8500 **Oral Abstract Session**

Surgical outcomes of patients with resectable non-small-cell lung cancer receiving neoadjuvant immunotherapy with nivolumab plus relatlimab or nivolumab: Findings from the prospective, randomized, multicentric phase II study NEOpredict-Lung.

Clemens Aigner, Bert Du Pont, Koen Hartemink, Marcel Wiesweg, Michel Vanbockrijck, Kaid Darwiche, Balazs Hegedus, Alexander Schramm, Hubertus Hautzel, Brigitte Maes, Dirk Theegarten, Hans-Ulrich Schildhaus, Paul Baas, Kristof Cuppens, Martin H. Schuler, Till Plönes; West German Cancer Center, University Medicine Essen - Ruhrlandklinik, Essen, Germany; Jessa Hospital, Hasselt, Belgium; Department of Surgery, The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; West German Cancer Center, University Hospital Essen, Essen, Germany; University Medicine Essen - Ruhrlandklinik, West German Cancer Center, Essen, Germany; Department of Medical Oncology, West German Cancer Center, University Hospital Essen, Essen, Germany; West German Cancer Center, Department of Nuclear Medicine, University Hospital Essen, Essen, Germany; Department of Pathology and Neuropathology, University Hospital of Essen, Univer, Essen, Germany; Institute for Pathology, University Hospital Essen, Essen, Germany; Department of Thoracic Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; Jessa Hospital Belgium, Hasselt, Belgium; Essen University Hospital, Essen, Germany

Background: Feasibility of surgical resection for non-small-cell lung cancer (NSCLC) after preoperative immune checkpoint inhibitor therapy (PICIT) with PD-1/PD-L1 and CTLA-4 inhibitors has been established. This study reports the first data on surgery after preoperative LAG-3 inhibition in NSCLC patients. **Methods:** Patients with histologically confirmed NSCLC stage IB, II or IIIA (UICC 8th edition) were randomized to receive two preoperative doses (q14d) of nivolumab (240 mg, arm A), or nivolumab (240 mg) plus relatlimab (80 mg, arm B). Primary study endpoint was the number of patients undergoing curatively intended surgery within 43 days of initiation of PICIT. Surgery was performed following the institutional standards. Outcomes and perioperative events were prospectively recorded. **Results:** 60 patients (29 female) were randomized 1:1 from 4/2020 to 7/2022. All patients were operated within 43 days after initiation of PICIT. Median age in arm A was 65 (43-78) years and 67 (44-81) years in arm B. Clinical UICC stages were similar between both arms. Central tumor location was present in 50% in arm A and 45% in arm B. R0 resection was achieved in 57 patients (95% ITT population, 98,3% curatively resected population). Two patients had pleural carcinosis only detected at surgery, and 1 patient had R1 resection. Resection was performed by lobectomy (n=23 and 24), bilobectomy (2 and 1), sleeve lobectomy (5 and 4) and combined lobectomy+segmentectomy (0 and 1). Surgical approach was either by videothoracoscopy (n=60% and 63,3%) or thoracotomy (n=40% and 36,6%). Conversion was required in 3 vs. 2 patients. Median operation time was 149 (77-234) and 165 (61-205) minutes. Median number of resected lymph nodes was 15 (3-52) and 10 (3-50). Intraoperative bleeding from the pulmonary artery was observed in 1 patient in each arm and was managed without sequelae. Postoperative complications occurred in 33,3% and 26,6%. Median hospital stay was 7 (2-22) and 5,5 (2-24) days. Complete or major histopathological response was observed in 27% and 30%. Overall perioperative 30-day mortality was 0%. No negative impact on adjuvant therapy was observed. The 12 months OS rate across both arms was 96% (95% CI: 83-99%), the DFS rate was 91 % (78-97%). **Conclusions:** Curative surgical resection following neoadjuvant combined PD-1/LAG-3 inhibition was equally safe and feasible as after PD-1 inhibition alone. Perioperative course, complications rate and outcome are comparable to other neoadjuvant regimens. Standard adjuvant therapies can be safely administered in this setting. Clinical trial information: NCT04205552. Research Sponsor: Bristol Myers Squibb.

8501 **Oral Abstract Session**

Perioperative toripalimab + platinum-doublet chemotherapy vs chemotherapy in resectable stage II/III non-small cell lung cancer (NSCLC): Interim event-free survival (EFS) analysis of the phase III NEOTORCH study.

Shun Lu, Lin Wu, Wei Zhang, Peng Zhang, Wenxiang Wang, Wentao Fang, Wenqun Xing, Qixun Chen, Jiandong Mei, Lin Yang, Lijie Tan, Xiaohong Sun, Shidong Xu, Xiaohua Hu, Guohua Yu, Dongliang Yu, Jinlu Shan, Nong Yang, Yuping Chen, Hui Tian, Shanghai Junshi Biosciences; Shanghai Chest Hospital, Jiao Tong University, Shanghai, China; Hunan Cancer Hospital, Changsha, China; The First Affiliated Hospital of Nanchang University, Nanchang, China; Department of Pulmonary, Shanghai Pulmonary Hospital, Jiaotong University, Shanghai, China; Department of Thoracic Surgery, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; Cancer Hospital Affiliated to Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China; Cancer Hospital of the University of Chinese Academy of Sciences, Hangzhou, China; Institute of Thoracic Oncology and Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu, China; Shenzhen People's Hospital, Shenzhen, China; Zhongshan Hospital, Fudan University, Shanghai, China; Cancer Hospital Affiliated to Xinjiang Medical University, Urumqi, China; Harbin Medical University Cancer Hospital, Harbin, China; Guangxi Medical University Affiliated Tumor Hospital, Nanning, China; Weifang People' s Hospital, Weifang, Shandong, China; The Second Affiliated Hospital Of Nanchang University, Nanchang, China; Army Characteristic Medical Center of PLA, Chongqing, China; Lung & Gastrointestinal Oncology Department, Hunan Cancer Hospital, Changsha, China; Cancer Hospital of Shantou University Medical College, Shantou, China; Qilu Hospital of Shandong University, Jinan, China

Background: Adjuvant and neoadjuvant immunotherapy have been approved by US FDA to treat early-stage NSCLC. However, the optimal neoadjuvant and adjuvant treatment, including duration of treatment, are unknown. We present the interim results of a randomized, double-blind, placebo-controlled, Phase III trial to evaluate the efficacy and safety of perioperative toripalimab plus chemotherapy followed by toripalimab maintenance vs chemotherapy in resectable stage III NSCLC. **Methods:** Patients with stage II/III resectable NSCLC, without EGFR/ALK alterations for non-squamous NSCLC, were randomized 1:1 to receive 240 mg toripalimab or placebo combined with chemotherapy Q3W for 3 cycles before surgery and one cycle after surgery, followed by toripalimab or placebo monotherapy Q3W for 13 cycles. Stratification variables for randomization included disease stage, histopathologic subtype, PD-L1 expression and surgical procedure. Primary endpoints were EFS by investigator and major pathological response (MPR) rate by a blinded independent pathologic review (BIPR) in the stage III and the ITT populations. Secondary endpoints included overall survival (OS), pathologic complete response (pCR) rate, EFS by independent review committee (IRC), and safety. A planned interim analysis was performed on the primary endpoint of EFS in the stage III subjects. **Results:** A total of 404 stage III NSCLC patients were randomized to toripalimab (n=202) or placebo (n=202). By the data cutoff date (November 30, 2022), the median follow-up was 18.3 months. Baseline characteristics were well balanced between the two arms. EFS was significantly improved in the toripalimab arm, HR=0.40, 95% CI (0.277-0.565), $P<0.0001$, and crossed the pre-specified efficacy boundary. The median EFS was not reached in the toripalimab arm and 15.1 months in the placebo arm. A consistent effect on EFS, favoring toripalimab, was observed in all subgroups. The MPR and pCR rates per BIPR were also higher in the toripalimab arm, 48.5% vs 8.4% and 24.8% vs 1.0%, respectively. The OS results showed a trend favoring toripalimab. The incidence of Grade $\geq$3 adverse events (AEs) (63.4% vs 54.0%), fatal AEs related to toripalimab/placebo (0.5% vs 0%) and AEs leading to discontinuation of toripalimab/placebo (9.4% vs 7.4%) were comparable between the two arms. However, the incidence of immune-related AEs (42.1% vs 22.8%) was more frequent in the toripalimab arm. **Conclusions:** The addition of toripalimab to perioperative chemotherapy showed statistically significant improvements in EFS for stage III NSCLC patients with a manageable safety profile. Patients will be followed for overall survival. Clinical trial information: NCT04158440. Research Sponsor: Shanghai Junshi Biosciences Co.,Ltd.

8502 **Oral Abstract Session**

First-in-human dose-escalation trial of BI 764532, a delta-like ligand 3 (DLL3)/CD3 IgG-like T-cell engager in patients (pts) with DLL3-positive (DLL3+) small-cell lung cancer (SCLC) and neuroendocrine carcinoma (NEC).

Martin Wermke, Enriqueta Felip, Yasutoshi Kuboki, Daniel Morgensztern, Cyrus Sayehli, Miguel F. Sanmamed, Edurne Arriola, Zohra Oum'Hamed, Eric Song, Matus Studeny, Valentina Gambardella; Technical University Dresden, NCT/UCC Early Clinical Trial Unit, Dresden, Germany; Department of Medical Oncology, Vall d'Hebron University Hospital & Vall d'Hebron Institute of Oncology, Barcelona, Spain; Department of Experimental Therapeutics, National Cancer Center Hospital East, Kashiwa, Japan; Washington University School of Medicine, St. Louis, MO; Interdisciplinary Study Center with ECTU, Medical Clinic and Polyclinic II of the University Hospital, Wuerzburg, Germany; Department of Immunology and Oncology, Clínica Universidad de Navarra, Pamplona, Spain; Department of Medical Oncology, Hospital del Mar-CIBERONC (Centro de Investigación Biomédica en Red de Oncología), 08003 Barcelona, Spain; Cancer Research Program, IMIM (Institut Hospital del Mar d'Investigacions Mèdiques), 08003 Barcelona, Spain; Boehringer Ingelheim France S.A.S., Reims, France; Boehringer Ingelheim (China) Investment Co., Shanghai, China; Boehringer Ingelheim International GmbH, Ingelheim, Germany; Department of Medical Oncology, Hospital Clínico Universitario, INCLIVA Biomedical Research Institute, University of Valencia, Valencia, Spain

Background: The inhibitory Notch ligand, DLL3, is highly expressed on the cell surface of SCLC and NEC tumors and is a promising drug target. BI 764532 is a DLL3/CD3 T cell engaging bispecific antibody that has shown potent preclinical anti-tumor activity in DLL3+ cells and xenograft models. NCT04429087 is an ongoing phase I first-in-human, open-label, dose-escalation trial of BI 764532 in adults with locally advanced/metastatic DLL3+ (confirmed centrally) SCLC, NEC or small cell carcinoma of any other origin (grouped as NEC), or large cell NEC (LCNEC). **Methods:** BI 764532 was administered intravenously using three different regimens: Regimen (R) A (fixed iv dose q3w); RB1 (fixed iv dose qw); RB2 (step-in doses followed by a fixed dose). Treatment (Tx) continued until progressive disease (PD), unacceptable toxicity, other withdrawal criteria, or maximum Tx duration (36 mos). The main objective was to determine the maximum tolerated dose (MTD) and/or recommended dose for expansion of BI 764532, based on dose-limiting toxicities (DLTs) during the MTD evaluation period. Further objectives were safety, tolerability, PK/PD and preliminary efficacy based on investigator review (RECIST v1.1). **Results:** As of 28th Dec 2022, 90 pts received ≥1 dose of BI 764532 (RA: n = 24, 8 dose levels; RB1: n = 10, 3 dose levels; RB2: n = 56, 6 dose levels; starting dose: 0.03 μg/kg). Median age: 60 years (32–78); ECOG PS 0/1: 24/74%; prior PD1/PD-L1 Tx: 40%; ≥2 prior lines of Tx: 69%. SCLC/NEC/LCNEC: 52/41/4%. Median Tx duration: 43 days (range 1–443); 25 pts are ongoing. DLTs were seen in 1 pt on RA (Grade 3 confusion) and 4 pts on RB2 (Grade 4 cytokine release syndrome [CRS]; Grade 3 CRS, Grade 3 nervous system disorder, Grade 2 infusion-related reaction). MTD has not been reached and dose escalation is ongoing. Overall, the most common treatment-related AEs were (any/Grade 3+): CRS (58/2%); pyrexia (19/0%); decreased lymphocytes (18/14%); asthenia (17/1%); dysgeusia (14/0%). CRS was managed with supportive care, corticosteroids, and/or anti-IL-6R antibodies. With RB2, most CRS and neurological events occurred early, and were reversable. Tumor response data were available for 70 pts (RA/RB1/RB2: n = 19/8/43). In pts with SCLC (n = 24) or NEC (n = 23) who received ≥ target dose of BI 764532, ORR was 33% and 22% across all regimens, respectively. One pt with LCNEC was also evaluable for response and achieved PR. **Conclusions:** BI 764532 showed clinically manageable tolerability and MTD has not been reached at the doses administered to date. Promising efficacy has been observed, not only in SCLC but also in difficult to treat entities such as NEC and LCNEC. The study is ongoing; updated data will be presented. Clinical trial information: NCT04429087. Research Sponsor: Boehringer Ingelheim.

8503 **Oral Abstract Session**

Exploratory biomarker analysis of the phase 3 KEYNOTE-604 study of pembrolizumab plus etoposide for extensive-stage SCLC.

Charles M. Rudin, Hye Ryun Kim, Alejandro Navarro, Maya Gottfried, Solange Peters, Tibor Csoszi, Parneet Kaur Cheema, Delvys Rodriguez-Abreu, Mira Wollner, James Chih-Hsin Yang, Julien Mazieres, Terufumi Kato, Gregory Peter Kalemkerian, Elisha Dettman, Mackenzie Edmondson, Amir Vajdi, Andrey Loboda, Hazem Edmond El-Osta, Bin Zhao, Mark M. Awad; Memorial Sloan Kettering Cancer Center, New York, NY; Yonsei Cancer Center, Seoul, South Korea; Vall d'Hebron University Hospital, Barcelona, Spain; Meir Medical Center, Kfar-Saba, Israel; Lausanne University Hospital, Lausanne, Switzerland; Hetenyi G Korhaz Onkologiai Kozpont, Szolnok, Hungary; William Osler Health System, University of Toronto, Brampton, ON, Canada; Complejo Hospitalario Universitario Insular Materno-Infantil de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Las Palmas De Gran Canaria, Spain; Rambam Medical Center, Haifa, Israel; National Taiwan University Hospital and National Taiwan University Cancer Center, Taipei, Taiwan; Centre Hospitalier Universitaire de Toulouse, Université Paul Sabatier, Toulouse, France; Kanagawa Cancer Center, Yokohama, Japan; University of Michigan, Ann Arbor, MI; Merck & Co., Inc., Rahway, NJ; Dana-Farber Cancer Institute, Boston, MA

Background: In the phase 3 KEYNOTE-604 study of extensive-stage small-cell lung cancer (ES-SCLC; NCT03066778), first-line pembrolizumab (pembro) plus etoposide and platinum (EP) significantly improved PFS vs placebo (pbo) plus EP (HR, 0.75; $P = 0.0023$), with favorable OS (significance threshold not met; HR, 0.80; $P = 0.0164$). PFS/OS were similar regardless of PD-L1 CPS. In this exploratory analysis, tumor mutational burden (TMB), 18-gene T cell–inflamed gene expression profile ($Tcell_{inf}GEP$) and SCLC transcriptional subtypes were assessed as correlates of survival. **Methods:** Patients (pts) eligible for this analysis of KEYNOTE-604 had previously untreated ES-SCLC with evaluable pretreatment tumor samples. TMB was assessed by whole-exome sequencing (WES) of tumor and matched normal DNA. RNA-seq was used to determine $Tcell_{inf}GEP$ and SCLC transcriptional subtypes (ASCL1, POU2F3, NEUROD1, YAP1, or inflamed). Associations of TMB, $Tcell_{inf}GEP$, and SCLC subtype with OS were analyzed using an adjusted Cox proportional hazards model. 1-sided (pembro + EP) and 2-sided (pbo + EP) *P* values were calculated for TMB and $Tcell_{inf}GEP$ (prespecified $\alpha = 0.05$); 2-sided *P* values were calculated for SCLC subtype (multiplicity-adjusted, $\alpha = 0.10$). Clinical utility was assessed using prespecified cutoffs of ≥175 mut/exome for TMB and the first tertile for $Tcell_{inf}GEP$. Clinical data cutoff date was Dec 2, 2019. **Results:** Of 453 pts randomized in KEYNOTE-604 (ITT), 318 had WES data (pembro + EP, n = 167; pbo + EP, n = 151), and 316 had RNA-seq data (pembro + EP, n = 159; pbo + EP, n = 157). High TMB was positively associated with OS in the pbo + EP group ($P = 0.005$) but not the pembro + EP group ($P = 0.450$). There was a positive association between higher $Tcell_{inf}GEP$ and OS in the pembro + EP ($P = 0.003$) and pbo + EP ($P < 0.005$) groups. SCLC subtypes were not associated with OS in either group (pembro + EP, $P = 0.960$; pbo + EP, $P = 0.999$). Clinical benefit of pembro + EP over pbo + EP was demonstrated for TMB <175 mut/exome, but not for TMB ≥175 mut/exome. Pembro + EP benefit over pbo + EP was consistent across $Tcell_{inf}GEP$ subgroups. **Conclusions:** In this exploratory analysis of biomarker subgroups of KEYNOTE-604, TMB and SCLC subtypes were not associated with OS in the pembro + EP group in pts with ES-SCLC. While $Tcell_{inf}GEP$ was positively associated with OS in both treatment groups, no additional OS benefit was observed with pembro + EP. Further research is warranted to better identify predictive biomarkers to immunotherapy. Clinical trial information: NCT03066778. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

		n	Median OS (95% CI), mo	HR (95% CI)
TMB <175 mut/exome	Pembro + EP	87	10.2 (8.5–14.4)	0.60 (0.43–0.85)
	Pbo + EP	73	7.7 (6.6–9.3)	
TMB ≥175 mut/exome	Pembro + EP	80	12.3 (8.3–15.5)	1.02 (0.72–1.45)
	Pbo + EP	78	12.0 (9.8–13.9)	
$Tcell_{inf}GEP$ <1st tertile	Pembro + EP	49	8.5 (8.1–12.5)	0.74 (0.49–1.11)
	Pbo + EP	56	7.9 (6.5–9.8)	
$Tcell_{inf}GEP$ ≥1st tertile	Pembro + EP	110	13.1 (9.7–17.5)	0.77 (0.56–1.06)
	Pbo + EP	101	10.6 (8.2–12.9)	

8504 **Oral Abstract Session**

SWOG S1929: Phase II randomized study of maintenance atezolizumab (A) versus atezolizumab + talazoparib (AT) in patients with SLFN11 positive extensive stage small cell lung cancer (ES-SCLC).

Nagla Fawzy Abdel Karim, Jieling Miao, Karen L. Reckamp, Carl Michael Gay, Lauren Averett Byers, Yingqi Zhao, Mary Weber Redman, Daniel R. Carrizosa, Wei-Lien Wang, William J. Petty, Kathan Mehta, Bryan A. Faller, Edem S. Agamah, Samer S. Kasbari, Rajini Katipamula Malisetti, Atul Kumar, John Schallenkamp, Krishna Chaitanya Alluri, Jhanelle Elaine Gray, Karen Kelly; Inova Schar Cancer Institute, University of Virginia, Fairfax, VA; SWOG Statistical Center, Fred Hutchinson Cancer Research Center, Seattle, WA; Cedars-Sinai Medical Center, Los Angeles, CA; Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; University of Texas MD Anderson Cancer Center, Houston, TX; SWOG Statistics and Data Management Center, Fred Hutchinson Cancer Center, Seattle, WA; Levine Cancer Institute, Charlotte, NC; Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX; Wake Forest College, Winston-Salem, NC; Independent Physician Researcher, Ocean Springs, MS; Missouri Baptist Medical Center, Saint Loius, MO; Southern Illinois University, Springfield, IL; Southeastern Medical Oncology Center, Goldsboro, NC; Minnesota Oncology Hematology PA - Coon Rapids, Minneapolis, MN; University of New Mexico Comprehensive Cancer Center, Albuquerque, NM; Billings Clinic, Billings, MT; St. Luke's Cancer Institute, Boise, ID; Moffitt Cancer Center, Tampa, FL; UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: In unselected patients (pts) with extensive-stage small cell lung cancer (ES-SCLC), the addition of immune checkpoint inhibitors (ICI) to chemotherapy resulted in a modest improvement in OS. In a retrospective analysis of a study with veliparib (PARP inhibitor [PARPi]) and temozolomide in patients with SCLC, Schlafen-11 (SLFN11) predicted PFS and OS benefit for the addition of PARPi. We evaluated whether the addition of PARPi (talazoparib) to standard-of-care maintenance ICI (atezolizumab) following frontline chemoimmunotherapy improved outcomes in pts with SLFN11-positive ES-SCLC. **Methods:** Participants with ES-SCLC expressing SLFN11 (H-score $\geq$ 1, evaluated centrally at MDACC) were randomized to maintenance atezolizumab (A) versus atezolizumab plus talazoparib (AT) following frontline chemotherapy and A. Randomization was stratified by Zebrod PS (0-1 vs 2) and use of consolidation thoracic radiation. The primary endpoint was PFS, and secondary endpoints included ORR, OS, and toxicity. The primary analysis was done using a 1-sided 10% level stratified log-rank test. Target sample size was 94 pts. **Results:** From June 2020 to December 2022, 309 pts were screened, of which 204 of 259 (79%) with evaluable tissue were SLFN11 positive, and 106 were randomized (52 A, 54 AT). Median follow up time is 5 months. Median age was 67 (45-84); 51 (48%) were females; 94 (89%) were white,102 (96%) were PS 0-1, and 26 (25%) had radiation prior to randomization. With 80 PFS events reported, PFS was significantly improved with AT (hazard ratio [80% CI]: 0.70 [0.52-0.94]; p = 0.056). Median PFS was 2.8 months (80% CI 2.0-2.9) for A and 4.2 months (80% CI 2.8-4.7) for AT. OS was not different (hazard ratio [80% CI]: 1.17 [0.80-1.71]; p = 0.30). Median OS was 8.5 months (80 % CI 7.4-12.7) for A and 9.4 months (80% CI 8.1-14.2) for AT. ORR was 16% (5/32, 80% CI 8-27%) for A and 12% (4/34, 80% CI 5-22%) for AT. Grade 3 or greater treatment related non-hematological adverse events (AEs) occurred in 13% pts in A and 15% in AT. Hematological AEs occurred 4% in A compared to 50% pts in AT (Expected for T) ($p < 0.001$). There were no treatment related grade 5 events. One participant on AT experienced grade 3 febrile neutropenia. The majority of grade 3 AEs were due to anemia (2% in A and 37% in AT). Only three pts discontinued treatment due to toxicity (2 in A and 1 in AT). **Conclusions:** This study met its primary endpoint demonstrating that maintenance AT improved PFS in SLFN11-selected patients with ES-SCLC. Hematologic toxicity was increased with AT as expected, with majority being grade 3 anemia. This study demonstrates the feasibility of conducting biomarker selected trials in SCLC, paving the way for future evaluation of novel therapies in selected SCLC populations. Clinical trial information: NCT04334941. Research Sponsor: U.S. National Institutes of Health; Genentech, Inc; NIH/NCI grants U10CA180888, U10CA180819, U10CA180820, U10CA180821; in whole or in part by funding from the Biomarker, Imaging, & QOL Studies Funding Program (BIQSFP) awarded by the National Cancer Institute; and in part by Genentech, a member of Roche Group. U01 CA213273, R01 CA207295, P50 CA070907.The University of Texas MD Anderson Cancer Center Lung Cancer Moonshot Program. The Andrew Sabin Family Fellowship.

