding of tepotinib in the brain, with unbound tepotinib in brain tissue being lower than in plasma (fu br = 0.4%, fu pl = 4%). Unbound tepotinib concentrations in the brain were 25% of plasma (Kp u,u = 0.25). Tepotinib treatment resulted in tumor regression in both PDXs (mean % tumor volume: –84% in LU5349, –63% in LU5406). As of 1 Jan 2020, 22/152 patients enrolled in Cohort A had baseline BM, with similar characteristics and comparable systemic response data (table) to the overall population. **Conclusion:** Tepotinib administration resulted in tumor regression in MET-driven lung cancer BM PDX models. Clinical activity in patients with NSCLC harboring METex14 skipping with baseline BM was consistent with the overall population in VISION. Cohort C aims to assess intracranial response. Previously presented at ESMO Congress 2020, "FNP:1286P", "Santiago Viteri et al." - Reused with permission

	BM-IRC subgroup	BM-INV subgroup
Number of patients with brain metastases; n		
Non-target lesions	14	12
Target lesions	0	1
Objective response rate; % (95% CI)	57.1% (28.9, 82.3)	53.8% (25.1, 80.8)
Best overall response; n		
Partial response	8	7
Stable disease	3	3

MO01.47

Tepotinib Exposure-Response Analyses of Safety and Efficacy in Patients with Solid Tumors

Wenyuan Xiong[1], Sofia Hietala[2], Joakim Nyberg[2], Orestis Papasouliotis[1], Richard Anziano[2], Karin Berghoff[3], Andreas Johne[4], Pascal Girard[1], Rainer Strotmann[5], Paul Paik[6]

[1]Quantitative Pharmacology, Merck, Lausanne, Switzerland, [2]Pharmetheus AB, Uppsala, Sweden, [3]Global Patient Safety, Merck KGaA, Darmstadt, Germany, [4]Global Clinical Development, Merck KGaA, Darmstadt, Germany, [5]Qualitative Pharmacology, Merck KGaA, Darmstadt, Germany, [6]Memorial Sloan Kettering Cancer Center, New York, United States

Background: Tepotinib is a highly selective, potent MET inhibitor that has shown clinical activity in patients with non-small cell lung cancer (NSCLC) harboring MET exon 14 skipping. The objective of this analysis was to evaluate the relationship between tepotinib and both safety and efficacy endpoints in patients with solid tumors. **Methods:** Data from patients receiving tepotinib 30 mg to 1400 mg once daily (QD) from four completed Phase I/II studies (NCT01014936, NCT01832506, NCT01988493, NCT02115373) and one ongoing Phase II study (VISION, NCT02864992) were used for exposure-safety analysis (n=499); exposure-efficacy analysis was performed using data from VISION cohort A (NSCLC patients with MET exon 14 skipping receiving tepotinib 500 mg QD; n=146). Exposure metrics of area under the curve over 24h (AUC24h) for safety, and at steady state (AUCτ,ss) for efficacy were derived from a population pharmacokinetic model. Safety or laboratory endpoints related to potential identified risks were evaluated, including edema (time to first event and maximum severity grade), aspartate aminotransferase and alanine aminotransferase concentrations, and serum lipase/amylase levels. Efficacy endpoints were objective response and duration of response based on independent review and investigator assessment. **Results:** Overall, no association of tepotinib exposure with safety or efficacy was observed. There was no clear association between exposure and first occurrence of edema event or severity of edema. There was no association between lipase elevation and tepotinib exposure. An observed trend towards increased amylase, and transient increases in aspartate aminotransferase and alanine aminotransferase, did not appear to be correlated with tepotinib exposure. There was no apparent difference in exposure for responders and non-responders by either assessment; the objective response rate was similar in all exposure quartiles. There was also no apparent association between exposure and duration of response. **Conclusion:** A flat exposure-response relationship was identified within the observed exposure range at dose levels of 30–1400 mg QD for safety and across the exposures observed in VISION at the clinical dose of 500 mg for efficacy. The exposure-response analyses confirm that 500 mg QD is an appropriate dose for tepotinib to be used in the clinic. Previously presented at ESMO Congress 2020, “FNP:584P”, “Paul K. Paik et al.” - Reused with permission

MO01.48

INSIGHT 2: Tepotinib + Osimertinib in EGFR-Mutant NSCLC with Resistance to 1st-Line Osimertinib due to MET Amplification

Egbert Smit[1], Enriqueta Felip[2], **Niki Karachaliou[3]**, Barbara Ellers-Lenz[4], Yi-Long Wu[5]
[1]Department of Thoracic Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands, [2]Department of Oncology, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, [3]Global Clinical Development, Merck KGaA, Darmstadt, Germany, [4]Department of Biostatistics, Merck KGaA, Darmstadt, Germany, [5]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital & Guangdong Academy of Medical Sciences, Guangzhou, China

Background: MET amplification is a mechanism of acquired resistance to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs), occurring in ~15% of patients who progress on 1st-line osimertinib therapy. Combination of osimertinib with a MET TKI may overcome MET-related osimertinib resistance. Tepotinib is an oral, once-daily (QD), highly selective, potent MET TKI. Tepotinib + gefitinib is associated with improved outcomes in patients with EGFR-mutant MET-amplified non-small cell lung cancer (NSCLC) and EGFR TKI resistance compared to chemotherapy (INSIGHT: NCT01982955); progression-free survival was 16.6 vs 4.2 months (hazard ratio [HR]=0.13; 90% CI: 0.04, 0.43) and overall survival was 37.3 vs 13.1 months (HR=0.08; 90% CI: 0.01, 0.51). **Methods:** INSIGHT 2 is a global, open-label, Phase II trial of tepotinib + osimertinib in patients with advanced EGFR-mutant NSCLC. Following a protocol amendment in April 2020, the study is enrolling patients with acquired resistance to 1st-line osimertinib due to MET amplification. Enrollment is allowed based on local fluorescence in situ hybridization (FISH) testing while awaiting central confirmation of MET amplification. Patients must be ≥18 years old, have ECOG PS of 0/1 and normal organ function. Patients will receive tepotinib (500 mg QD) + osimertinib (80 mg QD) until disease progression, unacceptable toxicity, or consent withdrawal. A safety run-in confirming the dose and regimen comprising ≥6 patients is ongoing (endpoint: dose-limiting toxicities). The study is anticipated to enroll 120 patients. Twelve patients will initially receive tepotinib monotherapy followed by combination of tepotinib + osimertinib upon disease progression. The primary endpoint is objective response rate by independent review committee (RECIST v1.1) in patients with MET amplification determined centrally by FISH. Secondary endpoints are objective response rate by investigator assessment, duration of response, disease control, progression-free survival, overall survival, pharmacokinetics, health-related quality of life, tolerability, and safety (NCI-CTCAE v5.0). Recruitment is ongoing, with >300 patients prescreened. Approximately 100 sites in 15 countries in Europe, Asia, and North America are expected to participate. **Results and conclusions:** As this is a trial in progress, results and conclusions cannot be shared yet. Previously presented at ESMO Congress 2020, "FNP:1415TiP", "Egbert F. Smit et al." - Reused with permission

MO01.49

Low Prognostic Nutrition Index Predicts Poorer Quality of Life in Late Stage Lung Cancer

Gengpeng Lin[1], Zhaohui Zhang[1], Xuefei Li[1]
[1]*Department of Pulmonary and Critical Care Medicine, The First Affiliated Hospital of Sun Yet-sen University, Guangzhou, China*

Quality of Life (QOL) is one of the most important endpoints in lung cancer care. However, most QOL questionnaires are time-consuming and they are not routinely performed in the daily clinic. The nutrition and immune status have been reported to correlate with QOL in lung cancer. The objective of this study was to investigate whether prognostic nutritional index, a reliable marker reflecting nutrition and immune status, can predict QOL in late stage lung cancer. Eighty patients with newly diagnosed NSCLC were included in the study. Clinical data including medical history, blood cytology and chemistry, definitive histopathology diagnosis, clinical tumor-node-metastasis (TNM) stage as well as ECOG performance status were obtained. The FACT-L questionnaire in Chinese versions 4 were performed on every patient. Of the eighty lung cancer patients of late stage enrolled in the study, 16 were stage III and 64 were stage IV. The average PNI value was 44.24±5.53. The average FACT-L score was 99.58±21.84, demonstrating an impaired quality of life. The FACT-L score in stage IV group was significantly lower than that in stage III group (P=0.001), especially in scales of physical well-being, social/family wellbeing, emotional well-being, and functioning well-being. In stage IV group, the FACT-L score in high PNI group was significantly higher than that in low PNI group (P=0.042), with especially higher score in physical well-being. PNI was significantly related to FACT-L score (r=0.3265, P=0.0085). Further correlation analysis showed that PNI was positively related to the aspect of physical wellbeing. PNI is a valuable marker in predicting quality of life in stage IV lung cancer patients. Lower level of PNI may indicate the need of detailed quality of life evaluation and intervention. Thus, PNI could be a simple and novel biomarker in lung cancer management.

figure.jpg

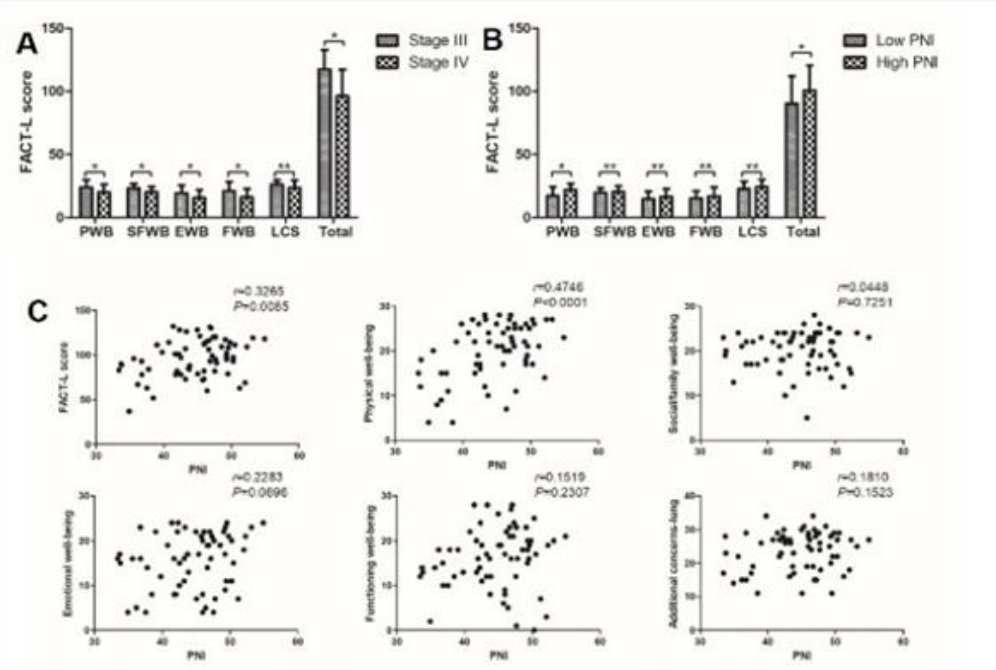


Figure 1 A. Comparison of FACT-L in stage III and stage IV **B**. Comparison of FACT-L in low PNI and high PNI group **C**. Correlation of PNI and FACT-L in stage IV group

figure.jpg

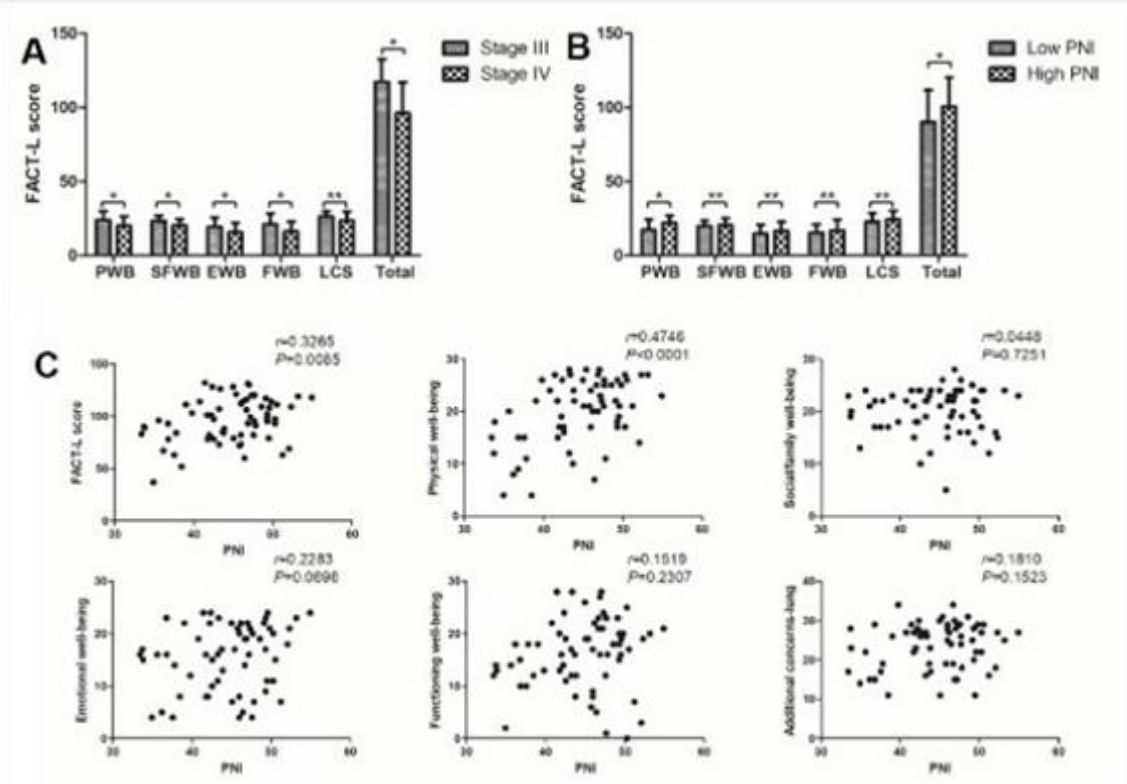


Figure 1 A. Comparison of FACT-L in stage III and stage IV **B**. Comparison of FACT-L in low PNI and high PNI group **C**. Correlation of PNI and FACT-L in stage IV group

MO01.50

Tislelizumab Plus Standard Chemotherapy for Treatment of Advanced Squamous Non-Small Cell Lung Cancer: Patients' Health Related Quality of Life

J. Wang[1], X. Yu[2], **Gisoo Barnes[3]**, J. Li[3], S.J. Leaw[4], X. Lin[4], B. Tang[3]
[1]National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, [2]Zhejiang Cancer Hospital, Hangzhou, China, [3]BeiGene USA, Inc., San Mateo, United States, [4]BeiGene (Shanghai) Co., Ltd., Shanghai, China

Squamous non-small cell lung cancer (SQ NSCLC) accounts for 20% to 30% of lung cancer. SQ NSCLC patients treated with chemotherapy experience substantial reductions in health-related quality of life (HRQoL). The objective of the current study was to assess whether the addition of tislelizumab to first-line standard-of care chemotherapy could improve HRQoL of patients with advanced and metastatic squamous NSCLC. Patients in this open-label, randomized, multicenter Phase 3 study conducted in China were randomized to 3 arms: tislelizumab combined with carboplatin and paclitaxel (Arm A), tislelizumab combined with carboplatin and nab-paclitaxel (Arm B), or paclitaxel plus carboplatin alone (Arm C). The primary endpoint was progression-free survival (PFS) by IRC in the comparisons of Arms A vs C and B vs C. HRQoL data was assessed using EORTC-QLQ-C30 and EORTC QLQ-LC13 in all three arms at baseline, cycles 3 and 5 while Arms A and B also completed HRQoL questionnaires up to cycle 17 in this data cut (12/6/2019). The analyses for this report are focused on baseline through cycle 5, for which all the three arms completed the HRQoL questionnaires. A total of 360 patients diagnosed with squamous NSCLC were randomized (n=120, Arm A; n=119, Arm B; n=121, Arm C). Patients were 91.7% male with a median age of 62 years (range 34, 74). Demographics and baseline characteristics were comparable across the 3 treatment arms and were representative of the target patient population. The global health status/QoL scores of the QLQ-30 improved for both Arms A [mean change=2.8 (SD=23.2)] and B [mean change=3.9 (SD=18.00)] by cycle 5, whereas it declined in Arm C [mean change=-1.3 (SD=19.4)]. For the symptoms measured by QLQ-LC13, Arm A [mean change = -20.1 (SD = 29.2)] and B [mean change = -12.7 (SD = 33.8)] both experienced a larger reduction in coughing symptoms at cycle 5 compared to Arm C [mean change = -7.3 (23.2)]. For dyspnea, change from baseline at cycle 5, both Arms A [mean -1.9 (SD = 18.1) and B [(mean change = -1.8 (SD = 15.2)] experienced a reduction in dyspnea while Arm C [mean change = 2.4 (SD = 15.2)] experienced more symptoms relative to baseline. Finally, all three Arms experienced a reduction in hemoptysis at cycle 5 with the larger reductions observed for Arms A [mean change = -9.4 (19.8)] and B [mean change = -9.4 (SD = 26.8)] compare to C [mean change = -2.3 (SD = 19.4)]. No clinical differences were observed between the three arms in pain items, all three reported reduction in pain sympto The addition of tislelizumab to platinum-based chemotherapy is associated with clinically meaningful improvements in SQ NSCLC patients' HRQoL, especially in general health status/ QoL and most importantly in the lung cancer specific symptoms including coughing, dyspnea and hemoptysis.