LBA8505 **Oral Abstract Session**

IND227 phase III (P3) study of cisplatin/pemetrexed (CP) with or without pembrolizumab (pembro) in patients (pts) with malignant pleural mesothelioma (PM): A CCTG, NCIN, and IFCT trial.

Quincy S. Chu, Maria Carmela Piccirillo, Laurent Greillier, Federica Grosso, Giuseppe Lo Russo, Marie Florescu, Manlio Mencoboni, Penelope Ann Bradbury, Alessandro Morabito, Fabiana Letizia Cecere, Sara Delfanti, Arnaud Scherpereel, Myriam Locatelli-Sanchez, Gerard Zalcman, David E Dawe, Joana Sederias, Scott A. Laurie, Christopher W. Lee, Wei Tu, Lesley Seymour; Cross Cancer Institute, Edmonton, AB, Canada; Istituto Nazionale Tumori, IRCCS, Fondazione G.Pascale, Naples, Italy; Assistance Publique Hôpitaux de Marseille (AP-HM), Marseille, France; Mesothelioma and Rare Cancer Unit, Azienda Ospedaliera SS Antonio e Biagio e Cesare Arrigo, Alessandria, Italy; Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; CHUM, Montréal, QC, Canada; AZ Ospedaliera Villa Scassi, Genova, GE, Italy; Princess Margaret - University Health Network, Toronto, ON, Canada; National Cancer Institute of Naples, Napoli, Italy; Istituto Nazionale dei Tumori Regina Elena, Roma, Italy; University Hospital of Lille, Lille, France; Lyon URCOT, Pierre-Bénite, France; Université Paris Cité, Thoracic Oncology Department & CIC Inserm 1425, Hôpital Bichat Claude Bernard, AP-HP.Nord, Paris, France; CancerCare Manitoba, Winnipeg, MB, Canada; Canadian Cancer Trials Group, Queen's University, Kingston, ON, Canada; Ottawa Hospital Cancer Centre, University of Ottawa, Ottawa, ON, Canada; BC Cancer Surrey, Surrey, BC, Canada

The full, final text of this abstract will be available at meetings.asco.org on the day of presentation and in the online supplement to the June 10, 2023, issue of the *Journal of Clinical Oncology*.

8506 **Oral Abstract Session**

Efficacy, cellular and molecular determinants of PD-1 checkpoint inhibition in relapsed mesothelioma.

Dean Anthony Fennell, Sean Ewings, Kayleigh Hill, Charlotte Poile, Essa Baitei, Zisen Zhou, James Harber, Tamihiro Kamata, Hongji Yang, Joanna Dzialo, Daniel Faulkner, Christian H.H Ottensmeier, Sarah Danson, Nicola Steele, Kim Mallard, Peter Wells-Jordan, Catherine Jane Richards, Min Zhang, Jason Lester, Gareth Owen Griffiths, CONFIRM investigators; University of Leicester and Leicester University Hospitals, Leicester, United Kingdom; University of Southampton, Southampton, United Kingdom; University of Leicester, Leicester, United Kingdom; Harry Perkins Institute of Medical Research, The University of Western Australia Centre for Medical Research, Perth, Australia; University of Liverpool, Liverpool, United Kingdom; Weston Park Hospital, Sheffield, Sheffield, United Kingdom; Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; University of Southampton Clinical Trials Unit, Southampton, United Kingdom; Leicester Royal Infirmary, Leicester, United Kingdom; Novogene, Beijing, China; South West Wales Cancer Centre, Swansea, United Kingdom; University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom

Background: Leveraging adaptive immunity to control mesothelioma is now a standard approach, however the factors that underpin clinical response are poorly understood. Here we report the final analysis of the CONFIRM trial (NCT03063450), a double-blind phase III randomized study of the PD-1 inhibitor nivolumab (N) versus placebo (P) in patients (pts) with unresectable mesothelioma. Genomic, transcriptomic and multiplex spatial phenotypic correlates were explored in mesotheliomas exhibiting either partial response or progressive disease as their best outcome. **Methods:** Pts with relapsed pleural or peritoneal mesothelioma with ECOG performance status 0–1 were randomized 2:1 to N (3 mg/kg) or P once every 2 weeks until progression, or a maximum of 12 months. Pts were stratified by epithelioid (E) vs non-epithelioid (NE) histology. Co-primary endpoints were progression-free survival (PFS) and overall survival (OS); key secondary endpoints included best overall response, safety and tolerability. PD-L1 tumour proportion score (TPS, Dako22C3) was evaluated. To decipher correlates response to N, blinded multi-omic analysis was conducted in a subset of responders (R, n=16) versus progressors (NR, n=13). Whole exomes (WES) and transcriptomes were sequenced, with immune landscapes profiled by 19x depth 4-panel multiplex immunofluorescence. Acquired resistance was explored by WES in a biopsied responder at the time of progression. **Results:** Between April 2017-March 2020, 332 pts were randomised to N (n=221) or P (n=111). Median follow up was 37.2m. Baseline characteristics were balanced between arms. Histology: E 88.3%, 3rd line or greater 69.9%. PFS was longer for N vs P (events=324; median, 2.9 vs 1.6 months; HR 0.65; 95% CI, 0.51 – 0.82; $P<0.001$). Crossover from P was 18.0% (due to widespread availability of N during the covid19 pandemic). OS curves crossed at 32m; 9.5 vs 6.8 months; HR, 0.81; 95% CI, 0.64 – 1.04; $P=0.096$). Grade 3-4 treatment-related toxicity occurred in 20.4% vs 7.2% of pts; discontinuation occurred in 13.6% (N) versus 9.9%. PD-L1 TPS was not predictive of PFS or OS. The R-subgroup had longer PFS versus NR (319 versus 30 days, Hazard ratio, HR 0.02, $p<0.001$) and OS (670 vs 122 days HR 0.19, $p<0.001$). The R-group were enriched for BAP1 inactivation, CD8+ T-cell infiltration, T cell co-stimulation, cytolytic activity and mature tertiary lymphoid structures (TLSs). Conversely, the NR group had significantly more aneuploidy (notably uniparental disomy, UPD), and enrichment of epithelial mesenchymal transition, TGF beta signalling, and E2F transcription. Acquired resistance was associated with increased aneuploidy (UPD) and subclonal evolution including a new DNMT3A c2204A>G mutation. **Conclusions:** N met its co-primary endpoint of PFS with responding mesotheliomas harbouring a TLS enriched, inflamed tumour microenvironment and stable genome compared to non-responders. Clinical trial information: NCT03063450. Research Sponsor: Stand Up to Cancer, Cancer Research UK; BMS.

8507 **Oral Abstract Session**

Association of somatic mutations and histologic subtype/grade on prognosis and PD-L1 expression in mesothelioma.

Allen Zhu, Aliya N. Husain, Andrew Hermina, Owen Mitchell, Jeffrey S. Mueller, Michael William Drazer, Hedy L. Kindler, Jung Woo Kwon; University of Chicago, Chicago, IL; Section of Hematology/Oncology, Department of Medicine, The University of Chicago Medicine, Chicago, IL; University of Chicago Bucksbaum Institute for Clinical Excellence, Chicago, IL

Background: Mesothelioma includes epithelioid, sarcomatoid, and biphasic histologic subtypes, and the epithelioid subtype is histologically graded based on mitotic count and nuclear atypia. Correlation between the most common somatic mutations (*BAP1*, *NF2*, *TP53*, *CDKN2A*), and overall survival is poorly understood. High PD-L1 expression is a poor prognostic factor for survival and may be a predictor of response to immunotherapy. Few studies have evaluated the relationships between these factors. **Methods:** We performed a retrospective study in 217 patients with pleural, peritoneal and bicavitary mesothelioma as part of an IRB-approved biobanking protocol. Histologic subtype, grade of epithelioid mesothelioma, tumor stage, and overall survival time were determined. Next-generation DNA sequencing (NGS) was used to identify the prevalence of somatic mutations. PD-L1 immunohistochemistry was obtained on 184 samples and quantified as percentage of tumor cells. Histologic subtype, nuclear grade, clinical stage, PD-L1 expression, survival time, and the prevalence of each mutation were compared using chi-squared, Kruskal-Wallis, or Cox proportional hazard tests. All p-values were determined in R version 4.2.0 using a two-sided alpha error of 0.05 to mark statistical significance. **Results:** The most frequent somatic mutations were found in *BAP1* (99/217, 45.6%), *CDKN2A* (47/217, 21.7%), *TP53* (37/217, 17.1%), and *NF2* (31/217, 14.3%). Patients with *CDKN2A*-mutated mesothelioma experienced shorter survival (p=0.032). *TP53* mutations were associated with higher nuclear grade (p=0.015), higher mitotic count (p=0.013), and greater nuclear atypia (p=0.015). *TP53* mutations were more prevalent in pleural than peritoneal mesothelioma (p=0.016) and in tumors without lymph node metastasis (p=0.05). As expected, patients with epithelioid mesothelioma had superior overall survival (p=0.02) and their tumors had lower PD-L1 expression (p=0.007) than either sarcomatoid or biphasic mesotheliomas. Neither PD-L1 expression nor mutations in *BAP1*, *NF2*, *CDKN2A*, or *TERT* were associated with nuclear grade, atypia, or mitotic count. No association was found between *BAP1* or *NF2* mutations and tumor stage, lymph node metastasis, or PD-L1 expression. **Conclusions:** To our knowledge, this is the first study of this scale to correlate PD-L1 expression, somatic mutation data, histologic features, and survival in mesothelioma patients. The most significant findings were that patients with *CDKN2A* mutations had shorter survival and *TP53* mutations, which were more prevalent in pleural mesotheliomas, were associated with higher nuclear grade, higher mitotic count, and greater nuclear atypia. An ongoing analysis evaluates the contribution of germline mutations, which occurred in a significant proportion (15.7%) of this mesothelioma patient cohort. Research Sponsor: Supported, in part, by John D. Cooney and the firm of Cooney and Conway through the University of Chicago Comprehensive Cancer Center.

8508 **Clinical Science Symposium**

Phase II trial of neoadjuvant osimertinib for surgically resectable *EGFR*-mutated non-small cell lung cancer.

Jacqueline V. Aredo, Anatoly Urisman, Matthew A. Gubens, Claire Mulvey, Greg M. Allen, Julia K. Rotow, Daniel Lucas Kerr, Turja Chakrabarti, Bianca Bacaltos, Megan Gee, Kirk Jones, Dara L. Aisner, Tejas Patil, Erin Lynn Schenk, Trever G. Bivona, Jonathan W. Riess, Melissa Coleman, Johannes Ruediger Kratz, David Jablons, Collin M. Blakely; University of California, San Francisco, San Francisco, CA; Dana-Farber Cancer Institute, Boston, MA; The University of California, San Francisco, San Francisco, CA; University of Colorado, Aurora, CO; University of Colorado Comprehensive Cancer Center, Aurora, CO; University of Colorado - Anschutz Medical Campus, Aurora, CO; UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: Osimertinib is a third-generation EGFR tyrosine kinase inhibitor (TKI) effective in treating advanced *EGFR*-mutated non-small cell lung cancer (NSCLC). Adjuvant osimertinib significantly decreases disease recurrence in stage IB-IIIA *EGFR*-mutated NSCLC. However, the benefit of neoadjuvant osimertinib prior to surgical resection remains unknown. **Methods:** This was a multi-institutional phase II trial of neoadjuvant osimertinib for patients with surgically resectable stage I-IIIA (AJCC V7) *EGFR*-mutated (L858R or exon 19 deletion) NSCLC (NCT03433469). Patients received osimertinib 80 mg orally daily for up to two 28-day cycles prior to surgical resection. The primary endpoint was major pathological response (mPR) rate ($\leq$10% residual viable tumor). 27 evaluable patients provide 87% power to detect a mPR rate of 50% with $\alpha = 0.05$. Secondary endpoints included pathological response (PR) rate ($\leq$50% residual viable tumor), pathological complete response (pCR) rate, unconfirmed objective response rate (ORR), rate of lymph node downstaging, unanticipated delays to surgery, surgical complication rate, disease-free survival (DFS), overall survival (OS), safety, and tumor mutational profile. **Results:** A total of 27 patients with early-stage (8 stage IA/B, 10 stage IIA/B, 9 stage IIIA) *EGFR*-mutated (11 exon 19 del, 16 L858R) NSCLC were treated with neoadjuvant osimertinib for a median 56 days prior to surgical resection. 24 (89%) patients underwent subsequent surgery; 3 (11%) patients were converted to definitive chemoradiotherapy. The mPR rate was 15% (4/27 patients) by intention-to-treat analysis. The PR rate was 48% (13/27). No pCR's were observed. Partial responses by radiography were observed in 52% (14/27) of patients and stable disease in 44% (12/27) of patients. Lymph node downstaging was achieved in 44% (4/9) of patients with positive lymph nodes. Median DFS after surgical resection was 32 months (95% CI 26-not reached) with a median follow-up of 11 months. OS data are immature. Significant adverse events occurred in 3 patients with grade 2 (G2) dyspnea, grade 3 (G3) pulmonary embolism, and G3 atrial fibrillation. One patient developed G2 treatment-related pneumonitis that resolved without steroids. Perioperative complications occurred in 38% (9/24) of patients; most involved rapidly reversible postoperative G2 atrial fibrillation (6/9) unrelated to study drug. Tumors were evaluable for genetic alterations from 16 patients. 4/6 patients who did not achieve a PR had tumors that harbored loss of function mutations in *RBM10* as compared to 0/10 patients who achieved a PR ($p < 0.01$). **Conclusions:** Neoadjuvant osimertinib in surgically resectable *EGFR*-mutated NSCLC achieved a 15% mPR, which did not meet the primary endpoint. Treatment was safe and may induce pathological responses and lymph node-downstaging of disease. Co-mutations in *RBM10* may limit response. Clinical trial information: NCT03433469. Research Sponsor: AstraZeneca.

8509 **Rapid Abstract Session**

Pembrolizumab and ramucirumab neoadjuvant therapy for PD-L1-positive stage IB-IIIA lung cancer (EAST ENERGY).

Keiju Aokage, Yoshihisa Shimada, Kiyotaka Yoh, Masashi Wakabayashi, Miki Fukutani, Hideki Furuya, Kotaro Nomura, Tomohiro Miyoshi, Kenta Tane, Joji Samejima, Shogo Kumagai, Shohei Koyama, Hiroyoshi Nishikawa, Tetsuro Taki, Takuo Hayashi, Jun Matsubayashi, Genichiro Ishii, Norihiko Ikeda, Masahiro Tsuboi; Department of Thoraci surgery, National Cancer Center Hospital East, Kashiwa, Japan; Division of Thoracic and Thyroid Surgery, Tokyo Medical University, Tokyo, Japan; Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan; Division for the Promotion of Drug and Diagnostic Development, National Cancer Center Hospital East, Kashiwa, Japan; Clinical Research Support Office, National Cancer Center Hospital East, Kashiwa, Japan; Department of Thoracic Surgery, National Cancer Center Hospital East, Kashiwa, Japan; Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Kashiwa, Japan; Division of Cancer Immunology, Exploratory Oncology Research and Clinical Trial Center, National Cancer Center Hospital East, Kashiwa, Japan; Division of Cancer Immunology, Exploratory Oncology Research & Clinical Trial Center, National Cancer Center, Chiba, Japan; Department of Pathology and Clinical Laboratories, National Cancer Center Hospital East, Kashiwa, Japan; Department of Human Pathology, Juntendo University School of Medicine, Tokyo, Japan; Division of Anatomic Pathology Tokyo Medical University, Tokyo, Japan; Tokyo Medical University, Tokyo, Japan

Background: Neoadjuvant treatments for resectable non-small cell lung cancer (NSCLC) using novel combination therapies are being developed. Angiogenesis inhibitors have been reported to modify tumor immunity, and the efficacy and safety of treatments added to immune checkpoint inhibitors (ICIs) have been investigated in advanced NSCLC. In this multi-institutional phase II study, we evaluated the efficacy and feasibility of neoadjuvant therapy with pembrolizumab and ramucirumab, a direct vascular endothelial growth factor (VEGF) receptor-2 antagonist, followed by surgery, in patients with PD-L1 positive, clinical stage IB-IIIA NSCLC. **Methods:** Patients (aged ≥20) with pathologically proven NSCLC harboring PD-L1 expression ≥1% (22C3), resectable clinical stage IB-IIIA NSCLC, and performance status of 0 to 1 were eligible. Patients received two cycles of pembrolizumab (200 mg/body) and ramucirumab (10 mg/kg) every three weeks. Surgery was scheduled 4-8 weeks after the last dose. The primary endpoint was to determine the major pathologic response (MPR) rate. The sample size was calculated based on the exact binomial distribution, considering a threshold MPR rate of 20%, an expected MPR rate of 45%, a one-side alpha of 5%, and a desired power of 80%. **Results:** A total of 24 eligible patients, with a median age of 75 years (range 50-78), were enrolled between July 2019 and April 2022; 18 patients were male. The histological subtype was adenocarcinoma in 12 patients, and the clinical stage was IB, IIA, IIB, and IIIA in 1, 4, 9, and 10 patients, respectively. PD-L1 was ≥50% in nine patients (37.5%). The MPR rate by the blinded independent central review of three pathologists was 50.0% (90% confidence interval, 31.9-68.1%); therefore, the primary endpoint was met. Six of the 12 patients who achieved MPR showed pathological complete response. One patient developed pneumonia before neoadjuvant treatment and one patient showed progressed disease after neoadjuvant treatment. Grade 3 adverse events (AEs) occurred in nine of 24 patients (37.5%) during the protocol treatment. Postoperative complications of grade 3 AEs, including postoperative hematoma, pulmonary fistula, and intraoperative arterial injury, were observed in three patients. Immune-related AEs related to protocol treatment were thyroid dysfunction, acute tubulointerstitial nephritis, and hepatic dysfunction in three, two, and two patients, respectively; however, no grade 3 or high AEs were observed. Twenty-one patients achieved R0 resection and one patient underwent R1 resection. There were no wound-healing adverse events of concern due to the anti-VEGF action of ramucirumab. **Conclusions:** The results of this study demonstrated that this new neoadjuvant combination of ICI and anti-VEGF agent (pembrolizumab and ramucirumab) is feasible and showed encouraging results. Clinical trial information: NCT04040361. Research Sponsor: MSD and Eli Lilly.

8510 **Rapid Abstract Session**

Preliminary results from the Female Asian Nonsmoker Screening Study (FANSS).

Elaine Shum, Wenyuan Li, Lecia V. Sequist, Sai-Hong Ignatius Ou, Judith D. Goldberg, Abraham Chachoua, Kwok-Kin Wong; NYU Langone Perlmutter Cancer Center, New York, NY; NYU Perlmutter Cancer Center, New York, NY; Massachusetts General Hospital, Boston, MA; Chao Family Comp Cancer Ctr, Orange, CA; NYU Grossman School of Medicine, Department of Population Health, Division of Biostatistics, New York, NY

Background: Lung cancer (LC) is the leading cause of cancer death in Asian Americans and unfortunately the majority are diagnosed at advanced or late stages. In Asia, approximately 60-80% of female LC patients are never smokers. Current screening in the U.S. with low-dose CT (LDCT) Chest scans is offered only to current or former smokers based on the National Lung Screening Trial (NLST). The LC detection rate in NLST was 1.1%. The TALENT study, a LC screening study for high-risk nonsmokers in Taiwan reported a LC detection rate of 2.6% which included invasive adenocarcinoma (adeno), adeno in situ, minimally invasive adeno and adenosquamous carcinoma. Invasive adeno detection rate was 1.52%. We are conducting the ongoing FANSS in the U.S. to screen female Asian nonsmokers with LDCT Chest scans to evaluate the feasibility of a LC screening program in this population. We report preliminary results here. **Methods:** This is an IRB-approved, prospective, multicenter study (NYU, MGH, UCI). Inclusion criteria are women, age between 40-74 years old (yo), never smoked or smoked $<$100 cigarettes in one's lifetime and identify as from Asian descent (report ancestry or race from the continent of Asia). Participants (pts) with history of LC or treatment of any cancer $<$5 years ago are excluded. Following informed consent, eligible pts undergo a shared-decision making discussion prior to obtaining a baseline LDCT Chest scan, read according to Lung-RADS 1.1 with plan for annual LDCT for two additional years. A plasma-based assay to analyze cell-free DNA (cfDNA) fragments for early detection of cancer by Delfi Diagnostics (Baltimore, MD) is sent at the time of each scan. A questionnaire regarding ethnicity, family history and environmental exposures is collected at baseline. **Results:** From 3/1/21 to 1/15/23, 222 pts signed consent and 201 had a baseline LDCT at NYU. Age range was 40-74 yo and median age of 56.8 yo. 83 (41%) reported a family history of LC. Of 201 pts who completed a baseline LDCT, 87 (43%) were Lung-RADS 1, 101 (50%) were Lung-RADS 2, 6 (3%) were Lung-RADS 3 and 7 (3.5%) were Lung-RADS 4. 5 pts with Lung-RADS 3 and 3 pts with Lung-RADS 4 have solid, subsolid or groundglass nodules $>$6mm that remain in close follow-up. 3 pts were diagnosed with invasive lung adeno for a LC detection rate of 1.5%; 2 are stage IIB and 1 is stage IIIC. All pts were surgically resected, EGFR mutation positive and are receiving adjuvant osimertinib. Analysis of the cfDNA fragmentation profiles is ongoing. **Conclusions:** Our data shows that LC screening in Asian female nonsmokers is feasible. Preliminary results demonstrate an invasive adeno detection rate comparable with TALENT and higher than in NLST. Early detection brings new meaning with the recent FDA approval for adjuvant targeted therapy in early stage LC. The expansion of LC screening guidelines to other high-risk populations warrants further attention. FANSS is continuing to accrue at additional U.S. sites this year. Clinical trial information: NCT05164757. Research Sponsor: NYU Lung Cancer Center; Delfi Diagnostics.

8511 **Rapid Abstract Session**

Bemcentinib and pembrolizumab in patients with relapsed mesothelioma: MIST3, a phase IIa trial with cellular and molecular correlates of efficacy.

Matthew G Krebs, Amy Branson, Shaun Barber, Charlotte Poile, Amy King, Alastair Greystoke, Sam Moody, Luke Nolan, Molly Scotland, Liz Darlison, Amrita Bajaj, Bruno Morgan, Cassandra Brookes, Peter Wells-Jordan, Catherine Jane Richards, Anne L. Thomas, Dean Anthony Fennell; The University of Manchester and The Christie NHS Foundation Trust, Manchester, United Kingdom; University of Leicester, Leicester, United Kingdom; University Hospitals of Leicester NHS Trust, Leicester, United Kingdom; Northern Centre for Cancer Care, University of Newcastle, Newcastle-upon-Tyne, United Kingdom; The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, United Kingdom; University Hospital Southampton, Hampshire, United Kingdom; University Hospitals Leicester, Leicester, United Kingdom; Leicester Clinical Trials Unit - University of Leicester, Leicester, United Kingdom; Leicester Royal Infirmary, Leicester, United Kingdom; University of Leicester and University Hospitals of Leicester, Leicester, United Kingdom

Background: AXL receptor tyrosine kinase is a key facilitator of immune escape and drug resistance, conferring a more aggressive phenotype. Targeting the PD1-PDL1 axis has demonstrated significant efficacy in patients with relapsed malignant mesothelioma (MM), however, responses are only observed in a fraction of patients. Preclinical studies suggest that dual PD1 and AXL inhibition is synergistic. We developed a multi-centre, molecularly stratified phase IIa trial to evaluate the efficacy of AXL/PD-1 inhibition with bemcentinib (Bem)/pembrolizumab (Pem) and to uncover cellular and molecular determinants of efficacy as arm 3 of the Mesothelioma Stratified Therapy umbrella trial (NCT03654833, MiST3). **Methods:** Patients with pleural mesothelioma were enrolled. Key inclusion factors were ECOG performance status (PS) 0-1, prior platinum-based chemotherapy (maximum of 2 prior lines allowed), evidence of disease progression with measurable disease by CT (Modified RECIST 1.1), and adequate haematological/organ function. All patients received 200mg Pem IV q3W in combination with Bem, loading dose 400mg PO for the first 3 days and then 200mg od q3w. Primary endpoint was disease control rate at 12 weeks (DCR12w). Secondary endpoints: DCR at 24 weeks (DCR24w), best objective response rate (ORR) and toxicity (NCI CTCAE 4.03). Pre-treatment fresh biopsy was required to enable multiplex immunofluorescence, whole exome and RNA transcriptome sequencing. Gut microbiome 16s RNA sequencing also was undertaken at baseline (n=21). **Results:** Between September 2020 and March 2022, 26 patients with MM started treatment and received at least one dose of Pem Bem. Median age was 72.5 (range, 55-85) years, 88% were male 12% were female, Histology: 88% epithelioid, 8% Biphasic, 4% Sarcomatoid, ECOG PS1 77%, $>$ 1 prior systemic therapy 35%. The median cycles of Pem Bem was 4 (IQR, 2-11). The DCR12w was 46.2% (12/26) (90% confidence limit (CI), 29.2% –63.4 %;), ORR was 15.4% (95%CI, 4.4- 34.9%; all PR)) with stable disease in 57.7% (36.9 – 76.6%); DCR24w was 38.5% (10/26) (95%CI, 20.2% – 59.4%). Adverse events (any cause): $\geq$ grade 3 toxicities affected 38% of pts and there were no treatment-related deaths. The most frequent adverse events recorded were fatigue in 12/26 (46%) patients and nausea in 11/26 (42%) patients. **Conclusions:** MiST3 met its primary endpoint and warrants further evaluation. Analysis of the cellular and molecular correlates of response are ongoing and will be presented. Clinical trial information: NCT03654833. Research Sponsor: Asthma and Lung UK and Victor Dahdaleh Foundation; Bergen Bio.

8512 **Poster Discussion Session**

Final survival data from a randomized phase II trial comparing high-dose with standard-dose twice-daily (BID) thoracic radiotherapy (TRT) in limited stage small-cell lung cancer (LS SCLC).

Bjorn H. Henning Gronberg, Kristin Toftaker Killingberg, Øystein Fløtten, Maria Moksnes Bjaanæs, Tesfaye Madebo, Tine Schytte, Seppo Wang Langer, Signe Leonora Risumlund, Nina Helbekkmo, Kirill Neumann, Odd Terje Brustugun, Øyvind Yksnøy, Georgios Tsakonas, Jens Engleson, Sverre Fluge, Thor Naustdal, Liv Ellen Giske, Jan Nyman, Tarje Onsøien Halvorsen; Norwegian University of Science and Technology (NTNU), Trondheim, Norway; Department of Thoracic Medicine, Haukeland University Hospital, Bergen, Norway; Department of Oncology, Oslo University Hospital, Oslo, Norway, Oslo, Norway; Stavanger University Hospital, Stavanger, Norway; Department of Oncology, Odense University Hospital, Odense, Denmark; Department of Oncology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; Department of Oncology, Rigshospitalet, Copenhagen, Denmark; Department of Oncology, University Hospital of North Norway, Tromsø, Norway; Department of Pulmonology, Akershus University Hospital, Lørenskog, Norway; Section of Oncology, Drammen Hospital, Vestre Viken HF, Drammen, Norway; Department of Pulmonology, Ålesund Hospital, Ålesund, Norway; Department of Oncology, Karolinska University Hospital, Stockholm, Sweden; Lund University Hospital, Lund, Sweden; Department of Pulmonology, Haugesund Hospital, Haugesund, Norway; Department of Medicine, Levanger Hospital, Levanger, Norway, Levanger, Norway; Department of Oncology, Innlandet Hospital Trust , Gjøvik, Gjøvik, Norway; Dep. of Oncology, Sahlgrenska University Hospital, Göteborg, Sweden; Department of Oncology, St. Olavs Hospital, Trondheim, Norway

Background: Concurrent chemotherapy and TRT is standard treatment of LS SCLC. BID TRT of 45 Gy/30 fractions is the most recommended schedule. Trials report 5-year survival rates of up to 36%, illustrating that some are cured but also need for better treatment. Many treatment failures are due to relapses within TRT fields, and it has been proposed that higher TRT doses might improve local control and consequently survival. However, high-dose once-daily (QD) TRT of 66-70 Gy do not prolong survival. We investigated whether high-dose BID TRT of 60 Gy/40 fractions was tolerable and improved survival compared with the established 45 Gy schedule (NCT02041845). Primary analyses presented at ASCO 2020 showed that the trial was highly positive for the primary endpoint, 2-year survival (60 Gy: 74.2%, 45 Gy: 48.1%, OR 3.09 [95% CI 1.62-5.89]; p=0.0005). We now present updated and final survival data. **Methods:** Patients ≥18 years with PS 0-2, confirmed SCLC, LS according to the IASLC definition after PET CT staging received 4 courses of platinum/etoposide and were randomized to receive 60 Gy or 45 Gy to PET CT positive lesions. TRT started concurrently with the 2nd chemotherapy course. Responders were offered QD prophylactic cranial irradiation of 25-30 Gy. All patients were followed for 5 years or until death. **Results:** 170 eligible patients were randomized at 22 Scandinavian hospitals from 2014-2018 (60 Gy: n=89, 45 Gy: n=81). Median age was 65, 31.2% were ≥70 years, 57.1% women, 89.4% had PS 0-1, 83.5% stage III disease, 7.6% pleural effusion and 20.0% ≥5% weight loss last three months before enrollment. Baseline patient and disease characteristics and TRT planning target volumes were well balanced between treatment arms. Completion rates of chemotherapy (60 Gy: 92.1%, 45 Gy: 87.7%) and TRT (60 Gy: 96.6%, 45 Gy: 91.4%) were similar. Patients on the high-dose arm did not experience more grade 3-4 esophagitis (60 Gy: 21.2%, 45 Gy: 18.2%; p=0.83) or pneumonitis (60 Gy: 3.4%, 45 Gy: 0.0%; p=0.39), other grade 3-4 toxicity or treatment related deaths. The 60 Gy group had numerically longer PFS (median PFS 60 Gy: 18.6 months [95% CI 11.6-25.6], 45 Gy: 10.9 months [95% CI 8.7-13.2], HR 0.76 [95% CI 0.53-1.08]; p=0.13). Results for the primary endpoint remain unchanged. The higher TRT dose significantly prolonged survival (median OS 60 Gy: 43.5 months [95% CI 30.4-56.6], 45 Gy: 22.6 months [95% CI 17.2-28.0], HR 0.69 [0.48-0.99]; p=0.043) and provided higher 4.5 year survival rate (60 Gy: 41.6% [95% CI 30.4-56.6], 45 Gy: 28.4% [95% CI 18.9-39.5], OR: 1.79 [95% CI 0.95-3.41]). 5-year survival rates will be presented at the meeting. **Conclusions:** Compared with LS SCLC patients who received standard TRT, patients receiving high-dose BID TRT of 60 Gy did not experience more toxicity, had a substantial prolongation of survival and a much higher long term survival rate. Clinical trial information: NCT02041845. Research Sponsor: The Norwegian Cancer Society; Norwegian University of Science and Technology; The Liaison Committee for Education, Research and Innovation in Central Norway.

8514 **Poster Discussion Session**

CRES^{3}T: A single-arm confirmatory trial of S-1 plus cisplatin with concurrent radical-dose radiotherapy followed by surgery for superior sulcus tumor.

Kazuya Takamochi, Kenji Suzuki, Morihito Okada, Seiji Niho, Satoshi Ishikura, Shunsuke Oyamada, Takuhiro Yamaguchi, Hirotoshi Horio, Fumihiro Tanaka, Satoshi Shiono, Tomohiro Haruki, Norihito Okumura, Ichiro Yoshino, Hiroyuki Ito, Hidetaka Uramoto, Masahiro Tsuboi, Advanced Clinical Trial chest surgery Group (ACTG); Department of General Thoracic Surgery, Juntendo University School of Medicine, Tokyo, Japan; Juntendo University School of Medicine, Bunkyo-Ku, Japan; Department of Surgical Oncology, Hiroshima University, Hiroshima, Japan; National Cancer Center Hospital Japan East, Kashiwa, Japan; Division of Radiation Oncology, Tokyo Bay Makuhari Clinic for Advanced Imaging, Cancer Screening, and High-Precision Radiotherapy, Makuhari, Japan; Department of Biostatistics, JORTC Data Center, Tokyo, Japan; Division of Biostatistics, Tohoku University Graduate School of Medicine, Miyagi, Japan; Department of Thoracic Surgery, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan; University of Occupational and Environmental Health, Kitakyushu, Japan; Department of Thoracic Surgery, Yamagata Prefectural Central Hospital, Yamagata, Japan; Division of General Thoracic Surgery, Department of Surgery, Faculty of Medicine, Tottori University, Tottori, Japan; Kurashiki Central Hospital, Kurashiki, Japan; Chiba University Graduate School of Medicine, Chiba, Japan; Division of Thoracic Surgery, Thoracic Oncology, Kanagawa Cancer Center, Yokohama, Japan; Division of Thoracic Surgery, Saitama Cancer Center, Saitama, Japan; Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Chiba, Japan

Background: A multicenter, single-arm, confirmatory trial (CRES^{3}T) was conducted to investigate the efficacy and safety of S-1 plus cisplatin and concurrent radical-dose thoracic radiotherapy (TRT) followed by surgery in patients with superior sulcus tumor (SST). To date, no clinical trials on radical-dose TRT in the induction setting for SST have been conducted. **Methods:** SST was defined as a tumor that directly invades the chest wall including the first rib or more cephalad, subclavian artery, or subclavian vein according to CT or MRI scans. Eligible patients were 20 to 75 years old and had pathologically proven non-small cell lung cancer, performance status of 0–1, and no history of prior treatment. The patients received induction therapy consisting of three cycles of S-1 plus cisplatin with concurrent TRT (66 Gy in 33 fractions) followed by surgery. S-1 was administered orally at 40 mg/m^2 twice per day, on days 1–14 along with an intravenous infusion of cisplatin (60 mg/m^2) on day 1. The treatment cycles were repeated every four weeks. The primary endpoint was the 3-year overall survival (OS) rate, and key secondary endpoints included progression-free survival (PFS) rate, objective response rate (ORR), pathological complete remission (pCR) rate, and toxicity. **Results:** Between June 2014 and March 2019, 61 patients registered and received induction therapy. Pathological diagnoses were 30 adenocarcinoma, 20 squamous cell carcinoma, and 11 others. Radiologically diagnosed tumor invasion sites were the chest wall (n=57), subclavian artery (n=18), and subclavian vein (n=10). One patient with distant metastasis that manifested after starting induction therapy was removed from this study. Forty-nine patients underwent lobectomy and resection of the involved sites. The complete resection rate was 98% (48/49). Median follow-up time was 54 months. The 3-year OS and PFS rates were 73% (95% CI: 60–83%) and 53% (95% CI: 40–65%), respectively. The ORR and pCR rate were 42% (25/60, 95% CI: 29–54%) and 33% (16/49, 95% CI: 20–46%), respectively. Grade (G) 3 or 4 toxicities during induction therapy included neutropenia (28%), anemia (13%), thrombocytopenia (5%), and hyponatremia (8%). Two (3%) cases of pneumonia resulted in death. G3 surgical complications such as supraventricular arrhythmia, chylothorax, pleural effusion, pneumonia, mediastinitis, wound infection, and arm neuropathy developed in one (2%) patient each. One (2%) cardiac arrest on postoperative day 3 resulted in death. **Conclusions:** CRES^{3}T demonstrated that induction therapy using S-1 plus cisplatin and concurrent radical-dose TRT followed by surgery was safe and effective in treating SST. Therefore, this strategy is potentially a new standard treatment for SST. (UMIN: 000014386, jRCT: s031180401.). Clinical trial information: UMIN000014386. Research Sponsor: None.

8516 **Poster Discussion Session**

The prognostic value of patient reported outcomes (PROs) and clinical/demographic variables in the CASPIAN study.

Apar Kishor Ganti, Sukhvinder Johal, Daniel Jackson, Nenad Medic, Kieran Davey, Lance Brannman; University of Nebraska Medical Center, Omaha, NE; AstraZeneca, Cambridge, United Kingdom; AstraZeneca, Gaithersburg, MD

Background: PROs have been shown to predict outcomes in non-small cell lung cancer and, using the FACT-G PRO instrument, in extensive stage small cell lung cancer (ES-SCLC). This study explored the relationships between EORTC QLQ-C30 domains and overall survival (OS) and progression free survival (PFS) in the phase III ES-SCLC CASPIAN trial, with and without adjustments for treatment (tx) and baseline clinical and demographic variables. **Methods:** CASPIAN had 3 treatment arms: durvalumab plus platinum–etoposide; durvalumab plus tremelimumab plus platinum–etoposide; and platinum–etoposide alone. It included the EORTC QLQ-C30, a PRO instrument consisting of 5 functioning scales (physical, role, emotional, cognitive, social), a global health status/quality of life (QoL) scale, 3 symptom scales (fatigue, nausea/vomiting, pain), 5 single item symptom assessments (dyspnea, insomnia, appetite loss, constipation, diarrhea) and a single financial difficulties item. Higher functional and QoL scores indicate better health status/function (anticipated positive OS/PFS associations) while higher symptom and financial difficulty scores represent a greater burden (anticipated negative OS/PFS associations). Baseline PRO scores were pooled across the 3 CASPIAN arms to obtain the most PRO information and used in 3 Cox proportional hazard models for OS and PFS: (A) scores only, (B) scores with a tx category for each CASPIAN arm, and (C) scores with tx categories and other baseline covariates (sex, age [< 65, ≥ 65], ECOG performance status [0, $> = 1$], smoker [Y/N], CNS metastasis [Y/N], race [Asian, non-Asian], stage [III, IV], region [Asia, Europe, North and South America]). Models B and C were stratified by the type of platinum received. Backwards selection found the set of variables most associated with OS and PFS. There was no correction for multiplicity and nominal P-values < 0.05 were used to assess importance. **Results:** The outcomes and models associated with more favorable baseline PRO scale/item scores were: (i) better OS and PFS across all 3 Cox models [physical, role, social, QoL, fatigue, pain]; (ii) better OS [emotional (models A,C), nausea/vomiting (model C), dyspnea (model C)], and (iii) better PFS [emotional (model C), financial difficulties (models A,B,C)]. Among the 90 estimated Cox hazard ratios, 82 had the anticipated directions for OS and PFS with 54/90 of the estimates having $P < 0.05$. In each Cox model, more favorable baseline diarrhea scores were associated with reduced OS. All 15 baseline PRO score domains for OS and 10/15 for PFS were important in the stepwise selection process. **Conclusions:** The results largely indicate that baseline PROs had prognostic value in the CASPIAN trial across different specifications, some including tx and baseline clinical and demographic values. A better understanding of the relationship between tx and PROs may aid tx decisions. Clinical trial information: NCT03043872. Research Sponsor: AstraZeneca.

8518 **Poster Discussion Session**

Phase II study of durvalumab plus olaparib as maintenance therapy in extensive-stage small-cell lung cancer (TRIDENT): Preliminary efficacy and safety results.

Yan Huang, Jun Jia, Qiming Wang, Xianling Liu, Li Zhang; State Key Laboratory of Oncology in South China, Guangzhou, China; Dongguan Key Laboratory of Precision Diagnosis and Treatment for Tumors, Affiliated Dongguan Hospital, Southern Medical University, Dongguan, China; Department of Internal Medicine, Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China; Department of Oncology, The Second Xiangya Hospital, Central South University, Changsha, China; Sun Yat-Sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center of Cancer Medicine, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Sun Yat-sen University, Guangzhou, China

Background: First-line durvalumab in extensive-stage small-cell lung cancer (ES-SCLC) demonstrated significant improvement of OS in phase III CASPIAN trial. PARP inhibitors have the potential to confer antitumor activity, modify tumor immunogenicity, and sensitize tumors to anti-PD-1/PD-L1 therapy. Durvalumab in combination with Olaparib (a PARPi) had clinical activity in relapsed SCLC in a phase I/II study. This phase II study aimed to assess the efficacy and safety of durvalumab plus olaparib as maintenance therapy in patients with ES-SCLC. **Methods:** TRIDENT is a single arm, multicenter, phase II study. Treatment-naive ES-SCLC aged ≥18 with ECOG PS 0-2 were eligible. Durvalumab (1500 mg) was concurrently administered with platinum–etoposide every 3 weeks for 4 cycles, followed by durvalumab 1500 mg every 4 weeks plus olaparib 300 mg twice daily until disease progression or unacceptable toxicity. The primary endpoint was the rate of progression free survival (PFS) at 12 months, the secondary endpoints included progression free survival, objective response rate (ORR) according to RECIST 1.1, duration of response (DoR), overall survival (OS) and safety profile. All patients should provide tumor sample for biomarker analysis (exploratory endpoint). **Results:** Between August 2021 and August 2022, 60 eligible patients were enrolled from 4 sites in China. At data cut-off (Jan 16th, 2023), 18 (30%) patients were still on treatment. The median age was 63 years (range 57-68). The median cycle of durvalumab was 7 (range 1-17), and durvalumab plus olaparib as maintenance therapy was 3.5 (range 1-13). The PFS rate at 6-, 9-, 12-month were 49.7% [95%CI 37.8%-65.4%], 26.3% [95%CI 13.8%-40.3%] and 18% [95%CI 9.3%-34.7%], respectively. ORR was 75% (45/60), the median DoR was 5.0 months [95%CI 3.8-6.5]. With a median follow-up of 10.5 months, the median PFS was 5.8 months [95%CI 4.9-7.7] as calculated from the first cycle of durvalumab plus chemotherapy. The median OS was not reached [95%CI 10-NA]. Of all, treatment emergent adverse event (AE) occurred in 93.3% (56/60) patients, and AEs ≥ grade 3 occurred in 36.7% (22/60) patients. There were no unexpected adverse events identified in this study. There were 5 patients (8.3%) discontinued treatment and 1 death (1.6%) due to AE. Biomarker analysis is still on-going and will be presented in the meeting. **Conclusions:** TRIDENT is the first study to evaluate the efficacy and safety of durvalumab plus olaparib as maintenance therapy in Chinese ES-SCLC patients to date. The preliminary result warrant further investigation of this treatment modality in ES-SCLC. Clinical trial information: NCT05245994. Research Sponsor: This study is sponsored by Sun Yat-sen University Cancer Center; This study is partly supported by AstraZeneca.

8519 **Poster Discussion Session**

Associations between patient-reported nutritional status, survival, and toxicity among patients with limited stage small-cell lung cancer (LS SCLC) in a randomized trial of high-dose, twice-daily (BID) thoracic radiotherapy (TRT).