Nursing & Allied Health Posters

NU01.01

Real World Data on Maintenance Therapy Utilization and Overall Survival Among Advanced Non-Small Cell Lung Cancer Patients Treated with Pemetrexed in combination with Pembrolizumab and Platinum Chemotherapy in the US

Kayonda Bayo[1], Himani Aggarwal[2], Yimei Han[2], Catherine Muehlenbein[2], Yajun Emily Zhu[2], Jong Seok Kim[2]
[1]Thomas Jefferson University, Philadelphia, United States, [2]Eli Lilly & Company, Indianapolis, United States

Background: First-line (1L) treatment with pemetrexed+pembrolizumab+platinum chemotherapy (pem+pembro+plat) had demonstrated improved survival versus pem+plat among metastatic non-squamous (NSQ) non-small cell lung cancer (NSCLC) patients in the KEYNOTE-189 trial. In the trial patients received 4 cycles of pem+pembro+plat followed by maintenance therapy (MT) with pem and pembro until progression or intolerable toxicity. This study examined MT utilization and overall survival (OS) among patients treated with pem+pembro+plat in real world. **Methods:** Adult patients in the US with advanced NSQ NSCLC who received 1L treatment with pem+pembro+plat between May 1, 2017 and October 31, 2019 were selected from the Flatiron Health electronic health record-derived database. Descriptive statistics were used to summarize patients' baseline characteristics and treatment patterns. Kaplan-Meier survival analysis was conducted to examine OS. **Results:** Of 2488 patients who received pem+pembro+plat in 1L, 43.9% received MT with pem+pembro (16.4%), pembro (18.1%), pem (0.16%), or a mix MT (9.2%). The mix MT comprised a switch from pembro to pem+pembro (7.4%), pem+pembro to pem (1.29%), pembro to pem (0.08%), or pembro to pem+pembro and then to pem (0.44%). Baseline characteristics were similar between the overall and MT populations (Table 1). The median number of cycles was 4 for both pem and pembro in pem+pembro MT and 6 for pembro MT. The median OS was 11.8 months (95% CI 10.82 – 12.76) for the overall, 21.0 months (95% CI 19.31 – 25.16) for the MT population and 9.1 months (95% CI 7.04 – 12.70) for patients who did not receive MT upon completion of 4 cycles of 1L treatment. **Conclusion:** In real world, a slightly less than half of advanced NSQ NSCLC patients in the US received MT following pem+pembro+plat in 1L. The median OS among the MT population was comparable to the median OS in the KEYNOTE-189 trial.

Table 1. Patients Baseline Characteristics and OS

Variable	Overall population (n=2488)	MT population (n=1091)
Mean age (SD), years	67.4 years (9.6)	67.0 years (9.4)
Male	54.5%	53.3%
White	68.1%	67.8%
History of smoking	89.3%	89.7%
ECOG Performance Status (PS) 0 or 1	61.3%	66.1%
ECOG PS ≥2	13.5%	9.3%
ECOG PS Unknown	25.2%	24.7%
Stage IV at Initial Diagnosis	83.5%	83.1%

Oligometastatic Posters

OL01.01
Real-World Clinical Outcomes in Patients with Advanced Non-Small Cell Lung Cancer (aNSCLC) in the US

Eric Nadler[1, 2], J. Chang[3], X. Zhang[4], K. Aguilar[2], J. Zhou[2], B. Arondekar[3], V. Pawar[4]
[1]Texas Oncology, Dallas, United States, [2]McKesson Life Sciences, The Woodlands, United States, [3]Pfizer Inc., New York, United States, [4]EMD Serono Research & Development Institute, Billerica, United States

While immuno-oncology (IO) regimens have demonstrated promising clinical benefits for patients with aNSCLC in clinical trials, evidence on their real-world (RW) outcomes remains limited. Identifying RW clinical benefits is often subject to bias. To mitigate confounding, this study employed a propensity score (PS) approach to assess time-to-treatment discontinuation (TTD) and overall survival (OS) among patients with aNSCLC treated within the US Oncology Network. This retrospective study included patients with aNSCLC who initiated chemotherapy, targeted therapy (TT), or IO therapy as first-line (1L) treatment from 1/3/15-1/8/18. Data were sourced from electronic healthcare records through 1/2/19. Inverse probability of treatment weighting (IPTW) was performed to mitigate confounding effects. Generalized boosted model, a nonparametric machine-learning classifying technique, was used to generate PS in a way that would have optimum balance in baseline covariates between each treatment group and the entire patient population. IPTW-weighted Cox model was used to estimate the hazard ratios for TT, IO monotherapy, and IO combination therapy (eg, IO-IO [0.5% of all regimens], IO-chemotherapy) vs chemotherapy. Weighted Kaplan-Meier curves were also constructed. In total, 7,746 patients were included. Based on the weighted Cox model, receipt of 1L IO therapy (alone or in combination) or TT was associated with decreased risk of treatment discontinuation vs chemotherapy ($p<0.0001$ for all). Receipt of 1L IO monotherapy or TT was associated with a reduced risk of death compared with chemotherapy ($p<0.0001$ for both). Figures 1-2 present adjusted Kaplan- Meier estimates. These results suggest that 1L IO-based treatment is associated with improved TTD; IO monotherapy and TT also improved OS vs chemotherapy. However, the survival benefit for IO combination therapy vs chemotherapy alone was nominal. Future RW studies should further explore how patient characteristics such as programmed death-ligand 1 (PD-L1) expression may have influenced outcomes, particularly between IO monotherapy and combination regimens.

figure 1.jpg

Figure 1. Inverse probability weighting estimates of time-to-treatment discontinuation

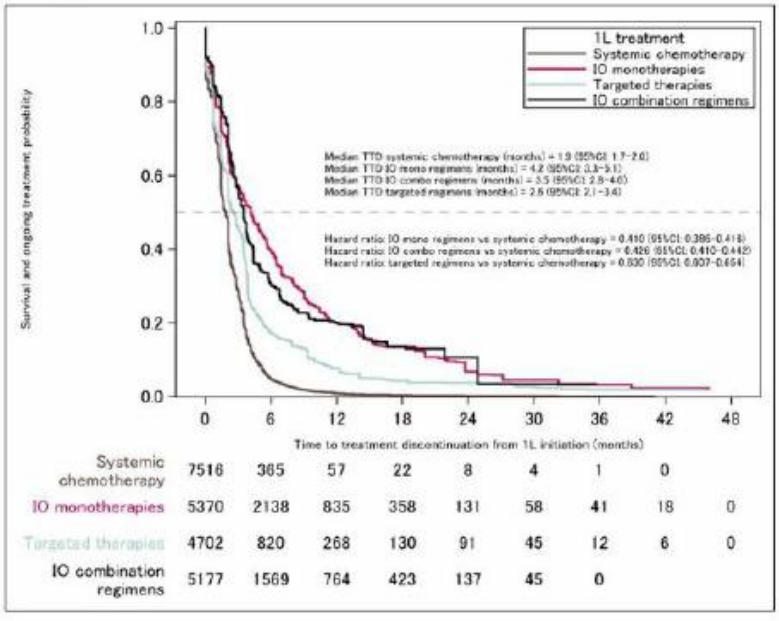


figure 2.jpg

Figure 2. Inverse probability weighting estimates of overall survival

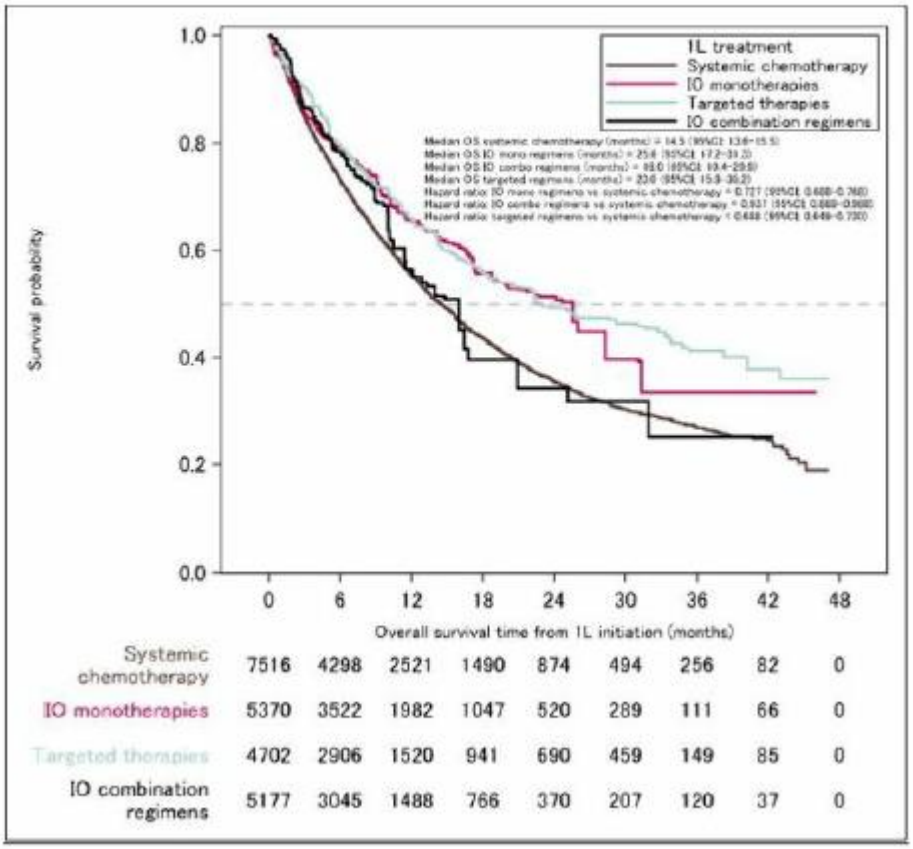


figure 1.jpg

Figure 1. Inverse probability weighting estimates of time-to-treatment discontinuation

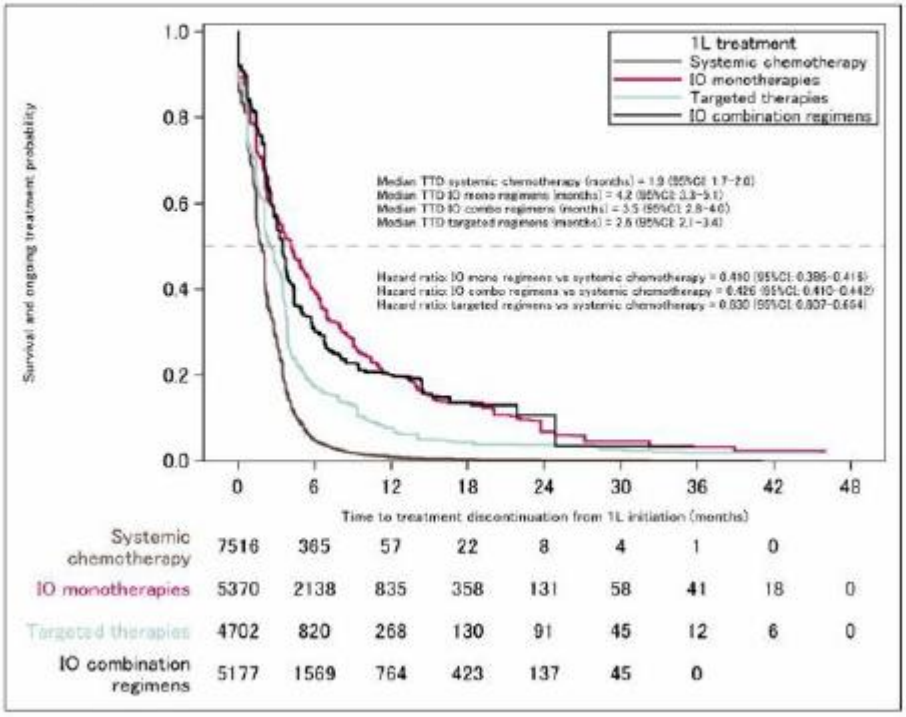
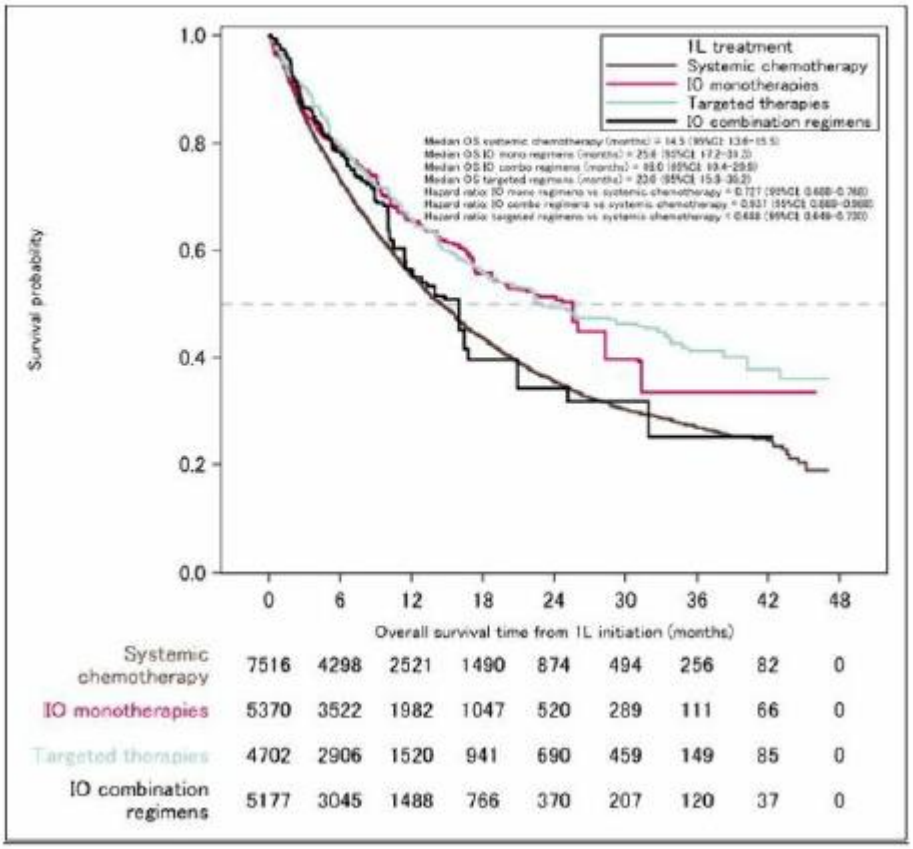


figure 2.jpg

Figure 2. Inverse probability weighting estimates of overall survival



Pathology Posters

PATH01.01

Diagnostic and Economic Value of Next-Generation Sequencing (NGS) in Genotyping Non-Small Cell Lung Cancer Tumors (NSCLC): A Literature Review

Ying Zheng[1], Helene Vioix[2], Frank X Liu[1], Barinder Singh[3], Sakshi Sharma[3], Sheetal Sharma[3]
[1]EMD Serono Inc., Rockland, United States, [2]Merck KGaA, Darmstadt, Germany, [3]Parexel, Access Consulting, Mohali, India

Background: The diagnostic and economic value of NGS in identifying appropriate therapies for patients with NSCLC has not been clearly defined. This literature review examined published evidence describing the diagnostic and economic outcomes of NGS vs. conventional molecular testing strategies (eg, single-gene only, single-gene sequential) in adults with unresectable, advanced, or metastatic NSCLC. **Methods:** Embase and MEDLINE were searched for articles (2015–2020) and conference abstracts (2017–2020) were manually searched. Eligible studies included clinical trials, observational studies, surveys, and economic evaluations published across the globe (assessing >100 patients/samples). Included studies compared NGS with single-gene testing techniques. **Results:** Of 375 full-text studies identified, 15 studies (7 US) were included. Of these 15 studies, 6 (2 US) reported diagnostic outcomes and 11 (5 US) reported economic evidence (2 non-US studies reported both) in patients with NSCLC. Among 6 diagnostic studies, 3 reported concordance rates of NGS vs. conventional molecular testing ranging from 70% to 99.1% across mutations examined. One US study reported higher rates of test initiation and completion, while using less tissue compared with single-gene testing for ≥4 biomarkers. Among 11 economic studies, 6 assessed cost-effectiveness, 2 assessed budget impacts, 1 reported a cost consequence analysis, and 2 reported costs. Among the 5 US economic studies, 2 found tumor tissue NGS vs. sequential exclusionary testing or hotspot panel testing (excluding treatment costs) to be cost saving, 2 found tumor tissue NGS vs. single-gene testing (including treatment costs) to be minimally cost additive, and 1 found circulating tumor DNA NGS vs. no additional genomic testing among patients with incomplete tissue genotyping to be cost saving. An additional 7-10% more patients were identified with targetable mutations and the expected survival was 0.06 years longer for NGS vs single gene testing. Median turnaround times were longer using NGS vs. single-gene testing (14–16.5 vs. 6.9–11.3 days), but not substantially longer if sequential single-gene tests were required. Studies conducted in other regions (eg, Europe, Asia) were aligned with US studies regarding economic and diagnostic outcomes. **Conclusion:** NGS has been validated to be highly concordant with conventional molecular testing in patients with NSCLC. NGS leads to a greater proportion of patients correctly assigned to targeted therapy and increased life years gained while being cost neutral or cost saving.