Evgenia Taranova, Bjorn H. Henning Gronberg, Tarje Onsøien Halvorsen, Kristin Toftaker Killingberg, Marit Slaaen, Marianne Aanerud; University of Bergen, Bergen, Norway; Norwegian University of Science and Technology (NTNU), Trondheim, Norway; Department of Oncology, St. Olavs Hospital, Trondheim, Norway; Sykehuset Innlandet, Hamar, Norway

Background: Up to 1/3 of LS SCLC patients are cured by chemoradiotherapy (CRT), but severe toxicity is frequent and population-based studies show that many patients do not receive standard CRT. More knowledge on how to predict who experiences side-effects or achieves long term disease control is needed. Poor nutritional status is strongly associated with inferior survival in many types of cancer including non-small cell lung cancer, but little is known about whether this is the case in LS SCLC. We investigated whether nutritional status reported by patients on the Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF) was associated with toxicity and survival among participants in a trial comparing high dose with standard dose twice-daily TRT in LS-SCLC (NCT02041845, n=170). **Methods:** Patients received four courses of platinum/etoposide chemotherapy and were randomized to TRT of 60 Gy/40 fractions or 45 Gy/30 fractions. Patients completed PG-SGA SF before treatment commenced and were categorized as having low (PG-SGA SF score 0–3.9), intermediate (4.0–8.9) and high ($\geq$9) risk of malnutrition. Toxicity was graded according to CTCAE 4.0. Median follow-up for survival was 49 months. **Results:** 113/170 (66.5%) patients completed PG-SGA SF at baseline. Median age was 65 years, 46.0% were men, 88.5% had PS 0-1, 87.6% stage III disease and 22.1% weight loss of $>$5% the three months before inclusion. Median PG-SGA SF score was 3.0, 52.2% of patients had low, 29.2% intermediate, and 18.6% high risk of malnutrition. Numerically, there were more patients with stage III, PS 1-2 and pleural fluid among those at high risk. There was no difference in mean no. of chemotherapy courses (low: 3.85, intermediate: 3.88, high: 3.90, p=0.95) or TRT completion (low: 96.6%, intermediate: 97.0%, high: 95.2%, p=1.0). There were no statistically significant differences in proportions who experienced grade 3-4 toxicity (low: 88%, intermediate: 91%, high: 86%, p=0.86), median PFS (low: 15.1 months, intermediate: 11.8 months, high: NR, p=0.23), 2-year survival (low: 68%, intermediate: 52%, high: 67%, p=0.28) or median OS (low: 38.1 months, intermediate: 25.8 months, high: NR, p=0.15). Patients with weight loss $>$5% did not experience more grade 3-4 toxicity (92% vs. 87%, p=0.73), had similar median PFS (24.0 vs. 15.9 months, p=0.69), 2-year survival (64.0% vs. 66.2%, p=0.84) and median OS (30.6 vs. 35.1 months, p=0.93) as those without. **Conclusions:** Our study suggest that LS SCLC patients tolerate and should receive concurrent chemotherapy and twice-daily TRT regardless of nutritional status and weight loss. Research Sponsor: University of Bergen; Norwegian Cancer Society; The Liaison Committee for education, research and innovation in Central Norway; Norwegian University of Science and Technology; the Nordic Cancer Union.

8520 **Poster Discussion Session**

Pembrolizumab vs placebo for early-stage non–small-cell lung cancer after resection and adjuvant therapy: Subgroup analysis of patients who received adjuvant chemotherapy in the phase 3 PEARLS/KEYNOTE-091 study.

Kersti Oselin, Byoung Yong Shim, Morihito Okada, Maciej Bryl, Laura Bonanno, Guzin Demirag, Ida Colantonio, Martin Kimmich, Urska Janzic, Johan F. Vansteenkiste, Reyes Bernabe Caro, Amina Scherz, Alessandra Curioni-Fontecedro, Martin Früh, Mira Wollner, Jing Yang, Nazly Shariati, Sandrine Marreaud, Solange Peters, Mary ER O'Brien; North Estonia Medical Centre, Tallinn, Estonia; The Catholic University of Korea, St. Vincent's Hospital, Suwon, Korea, Republic of (South); Hiroshima University Hospital, Hiroshima, Japan; Wielkopolskie Centrum Pulmonologii i Torakochirurgii im. Eugenii i Janusza Zeylandów, Poznań, Poland; Medical Oncology 2, Istituto Oncologico Veneto IOV IRCCS, Padova, Italy; Ondokuz Mayıs Üniversitesi Tıp Fakültesi, Samsun, Turkey; Azienda Ospedaliera S. Croce e Carle Cuneo, Cuneo, Italy; Robert-Bosch-Krankenhaus - Klinik Schillerhöhe, Stuttgart, Germany; Klinika Golnik, Golnik, Slovenia; University Hospital KU Leuven Leuven, Leuven, Belgium; Hospital Universitario Virgen del Rocío, Sevilla, Spain; Inselspital, Universitätsspital Bern, Bern, Switzerland; Cantonal Hospital and University of Fribourg, Fribourg, Switzerland; Kantonsspital St. Gallen, St. Gallen, Switzerland; Rambam Medical Center, Haifa, Israel; Merck & Co., Inc., Rahway, NJ; European Organisation for Research and Treatment of Cancer, Brussels, Belgium; CHUV University Hospital of Lausanne, Lausanne, Switzerland; Lung Unit, Royal Marsden Hospital, London, United Kingdom

Background: In the randomized, triple-blind, phase 3 PEARLS/KEYNOTE-091 study (NCT02504372), at the second interim analysis, pembrolizumab (pembro) significantly prolonged DFS vs placebo (pbo) in the overall population of patients (pts) with completely resected stage IB–IIIA NSCLC per AJCC v7 who may or may not have received adjuvant chemotherapy (chemo; up to 4 cycles) as recommended per local guidelines (n = 1177; HR, 0.76 [95% CI, 0.63–0.91]; $P = 0.0014$). Here we present outcomes for those pts who received 1–4 cycles of prior adjuvant chemo, per protocol. **Methods:** Eligible adults had pathologically confirmed, completely resected stage IB (T ≥4 cm), II, or IIIA NSCLC (AJCC v7) of any PD-L1 expression, ECOG performance status of 0 or 1, and had not received neoadjuvant radiotherapy or chemo. Pts were randomized 1:1 to pembro 200 mg or pbo Q3W for 18 doses (~1 year); receipt of adjuvant chemo (yes vs no) was one of the stratification factors. Dual primary endpoints were DFS in the ITT and PD-L1 TPS ≥50% populations. No alpha was assigned to this subgroup analysis of pts who received adjuvant chemo for 1–4 cycles per local guidelines. **Results:** Of 1177 pts in the ITT population, 1010 (85.8%) received adjuvant chemo and were included in this analysis (pembro, n = 506; pbo, n = 504). Pts received a median of 17 and 18 study doses, respectively. As of data cutoff (Sep 20, 2021), 52.6% in the pembro arm vs 64.9% in the pbo arm had completed treatment. Median time from randomization to data cutoff was 37.4 mo. Median (95% CI) DFS was 58.7 mo (39.2 mo–not reached [NR]) in the pembro arm vs 34.9 mo (28.6 mo–NR) in the pbo arm (HR, 0.73 [95% CI, 0.60–0.89]). Estimated 18-mo DFS rates were 73.8% and 63.1%, respectively. In pts with PD-L1 TPS ≥50% (pembro, n = 143; pbo, n = 141), median DFS was NR in both treatment arms (HR, 0.80 [95% CI, 0.54–1.20]). Grade 3–5 adverse events (AEs) occurred in 170 pts (34.3%) in the pembro arm and 128 (25.7%) in the pbo arm (grade 5, 2.2% vs 1.0%). Immune-mediated AEs and infusion reactions occurred in 195 pts (39.3%) in the pembro arm and 69 (13.8%) in the pbo arm. **Conclusions:** Consistent with the ITT population, pembro substantially improved DFS vs pbo in the subgroup of pts with stage IB (T2a ≥4 cm), II, or IIIA NSCLC who received adjuvant platinum-based chemo following complete resection. Based on these results, pembro was approved for adjuvant treatment in this pt population by the US FDA. Clinical trial information: NCT02504372. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

8521 **Poster Discussion Session**

Clinical outcomes with neoadjuvant nivolumab (N) + chemotherapy (C) vs C by definitive surgery in patients (pts) with resectable NSCLC: 3-y results from the phase 3 CheckMate 816 trial.

Jonathan Spicer, Patrick M. Forde, Mariano Provencio, Shun Lu, Changli Wang, Tetsuya Mitsudomi, Stephen Broderick, Scott Swanson, Mark M. Awad, Enriqueta Felip, Julie R. Brahmer, Keith Kerr, Gene Brian Saylors, Ke-Neng Chen, Fumihiro Tanaka, Junliang Cai, Javed Mahmood, Nan Hu, Phuong Tran, Nicolas Girard; McGill University Health Center, Montreal, QC, Canada; Johns Hopkins Medicine, The Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; Hospital Universitario Puerta de Hierro, Madrid, Spain; Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai JiaoTong University, Shanghai, China; Tianjin Lung Cancer Center, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; Kindai University Faculty of Medicine, Ohno-Higashi, Osaka-Sayama, Japan; Dana-Farber Cancer Institute, Boston, MA; Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; Aberdeen Royal Infirmary, Aberdeen, United Kingdom; Charleston Oncology, Charleston, SC; Peking University Cancer Hospital and Institute, and Beijing Cancer Hospital, Beijing, China; University of Occupational and Environmental Health, Kitakyushu, Japan; Bristol Myers Squibb, Princeton, NJ; Institut du Thorax Curie-Montsouris, Institut Curie, Paris, France

Background: In CheckMate 816, neoadjuvant N + C demonstrated statistically significant and clinically meaningful improvements in event-free survival (EFS) and pathologic complete response (pCR) vs C in pts with resectable NSCLC. Here, we report clinical outcomes in pts with or without definitive surgery following neoadjuvant treatment (tx). **Methods:** Adults with stage IB (tumors ≥ 4 cm) to IIIA (per AJCC 7th ed) resectable NSCLC, ECOG PS ≤ 1, and no known *EGFR*/*ALK* mutations were randomized 1:1 to 3 cycles of N 360 mg + C Q3W or C Q3W, followed by definitive surgery within 6 wk of tx. Primary endpoints were EFS and pCR, both per blinded independent review. Exploratory analyses included EFS (secondary definition; no censoring for subsequent tx), time to death or distant metastasis (TTDM), and EFS2 (EFS on next-line tx) in pts with or without surgery. **Results:** Among 358 randomized pts, 149 (83%; N + C) and 135 (75%; C) had definitive surgery. Baseline characteristics were similar in pts with or without surgery (N + C, 30; C, 44) and between tx arms, except that a higher proportion of pts who did not have surgery had ECOG PS 1 (both arms) or were from Europe (N + C arm). Surgery was canceled due to progressive disease (PD) in 11 (N + C) and 17 (C) pts; PD was locoregional in 4 and 15 pts and distant in 3 and 2 pts, while 4 pts in the N + C arm had both locoregional and distant PD. At database lock (October 14, 2022; median f/u: 41.4 mo), EFS, TTDM, and EFS2 were numerically improved in pts with vs without surgery, regardless of tx arm. In pts with surgery, median TTDM was not reached (NR) vs 46.8 mo (HR, 0.55) with N + C vs C, respectively; 3-y TTDM rates were 77% vs 59%. In pts without surgery, median TTDM was 24.8 vs 15.6 mo (HR, 0.63) with N + C vs C; 3-y rates were 36% vs 13%. Among pts without surgery, 17 (57%) vs 28 (64%) pts in the N + C vs C arms, respectively, received subsequent tx: radiotherapy 37% vs 41%; surgery 3% vs 2%; systemic tx 50% vs 52%. Grade 3/4 tx-related AEs occurred in 38% (N + C) and 36% (C) in pts with surgery, and 26% and 46% in pts without surgery. **Conclusions:** In CheckMate 816, neoadjuvant N + C demonstrated long-term clinical benefit vs C in pts with resectable NSCLC who received definitive surgery. In pts who did not receive definitive surgery, these exploratory analyses showed that neoadjuvant N + C was associated with numerically improved TTDM. Clinical trial information: NCT02998528. Research Sponsor: Bristol Myers Squibb.

	With surgery			Without surgery		
	N + C (n = 149)	C (n = 135)	HR (95% CI) N + C vs C	N + C (n = 30)	C (n = 44)	HR (95% CI) N + C vs C
mEFS,[a] mo (95% CI)	NR (44.4–NR)	31.8 (18.0–NR)	0.67 (0.47–0.95)	6.7 (2.7–24.9)	4.1 (2.5–11.2)	0.75 (0.44–1.28)
3-y EFS rate, %	62	49	–	8	10	–
mTTDM, mo (95% CI)	NR	46.8 (34.3–NR)	0.55 (0.36–0.84)	24.8 (6.7–37.8)	15.6 (11.2–18.6)	0.63 (0.34–1.16)
3-y TTDM rate, %	77	59	–	36	13	–
mEFS2, mo (95% CI)	NR	NR	0.60 (0.39–0.95)	12.3 (8.4–37.8)	15.5 (10.2–18.6)	0.94 (0.53–1.66)
3-y EFS2 rate, %	80	69	–	33	24	–

[a]Secondary definition. m, median.

8522 **Poster Discussion Session**

IMpower010: Exploratory analysis of disease-free survival by KRAS status in patients with stage II-IIIA NSCLC treated with adjuvant atezolizumab vs best supportive care.

Martin Reck, Minu K Srivastava, Heather A. Wakelee, Enriqueta Felip, Nasser K. Altorki, Tibor Csoszi, Vladimir Moiseyenko, Andrey Akopov, Alexey Smolin, Antonio Chella, Eric Vallieres, Alex Martinez-Marti, Wei Zou, V. McNally, Elizabeth Bennett, Hen Prizant, Barzin Nabet, Marcus Ballinger, Barbara J. Gitlitz, Caicun Zhou; Lung Clinic Grosshansdorf, Airway Research Center North, German Center of Lung Research, Grosshansdorf, Germany; Genentech Inc, South San Francisco, CA; Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA; Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; New York-Presbyterian Hospital, Weill Cornell Medicine, New York, NY; Jasz-Nagykun-Szolnok Megyei Hetenyi Geza Korhaz-Rend. Int., Szolnok, Hungary; GBUZ Saint Petersburg Clinical Research Center of Specialized Types of Care (Oncology), Saint Petersburg, Russian Federation; Pavlov State Medical University, Saint Petersburg, Russian Federation; Principal Military Clinical Hospital n.a. N.N. Burdenko, Moscow, Russian Federation; Pneumology Unit, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy; Swedish Cancer Institute, Seattle, WA; Genentech Inc., South San Francisco, CA; Roche Products Limited, Welwyn Garden City, United Kingdom; Genentech Inc., South San Fransico, CA; Tongji University Affiliated Shanghai Pulmonary Hospital, Shanghai, China

Background: The Phase III IMpower010 trial (NCT02486718) met its primary disease-free survival (DFS) endpoint leading to approval of atezolizumab after adjuvant platinum-based chemotherapy for completely resected PD-L1 TC ≥1% or ≥50% stage II-IIIA NSCLC in the US, EU and other regions. Mutant KRAS (mKRAS) is the most prevalent oncogenic driver in metastatic NSCLC (27% mKRAS [KRAS G12C,11%]; Osta et al, J Thorac Oncol 2019). Here, we report exploratory DFS outcomes by KRAS mutational status in patients from IMpower010. **Methods:** The study design and primary results of IMpower010 have been reported (Felip et al, Lancet 2021). After complete resection, patients received cisplatin-based doublet chemotherapy (1-4 21-day cycles) and were subsequently randomized to receive atezolizumab 1200 mg q3w (16 cycles) or best supportive care (BSC). This post hoc analysis evaluated DFS in subgroups of patients by KRAS mutational status. KRAS mutational status was assessed retrospectively using whole-exome sequencing (WES) on resected tumor tissue. Analyses were conducted in patients whose tumors harbored any mKRAS type, including G12C. A separate analysis of the KRAS G12C subgroup was not conducted due to limited patient numbers. **Results:** Of the 1005 patients in the intention-to-treat population (all randomized patients with stage IB-IIIA NSCLC), 603 comprised the WES biomarker-evaluable population (WES-BEP), and of these, 536 had stage II-IIIA NSCLC. Within the stage II-IIIA WES-BEP, the prevalence of mKRAS and KRAS G12C was 22% (n=118) and 10% (n=52), respectively. mKRAS was enriched in White, non-squamous and smoker populations. Atezolizumab showed DFS improvement vs BSC regardless of KRAS status in the stage II-IIIA WES-BEP (Table). In the mKRAS stage II-IIIA WES-BEP, atezolizumab showed DFS improvement vs BSC regardless of PD-L1 status. **Conclusions:** In IMpower010, the prevalence of mKRAS and KRAS G12C was similar to that seen in metastatic NSCLC. Despite limited patient numbers in this exploratory analysis, DFS appeared to be consistent and in favor of atezolizumab across subgroups regardless of KRAS status. Clinical trial information: NCT02486718. Research Sponsor: F. Hoffman-La Roche, Ltd.

	Atezolizumab median DFS, mo	BSC median DFS, mo	DFS HR (vs BSC) 95% CI
Stage II-IIIA WES-BEP	NR n=270	31.4 n=266	0.70 0.54, 0.91
KRAS WT stage II-IIIA WES-BEP	42.3 n=208	31.4 n=210	0.74 0.55, 1.00
mKRAS stage II-IIIA WES-BEP	NR n=62	25.2 n=56	0.56 0.32, 0.99
mKRAS SP263-evaluable stage II-IIIA WES-BEP	NR n=61	25.2 n=56	0.57 0.32, 1.02
mKRAS SP263-evaluable PD-L1 TC ≥1% stage II-IIIA WES-BEP	NR n=39	21.7 n=32	0.52 0.25, 1.08
mKRAS SP263-evaluablePD-L1 TC <1% stage II-IIIA WES-BEP	NR n=22	31.6 n=24	0.67 0.26, 1.73

NR, not reached; WT, wild type.

8523 **Poster Discussion Session**

Response to neoadjuvant immune checkpoint inhibitor (ICI)-based therapy in oncogene-driven resectable non-small cell lung cancer (NSCLC).

Samuel Rosner, Lavanya Sivapalan, Marianna Zahurak, Rohit Thummalapalli, Roni Rayes, Sydney Connor, Khaled Sanber, Joshua E. Reuss, Gavin Pereira, Kellie Nicole Smith, Valsamo Anagnostou, Stephen Broderick, David Randolph Jones, Julie R. Brahmer, Kristen A. Marrone, Jonathan Spicer, Jamie E. Chaft, Patrick M. Forde; Johns Hopkins University, Baltimore, MD; Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD; Memorial Sloan Kettering Cancer Center, New York, NY; RI-MUHC, Montreal, QC, Canada; Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC; Johns Hopkins University School of Medicine, Baltimore, MD; Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins School of Medicine, Baltimore, MD; Johns Hopkins Medicine, The Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; Johns Hopkins Hospital, Baltimore, MD; McGill University Health Center, Montreal, QC, Canada

Background: Neoadjuvant (NEO) chemotherapy (chemo) plus nivolumab (nivo) has received FDA approval for treatment of resectable NSCLC, demonstrating superior event-free survival compared to chemo alone. However, outcomes of NEO ICI-based therapies in patients (pts) with oncogene-driven (OD)-NSCLC remains an unanswered question. **Methods:** We conducted a retrospective secondary analysis of pts enrolled in the clinical trial NCT02259621 with clinical stage I-IIIA NSCLC, treated with NEO ICI-based therapies: nivo alone, nivo+ipilimumab (ipi), or nivo+chemo followed by surgery. Pts underwent baseline genomic profiling using NGS. Pts with *KRAS*, *EGFR*, *MET*, *BRAF*, *ALK*, *HER2*, *ROS1*, *RET* or *NTRK* alterations were identified as OD-NSCLC. *STK11* and *KEAP1* mutations (muts) were also recorded. For pts who underwent definitive resection (DR) and baseline NGS testing, association of OD-status and clinical outcomes, including major pathologic response (MPR) and recurrence-free survival (RFS) are reported. Proportions are reported with exact 95% binomial confidence intervals (CI). Binomial probabilities are compared with Chi-square or Fisher's exact tests. RFS and median follow-up (f/u) are reported using the Kaplan-Meier (KM) and reverse KM methods, respectively. **Results:** 61 pts received NEO ICI-based therapy: 60% treated with nivo alone, 15% with ipi+nvo and 25% with chemo+nivo. 92% of pts underwent DR. Pathologic complete response (pCR) and MPR rates were, 12.5% and 37.5%, respectively. Baseline NGS testing was available for 47 pts, of whom, 49% had OD-NSCLC, with the majority (78%) harboring a *KRAS* mut. Additional OD alterations included non-classical *EGFR* (9%), *METex14* skipping (9%) and *ROS1* fusion (4%), of whom, 3/5 pts had a MPR after NEO-ICI. *STK11* muts were noted in 16% pts, and co-altered with *KRAS* in 9%. Median f/u for OD-NSCLC was 42.58 months. Pts with OD-NSCLC had comparable RFS after NEO-ICI compared to those with non-OD-NSCLC (HR 0.64, CI 0.19-2.13, p=0.5), including those with *KRAS*+ disease (HR 0.73, CI 0.2-2.73, p=0.6). Pts with co-mut *KRAS*+*STK11*+ trended toward shorter RFS compared to *KRAS*+*STK11*- (HR 6.36, CI 0.56-72.82, p=0.1). *STK11*+ also trended toward shorter RFS without reaching statistical significance (HR 2.51, CI 0.67-9.35, p=0.17). No significant associations between OD-status and MPR rates were seen, however *KRAS*+ (4/18) vs. *Kras*- (13/29) trended toward lower MPR rate (p=0.1). Four of 5 pts with disease progression preventing DR harbored an *STK11* or *KEAP1* mut. **Conclusions:** Findings from this cohort treated with various NEO ICI-based therapies, suggests comparable RFS, regardless of OD status- with the majority harboring *KRAS* muts. Lower MPR rates were observed for pts with *KRAS*+ tumors. *STK11* mut and *KRAS*+*STK11*+ co-mut status both trended toward shorter RFS, though definitive conclusions are limited by cohort size and treatment heterogeneity. Research Sponsor: BMS; Stand Up 2 Cancer (SU2C).

8524 **Poster Session**

Predictive value of co-existing genetic alterations and tumor mutation burden for patients with completely resected non-small cell lung cancer harboring EGFR mutation: Biomarker analysis of phase III IMPACT study.

Satoshi Ikeda, Masahiro Tsuboi, Kazuko Sakai, Toshihiro Misumi, Hiroaki Akamatsu, Yasuo Iwamoto, Noriaki Sakakura, Atsushi Nakamura, Yasuhisa Ohde, Hidetoshi Hayashi, Kyoichi Okishio, Morihito Okada, Ichiro Yoshino, Jiro Okami, Kazuhisa Takahashi, Norihiko Ikeda, Tetsuya Mitsudomi, Hirohito Tada, Kazuhiko Nakagawa, Kazuto Nishio; Kanagawa Cardiovascular and Respiratory Center, Yokohama, Japan; National Cancer Center Hospital East, Kashiwa, Japan; Kindai University Faculty of Medicine, Osakasayama, Japan; Department of Data Science, National Cancer Center Hospital East, Kashiwa, Japan; Internal Medicine III, Wakayama Medical University, Wakayama, Japan; Hiroshima Citizens Hospital, Hiroshima, Japan; Aichi Cancer Center Hospital, Nagoya, Japan; Sendai Kousei Hospital, Sendai, Japan; Shizuoka Cancer Center, Sunto-Gun, Japan; Kindai University Faculty of Medicine, Osaka-Sayama, Japan; National Hospital Organization Kinki-Chuo Chest Medical Center, Sakai, Japan; Hiroshima University, Hiroshima, Japan; Chiba University Graduate School of Medicine, Chiba, Japan; Osaka International Cancer Institute, Osaka, Japan; Division of Respiratory Medicine, Juntendo University Faculty of Medicine & Graduate School of Medicine, Tokyo, Japan; Tokyo Medical University, Tokyo, Japan; Kindai University Faculty of Medicine, Ohno-Higashi, Osaka-Sayama, Japan; Suita Tokushukai Hospital, Suita, Japan; Kindai University Faculty of Medicine, Osaka-Sayama, OSAKA-FU, Japan

Background: Although osimertinib has recently become an option for adjuvant therapy in many countries, biomarkers predicting the efficacy of adjuvant EGFR-TKI and the risk of postoperative recurrence in completely resected NSCLC harboring EGFR mutations have not been fully investigated. **Methods:** This IMPACT-TR study is an exploratory biomarker study for completely resected, EGFR-mutated NSCLC patients who received gefitinib or cisplatin plus vinorelbine (cis/vin) in a phase III IMPACT study (Trial registration number: UMIN000044738. Funding: AstraZeneca K.K.). Surgically resected lung cancer tissue specimens were analyzed for co-existing somatic mutations and tumor mutation burden (TMB) determined by Oncomine Tumor Mutation Load, and these data were matched with disease free survival (DFS) and overall survival (OS) data. **Results:** Of the 234 patients in the IMPACT study, 211 patients were enrolled, and 202 patients in the Per Protocol Set were analyzed. The most frequent co-existing somatic mutation was *TP53* (58.4%), followed by *CSMD3* (11.8%), *NOTCH1* (9.9%) and *SYNE1* (9.9%). The median TMB was 6.67 mutations/Mb, and only 15.2% had $\geq$10 mutations/Mb. EGFR mutation subtypes, *TP53* co-mutation and TMB were not associated with DFS or OS in either the gefitinib or cis/vin groups. In the gefitinib group, patients with *NOTCH1* mutation had significantly shorter OS (hazard ratio [HR] 4.18, 95%CI 1.65-10.61, p=0.003) and tended to have shorter DFS (HR 1.44, 95%CI 0.62-3.37, p=0.399) than those without *NOTCH1* mutation. In the cis/vin group, patients with *CREBBP* mutation had significantly shorter DFS (HR 2.70, 95%CI 1.05-6.97, p=0.040) and tended to have shorter OS (HR 3.05, 95%CI 0.90-10.37, p=0.074) than those without *CREBBP* mutation. **Conclusions:** This study suggested that *NOTCH1* mutation may be a biomarker to predict poor response to adjuvant gefitinib and *CREBBP* mutation to predict poor response to cis/vin in patients with completely resected, EGFR-mutated NSCLC. Clinical trial information: UMIN000044738. Research Sponsor: AstraZeneca K.K.

8525 **Poster Session**

Safety and efficacy of QL1706 plus carboplatin/etoposide (EC) as first-line (1L) treatment for extensive-stage small-cell lung cancer (ES-SCLC): The results from a phase II single-arm study.

Yun Fan, Zhehai Wang, Runxiang Yang, Xuhong Min, Huiwen Ma, Yan Wang, Zhendong Chen, Hongmin Wang, Huayuan Wang, Lianghua Fang, Xiaoyan Kang; Zhejiang Cancer Hospital, Hangzhou, China; Shandong Cancer Hospital and Institute, Jinan, China; Department of Medical Oncology, Yunnan Cancer Hospital, Kunming Medical University, Kunming, China; Anhui Chest Hospital, Hefei, China; Chongqing University Cancer Hospital, Chongqing, China; Harbin Medical University Cancer hospital, Harbin, China; Department of Oncology, The Second Affiliated Hospital of Anhui Medical University, Hefei, China; The first Affiliated Hospital of Zhengzhou University, Zhengzhou, China; Medicine Department, Qilu Pharmaceutical Co., Ltd., Jinan, China

Background: Although the combination of PD-L1 inhibitor and platinum-etoposide chemotherapy has been the preferred 1L treatment for patients (pts) with ES-SCLC, the clinical benefit of the addition of PD-L1 inhibitor was still modest. QL1706 is a novel bifunctional antibody, containing a mixture of anti-PD-1 IgG4 and anti-CTLA-4 IgG1 antibodies produced by MabPair. In phase I trials, QL1706 monotherapy has shown promising antitumor efficacy in nasopharynx cancer and cervical cancer, as well as other advanced solid tumors including SCLC (to be published). This study aims to assess the safety and efficacy of QL1706 plus EC in treatment-naïve ES-SCLC. **Methods:** In this phase II, open-label, single-arm, multi-center study, eligible pts (18-75 years, ECOG 0-1) received 4-6 cycles of QL1706 (5mg/kg, IV, Q3W) plus EC (etoposide, 100 mg/m^2, D1-3, Q3W; carboplatin, AUC = 5, D1, Q3W), followed by the maintenance therapy of QL1706 until disease progression, intolerable toxicity or other discontinuation events defined in the study protocol. Tumor imaging was performed every 6 weeks for the first year and every 9 weeks thereafter. The primary endpoint is safety. **Results:** From Apr 18, 2022 to Jul 27, 2022, a total of 40 pts were enrolled with a median age of 58.5 years (range, 38−73). 87.5% pts were men, 80% were smokers and 90% had ECOG PS of 1. As of data cutoff (Jan 16, 2023), the median QL1706-treatment duration was 5.9 (range, 0.7−8.9) mo. Twenty pts remained on treatment and 20 pts discontinued due to progressive disease (16, 40.0%) or patient decision (4, 10.0%). Thirty two (80.0%) pts had at least one TRAE (QL1706-related). Fifteen (37.5%) pts experienced grade 3-4 TRAEs, including neutropenia (8, 20%), thrombocytopenia (4, 10%), anemia (3, 7.5%), WBC count decreased (2, 5.0%), AST increased (2, 5.0%), ALT increased (1, 2.5%), gamma-GT increased (1, 2.5%), rash (1, 2.5%), and diarrhea (1, 2.5%). No grade 5 TRAE occurred. No AE led to discontinuation of any treatment. Of the 39 pts who had at least 1 post-baseline tumor assessment, 37 achieved PR (35 confirmed and 2 unconfirmed) and 1 achieved SD. Thus, the confirmed ORR was 89.7% (95% CI, 75.8%−97.1%), and the DCR was 97.4% (95% CI, 86.5−99.9%) (per RECIST v1.1). The mDoR was 4.5 (95% CI, 4.2−not evaluable) mo, with the longest response duration more than 7.2 mo and ongoing. The mPFS was 5.7 (95% CI, 5.4−7.1) mo, together with 3 mo- and 6 mo-PFS rates of 94.8 (95% CI, 80.8−98.7%) and 44.7% (95% CI, 27.3−60.6%), respectively. With a median follow-up time for OS of 6.2 mo, the mOS has not been reached. **Conclusions:** QL1706 plus EC chemotherapy showed tolerable safety profile and promising efficacy as first-line treatment for pts with ES-SCLC. These data support further clinical development of QL1706 in ES-SCLC. Clinical trial information: NCT05309629. Research Sponsor: Qilu Pharmaceutical Co., Ltd.

8526 **Poster Session**

Clinical and financial implications of ADUARA trial on a real-world population.

Bharathi Muthusamy, Emily Craig Zabor, Nathan A. Pennell; Cleveland Clinic, Cleveland, OH

Background: In the ADAURA trial, adjuvant (adj) osimertinib improved disease free survival (DFS) in resected, *EGFR*-mutant (*EGFR*m) Stage IB-IIIA NSCLC compared to placebo. Based on these results, the FDA approved osimertinib in the adj setting. In this study, we have evaluated the hypothetical clinical and financial effects of adj osimertinib on the early-stage, *EGFR*m NSCLC patients at Cleveland Clinic who were treated prior to the FDA approval. **Methods:** Starting in 2010, Cleveland Clinic has been performing targeted molecular testing in all resected NSCLCs. With this information, we created a database of patients from 01/2010 to 01/2021 with resected, non-squamous NSCLC. The standard of care (SOC) arm of this study consisted of patients with stage IB-IIIA, *EGFR*m disease from our internal database. Data for the adj osimertinib arm were obtained through a microsimulation study by first generating the per-stage DFS distribution in the SOC arm, and then applying the per-stage hazard ratios from ADAURA to obtain the parameters of the exponential DFS distribution with osimertinib treatment. Outcomes and costs, such as treatment and imaging, were directly calculated for the SOC arm based on the amount of time each patient spent in a recurrence-free or recurrent state, and whether there was CNS involvement at recurrence. Costs and outcomes were averaged across 1000 simulated datasets for the osimertinib arm. Based on ADAURA we assumed that 78.4%, 16.2%, and 5.4% of DFS events were CNS- recurrence, CNS+ recurrence, or death. **Results:** 1,487 patients were included in the database. 724 of these patients had stage IB-IIIA disease and *EGFR* testing. 82 patients were *EGFR*m+ (exon 19 deletion or the L858R mutation), and their survival outcomes were used in the SOC arm. At 5 years, 32 (39%) of the patients were alive and disease free. With the addition of adj osimertinib, an estimated average of 61 (71.4%) of patients would have been disease free and alive. This corresponds to an average improvement in 5-year DFS of 35.4%. The cost of testing all 724 patients would have been $2,865.80 per patient eligible for osimertinib with single-gene *EGFR* testing or $5,279.11 per eligible patient with targeted NGS testing. The total treatment and healthcare costs with adj osimertinib in the 82 patients would have been $49,057,952.75 or $598,267.72 per patient. With SOC (surveillance +/- adj chemotherapy + osimertinib only upon recurrence), total and per patients costs were $12,297,374.11 and $149,967.98 respectively. This corresponds to an average increase in total costs of $448,299.74 per person with the use of adj osimertinib. **Conclusions:** Over a decade at Cleveland Clinic, about 5.5% (82/1,487) patients with early stage NSCLC would have been affected by the adj osimertinib approval. In our simulation, we estimated adj osimertinib would have improved 5-year DFS by 35.4% (29 more patients) but with a significant financial cost of about $450,000 per eligible patient. Research Sponsor: None.

8527 **Poster Session**

A study of tumor neoantigen burden and HLA-LOH by whole-exome sequencing to characterize immune biomarkers of lung cancer.

Wei Wang, Wenting Liao, Baoling Zhen, Tianrong Ji, Chen Du, Shaochen Cheng, Yaru Chen, Jie Yang; Department of Thoracic Surgery, Renmin Hospital of Wuhan University, Wuhan, China; HaploX Biotechnology, Shenzhen, China; Wuhan Fourth Hospital, Wuhan, China

Background: Lung cancer is a leading cause of cancer-related death worldwide. Precision immunotherapy, such as the use of immune checkpoint inhibitors (ICIs), has been shown to improve the survival of lung cancer patients. Cancer cells with high amount of neoantigens are more likely to be captured by immune cells and thus patients with high Tumor Mutation Burden(TMB) and high Tumor Neoantigen Burden(TNB) are estimated to be prone to ICIs treatment. HLA class I is one of the main factors affecting the prognosis of ICI in treatment. Studies have indicated that patients with highly heterozygous HLA-I are more likely to have better responses to ICI treatment. Some specific HLA-I genotypes and somatic mutations can affect the prognosis of ICIs treatment. **Methods:** In this study, we performed whole-exome sequencing (WES) of 200 pairs of tumor and gDNA samples from lung cancer patients. Tumor sample comes from tumor tissue or paraffin-embedded tissue and gDNA is extracted from white blood cells from *peripheral blood.* We analyze the WES data to obtain the TMB and HLA types of each sample. Then the peptide affinity of MHC-I genes were quantified based on IC50(nM) by netMHCpan software, and the level of neoantigen affinity were classified as strong (IC50$\leq$50nM), weak (50nM $<$ IC50$\leq$500nM), and negative (IC50 $>$ 500nM). TNB is defined as the number of high- affinity neoantigens per megabase of interrogated genomic sequence. Then we conducted linear regression analysis to study the statistical relationship between TMB and TNB. Finally, we analyzed the LOH status at the major region of HLA (HLA-A, HLA-B, and HLA-C) and classified the individuals who have LOH at all three types of HLA as HLA-LOH strong positive, samples with one or two LOH among the three HLA types as weak positive, and samples have no LOH are classified as HLA-LOH negative. **Results:** Among the 200 samples, the median value of TMB and TNB is 3.25 Muts/Mb and 1.09 Neos/Mb, respectively. 8.5% of the sample have high TMB(TMB$\geq$10). TMB and TNB are also significantly positively correlated (p-value $<$ 0.0001). For HLA typing, 82.0% HLA-A, 96.0% HLA-B, and 92.5% HLA-C are heterozygous. The dominant HLA types are: (A*11:01), (A*02:01), (B*46:01), (B*40:01), (C*01:02), and (C*07:02). As for LOH status among the three HLA types, 14.57% of the individuals are HLA-LOH strong positive, 31.66% are HLA-LOH weak positive, and 53.77% of the samples are HLA-LOH negative. Lastly, the average numbers of detected high-affinity neoantigens are statistically significantly related to the occurrence of HLA-LOH (Analysis of Variance p-value $<$ 0.01). **Conclusions:** HLA-LOH occurs in nearly half of our lung cancer samples, and it is associated with TMB-High and TNB-High. The analysis of HLA-LOH refines the prediction of neoantigen and gain understanding of drug resistance and immunotherapy. Research Sponsor: None.

8528 **Poster Session**

Dynamic ctDNA to inform the precise management of resected NSCLC: LUNGCA-2 study.

Liang Xia, Qiang Pu, Ran Kang, Jiandong Mei, Lu Li, Ying Yang, Senyi Deng, Gang Feng, Lin Ma, Feng Lin, Hu Liao, Chengwu Liu, Yunke Zhu, Qingyun Li, Xiaolong Zhang, Lunxu Liu; Institute of Thoracic Oncology and Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu, China; Department of Lung Cancer Center, West China Hospital, Sichuan University, Chengdu, China; Genecast Biotechnology Co., Ltd, Wuxi, China; Department of Thoracic surgery,-Sichuan Provincial People's Hospital, Chengdu, China; Department of Thoracic Surgery, Chengdu Shangjinnanfu Hospital, Chengdu, China

Background: Circulating tumor DNA (ctDNA) has been reported to be valuable for minimal residual disease (MRD) detection, but there is a lack of studies comprehensively assessing whether dynamic ctDNA monitoring can inform whole-course precise postoperative cancer management. In the present study (LUNGCA-2), we analyzed data obtained from longitudinal ctDNA monitoring of stage I-III NSCLC patients in the LUNGCA cohort, and sought to assess the use of dynamic ctDNA monitoring for precise whole-course postoperative management of NSCLC patients. **Methods:** All eligible NSCLC patients underwent curative-intent surgery and subsequently received adjuvant therapies when indicated by clinical practice guidelines for NSCLC. The clinical follow-up was scheduled to be every 3-6 months mainly involving CT and/or MRI. Fresh frozen or paraffin-embedded tissues of primary tumors were collected intraoperatively for baseline somatic mutation profiling. Blood samples were collected before surgery, at 3 days and 1 month after surgery, and then every 3-6 months at clinical visits up to 3 years postoperatively. 233 patients with a total of 2123 plasma samples were ultimately included in the longitudinal ctDNA analysis in the current study. NGS assays were performed with a custom-designed panel that covered 769 cancer-related genes via the MinerVA platform (Genecast Biotechnology Co., Ltd). **Results:** Among the cohort, 166 patients harboring targetable mutations in the primary tumor tissue, 15 were preadjuvant ctDNA positive, and among them, only 25% patients treated with adjuvant TKI therapy experienced relapse during follow-up, and patients received ACT or no adjuvant therapy had a relapse rate of 100%. TKI treatment tended to improve RFS compared with no treatment (HR 0.1, $P = 0.025$), but ACT failed to improve RFS (HR 1.1, $P = 0.834$). Among all 82 patients receiving adjuvant therapy, the pre- and post-adjuvant therapy postoperative ctDNA status with a negative-negative or positive-negative pattern had similar and favorable RFS ($P = 0.545$) but that patients with a positive-positive or negative-positive pattern had significantly inferior RFS than those with a negative-negative pattern (both $P < 0.001$). For recurrence monitoring, posttreatment ctDNA MRD status had a positive predictive value of 100% and a negative predictive value of 91.8%, and the sensitivity of MRD detection was affected by the organ of relapse. Among positive ctDNA MRD patients, faster increase of ctDNA concentration correlated with more imminent clinical relapse. The median lead time from ctDNA detection to radiological relapse was 273 days. Moreover, ctDNA negativity after relapse was associated with favorable survival. **Conclusions:** These findings highlight the clinical significance of ctDNA dynamics for the precise whole-course postsurgical management of NSCLC patients. Research Sponsor: the National Natural Science Foundation of China; the Major Research Project of Sichuan Province.

8529 **Poster Session**

Differential expression analysis of circRUNX1 in patients with early resected EGFR-mutant NSCLC.

Carlos Pedraz, Masaoki Ito, Ana Giménez-Capitán, Stavros Giannoukakos, Miguel Angel Molina Vila, Rafael Rosell; Pangaea Oncology, Laboratory of Molecular Biology, Barcelona, Spain; Surgical Oncology, Institute of Biomedical & Health Sciences, Hiroshima University, Hiroshima, Japan, Hiroshima, Japan; University of Granada, Department of Genetics, Granada, Spain; Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol (IGTP), Badalona, Barcelona, Spain

Background: In the ADAURA study, patients with stage IB-IIIA of resected EGFR mutated lung adenocarcinoma receiving adjuvant osimertinib had a 2-year survival of 89% versus 52% in the placebo group ($p<0.001$), however, predictive markers of response and recurrence are still needed. Circular RNA (circRNA) is a type of RNA which forms a covalently closed continuous loop. Some circRNAs have been reported as essential for tumor cell proliferation through functions distinct from the canonical linear RNA. In this project, we studied circRNA expression levels in formalin-fixed paraffin-embedded (FFPE) lung tumor samples in order to explore potential biomarkers that could predict the benefit of adjuvant EGFR TKIs in EGFR-mutant NSCLC patients. **Methods:** FFPE tumor samples from patients with EGFR-mutant, stage I-IIIB NSCLC (n=79) were collected. RNA was purified using the High Pure FFPET RNA Isolation Kit (Qiagen) and quantified by Nanodrop 2000 (Thermo Scientific). A total of 250 ng of RNA were subjected to overnight hybridization and downstream nCounter processing (NanoString) following manufacturer's instructions for our circRNA custom panel. Differential expression analysis was performed using Excel (Microsoft) and Prism GraphPad (Dotmatics) software. **Results:** Analysis of the 79 samples included in the study shown a cluster of 3 circRNAs significantly upregulated ($p<0.05$ and >2 fold-change) in EGFR mutation-positive NSCLC relapsing withing the 36 months after resection, including circRUNX1, circFUT8 and circAASDH. Disease-free survival (DFS) was significantly shorter for the subgroup of patients with high versus low circRUNX1 expression. Additional multivariate analysis identified circRUNX1 expression and tumor stage as the only statically significant prognostic factors (circRUNX1 hazard ratio = 4.480, confidence interval = 2.172-9.239, $P < 0.001$; pathological stage hazard ratio = 2.237, confidence interval = 1.183- 4.231, $P = 0.008$). **Conclusions:** CircRUNX1 could be a novel biomarker to predict the benefit of adjuvant EGFR TKIs with regards to DFS in EGFR-mutant resected NSCLC patients. Research Sponsor: None.

8530 **Poster Session**

Elucidating the genomic and transcriptomic landscape of L858R vs ex19del EGFR-mutated NSCLC.

Stephanie Pei Li Saw, Mengyuan Pang, Jia Chi Yeo, Jacob Alvarez, Ngak Leng Sim, Win Pin Ng, Gillianne Lai, Aaron C. Tan, Amit Jain, Wan Ling Tan, Ravindran Kanesvaran, Quan Sing Ng, Darren Wan-Teck Lim, Mei-Kim Ang, Tony Kiat Hon Lim, Boon-Hean Ong, Kevin Lee Min Chua, Daniel Shao-Weng Tan, Anders Skanderup; National Cancer Centre Singapore, Singapore, Singapore; Genome Institute of Singapore, Singapore, Singapore; Singapore General Hospital, Singapore, Singapore; National Heart Centre Singapore, Singapore, Singapore

Background: Epidermal growth factor receptor (EGFR)-mutated non-small cell lung cancer (NSCLC) is heterogeneous and L858R derive less benefit from osimertinib than ex19del in both the metastatic and adjuvant setting, which remains poorly understood. We sought to examine the genomic and transcriptomic features of L858R vs ex19del. **Methods:** Consecutive patients with AJCC7 Stage IA-IIIA EGFR-mutated NSCLC diagnosed 1/1/2010 – 31/12/2019 who underwent surgery at National Cancer Centre Singapore were included. Patients who received neoadjuvant therapy were excluded. Fresh frozen tumour and normal samples were subject to whole exome sequencing (WES) at 400X and 100X coverage respectively, with approximately 50 million paired-end reads for RNA-seq per sample. Wilcoxon and Fisher's exact test were used for association analysis. **Results:** A total of 203 patients were included. Median age at diagnosis was 66, 66.0% (134/203) were females and 84.2% (171/203) never-smokers. Stage IA comprised 44.3% (90/203), IB 28.6% (58/203), II 15.8% (32/203) and IIIA 11.3% (23/203). Median tumour mutational burden (TMB) was 1.3 mutations/megabase (range 0.3 – 44.3). Ex19del represented 46.3% (94/203) and L858R 41.9% (85/203). Whole genome doubling (WGD) was found in 70.0% (142/203) and was more common in *TP53*-mutated compared to *TP53*-wildtype (81.1% vs. 63.6%, p=0.01). *TP53* mutations were more common in stage II/IIIA tumours compared with stage IB and IA (50.9% vs 32.8% vs 30.0%, p=0.035). Comparing ex19del and L858R, there was no difference in stage distribution (p=0.337), proportion of TMB≥10 (1.1% vs 5.9%, p=0.103), number of cancer co-driver mutations (p=0.174), *TP53* mutations (39.4% vs 32.9%, p=0.437) and WGD (69.1% vs 76.5%, p=0.316). L858R had a higher incidence of smoking mutational signature (median 0.35 vs 0.28, p=0.018) compared to ex19del despite similar smoking history (15.3% vs 12.8%, p=0.67), whereas APOBEC mutational signature was higher in ex19del (median 0.06 vs 0.04, p=0.015). L858R tumors were associated with a higher incidence of co-mutations in *RBM10* (21.2% vs 6.38%, p=0.004), *RNF213* (10.6% vs 1.06%, p=0.007) and amplification of *NTHL1* (15.3% vs 2.13%, p=0.001) and *AXIN1* (17.6% vs 3.19%, p=0.002) compared to ex19del. Transcriptomic subtype differed significantly by EGFR mutation with a higher representation of TRU subtype among L858R than ex19del (51.0% vs 35.3%, p=0.010), while GEP score was similar (median 0.189 vs 0.325, p=0.122). **Conclusions:** L858R have distinct co-mutations and copy number alterations compared to ex19del, in addition to a higher representation of smoking mutational signature and TRU subtype. *TP53* co-mutations are more frequently observed in higher stage tumours and are associated with WGD. Our findings highlight the molecular heterogeneity of resected EGFR-mutated NSCLC, which could contribute to the differential outcomes to adjuvant osimertinib between ex19del and L858R. Research Sponsor: National Medical Research Council Singapore; Duke-National University of Singapore Oncology Academic Clinical Programme.