PATH01.02

Diagnostic and Economic Value of Liquid vs. Solid Tissue Biopsy Procedures for the Detection of Targetable Mutations in Non-Small Cell Lung Cancer (NSCLC) Tumors: A Literature Review

Ying Zheng[1], Helene Vioix[2], Frank X Liu[1], Barinder Singh[3], Sakshi Sharma[3], Deepti Sharda[3]
[1]EMD Serono Inc., Rockland, United States, [2]Merck KGaA, Darmstadt, Germany, [3]Parexel, Access Consulting, Mohali, India

Background: The role of less invasive liquid biopsy (LBx) techniques (eg, plasma samples, bronchoalveolar lavage, circulating tumor DNA, urine) compared with solid tissue biopsy (TBx) for diagnostic characterization of NSCLC has not been clearly defined. This literature review examined published evidence describing the diagnostic and economic outcomes of LBx vs. TBx in patients with unresectable, advanced, or metastatic NSCLC. **Methods:** Embase and MEDLINE were searched for articles (2015–2020) and conference abstracts (2017–2020) were manually searched for published evidence related to LBx vs. TBx procedures in patients with NSCLC. Eligible studies included clinical trials, observational studies, surveys, and economic evaluations published internationally (assessing ≥100 patients). **Results:** Of 375 full-text studies identified, 25 studies (≈14,000 patients total) reported diagnostic evidence pertaining to LBx vs. TBx; 3 studies reported economic impact. The majority of diagnostic studies were observational (88%). Median age of patients ranged from 57 to 70 years (n=11 studies); 32% to 70% of patients were male (n=16 studies). The range of specificity values reported across mutations and across studies was 42.5-100%, with 9 of 17 studies reporting specificity ≥90% for all tests. The range of sensitivity values reported across mutations and across studies was 0-100%, with 8 of 18 studies reporting sensitivity ≥60% for all tests. In 17 studies reporting concordance rates in LBx vs. TBx, concordance rates for all mutations tested were ≥70% in 15 studies (>90% in 4). In 9 studies reporting positive predictive values (PPV) for LBx vs. TBx, the range of PPVs for clinically actionable mutations was 74.5-100%, with US studies reporting 100% PPV for all clinically actionable mutations except T790M (79%). While 7 studies reported negative predictive value (NPP) of LBx vs. TBx, the range of NPP for clinically actionable mutations was 67-98%. Faster turnaround times were reported for LBx vs. TBx (range across 3 studies, 2-10 vs 5-25 days). All 3 economic studies (US, Canada and Italy) found incorporating LBx into the treatment pathway was associated with lower testing cost per patient, while the Canadian study estimated higher life-time cost driven by higher treatment cost as more patients were identified to receive targeted therapy. **Conclusion:** The faster turnaround times and high PPV of LBx enable faster treatment decisions in patients with NSCLC who have targetable mutations. The testing cost per patient identified was lower when LBx was incorporated into the treatment pathway.

PATH01.03

Mutational Landscape and Prognosis Prediction for Immune Checkpoint Blockades of DNA Damage Response Pathways in Non-Small Cell Lung Cancer

L. Zhong[1], **Jing Zhao[2]**, X. Zhao[2], W. Xie[2], Y. Bai[2]
[1]Affiliated Hospital of Nantong University, Jiangsu, China, [2]3D Medicines Inc., Shanghai, China

DNA damage response (DDR) pathways which play a key role in maintaining the genome stability, have been reported to be associated with higher tumor mutational burden (TMB) and improved clinical benefit of immune checkpoint blockades (ICBs) in non-small cell lung cancer (NSCLC). Our study aimed to reveal the mutation landscape of DDR pathways and their association with TMB and PD-L1 in a Chinese NSCLC cohort, and explore the potential prognosis prediction in patients treated with ICBs. A total of 3428 NSCLC patients who underwent next-generation sequencing (NGS) with a 381 genes panel in 3DMed Clinical Laboratory and 350 NSCLC patients treated with ICBs downloaded from Cbioportal were included in our analysis. Non-synonymous mutation of 30 DDR genes across six pathways were analyzed. Pathway mutation was defined as at least one gene mutation in the corresponding pathway. Ridge regression was used to analyze the association of DDR genes mutation and TMB levels. There are 2161 (63.0%) male and 1267 (37.0%) female patients, with a median age of 62 (IQR range, 54-68). DDR mutation was prevalent in 30.0% patients. The top five mutated DDR genes were ATM (168, 4.9%), BRCA2 (1311, 3.8%), ATR (112, 3.3%), POLE (100, 2.9%) and FANCA (69, 2.0%). The DDR pathway mutation frequency were 531 (15.5%) for fanconi anemia, 460 (13.4%) for homologous recombination, 334 (9.7%) for damage sensor, 206 (6.0%) for nucleotide excision repair, 182 (5.3%) for mismatch repair, 167 (4.9%) for base excision repair and 55 (1.6%) for non-homologous end joining. A total of 305 (8.9%) harbor at least two DDR genes mutation and 575 (16.8%) at least two DDR pathways mutation. In ridge regression, 18 DDR genes were significantly associated with TMB (FDR < 0.001). Among them, ATM, ATR, BRCA2, MLH1 and POLD1 had the highest coefficients. DDR mutation, TMB and PD-L1 expression on tumor cells were available for 2403 patients. In 730 patients with at least one DDR gene mutation, 184 (25.2%) patients were not in the group of TMB-high (top 20%) or positive PD-L1 (PD-L1 expression on tumor cells ≥1%). In 350 NSCLC patients treated with ICBs, DDR mutation (defined by DDR genes with FDR < 0.001 in ridge regression and mutation frequency > 1.5%) was significantly associated with prolonged overall survival (Hazard ratio = 0.70; 95% confidential interval = 0.51-0.97, P = 0.03). Our results indicated the wide prevalence of DDR pathways mutations in Chinese patients with NSCLC and validated the potential prognosis prediction of ICBs, which provide evidence for precise immune treatment in NSCLC.

Prevention, Smoking Cessation, Screening and Early Detection Posters

PR01.01
Evaluation of Circulating Tumor Cells for Non-Invasively Discerning Lung Primary from Metastasis

Darshana Patil[1], Sewanti Limaye[2], **Dadasaheb Akolkar[1]**, Pradip Fulmali[1], Pooja Fulmali[1], Archana Adhav[1], Sachin Apurwa[1], Sushant Pawar[1], Shoeb Patel[1], Rohit Chougule[1], Vishal Ranjan[1], Pradyumna Shejwalkar[1], Shabista Khan[1], Raja Dhasarathan[1], Vineet Datta[1], Stefan Schuster[1], Cynthe Sims[1], Prashant Kumar[1], Pradip Devhare[1], Ajay Srinivasan[1], Rajan Datar[1]
[1]Datar Cancer Genetics, Mumbai, India, [2]Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Mumbai 400053, India

Background: Lungs are the most common site of primary malignancy as well as metastasis from primary malignancies in other organs. Radiological imaging scans often present a diagnostic conundrum where suspicious lesions are observed in various organs including the lungs thus necessitating an invasive biopsy for histopathological diagnosis which remains the standard for diagnosis and disambiguation of primary lung malignancy and metastatic deposit. We present a non-invasive means for discerning primary lung malignancy from metastatic deposit based on Immunocytochemistry (ICC) profiling of Circulating Tumor Cells (CTCs) from peripheral blood. Methods: We collected peripheral blood from 229 individuals with suspicious findings on radiological scans involving the lung and various other organs such as the liver, chest wall, colon, hepatobiliary tract or the gastroesophageal tract. Patients underwent an invasive biopsy of the lungs to obtain tumor tissue for histopathological examination (HPE) which were initially blinded. Peripheral blood mononuclear cells (PBMCs) were isolated from blood samples and treated with an epigenetically activating medium which induces cell death in normal (non-malignant) hematolymphoid cells as well as epithelial cells in peripheral blood, but selectively confers survival privilege on apoptosis resistant tumor-derived Circulating Tumor Cells (CTCs). CTCs were profiled by ICC using IVD approved antibodies against organ and subtype specific (OSS) antigens to determine the tissue of origin (TOO). ICC findings were compared with the HPE results to determine concordance. **Results:** Among the 229 individuals, 10 each were diagnosed with a primary malignancy of the breast, colon and lungs, 5 each of esophagus and stomach, 4 of liver and 3 of pancreas. ICC profiling of CTCs for OSS antigens indicated a 96.9% overall concordance with HPE findings. ICC profiling of CTCs accurately discerned primary malignancies of the lungs, colon, esophagus, pancreas and stomach with 100% accuracy, of the breast with 90% accuracy and of the liver with 75% accuracy. **Conclusion:** The findings suggest that ICC profiling of CTCs can non-invasively discern primary malignancy of the lungs from metastatic deposits in the lungs with high accuracy. In the clinical setting, this approach will be useful for diagnostic triaging in individuals with confounding radiological findings, especially where a biopsy of the lungs (or any other organ) is not possible owing to anatomical considerations or patient's co-morbidities.

PR01.02

Smoking Cessation After Lung Cancer Diagnosis and Risk of Second Primary Lung Cancer: The Multiethnic Cohort Study

Eunji Choi[1], Sophia Luo[1], Martin Tammemägi[2], Jacqueline Aredo[3], Loïc Marchand[4], Iona Cheng[5], Heather Wakelee[3,6], Summer Han[1,3,6,7]

[1]Quantitative Sciences Unit, Department of Medicine, Stanford University, Palo Alto, United States, [2]Department of Health Sciences, Brock University, St. Catharines, Canada, [3]Stanford University School of Medicine, Stanford, United States, [4]Cancer Epidemiology Program, University of Hawaii Cancer Center, Honolulu, United States, [5]Department of Epidemiology and Biostatistics, University of California, San Francisco, United States, [6]Stanford Cancer Institute, Stanford University School of Medicine, Stanford, Unites States, [7]Department of Neurosurgery, Stanford University School of Medicine, Stanford, United States

Background: Smoking cessation provides significant mortality benefits to patients diagnosed with lung cancer. However, little is known about whether lung cancer diagnosis impacts changes in smoking behaviors. Furthermore, the effects of smoking cessation on the risk of second primary lung cancer (SPLC) have not been established yet. This study aims to examine the smoking behavioral changes after initial diagnosis of lung cancer and to estimate the effect of smoking cessation on SPLC risk. **Methods:** Data were derived from the 7,299 participants diagnosed with initial primary lung cancer (IPLC) between 1993 and 2017 in the Multiethnic Cohort (MEC), a population-based prospective study that enrolled adult participants in 1993-1996 (baseline). Smoking data were assessed longitudinally at baseline and 10-year follow-up (2003-2006). Our study cohort consisted of 986 participants who were healthy current smokers at baseline and provided updated smoking information at 10-year follow-up. Incident lung cancers were identified through SEER registries. Participants had incident IPLCs which developed either before or after 10-year follow-up and then were followed for a subsequent SPLC diagnosis. The primary outcome was a change in smoking status from “current” at baseline to “former” at 10-year follow-up (i.e. smoking cessation), which was analyzed using logistic regression in association with whether IPLC diagnosis occurred between the baseline and the follow-up. The second outcome was the incidence of SPLC after the IPLC diagnosis and the 10-year follow-up, which was analyzed using Fine-Gray competing risk regression in association with smoking cessation. **Results:** Among 986 participants who were current smokers at baseline, 504 (51.1%) reported having quit smoking at 10-year follow-up. The smoking cessation rate was significantly higher (80.6%) among those who were diagnosed with IPLC between baseline and 10-year follow-up versus those without IPLC diagnosis during the 10-year period (45.4%), with an odds ratio (OR) of 5.87 (P=3.42x10-14). Competing risk analysis showed that the incidence of SPLC was significantly lower (hazard ratio, HR=0.41, P=0.031) among the 504 participants who reported smoking cessation at follow-up, compared to those without smoking cessation. Among participants whose IPLC was diagnosed between baseline and 10-year follow-up (N=156), a stronger association was observed between smoking cessation after initial diagnosis and a reduced SPLC risk (HR=0.16; P=0.0016). **Conclusion:** Lung cancer diagnosis has a significant impact on smoking cessation based on a large population-based study with a long-term follow-up. Quitting smoking after the initial diagnosis of lung cancer reduces the risk of developing a subsequent malignancy in the lungs.

PR01.03

A Novel 27-Gene Signature Associated with Better Outcomes for NSCLC Patients Treated with IO Therapies with PD-L1 Expression >50%.

David Hout[1], **Robert Seitz[1]**, D. Bailey[1], B. Schweitzer[1], Tyler Nielsen[1], G. Vidal[2]
[1]*Oncocyte Corporation, Nashville, United States*

We have previously demonstrated the performance of a novel 27-gene signature that was developed to report an Immunomodulatory (IM) positive or negative score as a predictor of response to immune checkpoint inhibitors (ICIs) when compared to PD-L1 staining. The previous study used a PD-L1 expression cutoff of >1% positive, as had been accepted based on FDA clearance guidelines. However, current guidelines from the National Comprehensive Cancer Network (NCCN) suggest using a cutoff for PD-L1 expression of greater or equal to 50% positive by tumor proportion score (TPS) to determine when and whether to treat with ICIs alone or in combination with standard chemotherapy. This study compares the novel IM score against the current NCCN guideline of >50% positive for PD-L1 expression. In the original study, archival tumor tissue from a cohort of NSCLC patients was tested with the novel 27-gene IM signature, and compared against immunohistochemistry (IHC) PD-L1 testing. Of the 66 patients from the original cohort that had PD-L1 expression data available, the PD-L1 expression levels for 56 of the patients were reported as a numerical percentage, while ten were listed as positive or negative. In order to accurately capture which patients were above the 50% positive threshold for PD-L1 positivity, we restricted our analysis to the 56 patients with numerical TPS values for PD-L1 expression. Of these 56 patients, 27 were considered positive based on PD-L1 expression >50% while 29 were negative. When measured by the prospectively locked down algorithm for the 27-gene IM signature, 30 patients were considered positive, while 26 were negative. We then compared one-year progression free survival (PFS) rates among the positive and negative groups when determined by the 27-gene IM signature and the new >50% positive cutoff for PD-L1 expression. The one-year PFS for the 27 gene predictor was 76% for IM+ and 42% for IM- (cox proportional hazard = 0.33 (95% CI = 0.13, 0.81), $p < 0.02$). For PD-L1 staining, one-year PFS was 62% for > 50% positive staining and 58% for < 50% (cox proportional hazard = 0.82 (95% CI = 0.35, 1.9), $p = 0.65$). When looking at one-year PFS in the 29 patients below the 50% cutoff, the IM score finds an additional 11 responders with only 2 false negatives (84.6% sensitivity and 62.5% specificity). When considering objective response, odds ratios were calculated to compare non-responders (progressive disease or stable disease) to responders (partial response or complete response): The PD-L1 >50% group had an odds ratio of 1.381 (0.475-4.098) ($p=0.553$). The IM Signature group had an odds ratio of 3.75 (1.253-12.025) ($p=0.018$). In this small study, the 27-gene IM signature does a better job predicting response and non-response to immune checkpoint inhibitors than PD-L1 expression when using the >50% positive cutoff from the latest NCCN guidelines. If used reflexively, the novel 27-gene IM signature test could potentially identify additional patients who would benefit from ICI therapy that fall below the >50% positive threshold. Further studies are planned to test this in larger populations.

PR01.04

A Novel Immunomodulatory Signature Improves Prediction of Response to Immunotherapy Compared to PD-L1 IHC in NSCLC Patients.

David Hout[1], **Tyler Nielsen[1]**, B. Schweitzer[1], Robert Seitz[1], G. Vidal[2]
[1]Oncocyte Corporation, Nashville, United States, [2]West Cancer Center and Research Institute, Memphis, United States

Recent National Comprehensive Cancer Network (NCCN) Guidelines show immune checkpoint inhibitors (ICIs) as the standard of care for first- and secondline therapy in patients with advanced non-small cell lung cancer (NSCLC). However, determining who will respond to immunotherapy remains a vital clinical question as more is being learned about the therapeutic toxicities and costs of these drugs. The use of PD-L1 immunohistochemistry (IHC) as a predictive biomarker is the standard for immunotherapeutic selection but its utility is confounded by data demonstrating strong responses among patients with low or undetectable PD-L1 staining. A novel 27-gene signature has been developed which provides an immunomodulatory (IM) score to classify whether a tumor microenvironment is immune active (hot) or quiescent (cold), independent of PD-L1. Previously, we have demonstrated this 27-gene signature has an improved predictive value over both PD-L1 and TMB. To further elucidate where this test outperforms the standard approach, net reclassification improvement (NRI) evaluation was conducted on a cohort of NSCLC patients who had received immunotherapies independent of PD-L1 staining. The NRI method is used to evaluate improvements between models to measure risk predictions. In this retrospective study, archival FFPE tumor tissue from patients treated by immunotherapy either as a single agent or in combination with standard chemotherapy, were classified with the IM score which is obtained using a proprietary algorithm based off of a 27-gene qPCR panel. A 64-patient cohort of advanced stage NSCLC from which PD-L1 testing was performed, but not required for prescription of immunotherapy regimens, was used to calculate NRI in terms of IM score against PD-L1 positivity based on objective response. In cooperation with West Cancer Center, funding for the study was provided by Oncocyte. This study was approved by the West Cancer Clinic Review Board. A total of 71 patients were in the advanced stage NSCLC cohort, all receiving immunotherapy treatment. Of this cohort, 64 patients had PD-L1 IHC staining performed with 46 patients being ≥1% positive (Response = 30, 65%), 27 patients ≥50% (Response = 17, 63%), and 18 patients were negative (Response = 11, 61%). The NRI observed for the IM score against PD-L1 ≥1% was 0.07 (p=0.0044; Net Reclassified 3/46), PD-L1 ≥50% positive was 0.07 (p=0.0557; Net Reclassified 2/27), and the PD-L1 negative group was 0.22 (p=0.0009; Net Reclassified 4/18). When considering response to immunotherapies by all patients given a single agent immunotherapy and applying the NCCN Guideline of PD-L1 ≥50% we observed an NRI of 0.09 (p=0.0002). When looking at the full cohort given combination therapy (n=11) the NRI was 0.18 (p=0.0733) and PDL1 negative given a combination therapy (n=5) the NRI was 0.6 (p=0.0399). These data demonstrate improved outcomes in patients classified with the 27-gene IM signature compared to PD-L1 positive and negative cohorts. Importantly, this study demonstrates there are patients classified as PD-L1 negative who demonstrate durable responses to immunotherapies. As also demonstrated by other studies, this work suggests that an improved predictive biomarker can identify patients who are underserved by current standard predictive biomarkers.

PR01.05

Racial Differences in Eligibility for Low Dose CT Screening and Burden of Metastatic Disease at Diagnosis of Lung Cancer in the United States

Manoj P Rai[1], P. Bedi[2], B. Ansari[3], S. Siddappa Malleshappa[4], P. Neupane[3], C. Huang[3], J. Zhang[3], K. Mehta[3]
[1]Asante Rogue Regional Medical Center, Medford, United States, [2]UPMC East, Pittsburgh, United States, [3]University of Kansas Medical Center, Kansas City, United States, [4]Bay State Medical Center, Springfield, United States

The impact of the implementation of low dose CT screening (LDCT) in high-risk population in 2015, on the proportion of patients with metastatic disease at the time of diagnosis of Lung cancer in different racial subgroups is unknown. The racial difference in the proportion of population eligible for LDCT is also unknown. We conducted a cross-sectional study using SEER data to identify trends of the proportion of patients with metastatic disease at the time of diagnoses across 4 periods from 2007 to 2016. Period 1 (P1) and period 2 (P2) occurred before the publication of the National Lung Cancer Screening Trial (NLST) to establish baseline trends (2007-2009 and 2010- 2011 respectively). Period 3 (P3) and period 4 (P4) were after the publication of NLST (2012-2014) and LDCT implementation (2015-2016) respectively. We also analyzed the National Health and Nutrition Examination Survey (NHANES) to estimate the proportion of population meeting the LDCT criteria from 2015 to 2016. The population of interest was between the age of 55-79 years. The study included 471,300 patients with newly diagnosed Lung cancer with age of 55-79 years (mean age 68 years, 53% male, 83% white, and 11% African Americans [AA]). Among whites, the proportion of patients with metastatic disease at the time of diagnoses was stable before the publication of NLST (0.1% decline from P1 to P2, $p = 0.7$) and remained stable after the publication of NLST until the implementation of LDCT (0.3% decline from P2 to P3, $p = 0.2$). Compared with this baseline trend, implementation of LDCT was significantly associated with a decline in proportion of patients with metastatic disease at the time of diagnoses (3.6% decline from P3 to P4: difference in change, -3.5%, $p < 0.01$). In AA, compared to the baseline trend, implementation of LDCT was associated with a declining trend in the proportion of patients with metastatic disease at the time of diagnoses (2.1% decline from P3 to P4: difference in change, -1.7%, $p = 0.06$). However, the magnitude of decline was smaller and not statistically significant in AA compared to whites. From 2015 to 2016, the estimated proportion of the population with age of 55-79 years eligible for LDCT was significantly lower in AA compared to whites (2.1% vs 7.1%, $p < 0.01$). After the implementation of LDCT in 2015, the proportion of Lung cancer patients with metastatic disease at the time of diagnoses has declined in the US among whites but not yet in AA with age of 55-79 years. Further research is needed to identify if the observed racial difference is due to the underutilization of LDCT in AA.

PR01.06

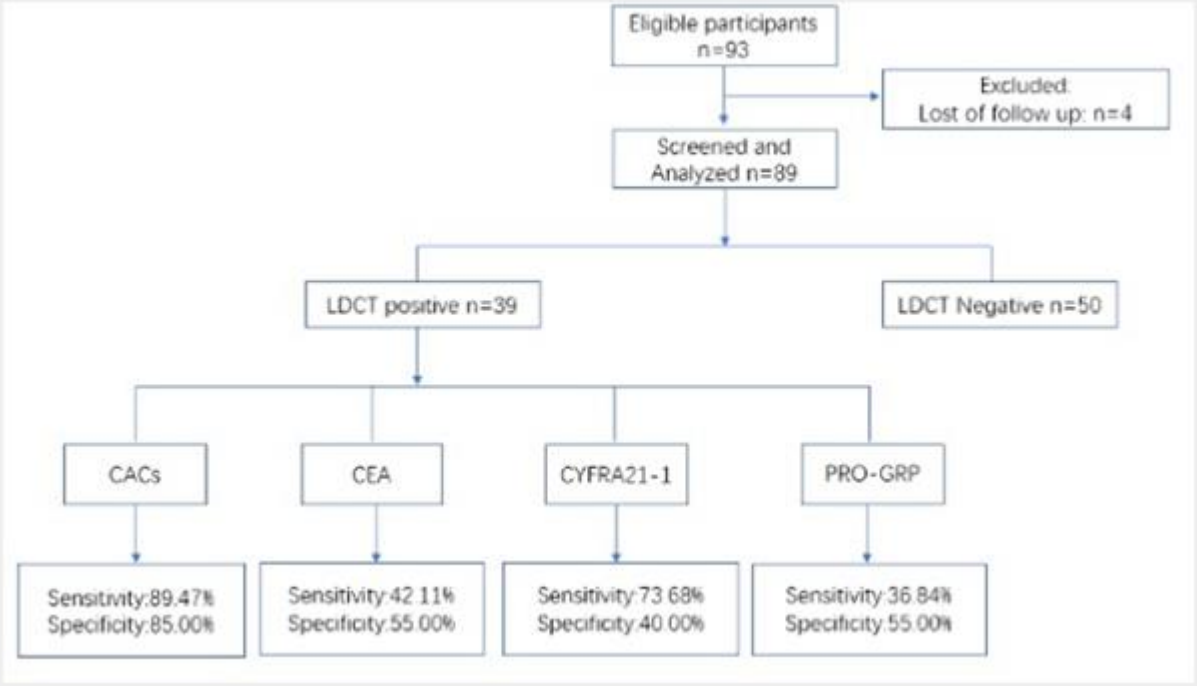
Integrating Circulating Genetically Abnormal Cells to Early Lung Cancer Screening in Chinese Bus Drivers

Baishen Chen[1], Yuelan Huang[2], Xiaozheng Yang[1], Xiaozheng Yang[3], Chuoji Huang[4], Xin Ye[5], Dongjiang Tang[5], Juncheng Zhang[5], Jinyan Zhang[6], Chunxue Bai[7]

[1]Sun Yat-Sen Memorial Hospital, Guangzhou, China, [2]The Fifth People's Hospital of Zhuhai, Zhuhai, China, [3]Zhuhai Sanmed biotech, Zhuhai, China, [4]Joint research center of liquid biopsy in Guangdong, Hong Kong and Macao, Zhuhai, China, [5]Zhuhai Sanmed Biotech, Zhuhai, China, [6]The Fourth Hospital of Hebei Medical University, Shijiazhuang, China, [7]Zhongshan Hospital, Shanghai, China

The current Chinese guidelines have identified people age≥40, with a history of environmental or occupational exposure as the high-risk population and recommended them to screen for lung cancer by LDCT annually. Bus drivers in urban Chinese cities might have a high risk of exposure to car exhaust hazardous and other harmful substances, but the lung cancer risk of this population is understudied. This study is aimed to evaluate the lung cancer risk in urban Chinese bus drivers, using LDCT combined with the circulating genetically abnormal cells (CACs) and traditional tumor markers. A total of 93 participants were recruited in October 2018. The inclusion criteria are 1) men and women age≥40; 2) full-time bus drivers with more than 5 years of working experience. All participants went through a baseline and follow-up LDCT screening in October 2018 and October 2019. Blood samples were obtained for a circulating genetically abnormal cells (CACs) test, as well as the tumor biomarker tests on the carcinoembryonic antigen (CEA), cytokeratin fragment 19(CYFRA21), and pro-gastrin-releasing peptide (ProGRP) on both screening periods. All participants who detected a pulmonary nodule by LDCT on the baseline or follow up screening endured a biopsy to classify benign and malignant nodules. 89 people have remained in the study after the follow-up section. Out of 39 participants who detected with pulmonary nodule by LDCT on the baseline or follow up screening, 19 were confirmed with stage IA lung cancer by histological test. The lung cancer rate is 21.34% (19/89)in this population. The CACs have the highest prediction value among the participants with a pulmonary nodule, with 89.47% sensitivity rate and 85% specificity rate. The sensitivity and specificity of CEA are 42.11%, 55%, CYFRA21 are 73.68%, 40.00%, and ProGRP are 36.84%, 55.00%. Three participants who had a positive CACs outcome but with a negative LDCT result on the baseline screening, pulmonary nodules were detected in the follow-up observation, and confirmed as cancerous by the histopathology test. The urban bus drivers have a much higher lung cancer incidence than the age adjusted Lung cancer incidence rate (36.71 per 100, 000) in China, which calls attention to early lung cancer screening programs in this population. On top, CACs might be more sensitive to malignant pulmonary nodules before its catchers by imaging tests, can be used as an accessible tool complementary with LDCT to increase the efficiency of early lung cancer screening in the highrisk population.

1.png



1.png

Eligible participants n=93
Excluded: Lost of follow up: n=4
Screened and Analyzed n=89
LDCT positive n=39
LDCT Negative n=50
CACs
CEA
CYFRA21-1
PRO-GRP
Sensitivity:89.47% Specificity:85.00%
Sensitivity:42.11% Specificity:55.00%
Sensitivity:73.68% Specificity:40.00%
Sensitivity:36.84% Specificity:55.00%

PR01.07

Predicting Changes in Lung Cancer Risk in the At-Risk Screen Ineligible Population

Andrew CL Lam[1], R Aggarwal[1], J. Huang[1], K. Hueniken[1], M. Tsao[1, 2], F. Shepherd[1, 2], W. Xu[1], J. Kavanagh[3], G. Liu[1, 2]
[1]Princess Margaret Cancer Centre, Toronto, Canada, [2]University of Toronto, Toronto, Canada, [3]University Health Network, Toronto, Canada

Emerging data suggest that lung cancer screening programs may benefit from risk calculators to select the highest risk participants for screening. The Prostate Lung Colorectal and Ovarian Six-year Lung Cancer Risk Model (PLCOM2012) is a high-performing risk calculator that has been shown prospectively to have higher sensitivity/specificity than the National Lung Screening Trial (NLST) eligibility criteria. However, programs using risk calculators for participant selection now must contend with whether/when to re-evaluate screen-ineligible participants; over time, changes in participant smoking history, lung cancer risk factors, and increasing age may change the status from ineligible to eligible. This study identified characteristics of a subpopulation among screen-ineligible participants at our centre who eventually met eligibility cutoff and developed a model that can predict changes in lung cancer risk over time. In a long-term research low-dose computed tomography lung cancer screening program, which had a very low initial threshold for eligibility (≥10 pack-years and ≥50 years old), PLCOM2012 risk scores were calculated for participants at two time-points: T0=baseline and T1=follow-up. The duration between T0-T1 varied among participants. Eligibility cutoffs of 3.25%, 2%, 1.5%, and 1% probability of developing lung cancer over six-years were evaluated. To focus on screen-ineligible participants, only participants with T0 risk scores less than the eligibility cutoff were included in each analysis. Rates of risk score change (%/year) were calculated at each threshold. Cox proportional hazards models were used to identify risk factors at T0 that predicted participant reaching cutoff by T1. Three predictive models were created and compared against the observed cohort: smoking-cessation model (all participants ceased smoking immediately after T0), expected model (participants continued with current habits), and Chronic Obstructive Pulmonary Disease (COPD) model (all participants develop COPD after T=0). Among screen-ineligible participants at T0 and using the 3.25% cutoff, 168/956 met cutoff at T1; using 2.0% cutoff, 130/755; using 1.5% cutoff, 149/652; and using 1.0% cutoff, 130/484. Twenty-four participants of the 956 (2.5%) developed lung cancer during a seven-year period. At the 3.25% cutoff, median increase in lung cancer risk for those who met cutoff at T1 was 0.35%/year (IQR= 0.19-0.59; p=0.002) compared to 0.02%/year (IQR= -0.49–0.096; p=0.55) in those not meeting cutoff at T1. Similar patterns were observed for the other three cutoffs. When comparing the three predictive models, the expected model most closely resembled the observed cohort. In the observed cohort, >30-year smoking duration and lower education at T0 were significantly associated with reaching cutoff at T1. In the expected model, having a >30-year smoking duration and a self-reported diagnosis of COPD at T0 were significantly associated with reaching cutoff at T1. Among lung cancer screen-ineligible participants, an identifiable subpopulation exists that exhibit a high rate of increase in their lung risk and eventually meet eligibility cutoffs for screening. Greater smoking duration, lower education, and development of COPD are each associated with meeting eligibility cutoff over time. Lung cancer screening programs should consider using the expected predictive model to prioritize re-evaluation of at-risk screen-ineligible participants for eventual lung cancer screening.