8531 **Poster Session**

Prevalence of *EGFR* mutations in patients with resected stage I-III non-squamous NSCLC: Results from the EARLY-EGFR study.

Ross A. Soo, Thanyanan Reungwetwattana, Herman Andres Perroud, Ullas Batra, Saadettin Kilickap, Luis Fernando Tejado Gallegos, Natalia Donner, Mohamed Alsayed, Reto Huggenberger, Tu Van Dao; National University Cancer Institute, National University Hospital, Singapore, Singapore; Division of Medical Oncology, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; Sanatorio de la Mujer, Rosario Argentina, Rosario, Argentina; Rajiv Gandhi Cancer Institute and Research Centre, New Delhi, India; Istinye University Faculty of Medicine, Department of Medical Oncology, Liv Hospital, Ankara, Turkey; AstraZeneca, Mexico City, Mexico; AstraZeneca, Cambridge, United Kingdom; AstraZeneca, Dubai, United Arab Emirates; AstraZeneca, Baar, Switzerland; Cancer Research and Clinical Trials Center, National Cancer Hospital, Ha Noi, Viet Nam

Background: The prevalence of *EGFR* mutations (*EGFRm*) in resected stage I-III NSCLC remains controversial as prior research studies were retrospective in nature. EARLY-EGFR is the first prospective, international study to determine the prevalence of *EGFRm* and treatment patterns in patients (pts) with early-stage NSCLC. **Methods:** EARLY-EGFR (NCT04742192), a non-interventional real-world study, captured data on *EGFRm* status, treatment patterns, demographic, clinical and pathological characteristics in consecutively enrolled pts with surgically resected stage IA-IIIB (AJCC 8th) non-squamous NSCLC (Mar 2021 – Oct 2022). The primary endpoint was prevalence of *EGFRm* and secondary endpoints included prevalence of *EGFRm* subtypes and treatment patterns. **Results:** Of 601 pts (median [range] age: 62 [30-86] yrs) enrolled at 33 centers across Middle East and Africa (n=16), Latin America (n=80), and Asia (n=505), 317 (52.7%) were females, 354 (58.9%) were never smokers. The majority had stage IA-IB NSCLC (64.1%) involving right lung (62.9%), no nodal involvement (81.5%), T1a-T2b tumor (82.7%), adenocarcinoma histology (98.7%), and 105/420 (25.0%) tumors were poorly differentiated. About 23.3% (130/559) were diagnosed through a screening program; 60/539 (11.1%) reported family history of lung cancer. The overall prevalence of *EGFRm* was 50.7% (300/592). *Exon-19* deletions accounted for 50.3%, *L858R* mutations for 35.7%, and compound mutations for 2.3% of mutations. *EGFRm* tumors were found to be PD-L1 positive in 38.5% of cases (15/39). Women had higher *EGFRm* rate than men (63.6% vs 36.2%). Compared with *EGFR wild type (wt)*, pts with *EGFRm* were more likely to be never smokers (39.5% vs 60.5%) and have stage I/II NSCLC (46.5% vs 53.5%) (Table). Of 216 stage II/III NSCLC pts, only 51.4% received systemic adjuvant therapy. Significantly higher *EGFRm* rates in stages I and II than in stage III NSCLC ($p<0.001$ and $p=0.050$) were found, while no significant difference was found between stages I and II NSCLC ($p=0.158$). **Conclusions:** In this first prospective, real-world study of *EGFRm* prevalence in resected NSCLC, stage III and smoking were independent predictors associated with decreased odds of *EGFRm*. The results highlight the need to adhere to ASCO adjuvant chemotherapy guidelines, as only half of stage II/III NSCLC pts received adjuvant systemic therapy. Clinical trial information: NCT04742192. Research Sponsor: AstraZeneca.

Proportion of *EGFRm* by smoking status, histology, and stage.

Variables		Overall (N=601), n (%)	Comparison of mutation rate			
***EGFRm* (N=300), n**	***EGFRwt* (N=292), n**	**Mutation rate (%)**	**p-value**			
Smoking status	Current	37 (6.2)	9	25	26.5	**<0.001[a]**
	Ex	160 (26.6)	58	101	36.5	
	Never	354 (58.9)	211	138	60.5	
Histology	Adenocarcinoma	592 (98.7)	296	288	50.7	0.502
	Others	6 (1.3)	4	2	66.7	
Stage	IA-B	385 (64.0)	210	170	55.3	**0.002[b]**
	IIA-B	129 (21.5)	60	65	48.0	
	IIIA-B	87 (14.5)	30	57	34.5	

Unknown/missing data not included [a]current and ex-smoker vs never smoker; [b]stage I and II vs stage III.

8532 **Poster Session**

Examining ultrafine particle pollution and lung cancer risk in a large, diverse cohort.

Arthur Bookstein, Justine Po, Iona Cheng, Anna H. Wu, Timothy V. Larson, Lani Park, Jun Wu, Salma Shariff-Marco, Pushkar Inamdar, Veronica Wendy Setiawan, Mindy DeRouen, Scarlett L. Gomez, Loic Le Marchand, Daniel Stram, Jonathan Samet, Beate Ritz, Scott A. Fruin; Keck School of Medicine of University of Southern California, Los Angeles, CA; University of California, San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA; University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA; Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA; Population Sciences in the Pacific Program, University of Hawai'i Cancer Center, Honolulu, HI; Division of Occupational and Environmental Medicine, University of California, Irvine, Irvine, CA; Greater Bay Area Cancer Registry, Fremont, CA; Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA; Helen Diller Family Comprehensive Cancer Center University of California San Francisco, San Francisco, CA; Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA; University of Hawai'i Cancer Center – University of Hawai'i at Mānoa, Honolulu, HI; Colorado School of Public Health, Denver, CO; University of California, Los Angeles Fielding School of Public Health, Los Angeles, CA

Background: Health effects associated with particles less than 2.5 μm in diameter ($PM_{2.5}$) have been well studied, leading to the establishment of air quality standards and routine monitoring. Additionally, there is growing experimental evidence that ultrafine particles (UFPs), defined as particles less than 0.1μm in diameter, may adversely affect lung health, eliciting greater injury than larger particles due to deeper penetration into airways and longer retention in the lung parenchyma. Only two epidemiological studies have investigated this topic, finding no associations between ambient UFPs and respiratory mortality or overall lung cancer incidence respectively. Given the limited epidemiologic investigation of UFPs and lung cancer, we examined the association between airport-related UFPs and lung cancer incidence in a large, racially and ethnically diverse cohort. **Methods:** We estimated airport-related UFP exposure for 71,387 participants of the Multiethnic Cohort, who lived within a 53 km×43 km grid area around the Los Angeles International Airport (LAX) from date of cohort entry (1993-1996) through December 31, 2013. Cox proportional hazards regression was used, with calendar month/year as the time variable, to examine associations between UFP exposure and lung cancer risk adjusting for demographics, lifetime smoking, neighborhood socioeconomic status, occupation and lifestyle factors. Subgroup analyses were conducted by racial and ethnic groups, lung cancer histology, and smoking status. Co-pollutant models were run to mutually adjust for other traffic-related air pollutants. **Results:** A per unit increase in the interquartile range (IQR) of airport-related UFP exposure was not associated with lung cancer risk overall [HR = 1.01, 95% CI: 0.97-1.05] or by race and ethnicity. UFP exposure was suggestive of a positive association with risk of lung squamous cell carcinoma (SCC) [HR per IQR = 1.08, 95% CI: 1.00-1.17]. No associations were observed for other histologies [P_{het} for histology = .05]. UFP exposure was associated with an increased SCC risk among current smokers [HR = 1.11, 95% CI: 1.01-1.22] but not among never or past smokers [P_{het} for smoking = 0.51]. **Conclusions:** This study suggests a possible association between airport-related UFP exposure and risk of SCC. These results may be explained by previous studies finding that UFPs activate genes involved in oxidative damage, TNF-α signaling via NF-κB, and secretion of inflammatory and cardiopulmonary disease biomarkers. These findings warrant further investigation in large epidemiologic cohorts. Research Sponsor: U.S. National Institutes of Health.

8533 **Poster Session**

Clinical validation of an activity-based enzyme assay for early stage lung cancer.

Paul W. Dempsey, Cristina-Mihaela Sandu Aparicio, Ricardo Gonzalezirias, Spencer Hantula, Mari Kagawa, Stefan H. Bossmann, Obdulia Covarrubias-Zambrano, Alykhan S. Nagji, Nirmal K Veeramachaneni, Nezih O. Ermerak, Derya Kocakaya, Tunc Lacin, Bedrettin Yildizeli, Sara Witting Christensen Wen, Line Nederby, Torben Hansen, Ole Hilberg; Hawkeye Bio, Inc., Torrance, CA; University of Kansas Medical Center (KUMC), Kansas City, KS; Marmara University, Istanbul, Turkey; Vejle Hospital, University Hospital of Southern Denmark, Vejle, Denmark

Background: The USPSTF guidelines recommend annual LDCT scans for 15.5 million adults with a heavy smoking history. While LDCT can reduce deaths by 20%, screening compliance remains low. A blood test with clinically useful, cost effective performance could improve compliance and access when integrated with the standard of care. We describe here a lyophilized nanosensor system for detecting protease enzyme activity in sera with clinically useful diagnostic activity in early stage lung cancer. We evaluated the performance of the assay by examination of prospectively collected sera for detection of cancer in high risk patients. **Methods:** Sera were obtained in multiple independent studies to include pathologically confirmed, treatment naive lung cancer patients and LDCT confirmed negative individuals. Protease activity was measured on 18 different nanosensors built with protease targets mainly selective for members of the Matrix Metalloproteinase and Cathepsin families. Lyophilized plates were incubated with serum and enzyme activity was measured indirectly as a continuous variable by a fluorescent plate reader. A machine learning modeling tool (Emerge) was used to detect signal associated with a cancer "fingerprint" of protease activity. The analysis stratified allocation into training and testing sets of 250 samples each and reserved a third out of sample validation set (250 samples) for reporting. **Results:** 750 clinical samples included 30% lung cancers, 63% males, 91% smokers, and an average age of 63 years (SD=9). Cancer cases were distributed across stages I (41%), II (17%), III (20%) and IV (20%) with 5% unknown. Histological classification included 59% adenocarcinoma, 31% squamous cell and 11% other subtypes. Using an Emerge model with only nanosensor activity and gender as inputs, we evolved a balanced algorithm. The algorithm can be further modified to favor sensitivity or specificity depending on the application by applying model weighting factors. We report the performance observed in the 250 out of sample validation set at three points on this spectrum (Table). Among Stage I cancer samples, the balanced algorithm had an accuracy of 90% (26/29). **Conclusions:** Current LDCT tools show low compliance. We demonstrate clinical validity of a cost effective tool to detect lung cancer in support of LDCT screening. Based on a simple blood sample, the current test may predict early stage lung cancer with an accuracy of 90%. The performance suggests applications in LDCT compliance, post LDCT management, and eventually screening. A clinically validated version of this technology is being evaluated as a triage tool for LDCT screening. Research Sponsor: Hawkeye Bio, Inc.

	Specificity Max	Balanced	Sensitivity Max
Sensitivity:	62%	90%	97%
(95% CI)*	*(49-73%)*	*(80-96%)*	*(90-100%)*
Specificity:	86%	82%	54%
(95% CI)*	*(80-91%)*	*(76-88%)*	*(47-62%)*

* Clopper Pearson Exact Method.

8534 **Poster Session**

Multi-genomic analysis of compound and uncommon EGFR mutations in patients with non-small cell lung cancer.

Jayoung Park, Yu Min Lee, Sojeong Ka, Seoree Kim, In-Ho Kim, Yeoun Eun Sung, Chan-Kwon Jung, Jung-Young Shin, Sang Hoon Chun, Young Ho Lee, Jin Hyoung Kang, Joori Kim; Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, South Korea; Research Center, E-BIOGEN Inc., Seoul, South Korea; Roche Pharmaceuticals, Seoul, South Korea; Division of Medical HematoOncology, Department of Internal Medicine, Bucheon St. Mary's Hospital, The Catholic University of Korea, Bucheon-Si, South Korea; Division of Oncology, Department of Internal Medicine, Seoul St. Mary's Hospital, Seoul, Korea, Republic of (South); Department of Hospital Pathology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea; Cancer Research Institute, College of Medicine, The Catholic University of Korea, Seoul, South Korea; Bucheon St. Mary's Hospital, Gyeonggi-Do, South Korea; Research Center for Bioconvergence Analysis, Korea Basic Science Institute (KBSI), Chungcheongbuk-do, Seoul, South Korea; Medical Oncology, Seoul St Mary's Hospital, The Catholic University of Korea, Seoul, South Korea; Seoul St.Mary's Hospital, College of Medicine, The Catholic University of Korea,, Seoul, South Korea

Background: There are similar and different properties between the epidermal growth factor receptor mutations (mEGFR), which are classified into common, uncommon, and compound mutation subtypes depending on their location and pattern on the EGFR gene. We investigated the RWD and RNA expression profile of uncommon and compound mutations in the mEGFR+ NSCLC patients. **Methods:** We collected the medical information for stage I-IIIA mEGFR+ NSCLC patients receiving curative surgical resection in Seoul St. Mary's Hospital. We explored the RNA expression profile using multiplex IF and High-Plex Digital Spatial Profiling. A total of 18,676 DEG libraries were constructed, and 151 significance genes with $>$ 2-fold changes, 4-log 2 normalized read counts, and p-value = 0.05 (up and down) were identified. **Results:** In hospital cohort, 941 mEGFR+ cases of total 6,609 cases consist of common, 860 (91.4%), uncommon, 60 (7.4%), and compound, 21 (2.2%). Median relapse-free survival in uncommon and compound mEGFRs (31.4M and 33.7M) was shorter than common mEGFRs (40.1M, p = 0.877), but median overall survival did not differ between the groups. CNS recurrence rates in the uncommon and compound mEGFRs (40.0% and 35.3%) tended to be higher than that of common mEGFRs (27.4%, p = 0.361). Spatial RNA-seq data of the ratio of deconvolution individual cells showed that genes involved in inflammatory and immune response were relatively lower in mEGFR+ groups. According to the difference in DEG library through clustering heat map, uncommon or compound mEGFR in the immune, inflammatory response category, extracellular matrix, RNA splicing gene category, JAK-STAT, p53, PI3K-AKT, and notch signaling pathway related genes were down regulated compared to common mEGFR+ group. Gene ontology string analysis revealed RNA expression of genes in compound mEGFR was functionally associated with chemokine production (23.4%), electron transfer activity (14.9%) and T cell selection (8.5%), and, in uncommon mEGFRs, was associated with regulation of oligopeptide transport (26.1%), hypermethylation of CpG island (21.7%), and CD4+ CD25+ $\alpha\beta$ regulatory T cell lineage commitment (13.0%), compared to common mEGFR+ groups. Based on the GSEA, relatively highly clustered genes in compound mEGFR were the protein modification process, G-protein coupled receptor, regulation of cytosolic calcium ion concentration, and IL-5 production pathways, and lower ES levels in oxidative phosphorylation and RNA processing pathways, when compared to common mEGFR+ groups. **Conclusions:** In conclusion, our results suggest that uncommon and compound mEGFR+ subtypes exhibiting distinguished RNA expression profile of functional signaling pathways and protein network be not same disease entity as common mEGFR+ subtype. Research Sponsor: Bucheon St. Mary's Hospital Clinical Research Laboratory Foundation made in the program year of 2021.

8535 **Poster Session**

Validation of recurrence prediction using circulating tumor DNA in patients with curatively treated early stage non-small cell lung cancer.

Milou Schuurbiers, Christopher Gareth Smith, Koen Hartemink, Robert Rintoul, Kim Monkhorst, Daan van den Broek, Nitzan Rosenfeld, Michel van den Heuvel; Department of pulmonary diseases, Radboud university medical center, Nijmegen, Netherlands; Neogenomics Ltd, Babraham Research Park, Cambridge, United Kingdom; Department of Surgery, The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; Department of Oncology, University of Cambridge, Cambridge, United Kingdom; Department of Pathology, The Netherlands Cancer Institute, Amsterdam, Netherlands; Department of Laboratory Medicine, The Netherlands Cancer Institute, Amsterdam, Netherlands; Cancer Research UK Cambridge Institute, University of Cambridge, Cambridge, United Kingdom

Background: Stage II-III non-small cell lung cancer (NSCLC) patients receive adjuvant chemotherapy after surgery as standard-of-care treatment, despite an absolute 5-year disease free survival benefit of only 5.8%. Stage I patients do not receive adjuvant treatment but may benefit. Identification of residual disease by circulating tumor DNA (ctDNA) after curative intent therapy may allow more accurate decisions. **Methods:** Tumor tissue and serial plasma samples were collected from stage I-III NSCLC patients enrolled in the LEMA trial (NCT02894853). Somatic mutations identified by tumor exome sequencing were used to design patient-specific RaDaR assays, targeting up to 48 variants per patient, to analyze ctDNA in serial plasma samples. Results were compared and combined with an independent dataset (LUCID; Gale et al, Annals Oncol 2022). **Results:** In LEMA, 129 patients (53% stage I, 18% stage II and 29% stage III) were treated with curative intent by surgery (n=117), chemoradiation (n=8) or stereotactic radiotherapy (n=4) and followed for a median of 3.4 years. The LUCID dataset included 88 patients (49%/28%/23% in stage I/II/III). Results in the two cohorts were highly concordant (Table) and were assessed in the combined dataset of 808 serial plasma samples. Before treatment, ctDNA was detected in 22%, 72% and 90% of patients with stage I, II and III disease. ctDNA was detected post-treatment (at least one positive samples $\geq$14 days after the end of therapy) in 41/65 (63%) of patients who developed radiographic recurrence of their primary cancer, and preceded recurrence by a median of 204 days. For recurrence prediction by ctDNA detection post-treatment, the sensitivity, specificity, positive and negative predictive value (PPV and NPV) in stage I patients were 53%, 99%, 91% and 90%. In stage II-III patients, sensitivity was higher but specificity and NPV were lower (67%, 93%, 91% and 74%, respectively). ctDNA detection after treatment was associated with shorter recurrence-free survival (hazard ratio (HR) 11.5, P=$1.8x10^{-32}$) and overall survival (HR 8.1, P=$1.2x10^{-17}$). **Conclusions:** ctDNA detection by RaDaR assays predicted recurrence in two independent cohorts, confirming the potential to identify patients for adjuvant treatment. In stage I patients with positive ctDNA, adjuvant treatment could be offered with confidence due to high specificity of 99% and PPV of 91%. In stage II-III patients, the primary cancer recurred in a quarter of patients with no ctDNA detected post-treatment (NPV 74%). Our results help identify the potential role for ctDNA analysis as a decision support tool for adjuvant therapy in NSCLC. Research Sponsor: None.

Recurrence prediction by ctDNA detection post-treatment.

	Sensitivity %	Specificity %	PPV %	NPV %
Combined (n=193)	63	97	91	84
Stage I	53	99	91	90
II-III	67	93	91	74
- LEMA	62	97	92	85
Stage I	50	100	100	89
II-III	68	93	89	77
- LUCID	64	96	90	82
Stage I	57	97	80	91
II-III	65	94	93	68

8536 **Poster Session**

Real-life efficacy of nivolumab plus ipilimumab combination in untreated, unresectable malignant pleural mesotheliomas: Result of French early access program—MESOIMMUNE – GFPC 04-2021.