PR01.08

Simultaneous Multi-Cancer Detection and Tissue of Origin Prediction Via Targeted Bisulfite Sequencing of Plasma Cell-Free DNA

Kathryn Kurtzman[1], Geoffrey Oxnard[2], Eric Klein[3], Michael Seiden[4], Earl Hubbell[1], Oliver Venn[1], Arash Jamshidi[1], Nan Zhang[1], John Beausang[1], Samuel Gross[1], Eric Fung[1], Jessica Yecies[1], Rita Shaknovich[1], Alexander Fields[1], Mikkael Sekeres[3], Donald Richards[5], Peter Yu[6], Alexander Aravanis[7], Anne-Renee Hartman[1], Minetta Liu[8]
[1]GRAIL, Inc. , Menlo Park , United States, [2]Dana Farber Cancer Institute, Boston , United States, [3]Cleveland Clinic , Cleveland, United States, [4]US Oncology Research, The Woodlands, United States, [5]Texas Oncology, Tyler, United States, [6]Hartford HealthCare Cancer Institute , Hartford, United States, [7]Illumina, Inc., San Diego , United States, [8]Mayo Clinic, Rochester , United States

Background: A minimally invasive cell-free DNA (cfDNA) blood test detecting multiple cancers at earlier stages could decrease cancer mortality. In earlier discovery work, whole-genome bisulfite sequencing outperformed whole-genome and targeted sequencing approaches for multi-cancer detection across stages at high specificity. Here, multi-cancer detection and tissue-of-origin (TOO) prediction using bisulfite sequencing of plasma cfDNA to identify methylomic signatures was evaluated in preparation for clinical validation, utility, and implementation studies. **Methods:** In all, 6,689 participants (2,482 cancer [>50 cancers, all stages]; 4,207 non-cancer) were included in this prespecified substudy from the Circulating Cell-free Genome Atlas (CCGA) study (NCT02889978) and the STRIVE study (NCT03085888) - prospective, multi-center, observational, case-control studies with longitudinal follow-up. Plasma cfDNA was subjected to a targeted methylation sequencing assay using high-efficiency methylation chemistry to enrich for methylation targets, and a machine-learning classifier determined cancer status and predicted TOO. Observed methylation fragments characteristic of cancer and TOO (cancer “signals”) were combined across targeted regions and assigned a relative probability of cancer and of a specific TOO. Test performance was also assessed in a subgroup of participants with clinical suspicion of cancer but without pathologic diagnosis or treatment at the time of enrollment. **Results:** Performance is reported at 99.3% specificity (95% confidence interval [CI], 98.3-99.8%) (ie, a combined false positive rate across all cancers of <1%—a level required for population-level screening). Across all cancers, stage I-III sensitivity was 43.9% (95% CI, 39.4-48.5%). Combined cancer detection sensitivity (95% CI) was 18% (13-25%) in stage I (n=185), 43% (35-51%) in stage II (n=166), 81% (73-87%) in stage III (n=134), and 93% (87-96%) in stage IV (n=148). TOO was predicted for 96% of all cancers detected; of these, TOO was correct in 93% of cases. Among participants enrolled with suspicion of cancer and subsequently confirmed to have cancer (n=75), cancer detection across all stages was 46.7% (35/75; 95% CI, 35.1-58.6%) and TOO prediction accuracy was 97.1% (34/35; 95% CI, 85.1-99.9%). None of the non-cancer participants in the subgroup (n=15) had a cancer signal (ie, specificity was 100%). **Conclusion**: Detection of multiple cancers across stages using methylation signatures in plasma cfDNA was achieved with a single, fixed, low, false positive rate, and simultaneously provided accurate TOO prediction. This targeted methylation assay is undergoing validation in preparation for prospective clinical investigation as a cancer detection diagnostic.

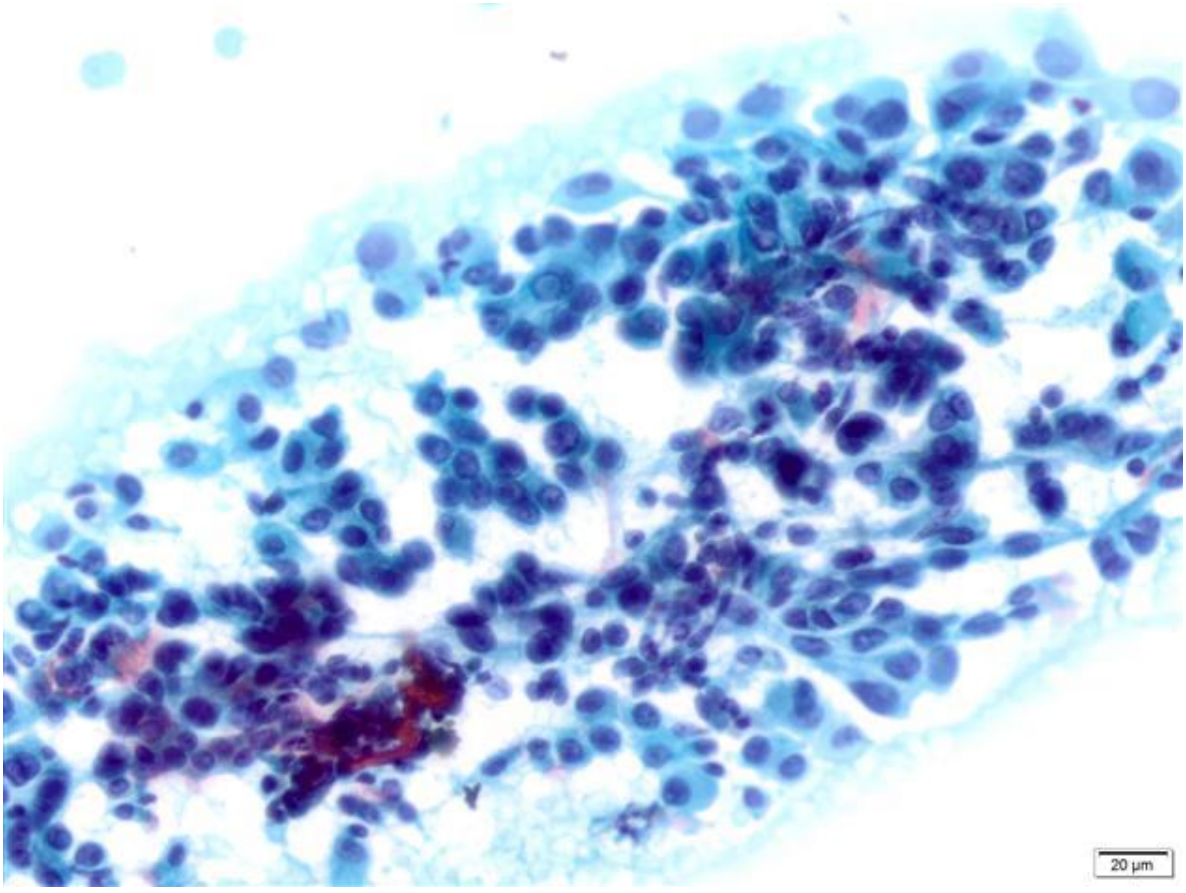
Pulmonary Posters

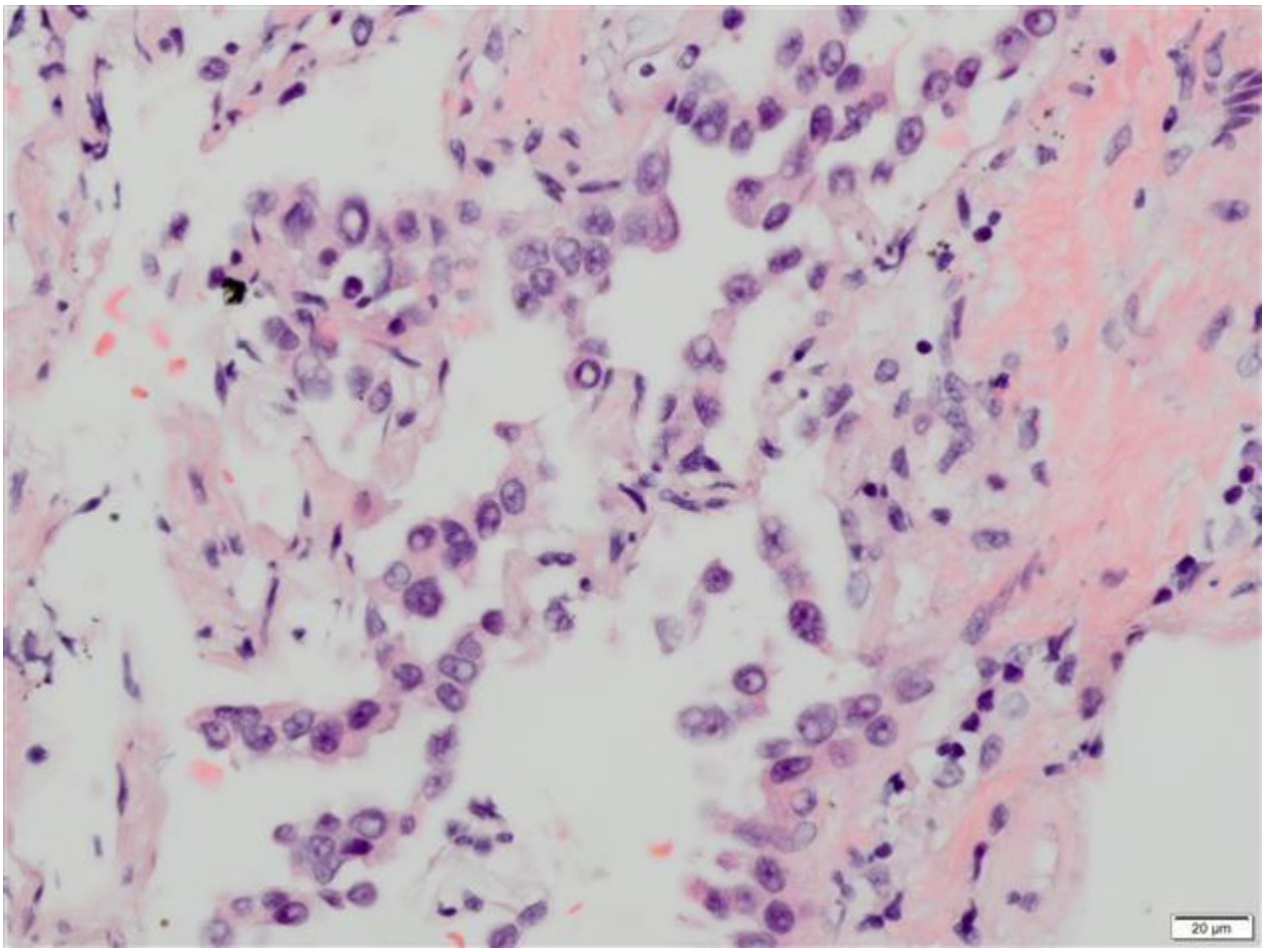
PUL01.01
Ground Glass Opacity: What's in a Name?

Eric L. Flenaugh[1,3], James Roberts[2], Geoffrey Smith[2], Frank Schneider[2], Gabriela Oprea-Ilies[2,3]
[1]Morehouse School of Medicine, Atlanta, US, [2]Emory Unversity Medical School, Atlanta, US, [3]Grady Memorial Hospital, Atlanta, US

Background: Ground glass opacity (GGO), consists of hazy opacity not obscuring the underlying bronchial structures or pulmonary vessels. the underlying pathology varies from benign conditions (pulmonary edema, infections - including COVID-19, cytomegalovirus, Pneumocystis jirovecii, etc), noninfectious interstitial lung diseases and adenocarcinomas. **Methods:** Following IRB approval our electronic files from January-July 2020 were searched for sampled GGO in comparison with other types of lung lesions found in our patients. Tissue was collected using tip-tracked guided procedures. We compared association of GGO with adenocarcinoma of the lung with lepidic spread (ADCC-L) (Image 1, 2). Results: 122 pathology cases (male=64) were identified: 40 benign and 82 malignant diagnoses. There were 39 cases of ADCC-L (median [interquartile range] age: 63 [60-71]) and 83 cases with various other lesions (age: 62 [57-67]). GGO were reported in 17 ADCC-L cases and 13 of the other cases. The Fisher exact test statistic demonstrated a statistically significant association between ADCC-L and GGO in our overall (n=122, p=0.0014*) and female (n=58, p=0.0151*) cohorts. **Conclusion:**

1. Tip-tracked guided procedures obtain diagnostic tissue from these challenging to sample lesions.
2. GGO statistically significant association with AADCC-L in our patient population indicates necessary appropriate follow-up for appropriate patient management.




20 µm

PUL01.02

AcceleRET Lung: A Phase 3 Study of First-Line Pralsetinib in Patients with RET-Fusion+ Advanced/Metastatic NSCLC

Benjamin Besse[1], Enriqueta Felip[2], Edward S. Kim[3], Corinne Clifford[4], Melinda Louie-Gao[4], Adam Yagui-Beltran[4], Sanjay Popat[5]

[1]Institut Gustave Roussy, Villejuif, France, [2]Vall d'Hebron University Hospital, Barcelona, Spain, [3]Levine Cancer Institute, Atrium Health, Charlotte, United States, [4]Blueprint Medicines Corporation, Cambridge, United States, [5]The Royal Marsden Hospital, London, United Kingdom

Background: RET gene fusions have been identified as oncogenic drivers in multiple tumor types, including 1–2% of non-small cell lung cancer (NSCLC). The investigational oral RET inhibitor, pralsetinib, potently and selectively targets oncogenic RET alterations, including those that confer resistance to multi-kinase inhibitors. In the registration-enabling phase 1/2 study (ARROW; NCT03037385), patients with RET-fusion+ NSCLC treated with pralsetinib 400 mg once daily (QD) after platinum-based chemotherapy (n=80) achieved an overall response rate (ORR) of 61% (95% CI 50, 72; two responses pending confirmation) per independent central review. In addition, an ORR of 73% (all centrally confirmed responses) was attained in the systemic treatment naïve cohort (n=26). Most treatment-related adverse events were grade 1–2 across the entire safety population treated with pralsetinib 400 mg QD (N=354). AcceleRET Lung, an international, open-label, randomized, phase 3 study, will evaluate the efficacy and safety of pralsetinib versus standard of care (SOC) in first-line treatment of advanced/metastatic RET fusion+ NSCLC (NCT04222972). This abstract was previously submitted to and presented at the American Society of Clinical Oncology 2020 annual meeting (May 29 to June 2, 2020). **Methods:** Approximately 250 patients with advanced/metastatic RET-fusion+ NSCLC will be randomized 1:1 to pralsetinib 400 mg QD or SOC (non-squamous histology: platinum/pemetrexed ± pembrolizumab followed by maintenance pemetrexed ± pembrolizumab; squamous histology: platinum/gemcitabine). Stratification factors include intended use of pembrolizumab, history of brain metastases, and Eastern Cooperative Oncology Group Performance Status 0 vs 1. Key eligibility criteria include no prior systemic treatment for advanced/metastatic NSCLC; RET-fusion+ tumor by local or central assessment, no additional actionable oncogenic drivers, no prior treatment with a selective RET inhibitor, and measurable disease per RECIST v1.1. Cross-over to receive pralsetinib upon disease progression will be permitted for patients randomized to SOC. The primary endpoint is progression-free survival (blinded independent central review; RECIST v1.1). Secondary endpoints include ORR, overall survival, duration of response, disease control rate, clinical benefit rate, time to intracranial progression, intracranial ORR, safety/tolerability, and quality of life. Recruitment has begun with sites (active or planned) in North America, Europe, Asia, and Australia.

PUL01.03

Effect of Tumor Size Change and Duration of Response on OS With First-Line Pembrolizumab Plus Pemetrexed-platinum For Metastatic Nonsquamous Non–Small-Cell Lung Cancer

Steven F. Powell[1], Silvia Novello[2], Marina C. Garassino[3], Delvys Rodríguez-Abreu[4], Meihua Wang[5], Jing Yang[5], Fabricio Souza[5], Jhanelle E. Gray[6]

[1]Sanford Health, Sioux Falls, United States, [2]University of Turin, Turin, Italy, [3]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, [4]Complejo Hospitalario Universitario Insular Materno-Infantil de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain, [5]Merck & Co., Inc., Kenilworth, United States, [6]Moffitt Cancer Center, Tampa, United States

Background: RECIST is the primary tool for assessing tumor response in patients with solid tumors. Immunotherapy agents have shown unique response patterns. Assessment of the contribution of such patterns to OS is of interest. This analysis evaluates early tumor size change (TSC) cutoffs for their association with OS, assesses whether deeper response had greater association with OS than the 30% RECIST cutoff, and quantifies the contribution of ORR and duration of response (DOR) to OS benefit among patients with metastatic nonsquamous non–small-cell lung cancer (NSCLC) receiving pembrolizumab + pemetrexed-platinum in KEYNOTE-189 (NCT02578680). **Methods:** For patients with metastatic nonsquamous NSCLC without sensitizing EGFR/ALK alteration who received pembrolizumab + pemetrexed-platinum in the randomized, double-blind, phase 3 KEYNOTE-189 study (data cutoff: May 20, 2019), we evaluated associations between OS and early TSC (percentage change from baseline in sum of target lesion diameters at study week 12) using recursive partition analysis and C-index, OS and deeper response (CR/PR with ≥30% target lesion reduction cutoffs) using Cox proportional hazard models, and OS and DOR using time-varying covariate analysis with proportion of treatment effect (PTE) analysis to quantify relative contribution. **Results:** −30% TSC at week 12 had greater association with OS than other cutoffs (C-index value [95% CI]: −10%, 0.55 [0.52–0.58]; −20%, 0.58 [0.55–0.62]; −30%, 0.60 [0.56–0.63]; −40%, 0.59 [0.56–0.62]) and was similar to ORR at week 12 (C-index value, 0.60; 95% CI, 0.57–0.63). Deeper response did not have greater association with OS than the 30% RECIST cutoff (OS HR [95% CI] for patients with/without response at TSC cutoff: −30%, 0.30 [0.23–0.38]; −50%, 0.29 [0.22–0.39]; −70%, 0.25 [0.16–0.39]). DOR coupled with response rate had higher PTE (0.57) than objective response (0.36) and −10% (0.08), −20% (0.09), or −30% (0.20) TSC. **Conclusions:** Among patients with metastatic nonsquamous NSCLC treated with first-line pembrolizumab + pemetrexed-platinum, early TSC of 30% was the optimal cutoff associated with OS, consistent with RECIST ORR. Deeper response did not have greater association with OS than the 30% RECIST cutoff. ORR by RECIST coupled with DOR explained ~60% of OS benefit from pembrolizumab + pemetrexed-platinum over pemetrexed-platinum alone.

Radiation Oncology Posters

RO01.01
Prospective Evaluation of Ipilimumab and Nivolumab in Patients with Non-Small Cell Lung Cancer Brain Metastasis

Aditya Juloori[1], Christine Bestvina, Sean Pitroda, Kelli Pointer, Michael Jelinek, Phil Hoffman, Everett Vokes, Jyoti Patel, Steve Chmura
[1]*The University of Chicago, Chicago, United States*

Background: Nivolumab combined with Ipilimumab (Ipi/Nivo) has been shown to improve overall survival compared to chemotherapy in first-line treatment of stage IV non-small cell lung cancer (NSCLC). Brain metastasis patients have often been excluded from many clinical trials. We examined outcomes of brain metastasis patients included on a phase 1 trial of combined immune checkpoint blockade and multi-site stereotactic body radiation therapy (SBRT) in newly diagnosed stage IV NSCLC. **Methods:** All patients underwent brain MRI as part of trial screening. Treatment naïve patients with advanced NSCLC were eligible for enrollment. Patients received SBRT to 1 to 4 extracranial metastases and were randomized to receive 1st cycle of Ipi/Nivo either during or after multi-site SBRT. Ipi/Nivo continued until progression, development of toxicity, or up to two years. Brain metastases > 3 mm in size were treated with radiosurgery or WBRT prior to starting systemic therapy and multi-site SBRT. **Results:** 35 patients were treated with multi-site SBRT and received at least one cycle of Ipi/Nivo. 9 patients had brain metastasis at diagnosis. 8 patients received SRS while one received WBRT. With a median follow-up time of 15 months for all patients, median OS for the brain metastasis cohort has not been reached. All 9 brain metastasis patients remain alive; 7 of these patients have remained alive for at least 15 months and continue on Ipi/Nivo. Two of 18 treated lesions (11%) developed radiation necrosis. Of 26 patients enrolled without brain metastases, 5 developed intracranial disease. Four of these 5 patients underwent salvage WBRT and remain alive, free of intracranial progression. The 1-year intracranial progression-free survival (PFS) was 81.7% and was 87.0% in those enrolled without brain metastasis. In the 9 patients with brain metastasis, only 3 went on to progress intracranially, notably within a short time frame (within 3 months). Median PFS did not differ between BM (13.1 months) and non-BM(5.86 months) cohorts (p=NS). Two patients in the brain metastasis cohort had lesions at diagnosis that were not treated with SRS which had complete response with immunotherapy alone. **Conclusions:** Ipi/nivo/SBRT is a successful treatment strategy in patients with NSCLC brain metastasis. Outcomes do not appear to be inferior for these patients compared to non-brain metastasis stage IV patients and they should be included in trials in the immunotherapy era. Intracranial control appears promising. Further intracranial efficacy of Ipi/Nivo and outcomes of brain metastasis patients will be explored in a phase II expansion.

Targeted Therapy - New Targets, New Treatments and New Diagnostics Posters

TT01.01

Real-World Outcomes in Patients with EGFR/ALK-Positive NSCLC Treated with Chemotherapy Following 1 or 2 Lines of TKI Therapy

Parneet Cheema[1], T. Ton[2], P. Lambert[2], D. Merritt[3], S. Morris[3], G. Shankar[2], A.K. Ganti[4]
[1]William Osler Health System, University of Toronto, Toronto, Canada, [2]Genetech, Inc., South San Francisco, United States, [3]F. Hoffmann-La Roche, Ltd., Basel, Switzerland, [4]VA Nebraska Western Iowa Health Care System and University of Nebraska Medical Center, Omaha, United States

Chemotherapy has been the primary option for patients with epidermal growth factor receptor–positive (EGFR+) or anaplastic lymphoma kinase–positive (ALK+) tumours whose cancer has progressed after several lines of tyrosine kinase inhibitors (TKIs). For these patients, atezolizumab in combination with carboplatin, paclitaxel, and bevacizumab had superior efficacy vs chemotherapy plus bevacizumab. However, in the real world, many patients with EGFR+/ALK+ tumours are not treated with bevacizumab-containing chemotherapy after TKIs. Understanding practice patterns and outcomes for patients subsequently treated with chemotherapy without bevacizumab can help identify unmet needs. Patients with EGFR+/ALK+ tumours diagnosed with advanced or metastatic NSCLC on or after 1 January 2011 and treated with platinum-paclitaxel or platinum-pemetrexed after 1 or 2 prior lines of TKIs were selected from the Flatiron Health electronic health records (EHR)–derived de-identified database. Those with ECOG ≥ 2 at the start of chemotherapy were excluded. Real-world progression was abstracted from clinic notes, radiology scans, and pathologic reports. Endpoints were real-world progression-free survival (rwPFS) and overall survival (OS). Descriptive statistics and time-to-event medians are reported. Patient characteristics are in the table. The median rwPFS from chemotherapy start after 1 line, 2 lines, and combined 1-2 lines of TKIs was 5.7 (95% CI: 4.2, 7.9), 4.1 (95% CI: 3.2, 5.3) and 4.9 (95% CI: 4.1, 6.4) months, respectively. Median OS in these three cohorts was 16.7 (95% CI: 13.2, 19.6), 9.1 (95% CI: 6.0, 12.5) and 14.2 (95% CI: 11.2, 18.0) months, respectively. 12- and 24-month survival was 63% and 35% in patients with 1 prior TKI; 31% and 12% for those with 2 prior TKIs; and 55% and 29% for the combined cohort. Over one-third of all patients received a TKI after chemotherapy, primarily osimertinib. In routine clinical practice, EGFR+/ALK+ patients receiving chemotherapy had prior TKIs reflecting US clinical guidelines. mOS in the combined population was similar to that observed in the PARAMOUNT trial of cisplatin and pemetrexed chemotherapy in an unselected patient population. mOS across cohorts was numerically lower than observed with chemotherapy and bevacizumab in EGFR+/ALK+ patients in the IMpower150 trial; Comparisons with randomized data remains a challenge given differences in patient populations and the likely impact on OS of high rate of osimertinib treatment after chemotherapy in this analysis. Outcomes remain poor for patients progressing on TKIs in this realworld cohort, highlighting the need for novel treatment options, such as PD-L1 and VEGFi combination regimens.

Table. Characteristics of Patients With EGFR/ALK-Positive Tumours Who Were Treated With Platinum-Paclitaxel or Platinum-Pemetrexed Following 1 or 2 Lines of TKIs[a] in Routine Clinical Practice

		1 Prior Line of TKI	2 Prior Lines of TKIs	1 or 2 Prior Lines of TKIs
Patients, n		114	46	160
Age at start of chemotherapy, median (IQR), years		66.5 (57.3, 73.0)	67.0 (57.3, 77.0)	66 (56.7, 73.3)
Aged ≥ 65 years at start of chemotherapy, n (%)		64 (56.2)	25 (54.3)	88 (55.0)
Female, n (%)		75 (65.8)	32 (69.6)	106 (66.2)
Caucasian, n (%)		62 (54.4)	33 (71.7)	96 (60.0)
Smoking history, n (%)		51 (44.7)	23 (50.0)	74 (46.2)
Stage at initial diagnosis, n (%)				
	IIII	10 (8.8)	3 (6.5)	13 (8.2)
	IIIV	101 (88.6)	42 (91.3)	143 (89.3)
	Unknown	3 (2.6)	1 (2.2)	4 (2.5)
ECOG PS, n (%)[b]				
	0	20 (17.5)	7 (15.2)	31 (19.4)
	1	36 (31.6)	21 (45.7)	59 (36.9)
	Unknown/Missing	58 (50.9)	18 (39.1)	70 (43.8)
Practice type, n (%)				
	Academic	15 (13.2)	11 (23.9)	25 (15.6)
	Community	99 (86.8)	35 (76.1)	135 (84.4)
Alterations, n (%)[c]				
	EGFR mutation only	102 (89.5)	40 (87.0)	142 (88.8)
	ALK rearrangement only	11 (9.6)	6 (13.0)	17 (10.6)
	ALK and EGFR double positive	1 (0.9)	0 (0.0)	1 (0.6)
2L/3L chemotherapy, n (%)				
	Platinum paclitaxel	14 (12.3)	4 (8.7)	18 (11.2)
	Platinum pemetrexed	100 (87.7)	42 (91.3)	142 (88.8)
Prior 1L TKI, n (%)				
	Among patients with EGFR-positive tumours[d]	103	40	143
	Erlotinib	87 (84.5)	32 (80.0)	129 (90.2)
	Afatinib	7 (6.8)	5 (12.5)	12 (8.4)
	Osimertinib	7 (6.8)	1 (2.5)	8 (5.6)
	Crizotinib	1 (1.0)	-	1 (0.7)
	Gefitinib	1 (1.0)	2 (5.0)	3 (2.1)
	Among patients with EGFR-positive tumours[d]	12	6	18
	Crizotinib	11 (91.7)	6 (100.0)	17 (94.4)
	Alectinib	1 (8.3)	-	1 (5.6)
	Treatment duration of 1L TKI, median (IQR), months	6.84 (3.35, 9.86)	8.24 (6.12, 12.43)	7.30 (4.34, 11.08)
Prior 2L TKI, n (%)				

	Among patients with EGFR-positive tumours[d]		40	40
	Osimertinib	-	21 (52.5)	21 (52.5)
	Afatinib	-	16 (40.0)	16 (40.0)
	Erlotinib	-	2 (5.0)	2 (5.0)
	Gefitinib	-	1 (2.5)	1 (2.5)
	Among patients with ALK-positive tumours[d]	-	6	6
	Ceritinib	-	3 (50.0)	3 (50.0)
	Alectinib	-	2 (33.3)	2 (33.3)
	Lorlatinib	-	1 (16.7)	1 (16.7)
	Treatment duration of 2L TKI, median (IQR), months	-	6.25 (2.95, 9.07)	6.25 (2.95, 9.07)
Any subsequent TKIs after chemotherapy, n (%)		52 (45.6)	7 (15.2)	59 (36.9)
Osimertinib in any line after chemotherapy, n (%)		28 (24.6)	6 (13.0)	34 (21.2)

1L, first line; 2L, second line; ECOG, Eastern Cooperative Oncology Group; FDA, US Food and Drug Administration; IQR, interquartile range; PS, performance status.

[a] alectinib, afatinib, crizotinib, ceritinib, erlotinib, gefitinib, osimertinib, brigatinib, lorlatinib.

[b] ECOG PS value closest to within −60 to +7 days of treatment initiation.

[c] Alterations with known or functional status at any time before index line of chemotherapy. EGFR alterations include Exon19 deletion, Exon20 insertion, L858R point mutation on Exon21, T790M, other mutation type, and unknown mutation type. ALK alterations include rearrangements.

[d] 1 patient had both an EGFR mutation and an ALK alteration.

TT01.02

Emergence of NOTCH2-NTRK1 After Osimertinib in a Patient with Lung Adenocarcinoma with Neuroendocrine Differentiation

Gengpeng Lin[1], Hui Li[2], Jia Shi[1]

[1]Department of Pulmonary and Critical Care Medicine, The First Affiliated Hospital of Sun Yet-sen University, Guangzhou, China, [2]Department of Pathology, The First Affiliated Hospital of Sun Yet-sen University, Guangzhou, China

Osimertinib is now the recommended treatment for EGFR T790M-positive lung cancer after prior EGFR tyrosine kinase inhibitor (TKI) treatment. But acquired resistance to osimertinib is inevitable and the mechanism is not well elucidated. Neurotrophic receptor tyrosine kinase gene (NTRK) fusions are oncogenic drivers in many malignant tumors. NTRK gene fusions frequency in lung cancer is less than 5%, but a response rate over 75% has been reported in patients with NTRK fusions. Here we report a NOTCH2-NTRK1-rearranged fusion in lung adenocarcinoma with neuroendocrine differentiation after osimertinib treatment. Section not applicable. CASE REPORT A 68-year-old woman was admitted to our hospital for massive right sided pleural effusion in July 2017. Positron emission tomography– computed tomography examination after drainage revealed pulmonary mass in the right upper lung and multiple metastatic lesions in the lungs, the right pleura and the bones. Ultrasonography-guided percutaneous lung biopsy revealed a pathological diagnosis of lung adenocarcinoma with neuroendocrine differentiation. Subsequent targeted next-generation sequencing (NGS) showed EGFR p.(L858R) c.2573T>G. The patient was treated with erlotinib 150mg daily as first-line treatment since 10 Aug, 2017 and achieved stable disease (SD) for 4 months. Detection of EGFR T79M was positive in plasma and the patient began osimertinib 80mg daily since the lesions in the lung slowly increased. However, after 6 months of treatment, slowly enlarged lung lesions and increased bone lesions revealed disease progression again. The patient received chemotherapy treatment consisting of pemetrexed and carboplatin for 4 cycles. Targeted sequencing of plasma-derived circulating tumor DNA revealed the emergence of NOTCH2-NTRK1 with pre-existing EGFR L858R. Since NTRK inhibitors were not available in China at that period, the patient continued pemetrexed treatment. The treatment was discontinued due to severe myelosuppression. Her functional status deteriorated, with her ECOG PS evaluated as 2. Re-biopsy of pleural lesions and subsequent NGS confirmed the emergence of NOTCH2-NTRK1 with EGFR L858R. Larotrectinib was obtained from abroad and administered to the patient at 100 mg twice daily from Feb 16, 2019 in combination with osimertinib. The patient had significantly improved clinical symptoms with her PS evaluated as 1, despite the absence of measurable change in the primary lung lesions. However, CT scan after 3 months showed brain and liver progression, suggesting the presence of other major signaling pathways besides EGFR and NTRK that are driving the oncogenic progression. Interestingly, sequencing at PD revealed the significant decrease in NOTCH2-NTRK1 fusion, suggesting the molecular efficacy of larotrectinib. The patient received 1 cycle of paclitaxel without benefit and shortly succumbed to the complications of metastatic disease with an overall survival of 21.5 months. In conclusion, our case suggested NOTCH2-NTRK1 could be another possible target of osimertinib resistance. Further research is needed to elucidate the mechanism.