Olivier Bylicki, Florian Guisier, Catherine Daniel, Aurélie Swalduz, Emmanuel Grolleau, Marie Bernardi, Stephane Hominal, Nicolas Cloarec, Simon Deshayes, Judith Raimbourg, Remi Veillon, Youssef Oulkhouir, Clarisse Audigier-Valette, Aurélien Gobert, Lionel Falchero, Lise Thibonnier, Matthieu Chasseray, Christine Raynaud-Donzel, Chantal Decroisette, Laurent Greillier; HIA SAINTE ANNE, Toulon, France; Univ Rouen Normandie, LITIS Lab QuantIF team EA4108, CHU Rouen, Inserm CIC-CRB 1404, Department of Pneumology, Thoracic Oncology and Respiratory Intensive Care, F-76000, Rouen, France; Institut Curie, Paris, France; Centre Leon BERARD, Service d'Oncologie Médicale, Lyon, France; Acute Respiratory Disease and Thoracic Oncology Department, Lyon Sud Hospital, Hospices Civils de Lyon, Lyon, France; CH du Pays D'Aix, Aix En Provence, France; Centre Hospitalier Annecy-Genevois, Annecy, France; Service d'Oncologie, Centre Hospitalier Henri Duffaut, Avignon, France; Chu De Caen, Caen, France; Institut de Cancérologie de l'Ouest, Saint-Herblain, France; CHU Bordeaux - Hôpital Haut Lévêque, Pessac, France; University Hospital CAEN, Caen, France; CHITS Toulon Sainte Musse, Pôle de Médecine à Orientation Oncologique, Toulon, France; St Gregoire Hospital, St Gregoire, France; Hôpitaux Nord-Ouest, Service de Pneumologie et Cancérologie Thoracique, Villefranche-Sur-Saone, France; Unicancer Clermont Ferrand, Clermont Ferrand, France; Centre Finistérien de Radiothérapie et d'Oncologie–Clinique Pasteur, Brest, France; CH Argenteuil, Argenteuil, France; CH Annecy Genevois, Epagny Metz-Tessy, France; Multidisciplinary Oncology and Therapeutic Innovations, Hôpital Nord, Marseille, France

Background: The SOC for unresectable malignant pleural mesothelioma (MPM) has changed in 2020 with the combination nivolumab plus ipilimumab (NIVO+IPI) results of CheckMate 743 study. As CheckMate 743 was therapeutic trial in selected MPM patients (pts), additional data would be of interest to confirm the results in real-life setting. **Methods:** The present multicenter, retrospective study assessed the outcomes of NIVO+IPI, via an early access program (EAP) in France, in pts with treatment naïve unresectable MPM. The primary objective was investigator-assessed real world progression-free survival (rwPFS) from initiation of NIVO+IPI, defined as time from first dose of NIVO+IPI to first documentation of objective disease progression or death from any cause. The secondary objectives were real world OS (rwOS), objective response rate (ORR), and safety of NIVO+IPI combination. **Results:** From April 1, 2021 to Feb 15, 2022 (last day of EAP) there were 143 pts included out of 350 pts treated by EAP for unresectable MPM in 44 centers. Population characteristics are described in the table. With a median follow-up of 14.1 months, median rwPFS was 7.8 months (95%CI 6.2-9.5). rwPFS rates no differ according to histological subtypes: rwPFS for epithelioid MPM was 8.1 months (95%CI 6.0-12.6) and 7.4 months (95% CI 5.3-11.2) for other histological subtypes. The median rwOS was not reached (NR), 1-year survival rate was 65% (95% CI 57-75%). Median rwOS was NR and 13.1 (95% CI 7.8- NA) in epithelioid and non-epithelioid MPM, respectively. At 1 year, 71.2% of pts with epithelioid MPM are still alive versus 51.2% in pts with other histological subtypes. ORR was 23.9% (95% CI 16.9-32.0%) with median time to response of 3.68 months (2.33-5.09) after introduction of NIVO+IPI. Disease control rate was 80.4%. Grade 3-4 adverse events (AE) occurred in 37.8%. Severe immune-related AE occurred in 13.9% of patients. Five deaths were associated with treatment-related AEs according to investigators judgment. **Conclusions:** While pt's characteristics differed from the pivotal trial, notably with older and unselected patients, efficacy outcomes that we observed here compares favorably with CheckMate 743 results. Tolerance looks acceptable in real-life setting despite 5 toxic deaths reported. Extended follow-up of our cohort will allow consolidation of the results. Clinical trial information: NCT05308966. Research Sponsor: BMS.

	Nivolumab + Ipilimumab (n=143)
Age, years (SD)	74.7 (9.42)
<65	20 (14.0%)
≥ 65 to ≤ 75	45 (31.5%)
≥ 75	78 (54.5%)
Sex	
Male	120 (83.9%)
Female	23 (16.1%)
Eastern Cooperative Oncology Group Performance status	
0	51 (39.8%)
1	66 (51.6%)
2	9 (7.0%)
≥2	2 (1.6%)
Smoking Status	
Current or former	71 (49.7%)
Never	64 (44.8%)
Unknown	13 (5.6%)
Histology	
Epithelioid	99 (69.7%)
Non-Epithelioid	43 (30.3%)
Sarcomatoid	13 (9.2%)
Mixed or other	30 (21.2%)
Stage	n=98
1	9 (9.2%)
2	10 (10.2%)
3	49 (50.0%)
4	30 (30.6%)

8537 **Poster Session**

Phase 1 trial of gavocabtagene autoleucel (gavo-cel, TC-210) in patients (pts) with treatment refractory mesothelioma and other mesothelin-expressing solid tumors.

Raffit Hassan, Marcus O. Butler, David Yoonsuk Oh, Roisin Eilish O'Cearbhaill, Lauren MacMullen, Erin Jeter, Udayan Guha, Viera P. Muzithras, Kevin Zikaras, Melissa Lynne Johnson, Janos Laszlo Tanyi, Azam Ghafoor, Robert Tighe, Munisha Smalley, Alfonso Quintas-Cardama, David S. Hong; Thoracic and GI Malignancies Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD; Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada; Department of Medicine, University of California, San Francisco, CA; Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY; TCR2 Therapeutics, Cambridge, MA; Sarah Cannon Research Institute, Nashville, TN; University of Pennsylvania, Media, PA; National Cancer Institute/National Institutes of Health, Bethesda, MD; University of Texas MD Anderson Cancer Center, Houston, TX

Background: We have conducted a Phase 1 trial of gavo-cel, an autologous genetically engineered anti-mesothelin T cell receptor fusion construct (TRuC™) cell therapy in pts with refractory mesothelin-expressing mesothelioma (MPM), ovarian cancer (OvC), cholangiocarcinoma (CHO), or non-small cell lung cancer (NCT03907852). **Methods:** T cells were engineered with a lentiviral vector to express an anti-mesothelin single domain antibody fused to the CD3ε subunit, which upon translation, integrated into and reprogrammed native T cell receptors to target mesothelin-expressing cancer cells in an HLA-independent manner. Eligibility required central laboratory confirmation of 2+ or 3+ mesothelin expression by IHC in ≥50% of tumor cells. Dose escalation followed a modified 3+3 design. **Results:** At data cut-off date (January 17th, 2023), 32 pts (23 MPM, 8 OvC, 1 CHO) received a gavo-cel infusion at one of 7 dose levels (DL): DL0 (n = 1, no lymphodepletion [LD]) and DL1 (n = 8), $5x10^7$ transduced cells/m^2; DL2 (n = 1, no LD) and DL3 (n = 13), $1x10^8$ transduced cells/m^2; DL3.5 (n = 5), $3x10^8$ transduced cells/m^2; DL4 (n = 1, no LD) and DL5 (n = 3), $5x10^8$ transduced cells/m^2. Median number of prior therapies was 5 (range, 1-13), including immune checkpoint inhibitors (ICI) in 87% of MPM pts. Bridging therapy was required in 24 (75%) pts. Two DLTs were reported: grade (gr) 3 pneumonitis at DL1 and gr5 bronchoalveolar hemorrhage at DL5. At the RP2D ($1x10^8$/m^2 after LD) 2/13 (15%) pts had reversible gr≥3 CRS. The ORR and disease control rate was 20% and 77%, respectively. The 6-month OS rate was 70.2%. The ORR of pts with MPM or OvC receiving gavo-cel after LD was 21% and 29%, respectively. The median PFS and OS in MPM was 5.6 and 11.1 mos and in OvC was 5.8 and 9.4 mos. Responses correlated with declines in soluble mesothelin related peptides. Peak expansion and persistence correlated with dose and LD administration. At the RP2D, the median C_{max} was 14,385 copies/ug gDNA (range, 64.4–100,782) and the median peripheral blood (PB) persistence was 84 days (range: 0-170). Consistent elevation in IL-6 and IFN-γ levels but minimal IL-8 and TNF-α were observed. Gavo-cel expanded preferentially in cancerous tissues, where it was detected long after becoming undetectable in PB. Gavo-cel therapy led to increased $CD3^+CD8^+$ T cell tumor infiltration. Non-responders exhibited upregulation of immunoinhibitory ligands (CD155, PDL1), indicating potential resistance mechanisms. **Conclusions:** A single IV gavo-cel infusion at the RP2D was associated with a manageable toxicity profile and high rates of disease control, including objective responses in pts with refractory MPM and OvC. A phase 2 study is underway testing the safety and efficacy of gavo-cel in combination with checkpoint inhibitors in pts with mesothelin-expressing solid tumors. Clinical trial information: NCT03907852. Research Sponsor: TCR2 Therapeutics.

8538 **Poster Session**

Long-term outcomes of single and five fraction schedules of stereotactic body radiation therapy for early-stage central or peripheral NSCLC: Neither fractionation nor location matter?

Karen Huang, Sharan Prasad, Sung Jun Ma, Austin Iovoli, Mark Farrugia, Nadia Karen Malik, Anurag K. Singh; Department of Radiation Medicine, Roswell Park Comprehensive Cancer Center, Buffalo, NY; Cornell University, Ithaca, NY; Roswell Park Comprehensive Cancer Center, Buffalo, NY; Roswell Park Cancer Institute, Buffalo, NY; Roswell Park Cancer Institute Department of Cancer Prevention and Population Sciences, Buffalo, NY

Background: Due to concerns with toxicity, treatment of early-stage non-small cell lung cancer (NSCLC) with stereotactic body radiation therapy (SBRT) often involves different fractionation schemes for peripheral and centrally located tumors. There is a paucity of long-term SBRT survival outcomes comparing peripheral versus central NSCLC. **Methods:** This is a single-institution observational cohort study of patients diagnosed with early-stage NSCLC (T1-2N0M0) who underwent 27 Gy in 1 fraction or 50 Gy in 5 fractions with heterogeneity correction at Roswell Park Comprehensive Cancer Center between September 2008 to December 2018. All patients treated with single-fraction SBRT had peripheral NSCLC and those treated with five-fraction SBRT had central NSCLC. Clinically relevant variables including age, gender, race, Karnofsky Performance Status (KPS), histology (adenocarcinoma, squamous cell carcinoma, NSCLC not otherwise specified), T stage, smoking status, tumor location, and the year of SBRT delivery were obtained retrospectively. Cox multivariable analysis (MVA), Kaplan-Meier plot, and log-rank test were performed to evaluate progression-free survival (PFS) and overall survival (OS). Fine-Gray competing risk MVA was performed to evaluate local failure (LF), nodal failure (NF), and distant failure (DF) with death as a competing event. To reduce selection bias, propensity score matching was performed between single- versus five-fraction SBRT cohorts. **Results:** A total of 265 patients (142 female [53.6%]; median age 77 years) met our criteria. There were 74 (27.9%) and 191 (72.1%) patients with central tumors treated with five-fraction SBRT and peripheral tumors treated with single-fraction SBRT, respectively. On Cox MVA, there was no statistically significant difference in OS (peripheral vs central tumors: adjusted hazards ratio [aHR] 1.04, 95% confidence interval [CI] 0.74-1.46, p=0.81) and PFS (peripheral vs central tumors: aHR 1.05, 95% CI 0.76-1.45, p=0.77). On Fine-Gray competing risk MVA comparing peripheral vs. central tumors, there was no statistically significant difference in LF, NF, and DF. After propensity score matching, 68 matched pairs were identified for peripheral vs. central tumors with similar results. **Conclusions:** Among patients with early-stage NSCLC treated with SBRT central versus peripheral location was associated with similar long-term survival and tumor recurrence outcomes. Research Sponsor: None.

8539 **Poster Session**

EGFR assessment using next generation sequencing as a reflex testing on surgically resected non-squamous non-small cell lung carcinoma.

Samantha Goffinet, Veronique Hofman, Christophe Bontoux, Jonathan Benzaquen, Charlotte Cohen, Charles-Hugo Marquette, Jean-Philippe Berthet, Marius Ilie, Paul Hofman; Laboratory of Clinical and Experimental Pathology, Pasteur Hospital, FHU OncoAge, Université Côte d'Azur, CHU Nice, Nice, France; Department of Pneumology, Pasteur Hospital, FHU OncoAge, Université Côte d'Azur, CHU Nice, Nice, France; Department of Thoracic Surgery, Pasteur Hospital, Université Côte d'Azur, CHU Nice, Nice, France; Department of Thoracic Surgery, Pasteur Hospital, CHU Nice, Université Côte d'Azur, Nice, France; Laboratory of Clinical and Experimental Pathology, Biobank Côte d'Azur, Pasteur Hospital, FHU OncoAge, Université Côte d'Azur, CHU Nice, Nice, France

Background: *EGFR* status assessment is mandatory in early stage (IB-IIIA) non-squamous non-small cell lung carcinoma (NS-NSCLC), but whether NGS methods should be used as reflex testing for this evaluation in daily practice is controversial. However, co-occuring mutations, notably *TP53* mutations, may have an impact on tumor behavior and prognosis, and so, on future adjuvant therapeutic strategies. **Methods:** *EGFR* mutations were assessed prospectively using NGS (Oncomine Precision Assay genes panel) in 720 NS-NSCLC surgically resected between January 2021 and September 2022 in a single institution (LPCE, Nice, France). PD-L1 expression was evaluated in all tumors. Disease free survival (DFS) analysis was available in 675/720 (94%) patients. **Results:** *EGFR* mutations were detected in 83/720 (11.5%) cases. A common non-compound *EGFR* mutation (L858R or del19) was observed in 62/83 (75%) cases. 12/83 (14%) and 9/83 (11%) tumors had a rare non-compound and compound *EGFR* mutations, respectively. 40/83 (48%) has a co-occuring mutation, including a *TP53* (30/40; 75%) mutation, mainly in exon 5, 7 or 8. *EGFR/TP53* mutated tumors were significantly associated with higher PD-L1 expression compared to *EGFR* mutated tumors. A significant correlation was noted between worse DFS and the detection of a mutation in *EGFR* exon 18 mutation, as well as the detection of a co-mutation in *TP53* exon 7 and in *MET* exon 14. **Conclusions:** Genomic alteration should be systematically evaluated using an NGS reflex testing in surgically resected NS-NSCLC, since future adjuvant therapeutic decision making may consider the presence of compound *EGFR* mutations as well as co-occuring mutations in other genes, especially in *TP53.* Research Sponsor: Centre Hospitalier Universitaire de Nice.

8540 **Poster Session**

Stereotactic body radiation therapy with sequential immunochemotherapy as neoadjuvant therapy in resectable non-small cell lung cancer (SACTION-01 study).

Ze-Rui Zhao, Shi-Liang Liu, Ting Zhou, Zhi-Chao Li, Jia-Di Wu, Mian Xi, Yong-Bin Lin, Hong Yang; Sun Yat-Sen University Cancer Center, Guangzhou, VA, China; Department of Radiation Oncology, Sun Yat-Sen University Cancer Center, Guangzhou, China; Department of Medical Oncology, Sun Yat-sen University Cancer Center & State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangzhou, Guangdong, China; Sun Yat-Sen University Cancer Center, Guangzhou, China; Sun Yat-sen University Cancer Center, Guangzhou, China

Background: Neoadjuvant PD-1 inhibitor plus chemotherapy increases pathological response for resectable non-small cell lung cancer (NSCLC) compared with chemotherapy alone. Previous phase II trial indicated that stereotactic body radiation therapy (SBRT) served as an immunomodulator and enhanced the effect of preoperative immuno-monotherapy. However, whether SBRT would further increase the efficacy of immunochemotherapy for NSCLC remains unknown. **Methods:** In this phase II trial, patients with resectable EGFR wild-type stage IIA to IIIB NSCLC were recruited to receive SBRT (24 Gy in 3 daily fractions) to the primary tumor followed by two cycles of PD-1 inhibitor tislelizumab (200 mg) plus platinum-based doublet chemotherapy (Q3W) before surgical resection. The primary endpoint was major pathological response (MPR) defined as no more than 10% of viable tumor cells in the specimen. Simon's optimal two-stage design was used for conducting the trial. The null hypothesis was that the MPR rate is 0.30, and the alternative hypothesis was that the true MPR rate was 0.50. More than 4 MPRs were needed in stage 1 (n=15) to continue, and if there were 19 or more MPRs in 46 patients by the end of stage 2, the null hypothesis can be rejected. The design controls the type I error rate at 0.05 and yields the power of 0.80. (NCT05319574). **Results:** Between May 2022 and Jan 2023, 32 patients were enrolled with 31 (96.9%) male and 19 (59.4%) having squamous cell lung cancer. Twenty-six (81.3%) patients had stage IIIA/B disease. All patients received at least one cycle of immunochemotherapy; 23 of the 25 patients (92.0%) who completed treatment had undergone R0 resections, except for one patient who had disease progression and the other one that unable to tolerate surgery because of grade 4 neutropenia. Twenty-two patients underwent minimally invasive approaches and 3 of them (13.6%) converted to thoracotomy. The median percentage of the viable tumor was 0 (interquartile range: 0-4.0%). Twenty patients achieved MPR, which surpassed the prespecified required number to reject the null hypothesis, resulting in the MPR rate of 80.0% (20/25) in the intention-to-treat population, and 87.0% (20/23) in the per-protocol population. Pathological complete response (pCR) was found in 14 patients (56.0% in the intention-to-treat population and 60.9% in the per-protocol population). Nodal clearance status (pN0) was found in 20 of 23 cN1/2 cases (87.0%). Grade 3-4 adverse events related to neoadjuvant treatment included neutropenia (13.0%), anemia (4.3%), and pneumonia (4.3%). No 30-day or 90-day mortality was observed. **Conclusions:** Neoadjuvant SBRT followed by immunochemotherapy yields unprecedently high MPR and pCR rates in NSCLC without EGFR mutation. The trial will continue to recruit 14 more patients to reach a final sample size of 46 participants. Clinical trial information: NCT05319574. Research Sponsor: None.

8541 **Poster Session**

The RESECT study: Factors associated with overall survival (OS) and relapse-free survival (RFS) among patients with stages I–III resected NSCLC without known EGFR mutations.

Jhanelle Elaine Gray, Rachel Salomonsen, Nefeli Georgoulia, Ignacio Diaz Perez, Alice Wang, Ling Cai, Graham Wetherill, Yang Xiao, Claire Fielden, Nasser K. Altorki; Moffitt Cancer Center, Tampa, FL; AstraZeneca, Gaithersburg, MD; AstraZeneca, Cambridge, United Kingdom; Weill Cornell Medicine, New York, NY

Background: Approximately one-third of patients with Stages I–III resected non-small-cell lung cancer (NSCLC) do not survive 5 years from diagnosis. This retrospective observational study analyzed factors associated with OS and real-world (rw) RFS among Stage I–III NSCLC patients before the introduction of immuno-oncology (IO) treatment. **Methods:** We analyzed data from the US CancerLinQ database for adult patients with no known *EGFR* mutations and no other cancers, who were diagnosed with Stage I–III NSCLC from 2014–2019 and had surgical resection within 140 days after initial diagnosis. 3081 patients met the study criteria of whom 1677 were Stage I, 853 were Stage II, and 551 were Stage III; 4 Stage I patients who received neoadjuvant or perioperative treatment were excluded (too few for analysis). Most patients received surgery only (71.5%); the rest also received adjuvant (24.7%), neoadjuvant (2.4%) or perioperative (1.5%) treatment, most often chemotherapy ± radiotherapy. Key demographics, clinical characteristics, treatment patterns, and relevant 2-way interactions were considered for inclusion in the model, based on Cox regression analyses and medical insights. Multivariable Cox regression analysis (backwards selection, $p<0.05$) was used to model OS and rwRFS. **Results:** In the multivariable analyses (in which no Stage I patients with neoadjuvant or perioperative treatment were included), factors associated with both OS and rwRFS ($p<0.05$) were disease stage, race, ethnicity, year of diagnosis, ECOG performance status, and neoadjuvant treatment. Factors associated with OS ($p<0.05$), but not rwRFS, were age, sex, time from diagnosis to surgery, and type of surgery. Factors associated with rwRFS ($p<0.05$), but not OS, were geographic region, nodal status, and adjuvant treatment in Stage II and III patients but not Stage I patients. **Conclusions:** This study identified several risk factors associated with OS and rwRFS, many of which are known. Notably, in this analysis, neoadjuvant treatment was associated with both improved OS and rwRFS in Stage II–III patients and was not evaluable in Stage I patients. However, adjuvant treatment was only associated with improved rwRFS, and only in Stage II–III patients. Based on these findings, there remains an unmet need for Stage I–III NSCLC patients. The recent introduction of IO treatment in this setting may help improve patient outcomes. Research Sponsor: AstraZeneca.

8542 **Poster Session**

Two-year lung cancer survival between 2000 to 2020: Results from 3 French nationwide cohorts.

Didier Debieuvre, Isabelle Monnet, Olivier Bylicki, Sophie Schneider, Francois Goupil, Benoit Godbert, Christine Dussopt, Herve Pegliasco, Laurent Portel, Reda Chikouche, Philippe Masson, Mohamad Jaafar, Clothilde Marty, Fethi EL Khanjari, Julie Obert, Marjorie Picaud, Anne Sophie Bravard, Herve Le Floch, Alexia Letierce, Hugues Morel; Service de Pneumologie, Groupe Hospitalier de la Région Mulhouse Sud-Alsace, hôpital Émile-Muller, Mulhouse, France; CHI De Creteil, Créteil, France; HIA SAINTE ANNE, Toulon, France; Hospital Center De La Cote Basque, Bayonne, France; Centre Hospitalier, Le Mans, France; Hôpital Robert Schuman, Service de Pneumologie, Metz, France; Hopital Nord Ouest (HNO), Villefranche-Sur-Saône, France; Hôpital Européen Marseille, Marseille, France; Centre Hospitalier Robert Boulin, Libourne, France; Centre Hospitalier Auxerre, Auxerre, France; Cholet Hospital Centre, Cholet, France; Centre Hospitalier Eure-Seine-Evreux, Evreux, France; Centre Hospitalier Saint Nazaire, Saint-Nazaire, France; Centre Hospitalier Blois, Blois, France; Centre Hospitalier le Raincy Montfermeil, Montfermeil, France; Centre Hospitalier Tourcoing, Tourcoing, France; CH Avranches, Avranches, France; Hôpital d'instruction des armées Percy, Clamart, France; Qualitystat, Morangis, France; Service Pneumologie Oncologie Thoracique, Orléans, France

Background: Each decade since 2000, the French College of General Hospital Pulmonologists (CPHG) conducts the KBP study, a real-life nationwide prospective multicenter study on LC in non-academic public hospital (NPH). Here, we report the two-year survival (2-y) rate among the 2020 cohort and the comparisons with the 2000 and 2010 cohorts. **Methods:** Collection of all consecutive diagnosed LC, all stage and all histology, between 01/01 and 12/31 in NPH pulmonology or oncology units in 2000, 2010 and 2020 with the same methodology. A Scientific Committee controlled inclusion exhaustivity and quality in each center. Survival rates were calculated using the Kaplan-Meier method and risk factors were assessed using Cox models. **Results:** 8,999 patients were included in 82 centers in 2020. The 2-y survival rate was 40.3%, the median overall survival was 15.3 months. Compared to 2000, mortality rates at 2 years decreased significantly (-19.1%), while early (1 month and 3 months) mortality remains similar. Survival improved in 20 years whatever histologic types (Table). Factors associated with 2-y survival were sex (36.1% vs 48.1% respectively for male and female respectively, significantly increased over 20 years: + 15.3% for M and + 24.5% for F), high age (>80 y-o), poor ECOG status (3 or 4) and advanced disease. As expected in 2020, TNM stage was still determining for 2-year mortality, 15.2 [12.6-17.7] stage I vs 75.6 [74.4-76.8] stage IV. In 2020 the Covid-19 infection (n=283) impacted the survival (HR = 4.02 95%CI [3.33-4.86]) on multivariate analysis adjusted to age, sex, tobacco consumption, histology, ECOG status, TNM stage. **Conclusions:** These results confirmed the major improvement in the last two decades for LC. 5-years survival will provide us more enlightenment. Research Sponsor: AstraZeneca, BMS, MSD, Janssen, Bayer, Boehringer Ingelhei, Lilly, Takeda, Sanofi, Roche, Chugai, Pfizer; Fondation du Souffle, Le Nouveau Souffle, Couleur Espoir, the labeling of InCa and FHF-CNCR.