TT01.03

Drug-Drug Interaction of Oral EGFR Inhibitor TAK-788 With Itraconazole and Rifampin in Healthy Volunteers

Steven Zhang[1], S. Jin[1], C. Griffin[1], Z. Feng[1], J. Lin[1], K. Venkatakrishnan[1], N. Gupta[1]
[1]*Millennium Pharmaceuticals, Inc., Cambridge, MA, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, United States*

TAK-788 is an investigational oral small molecule tyrosine kinase inhibitor targeting EGFR. The clinical development program for TAK-788 to treat NSCLC patients with EGFR exon 20 insertions is ongoing. We report the results of a phase 1, open-label, 2-period, fixed-sequence 2-part study (NCT03928327) to characterize the effect of a strong cytochrome P450 (CYP) 3A inhibitor, itraconazole (Part 1) and a strong CYP3A inducer, rifampin (Part 2) on the pharmacokinetics (PK) of TAK-788 and its 2 active metabolites, AP32960 and AP32914, in healthy adult volunteers. In Part 1, on Day 1 of Period 1, volunteers received a single 160 mg oral dose of TAK-788 and subsequently PK samples were collected up to 168 hours postdose. In Period 2, volunteers received 200 mg oral itraconazole qd alone from Days 1 to 4. On Day 5, volunteers received 200 mg itraconazole together with 20 mg oral TAK-788. On Days 6–14, volunteers received 200 mg oral itraconazole qd alone. PK samples were collected on Days 5–15. In Part 2, on Day 1 of Period 1, volunteers received a single 160 mg oral dose of TAK-788 and PK samples were collected up to 168 hours postdose. In Period 2, volunteers received 600 mg oral rifampin qd alone from Days 1 to 6. On Day 7, volunteers received 600 mg rifampin together with 160 mg oral TAK-788. On Days 8–13, volunteers received 600 mg oral rifampin qd alone. PK samples were collected on Days 7–14. In Part 1, daily itraconazole oral administration resulted in an approximately 283% increase in TAK-788 maximum observed concentration, Cmax (geometric least squares mean [LSM] ratio [90% CIs] of 3.83 [3.25, 4.50]) and a 743% increase in TAK-788 area under the concentration-time curve, from time 0 to infinity, AUC∞ (geometric LSM ratio of 8.43 [7.02, 10.12]), respectively. Similarly, the combined molar Cmax and AUC∞ of TAK-788, AP32960, and AP32914 were increased in the presence of itraconazole by approximately 186% (geometric LSM ratio of 2.86 [2.48, 3.30]) and 527% (geometric LSM ratio of 6.27 [5.20, 7.56]), respectively. In Part 2, rifampin oral coadministration resulted in lower plasma concentrations of TAK-788 and its 2 active metabolites, AP32960 and AP32914, throughout the 168-hour postdose interval. Plasma TAK-788 Cmax and AUC∞ were reduced in the presence of rifampin by approximately 95% (geometric LSM ratio of 0.05 [0.04, 0.07]) and 96% (geometric LSM ratio of 0.04 [0.03, 0.05]), respectively. Similarly, the combined molar Cmax and AUC∞ of TAK-788, AP32960, and AP32914 were reduced in the presence of rifampin by approximately 92% (geometric LSM ratio of 0.08 [0.07, 0.11]) and 95% (geometric LSM ratio of 0.05 [0.04, 0.07]), respectively. The strong CYP3A inhibitor itraconazole significantly increased systemic exposure of TAK-788 and its 2 active metabolites, while the strong CYP3A inducer rifampin significantly reduced the exposure of TAK-788 and its 2 active metabolites. Hence, coadministration of TAK-788 with moderate and strong CYP3A inhibitors and inducers is not recommended.

Translational Science Posters

TS01.01
HIF-1a Upregulates Muscarinic Receptor 3 and Promotes Invasion and Metastasis in NSCLC

Gengpeng Lin[1], Hui Li[2], Xuefei Li[1]
[1]*Department of Pulmonary and Critical Care Medicine, The First Affiliated Hospital of Sun Yet-sen University, Guangzhou, China,* [2]*Department of Pathology, The First Affiliated Hospital of Sun Yet-sen University, Guangzhou, China*

In our previous study, we found that muscarinic receptor 3(M3R) was overexpressed in NSCLC tissues. The expression intensity was strongly correlated to metastasis status of NSCLC patients, but conversely correlated to the 5-year survival rate. We found that M3R promoted invasion and metastasis of NSCLC via PI3K/Akt/MMP9 pathway. However, why M3R is highly expressed in NSCLC patients is still unclear. In this project, we aim to investigate the role of HIF-1α in M3R expression as well as invasion and metastasis of NSCLC. NSCLC tissue as well as NSCLC cell lines A549 and L78 were used to evalute the expression of M3R and HIF-1a. The relationship between HIF-1a and clinicalpathological charateristics of NSCLC patients were analyzed. The interaction between HIF-1α and M3R was assessed using Dual Luciferase reporter. We found that hypoxia-inducible factor 1α (HIF-1α) was overexpressed in NSCLC tissues. The expression intensity was strongly correlated to metastasis status of NSCLC patients, but conversely correlated to the 5-year survival rate. The expression level of HIF-1α was positively related to M3R in NSCLC tissues. NSCLC cell lines under hypoxia showed upregulation of M3R as well as enhanced ability of migration and invasion, and down-regulation of HIF-1α resulted in the inhibition of migration and invasion ability of NSCLC cell lines L78 and A549. Dual Luciferase reporter showed that HIF-1α upregulated the expression of M3R through binding to the promoter of M3R. Our study suggests that hypoxia upregulates M3R via HIF-1α, and this promotes invasion and metastasis of NSCLC. M3R could be another therapy target in treating lung cancer.

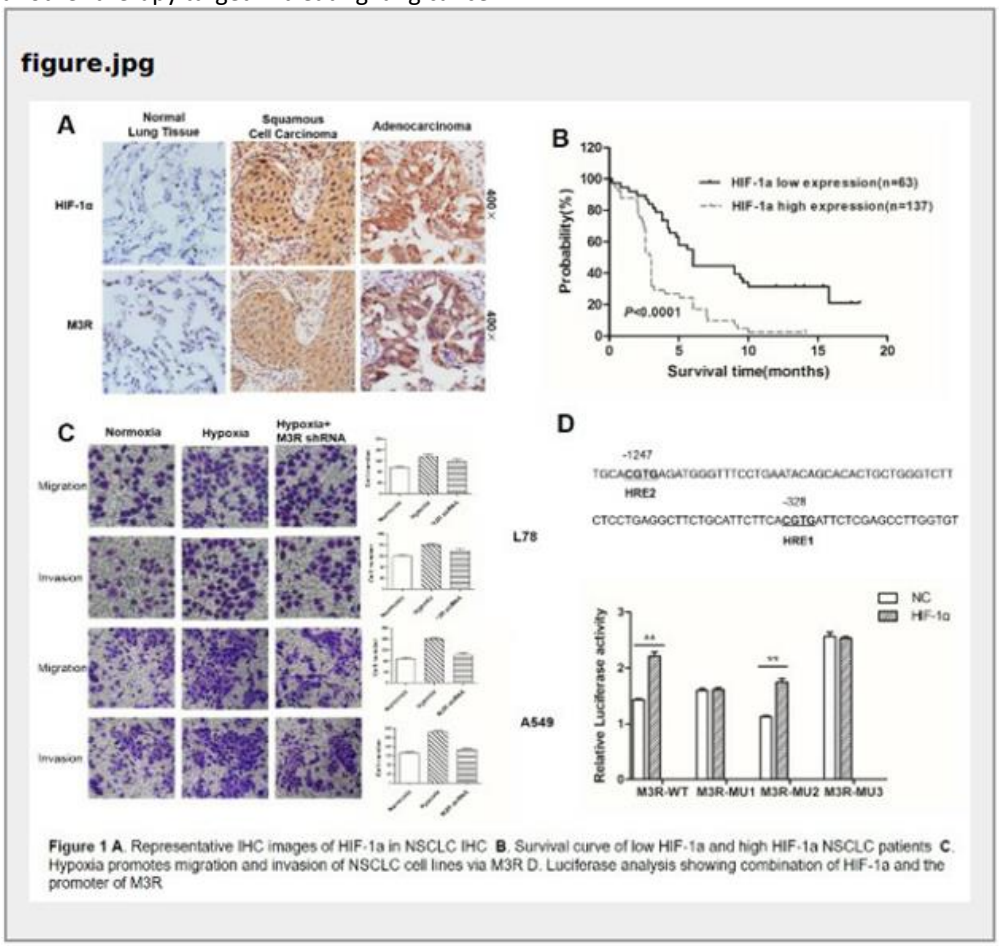


Figure 1 A. Representative IHC images of HIF-1a in NSCLC IHC **B**. Survival curve of low HIF-1a and high HIF-1a NSCLC patients **C**. Hypoxia promotes migration and invasion of NSCLC cell lines via M3R D. Luciferase analysis showing combination of HIF-1a and the promoter of M3R

figure.jpg

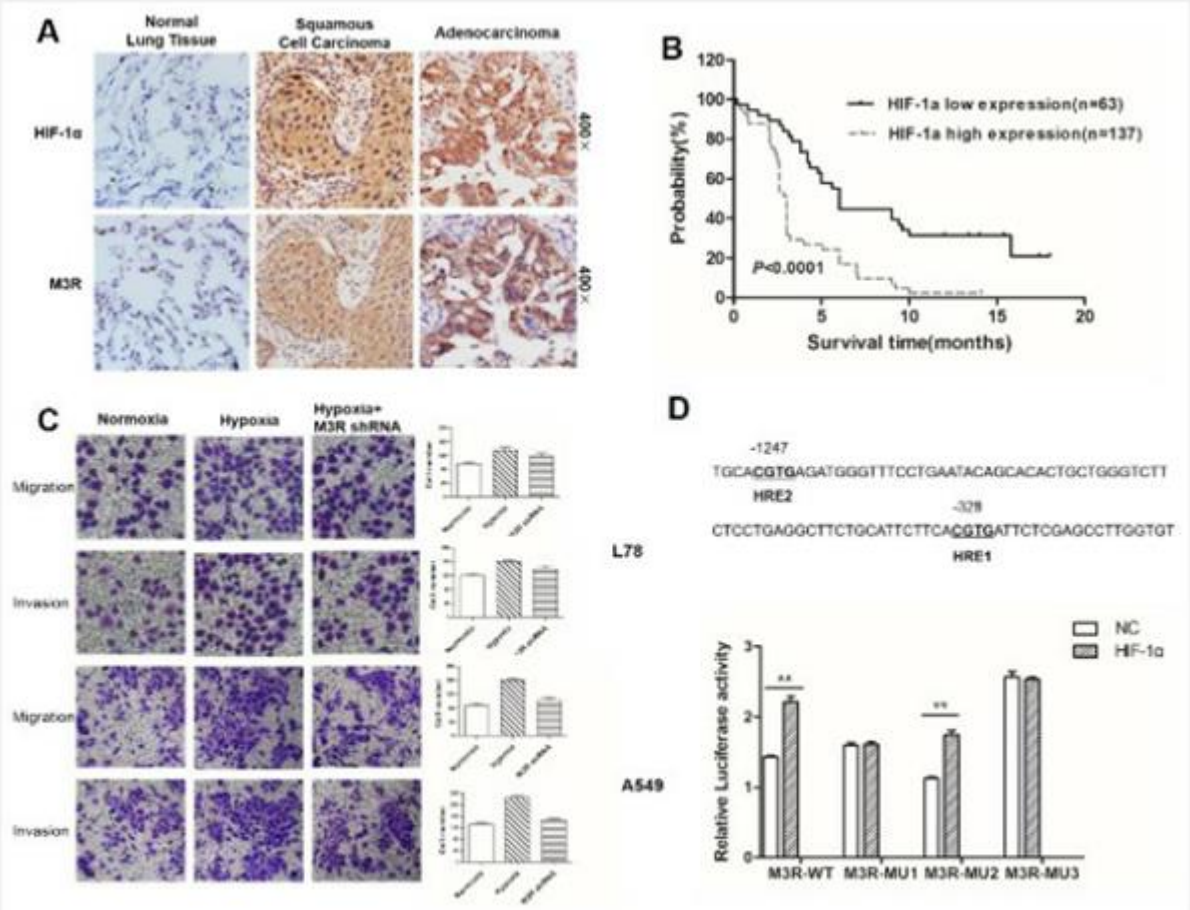


Figure 1 A. Representative IHC images of HIF-1a in NSCLC IHC **B**. Survival curve of low HIF-1a and high HIF-1a NSCLC patients **C**. Hypoxia promotes migration and invasion of NSCLC cell lines via M3R D. Luciferase analysis showing combination of HIF-1a and the promoter of M3R

TS01.02

Novel Anti–CTLA-4 Antibody Quavonlimab Plus Pembrolizumab as First-Line Therapy for NSCLC: Extended Follow-up From a Phase 1 Study

Byoung Chul Cho[1], Ruth Perets[2], Drew W. Rasco[3], Myung-Ju Ahn[4], David R. Spigel[5], Kiyotaka Yoh[6], Dong-Wan Kim[7], Martin Gutierrez[8], Dae Ho Lee[9], Adnan Nagrial[10], Miyako Satouchi[11], Dusan Kotasek[12], Corinne Maurice-Dror[2], Jiaxin Niu[13], Mohini Rajasagi[14], Shabana Siddiqi[14], Xiaoyun (Nicole) Li[14], Jobin Cyrus[14], Rachel A. Altura[14], Jair Bar[15]
[1]Yonsei Cancer Center, Seoul , South Korea, [2]Rambam Medical Center, Haifa, Israel, [3]START, San Antonio, USA, [4]Sungkyunkwan University of Medicine, Samsung Medical Center, Seoul, South Korea, [5]Sarah Cannon Research Institute, Nashville, USA, [6]National Cancer Center Hospital East, Kashiwa, Japan, [7]Seoul National University Hospital, Seoul, South Korea, [8]Hackensack University Medical Center, Hackensack, USA, [9]University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea, [10]Blacktown Hospital and University of Sydney, Sydney, Australia, [11]Hyogo Cancer Center, Japan, [12]Adelaide Cancer Centre and University of Adelaide, Adelaide, Australia, [13]Banner MD Anderson Cancer Center, Gilbert, USA, [14]Merck & Co., Inc., Kenilworth, USA, [15]Chaim Sheba Medical Center at Tel HaShomer, Ramat Gan, Israel

Background: In an open-label phase 1 study (NCT03179436), treatment with anti–CTLA-4 antibody quavonlimab (MK-1308) in combination with anti–PD-1 antibody pembrolizumab conferred encouraging antitumor activity as first-line treatment in advanced non–small cell lung cancer (NSCLC; median follow-up, 8 months). We present safety and efficacy outcomes after extended follow-up. **Methods:** Patients had newly diagnosed histologically/cytologically confirmed stage IIIB/IV NSCLC, measurable disease, and ECOG PS 0 or 1. In the dose-confirmation phase, patients received quavonlimab (25 mg or 75 mg) Q3W or Q6W in combination with pembrolizumab (200 mg) Q3W for up to 35 cycles. The primary objective was safety and tolerability. Secondary and exploratory objectives included ORR (centrally assessed), PFS, and OS. Response based on PD-L1 status was retrospectively evaluated using tumor proportion score (TPS) as a continuous variable. Data cutoff: January 3, 2020. **Results:** Overall, 134 patients with NSCLC from the dose-confirmation phase were included in this analysis; median follow-up was 16.9 months (IQR, 7.0-21.3). Any-grade AEs and treatment-related AEs (TRAEs) occurred in 98% and 85% of patients, respectively. Grade ≥3 TRAEs occurred in 36% (25 mg Q6W, 30%; 25 mg Q3W, 35%; 75 mg Q6W, 35%; 75 mg Q3W, 57%); most common were increased ALT (8%), pneumonitis (8%), and increased AST (6%). Efficacy outcomes are described in the Table. A higher TPS was significantly associated with better response (one-sided P=0.015); responses were observed regardless of PD-L1 status (PD-L1–positive [TPS ≥1%], 39% [95% CI, 29%-49%]; PD-L1–negative [TPS <1%], 33% [95% CI, 19%-52%]). **Conclusions:** Combination treatment with quavonlimab plus pembrolizumab conferred encouraging antitumor activity as first-line therapy for patients with advanced NSCLC and was generally well tolerated with no unexpected toxicities. Efficacy and safety data support 25 mg Q6W as the recommended phase 2 dose of quavonlimab when used with pembrolizumab. A phase 3 study is planned.

	Quavonlimab 25 mg Q6W + Pembro n=40	Quavonlimab 25 mg Q3W + Pembro n=40	Quavonlimab 75 mg Q6W + Pembro n=40	Quavonlimab 75 mg Q3W + Pembro n=14	Total N=134
ORR, % (95%, CI)	37.5 (22.7-54.2)	40 (24.9-56.7)	27.5 (14.6-43.9)	35.7 (12.8-64.9)	35.1 (27.0-43.8)
PFS, median (95%, CI), mo	7.8 (4.2-14.8)	6.0 (2.0-8.3)	6.0 (3.5-8.1)	3.4 (1.8-NE)	6.1 (4.2-7.3)
OS, median (95%, CI), mo	18.1 (14.2-NE)	18.1 (9.1-21.8)	17.1 (9.0-NE)	13.7 (3.5-NE)	16.5 (14.2-21.8)
DOR, median (95%, CI), mo	NR (4.0 to 21.6+)	7.9 (2.8 to 21.4+)	15.9 (3.4 to 21.4+)	NR (8.8+ to 16.3+)	13.6 (2.8 to 21.6+)

TS01.03

Efficacy and Safety Data From a Phase 1/2 Trial of Tislelizumab in Chinese Patients With Non-Small Cell Lung Cancer (NSCLC)

Qing Zhou[1], J. Zhao[2], J. Wang[3], Q. Zhang[4], H. Pan[5], L. Shen[2], Y. Yuan[6], Y. Bai[4], T. Liu[7], Y. Gao[8], Y. Li[8], J. Zhang[8], Y.-L. Wu[1]
[1]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital and Guangdong Academy of Medical Sciences, Guangzhou, China, [2]Beijing Cancer Hospital, Beijing, China, [3]Tumor Hospital of Chinese Medical Science Institute, Beijing, China, [4]Harbin Medical University Cancer Hospital, Harbin, China, [5]Sir Run Run Shaw Hospital, Zhejiang University, School of Medicine, Hangzhou, China, [6]The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China, [7]Zhongshan Hospital Fudan University, Shanghai, China, [8]8BeiGene (Beijing) Co., Ltd., Beijing, China

PD-(L)1 inhibitors have provided new treatment approaches for patients with NSCLC; however, resistance to PD-(L)1 inhibitors or low PD-L1 expression may limit clinical benefit. Tislelizumab, a monoclonal antibody with high affinity and specificity for PD-1, was recently approved in China for the treatment of previously treated classical Hodgkin lymphoma. Tislelizumab was engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti- PD-1 therapy. Preliminary reports from this study (NCT04068519) showed that tislelizumab monotherapy was generally well tolerated and demonstrated antitumor activity in Chinese patients with advanced solid tumors. We now present data from patients with NSCLC. This multi-arm, open-label, nonrandomized phase 1/2 study evaluated safety/tolerability, antitumor activity, and survival in patients with histologically/cytologically confirmed advanced solid tumors treated with tislelizumab. Eligible patients progressed on, or were intolerant to, their last standard antitumor treatment and were anti-PD-(L)1 therapy treatment-naïve. Patients received intravenous tislelizumab 200 mg every 3 weeks until loss of clinical benefit or unacceptable toxicity. Patients were considered PD-L1-positive if ≥10% of their tumor cells had PD-L1 membrane staining at any intensity using the VENTANA PD-L1 (SP263) assay. Antitumor response was assessed by RECIST v1.1, overall survival (OS) was estimated by Kaplan-Meier analysis, and safety/tolerability was examined by monitoring adverse events (AEs). As of 01 December 2018, 56 patients with NSCLC (nonsquamous, n=31 [55%]; squamous, n=25 [45%]) were enrolled. Forty patients (71%) were male, 53 (95%) had metastatic disease, and 23 (41%) had never smoked; one patient each had an EGFR mutation or ALK rearrangement. Patients were heavily pretreated, with 16 patients (29%) receiving ≥3 lines of prior systemic therapy. The most common treatment-related AEs (TRAEs) were increased AST (n=14; 25%), increased ALT (n=13; 23%), and rash (n=8; 14%). Increased AST (n=3; 5%) and increased ALT (n=2; 4%) were the only grade ≥3 TRAEs occurring in ≥2 patients. Immune-related AEs (irAE) were reported in 12 patients (21%) and were generally of low severity, including 1 patient with grade 2 pneumonitis; 4 patients (7%) experienced a grade ≥3 irAE. The objective response rate (ORR) was 18% (95% CI: 8.9, 30.4), with an ORR of 17% (95% CI: 4.7, 37.4) and 19% (95% CI: 7.5, 37.5) in patients who were PD-L1-positive (n=24) and PD-L1-negative (n=31), respectively. With a median follow-up of 14.6 months (95% CI: 12.0, 15.6), median OS was not reached in patients with NSCLC. Updated data with a follow-up of ≥2 years will be presented, including OS. Tislelizumab was generally well tolerated and demonstrated antitumor activity in NSCLC patients regardless of PD-L1 expression status. Tislelizumab is being evaluated as a single agent or with chemotherapy in phase 3 studies in NSCLC patients (NCT03358875, NCT03594747, and NCT03663205).

TS01.04
Racial Disparity in the Timely Treatment of Non-Small Cell Lung Cancer

Paige Neroda[1], Mei-Chin Hsieh[2], Xiao-Cheng Wu[2], Kathleen Cartmell[1], Rachel Mayo[1], Jiande Wu[2], Chindo Hicks[2], Lu Zhang[1]
[1]Clemson University, Clemson, United States, [2]Louisiana State University Health Sciences Center, New Orleans, United States

Background: Lung cancer is the leading cause of cancer death in the U.S. Non-small cell lung cancer (NSCLC) represents about 85% of all lung cancer cases. It has been well established that surgery and adjuvant treatment significantly improve nonmetastatic NSCLC survival. Delayed treatment has been associated with worse survival. While black patients have higher incidence and mortality of lung cancer than white patients, it is unknown whether there is racial disparity in receiving timely treatment. **Methods:** White and black patients diagnosed with stage I-IIIA NSCLC in Louisiana between 2004 and 2016 who received surgery were identified. Patients who received neo-adjuvant treatment or had unknown sequence of surgery and other treatment were excluded. Exposure variable was race (white vs. black). Outcome variables included delayed surgery (receiving surgery >3 weeks after tumor diagnosis) and delayed adjuvant treatment (receiving adjuvant treatment >6 weeks after surgery). Adjuvant treatment included chemotherapy, radiation, or immunotherapy. Multivariable logistic regression was applied adjusting for age, sex, marital status, insurance, census-tract level urbanicity and poverty, comorbidity, tumor size, grade, stage, lymph node involvement, and surgery type. **Results:** Out of 4,123 patients evaluated, 1,179 received adjuvant treatment. Black patients were more likely to be younger, unmarried, insured with Medicaid, living in urban or high poverty area. In addition, black patients had more positive nodal tumors than white patients. The median time interval between tumor diagnosis and surgery was 26 days for white patients and 40 days for black patients. The median time interval between surgery and adjuvant treatment was 44 days and 47 days, respectively, for the two racial groups. About 55.8% white vs. 68.0% black patients received delayed surgery (P<0.0001), and 52.9% white vs. 59.8% black patients received delayed adjuvant treatment (P=0.05). After adjusting for covariates, the odds ratio (OR) of receiving delayed surgery for black patients was 1.49 (1.25-1.78) compared to white patients, and the OR of receiving delayed adjuvant treatment was 1.18 (0.86-1.62). **Conclusion:** Compared to white NSCLC patients, black patients are more likely to have longer wait time from diagnosis to surgery, but not from surgery to adjuvant therapy. Interventions are needed to improve the timeliness of surgery for black patients.

TS01.05
Timely Treatment and Survival for Localized Lung Cancer

Lu Zhang[1], Mei-Chin Hsieh[2], Paige Neroda[1], Xiao-Cheng Wu[2], Lior Rennert[1], Chindo Hicks[2], Jiande Wu[2], Ronald Gimbel[1]
[1]Clemson University, Clemson, United States, [2]Louisiana State University Health Sciences Center, New Orleans, United States

Background: More and more lung cancers are diagnosed at an early stage with the advancement of early detection methods. However, the management of early-stage lung cancers, particularly the timing of treatment initiation, has been less studied. Current guidelines in this regard are inconsistent and not specific to histologic subtypes, which have different aggressiveness and prognosis. This study investigated the association between the timing of treatment initiation and survival for all localized lung cancers and by selected histologic subtypes. **Methods:** Patients diagnosed with localized lung cancer between 2004 and 2016 were identified from Surveillance, Epidemiology, and End Results Program public research database. Patients who did not receive lung cancer surgery, unknown timing of treatment initiation, or whose lung cancer was not first primary tumor, were excluded. Exposure variable was the time interval between tumor diagnosis and the treatment initiation (<1, 1-2, 2-3, and ≥3 months). The outcome was lung cancer-specific survival. Covariates included age, sex, race, marital status, tumor size, grade, and surgery type as well as histologic subtype (defined based on ICD-O-3 codes). Cox proportional hazards model was applied. **Results:** A total of 47,051 localized lung cancer patients were included. Th majority of the patients were older than 60, white, married, having tumor size <2cm. Adenocarcinoma (36.8%) and squamous cell carcinoma (23.3%) were the most prevalent subtypes. The average follow-up time was 54.5 months. The proportion of patients receiving treatment in <1, 1-2, 2-3, and ≥3 months from tumor diagnosis were 38.5%, 30.9%, 18.6%, and 12.0%; and the lung cancer-specific survival rate in the four groups were 63.3%, 59.5%, 57.5%, and 53.5%, respectively (P<0.0001). After adjusting for covariates, the hazard ratio of death from lung cancer was 0.97 (0.92-1.02), 1.03 (0.98-1.10), 1.11 (1.04-1.18) for those receiving treatment in 1-2, 2-3, and ≥3 months, compared to those in <1 month. The adjusted hazard ratio remained significant for adenocarcinoma (≥3 vs. <1 month: 1.14, 1.02-1.27), bronchioloalveolar (1-2 vs. <1 month: 1.39, 1.09-1.78), and large cell carcinoma (1-2 vs. <1 month: 0.62, 0.41-0.95; ≥3 vs. <1 month: 1.61, 1.07-2.42), but not significant for squamous or epidermoid carcinoma, adenosquamous carcinoma, carcinoids, and small cell lung cancer. **Conclusion:** Treatment initiation in 3 months or later after diagnosis was associated with worse survival for localized lung cancer. The association varied by histologic subtype. Future studies should use more specific time interval (in weeks) to investigate the effect of timely treatment, particularly for the more aggressive subtypes.

TS01.06
High-Plex Digital Spatial Profiling of Non-Small-Cell Lung Cancer (NSCLC)

Arutha Kulasinghe[1], James Monkman[1], Touraj Taheri[2], Majid Warkiani[3], Connor O'leary[1,4], Rahul Ladwa[4], Derek Richard[1], Ken O'Byrne[1,4]
[1]Queensland University Of Technology, Woolloongabba, Australia, [2]Royal Brisbane and Women's Hospital, Herston, Australia, [3]University of Technology Sydney, Sydney, Australia, [4]Princess Alexandra Hospital, Woolloongabba, Australia

Background: Profiling the tumour microenvironment (TME) has been informative in understanding the underlying tumour-immune interactions at play, which may be informative of outcome to therapy in non-small-cell lung cancer (NSCLC). Multiplex immunohistochemistry (mIHC) coupled with molecular barcoding technologies have revealed greater insights into the spatial biology of the TME. **Methods:** In this study, we utilised the Nanostring GeoMX Digital Spatial Profiler (DSP) platform to profile NSCLC tissue for protein markers across immune cell profiling, immuno-oncology (IO) drug target, immune activation status, immune cell typing, and pan-tumour protein modules. Regions of interest (ROIs) were selected that described tumour, tumour microenvironment and normal adjacent tissue (NAT) compartments. **Results:** Our data revealed that paired analysis (n=18) of patient matched compartments indicated that the TME was significantly enriched in CD27, CD3, CD4, CD44, CD45, CD45RO, CD68, CD163, and VISTA relative to tumour. Unmatched analysis indicated that the NAT(n=19) was significantly enriched in CD34, fibronectin, IDO1, LAG3, ARG1 and PTEN when compared to the TME (n=32). Univariate Cox proportional hazards indicated that the presence of cells expressing CD3 (HR:0.5, p=0.018), CD34 (HR:0.53, p=0.004) and ICOS (HR:0.6, p=0.047) in tumour compartments were significantly associated with improved overall survival (OS). **Conclusion:** We implemented both high-plex and high-throughput methodologies to the discovery of protein biomarkers and molecular phenotypes within biopsy samples and demonstrate the power of such tools for a new generation of pathology research.

TS01.07

Genomic HLA as a Predictive Biomarker for Survival Among Non-Small Cell Lung Cancer Patient Treated with Single Agent Immunotherapy.

Afaf Abed[1,2,3], Leslie Calapre[2], Johnny Lo[2], Mrs Suzana Correia[1], Samantha Bowyer[4], Abha Chopra[5], Mark Watson[5], Adnan Khattak[1,2,6], Michael Millward[3,4,6], Elin Gray[2]

[1]Department of Medical Oncology, Fiona Stanley Hospital, MURDOCH, Australia, [2]Edith Cowan University, JOONDALUP, Australia, [3]Linear Clinical Research, NEDLANDS, Australia, [4]Department of Medical Oncology, Sir Charles Gairdner Hospital, NEDLANDS, Australia, [5]Health Futures Institute, Murdoch University, MURDOCH, Australia, [6]St John of God Hospital, SUBIACO, Australia, [7]University of Western Australia, NEDLANDS, Australia

Background: We aimed to assess the role of genomic HLA-I/II homozygosity in the Overall Survival (OS) benefit in patients with unresectable locally advanced, metastatic non-small lung cancer treated by single agent PD1/PDL1 inhibitors. **Methods:** We collected blood from 170 advanced lung cancer patients treated with immunotherapy at two major oncology centres in Western Australia. High quality DNA was extracted from white blood cells and used for HLA-I/II typing. Correlation between genomic HLA-I/II, OS and Progression Free Survival (PFS) were assessed using log rank test. A multivariate analysis was carried out to define independent predictors that influenced OS and PFS using Cox regression analysis. We then investigated the correlation between individual HLA-A and -B supertypes with OS using log rank analysis. **Results:** Homozygosity at one or more HLA-I loci and the type of immune-checkpoint inhibitor used (anti-PD1 vs anti-PDL1) were the only statistically significant independent predictor of shorter OS (HR=2.17, 95%CI 1.13-4.17, P=0.02 and HR=3.16, 95%CI 1.66-5.99 respectively) in the univariate analysis. This was more significant in patients with tumour expressing PDL1 in more than 50% of cancer cells (HR=3.93, 95%CI 1.30-11.85, P<0.001). In the multivariate analysis, pre-treatment neutrophil to lymphocyte ratio (NLR) also emerged as a prognostic marker of OS (HR=2.17, 95% CI 1.12-4.20, P=0.02) together with HLA-I genotype (HR=2.07, 95% CI 1.07-4.01, P=0.03). The adverse effect of homozygosity at one or more HLA-I loci on PFS was only apparent after controlling for interactions between PD-L1 status and HLA-I genotype (HR= 2.37, 95%CI 1.12 – 5.01, P=0.02). No interactions were found between HLA-I and therapy type, and both were not found to be associated with PFS or OS advantage in the multivariate analysis. The presence of HLA-A02 supertype was the only type of HLA-I supertypes to be associated with improved OS (HR=0.56 95%CI 0.34-0.93, P=0.023). **Conclusion:** Overall, homozygosity at ≥1 HLA-I loci appears to predict worse OS and PFS in patients with advanced or metastatic NSCLC treated with single agent immunotherapy. HLA-A02 supertypes is the only positively influencing HLA-I supertype on OS.

	Univariate				Multivariate				Multivariate + Interactions			
	p-value	HR	95.0% CI		p-value	HR	95.0% CI		p-value	HR	95.0% CI	
OS			Lower	Upper			Lower	Upper			Lower	Upper
HLA-I (hetero vs homo)	**0.020**	**2.17**	**1.13**	**4.17**	**0.031**	**2.07**	**1.07**	**4.01**	**0.003**	**3.71**	**1.57**	**8.78**
Age (<65 vs ≥65)	0.534	0.83	0.45	1.51	0.862	0.95	0.51	1.76	0.855	1.06	0.57	1.99
PDL1 (≥50% vs <50%)	0.916	0.97	0.53	1.77	0.522	0.82	0.45	1.51	0.589	1.23	0.59	2.55
ECOG (≤1 vs ≥2)	0.400	1.56	0.56	4.36	0.246	1.85	0.65	5.25	0.263	1.82	0.64	5.17
NLR (≤5 vs >5)	0.059	1.78	0.98	3.24	**0.022**	**2.17**	**1.12**	**4.20**	**0.019**	**2.20**	**1.14**	**4.26**
Therapy type (αPD1 vs αPDL1)	**<0.001**	**3.16**	**1.66**	**5.99**	**<0.001**	**3.32**	**1.73**	**6.37**	**<0.001**	**3.33**	**1.72**	**6.45**
HLA-I*PDL1									0.061	0.23	0.05	1.07

	Univariate				Multivariate				Multivariate + Interactions			
	p-value	HR	95.0% CI		p-value	HR	95.0% CI		p-value	HR	95.0% CI	
PFS			Lower	Upper			Lower	Upper			Lower	Upper
HLA-I (hetero vs homo)	0.093	1.62	0.92	2.86	0.065	1.71	0.97	3.02	**0.024**	**2.37**	**1.12**	**5.01**
Age (<65 vs ≥65)	0.352	0.79	0.48	1.30	0.550	0.86	0.52	1.42	0.752	0.92	0.55	1.55
PDL1 (≥50% vs <50%)	0.347	1.26	0.78	2.06	0.608	1.14	0.70	1.86	0.283	1.38	0.77	2.46
ECOG (≤1 vs ≥2)	0.581	0.82	0.41	1.66	0.831	0.92	0.45	1.90	0.729	0.88	0.43	1.82
NLR (≤5 vs >5)	0.626	1.13	0.69	1.86	0.494	1.21	0.70	2.07	0.506	1.20	0.70	2.06
Therapy type (αPD1 vs αPDL1)	**<0.001**	**2.93**	**1.75**	**4.88**	**<0.001**	**2.84**	**1.67**	**4.84**	**<0.001**	**2.71**	**1.59**	**4.64**
HLA-I*PDL1									0.224	0.46	0.13	1.61

A

B

C

D

D

E

F

G

H

L

T

V

W

X

Y

Z