Mortality rates* - % [95% IC].

Overall mortality	Months	2000	2010	2020
	1	10.4 [9.6 - 11.2]	9.8 [9.1 - 10.4]	8.2 [7.7 - 8.8]
	3	24.6 [23.4 - 25.7]	23.3 [22.3 - 24.3]	20.2 [19.4 - 21.0]
	12	60.1 [58.8 - 61.4]	56.9 [55.7 - 58.0]	44.5 [43.4 - 45.5]
	24	78.8 [77.7 - 79.8]	74.2 [73.2 - 75.3]	59.7 [58.7 - 60.8]
	Median survival time (months)	*8.8 [8.4 - 9.1]*	*9.7 [9.4 - 10.1]*	*15.3 [14.6-16.1]*
Mortality / histology	**Months**	**2000**	**2010**	**2020**
SCLC	**24**	88.3 [86.0 - 90.3]	86.4 [84.0 - 88.4]	80.6 [78.0 - 82.9]
Squamous	**24**	75.6 [73.7 - 77.4]	70.9 [68.8 - 73.0]	61.5 [59.1 - 63.6]
Non-SCLC, non-squamous	**24**	76.5 [74.3 - 78.5]	72.3 [70.7 - 73.9]	54.4 [52.9 - 55.9]

*Preliminary results with 1291 missing data at Month 24 – Update will be available for the congress.

8543 **Poster Session**

Association of nuclear shape in the tumor epithelium with response to atezolizumab in NSCLC.

Patrick Leo, Namrata Srivastava Patil, Daniel Ruderman, Jennifer M. Giltnane, Eloisa Fuentes, Amber Schedlbauer, Barzin Nabet, Cleopatra Kozlowski; Genentech, South San Francisco, CA; Genentech, Inc., South San Francisco, CA; Genentech Inc, South San Francisco, CA; Rancho Bio-Sciences LLC, San Diego, CA; Genentech Inc., South San Francisco, CA

Background: Anti-PD-(L)1 treatment is the standard of care for advanced non-small cell lung cancer (NSCLC). However, additional biomarkers are needed to identify patients who will benefit from these therapies. In this study, we demonstrate the atezolizumab response score (ARS), which uses digital pathology features of the shape and size of nuclei in the tumor epithelium to predict response to the anti-PD-L1 antibody atezolizumab in NSCLC. **Methods:** Patients were drawn from two trials comparing atezolizumab to docetaxel in second-line advanced NSCLC. A single digitized slide stained for the epithelial cell marker pan-cytokeratin (CK) and CD8 was selected for each patient. OAK, a phase III trial, had 819 patients with images available and was used for training the ARS model. POPLAR, the phase II trial preceding OAK, had 168 evaluable patient images for validating ARS. Color deconvolution was used to identify the CK-positive regions in each image. Nuclei were segmented using the hematoxylin channel. The area, perimeter, eccentricity, solidity, and minor/major axis lengths were extracted from each nucleus in the CK-positive compartment of the pathologist-annotated tumor lesion, excluding necrosis and artifacts. Each measure's mean, median, standard deviation, skewness, and kurtosis across the slide was calculated, for a total of 30 features. Features with an interaction $p < 0.35$ with trial arm in a Cox model were used to fit an elastic-net regularized Cox model on the atezolizumab-treated training set patients, producing ARS. The ARS threshold maximizing atezolizumab overall survival (OS) benefit in the ARS-high group was identified in OAK and applied to POPLAR (the validation set). ARS performance was assessed in the validation set by OS concordance index (c-index) and by atezolizumab benefit in the high- vs. low-ARS groups by hazard ratio (HR) [95% confidence interval]. **Results:** ARS employs five features. Lower nuclear median and standard deviation of major axis length, higher perimeter mean and standard deviation, and higher area were associated with better atezolizumab response. In the validation set, high-ARS (prevalence = 42%) patients had longer OS on atezolizumab vs. docetaxel (HR = 0.42 [0.24-0.72]) while low-ARS patients did not (HR = 0.95 [0.62-1.47]). ARS was positively associated with OS in the validation set atezolizumab arm (c-index = 0.60 [0.54-0.66]), but not the docetaxel arm (c-index = 0.47 [0.41-0.54]). **Conclusions:** We validated a nuclear morphology-based biomarker for atezolizumab response in advanced NSCLC. This demonstrates the utility of digital pathology for biomarker development and motivates study into the identified responder phenotype. Combination of ARS with additional markers, such as PD-L1 expression, might further improve stratification. Research Sponsor: Roche.

8544 **Poster Session**

Radiation therapy (RT)-free pembrolizumab plus chemotherapy (P+C) for PD-L1 TPS ≥50% locally advanced non-small cell lung cancer (LA-NSCLC): An early report analyzing depth of response from multicenter single arm phase II study (Evolution trial: WJOG11819L).

Akito Hata, Taira Ninomaru, Hideaki Okada, Yoshihito Kogure, Masahide Oki, Nobuyuki Katakami, Takashi Kijima, Toshihide Yokoyama, Hirotaka Matsumoto, Yuki Sato, Terufumi Kato, Shunichi Sugawara, Takeshi Sawada, Kenichi Yoshimura, Takashi Seto, Nobuyuki Yamamoto, Kazuhiko Nakagawa; Kobe Minimally Invasive Cancer Center, Kobe, Japan; National Hospital Organization Nagoya Medical Center, Nagoya, Japan; Takarazuka City Hospital, Takarazuka, Japan; Hyogo Medical University, Nishinomiya, Japan; Kurashiki Central Hospital, Kurashiki, Japan; Hyogo Prefectural Amagasaki General Medical Center, Amagasaki, Japan; Kobe City Medical Center General Hospital, Kobe, Japan; Kanagawa Cancer Center, Yokohama, Japan; Sendai Kousei Hospital, Sendai, Japan; Kyoto University Hospital, Kyoto, Japan; Hiroshima University Hospital, Hiroshima, Japan; National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan; Internal Medicine III, Wakayama Medical University, Wakayama, Japan; Kindai University Faculty of Medicine, Osaka-Sayama, Japan

Background: Standard of care for unresectable LA-NSCLC is chemoradiation therapy (CRT) followed by durvalumab (D). Survival curves of P monotherapy/P+C for PD-L1 TPS ≥50% stage IV NSCLC suggested possible comparable survival to CRT for stage III patients (pts). Moreover, some studies of neoadjuvant C+immunotherapy (I) for stage III pts have demonstrated high pCR and MPR rates, implying potentially outstanding efficacy of C+I for earlier stage. We thus hypothesized P+C without RT in PD-L1 ≥50% LA-NSCLC pts provides a comparable efficacy to CRT followed by D while avoiding CRT-induced severe toxicities. **Methods:** This early report focuses on depth of response in a phase II study by WJOG. P with platinum plus pemetrexed (PEM) (non-squamous) or P with carboplatin plus nab-paclitaxel (squamous) was administered every 3 weeks without RT. After four cycles of induction P+C, P with PEM (non-squamous) or P alone (squamous) was continued until progression or 2 years. The primary endpoint was PFS rate at 2 years. **Results:** Between May 2020 and February 2022, 21 pts were enrolled. Median age was 74 (range, 53-89). Stage IIIA/B/C included 12 (57%)/6 (29%)/3 (14%), respectively. Histologic subtypes were 13 (62%) adeno, 5 (24%) squamous, and 3 (14%) others. Investigator-assessed best response: 8 (38%) CR; 10 (48%) PR; 2 (10%) SD; and 1 (5%) NE were confirmed, resulting in response rate (RR) of 86% and disease control rate of 95%. RR of TPS 50-79% and 80-100% were 78% and 92%, respectively. Deep response (DR): defined as tumor shrinkage ≥80% was obtained in 12 (57%) of 21 pts. DR was accomplished in 4 (44%) of 9 TPS 50-79% and 8 (67%) of 12 TPS 80-100%. Median time to response was 43 (range, 41-92) days. Early tumor shrinkage (ETS): PR-in at the time of first CT evaluation (6 weeks) was achieved in 16 (89%) of 18 CR+PR pts. At the time of data cut-off, median follow-up period was 18.5 (range, 0.3-29.0) months, and 14 (67%) of 21 pts were progression-free. All 12 pts achieving DR, including all 8 CR were progression-free, also in 14 (88%) of 16 ETS pts. Three pts after local progression received salvage definitive-CRT. Median number of P administrations was 20 (range, 1-35). AEs ≥grade 3 were observed in 11 (52%) pts, including: 2 (10%) pneumonitis; 2 (10%) pneumonia; 1 (5%) diarrhea; 1 (5%) ALT elevation; and 1 (5%) acute heart failure, excluding hematological AEs. There was one (5%) possible grade 5 AE (pneumonia). **Conclusions:** RT-free P+C exerted a notably high RR, including some CRs. The deeper/earlier response and higher PD-L1 TPS could be associated with the higher progression-free incidence at the data cut-off. To investigate our hypothesis: RT-free P+C can be a less toxic curative option in selected LA-NSCLC pts with PD-L1 TPS ≥50%, further matured data is warranted. Clinical trial information: NCT04153734. Research Sponsor: MSD.

8545 **Poster Session**

Phase I Beamion Lung 1 trial of BI 1810631, a HER2 tyrosine kinase inhibitor (TKI), as monotherapy in patients (pts) with advanced/metastatic solid tumors with HER2 aberrations: Updated data.

John Heymach, Frans Opdam, Minal A. Barve, Hai-Yan Tu, Yi-Long Wu, David Berz, Neil Gibson, Behbood Sadrolhefazi, Josep Serra, Kiyotaka Yoh, Noboru Yamamoto; Department of Thoracic/Head and Neck Medical Oncology, Division of Cancer Medicine, MD Anderson Cancer Center, University of Texas, Houston, TX; Department of Clinical Pharmacology, The Netherlands Cancer Institute, Amsterdam, Netherlands; Mary Crowley Cancer Research Center, Dallas, TX; Department of Medical Oncology, Guangdong Provincial People's Hospital, Guangzhou, China; Guangdong Lung Cancer Institute, Guangdong Province People's Hospital, Southern Medical University, Guangzhou, China; Valkyrie Clinical Trials, Inc, Los Angeles, CA; Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany; Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT; Boehringer Ingelheim España S.A., Barcelona, Spain; Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan; National Cancer Center Hospital, Tokyo, Japan

Background: There is an unmet need for effective TKIs against HER2 mutations in solid tumors, especially NSCLC. BI 1810631 is a highly potent and selective HER2 TKI that covalently binds to both wild-type and mutated HER2 receptors, including exon 20 insertions (ex20ins), while sparing EGFR. Beamion Lung 1 is an ongoing Phase Ia/Ib study to determine the safety, MTD, PK, PD, and preliminary efficacy of BI 1810631 in pts with HER2 aberration-positive solid tumors (NCT04886804). Preliminary results from Phase Ia are presented. **Methods:** In Phase Ia, pts with advanced/unresectable/metastatic solid tumors who were refractory or unsuitable for standard treatment (Tx) and had HER2 aberrations (e.g. overexpression, gene amplification, somatic mutation, or gene rearrangements) were enrolled. Pts received escalating doses of BI 1810631 BID starting from 15 mg or BI 1810631 QD starting from 60 mg via a Bayesian model. Phase Ib will initially include 30 pts with advanced HER2 tyrosine kinase domain mutation-positive, pre-treated NSCLC. Additional cohorts may be included. Primary endpoints: MTD based on DLTs; pts with DLTs (Phase Ia); ORR (Phase Ib). Secondary endpoints: number of pts with DLTs throughout entire Tx period and PK parameters (Phase Ia/Ib); DoR, DCR, duration of disease control, and PFS (Phase Ib). **Results:** As of 23 January 2023, 36 pts had been treated in the US, The Netherlands, Japan, and China. Pts had NSCLC (n = 22), colorectal cancer (n = 3), or other tumors (n = 11). Most pts (n = 26; ex20ins: n = 23) had a pathological *HER2* mutation. Median (range) lines of prior systemic Tx: 2.5 (1–8). Prior HER2-targeted Tx: 12 (33%). Pts received BI 1810631 at 15, 30, 60, 100, 150 mg BID (n = 3/3/4/4/3) or 60, 120, 180, 240, 300 mg QD (n = 5/4/5/4/1). Median number of cycles was 4 (range 1–14). Tx is ongoing in 20 pts. To date, 3 DLTs have been observed (grade 2 edema [60 mg BID], grade 3 anemia [60 mg QD], grade 3 elevated ALT [180 mg QD]). The MTD has not been reached with either schedule. Tx-related adverse events (TRAEs) were reported in 25 pts (69%). The most common TRAEs were diarrhea (n = 10), anemia (n = 5), increased alkaline phosphatase, increased creatinine, increased ALT, hypoalbuminemia (all n = 4), hypocalcemia, increased AST, dry skin, increased GGT (all n = 3). Three pts had grade 3 TRAEs (anemia/increased GGT [n = 1], increased ALT [n = 2]). Strong preliminary efficacy signals were observed across all dose levels. Of 22 evaluable NSCLC patients, 10 responded (all PRs; all ex20ins) and 11 had SD. Two patients with other tumors (esophagus; cholangiocarcinoma) also achieved PR. **Conclusions:** These preliminary data indicate that BI 1810631 is well tolerated and shows encouraging anti-tumor activity in pts with HER2 aberration-positive solid tumors. Recruitment into Phase Ia is ongoing. Updated data, including durability endpoints, will be presented. Clinical trial information: NCT04886804. Research Sponsor: Boehringer Ingelheim.

8546 **Poster Session**

A systematic comparison of whole genome sequencing and targeted panel sequencing for precision oncology.

Ji-Hyung Park, Erin Connolly-Strong, Young Tae Kim, Young Seok Ju; Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology, Daejeon, South Korea; Genome Insight, San Diego, CA; Seoul National University Cancer Research Institute, Department of Thoracic and Cardiovascular Surgery, Seoul National University Hospital, Seoul, South Korea; Genome Insight Inc., San Diego, CA

Background: The analysis of the cancer genome provides clinically meaningful information such as actionable cancer driver mutations. Whole genome sequencing (WGS) provides a complete mutational landscape at an affordable cost thereby having increase clinical utility compared to the usual approach of targeted panel sequencing (TPS). To understand the capabilities of WGS in oncology, we conducted a study in lung adenocarcinomas. **Methods:** We produced WGS (surgically resected tumor tissues and matched blood; mean coverage 42x) and TPS (tumor only; SNUH panel encompassing 75 cancer genes; mean coverage 904x) through the Illumina sequencing platform and conducted comprehensive bioinformatic analyses. Oncogenic driver events, including single base substitution (SBS), insertion or deletion (INDEL), complex deletion-insertion, and fusion oncogene, were investigated in both datasets. Lastly, we compared the pattern-based mutational features, such as tumor mutational burden (TMB), mutational signatures, and copy number changes which is associated with genomic instability. **Results:** In 60 lung adenocarcinomas, the TPS method identified 120 driver mutations from the 75 targeted genes. Of these, 114 mutations were also detected by the WGS method, showing 95.0% sensitivity of WGS in detection of core driver mutations. In uncovered genomic regions by TPS, WGS captured 9 additional driver mutations (such as loss-of-function mutations in PIK3R2, ARID2, and APC) and 37 copy number variations (such as amplification of LMO and SMO, deletion of PIK3R1 and APC) in the cancer genes. TMB calculation is straightforward in WGS however, sophisticated considerations were necessary in TPS for TMB, to remove false positives and germline mutations. TPS showed a good capability for identifying hypermutator tumor samples, but a quantitative estimation was not always feasible due to the substantial background fluctuation, particularly for INDELs. Mutational signatures are unique combinations of mutation types in a given sample, which can give important clues to the mechanism underlying mutations. TPS showed adequate mutational signatures (cosine similarity $>$ 0.7), but was not constantly satisfactory in tumors with high TMB ($>$ 20,000 genome wide SBS and INDELs). In TPS, approximately 30% of high TMB tumors represented marginal cosine similarity (0.5-0.7), and tobacco smoking related signature (SBS 4) found in WGS was captured only in 50% of the associated cases (9 out of 18). For DNA copy number changes and loss-of-heterozygosity analyses, WGS showed a much higher resolution. **Conclusions:** Our study demonstrates that WGS has comparable capabilities for the detection of driver mutations in core oncogenes and tumor suppressor genes. WGS was superior for pattern-based features, such as TMB, mutational signatures, and copy number changes. WGS is a medically necessary more comprehensive approach to precision oncology. Research Sponsor: None.

8547 **Poster Session**

SAKK 16/18: Immune-modulatory radiotherapy to enhance the effects of neoadjuvant PD-L1 blockade after neoadjuvant chemotherapy in patients with resectable stage III (N2) non-small cell lung cancer (NSCLC)—A multicenter phase II trial.

Laetitia A Mauti, Tobias Finazzi, Lisa Holer, Adrienne Bettini, David König, Martin Früh, Simon Haefliger, Alfredo Addeo, Michael Thomas Mark, Martin Buess, Patrizia Froesch, Wolf Dieter Janthur, Christine Waibel, Christoph J. Ackermann, Patrick Dorn, Bernhard Scheibe, Miklos Pless, Matthias Guckenberger, Spasenija Savic Prince, Sacha Rothschild; Department of Oncology, Kantonsspital Winterthur, Winterthur, Switzerland; Clinic of Radiotherapy and Radiation Oncology, University Hospital Basel, Basel, Switzerland; Swiss Group for Clinical Cancer Research (SAKK), Bern, Switzerland; Department of Oncology, HFR - Hôpital fribourgeois, Fribourg, Switzerland; Department of Medical Oncology and Comprehensive Cancer Center, University Hospital Basel, Basel, Switzerland; Department of Oncology/Hematology, Kantonsspital St. Gallen, St. Gallen, Switzerland; Department of Medical Oncology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; Department of Oncology, University Hospital HUG, Geneva, Geneva, Switzerland; Division of Oncology/Hematology, Kantonsspital Graubuenden, Chur, Switzerland; Department of Oncology, St. Claraspital Basel, Basel, Switzerland; Oncology Institute of Southern Switzerland, Bellinzona, Switzerland; Department of Oncology/Hematology, Kantonsspital Aarau, Aarau, Switzerland; Department of Oncology/Hematology, Kantonsspital Baden, Baden, Switzerland; Department of Oncology, Spital Thun, Thun, Switzerland; Department of Thoracic Surgery, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; Department of Radiation Oncology, University Hospital Zurich, Zurich, Switzerland; Pathology, Institute of Medical Genetics and Pathology, University Hospital Basel, Basel, Switzerland

Background: Neoadjuvant chemo-immunotherapy has become a new standard of care in locally advanced, resectable NSCLC. The SAKK 16/14 trial demonstrated a major improvement in pathological response (pCR), major pathological remission (MPR) and event-free survival (EFS) with the addition of perioperative durvalumab after standard induction chemotherapy (ChT) with cisplatin and docetaxel. Based on data suggesting a potential enhancement of immunotherapy efficacy, the ongoing SAKK 16/18 trial investigates the addition of immune-modulatory radiotherapy (RT) given concurrently with neoadjuvant durvalumab. **Methods:** In this non-comparative randomized phase II trial patients (pts) with resectable stage IIIA-B(N2) (cT1-3 or T4 due to size N2 M0) NSCLC receive 3 cycles of cisplatin 100mg/m2 and docetaxel 85mg/m2 followed by durvalumab (1500mg) and one of three randomized RT regimens before tumor resection and adjuvant durvalumab for 1 year. RT is delivered to the primary tumor only, using either 20x2 Gy, 5x5 Gy, or 3x8 Gy (deliverd inhomogenously). RT planning is optimized for strict organ at risk and mediastinal lymph node sparing. The primary endpoint is 1-year EFS. We report a preplanned interim analysis of the secondary endpoints safety, surgical outcomes and pathological response after surgery in 25 pts. **Results:** At data cut-off on Oct 8, 2022, 25 pts had reached post-operative day 30 and a total of 31 pts were included in the safety analysis. Thirty pts (97%) had at least one treatment related adverse events (TRAE). Eighty-eight % were attributed to neoadjuvant ChT (16% G3-4), 4% each to neoadjuvant durvalumab (1% G3) and RT (1% G4), and 8% to surgery (35% G3-4). One fatal TRAE occurred in a pt with COVID-pneumonia during neoadjuvant ChT. No difference in safety was seen between the three RT arms. There was no treatment-related cancellation or delay in surgery and 0% 30-day postoperative mortality. Eighty-one % of pts underwent tumor resection (96% R0). Non-resection was due to death (n = 1), progressive disease (n = 3), or unresectable tumor (n = 2). The pCR-rate was 28%, and MPR (≤10% viable tumor cells) was detected in 76% of all specimens. Details of pathological responses with regard to immune-modulatory RT regimen will be presented at the meeting. **Conclusions:** The preplanned interim safety analysis of the SAKK 16/18 trial did not show a relevant increase in TRAE due to immune-modulatory RT. Surgical feasibility and safety are confirmed and the trial continues enrolment to a planned total of 90 pts (30 per RT arm). Preliminary pathological responses are promising, and exploratory analyses will study potential differences between the RT regimens, in order to better understand the potential role of immune-modulatory RT in the multimodal treatment of resectable stage III(N2) NSCLC. Clinical trial information: NCT04245514. Research Sponsor: AstraZeneca.

8548 **Poster Session**

Sequential intravenous chemotherapy with drug-eluting bead bronchial arterial chemoembolization for the treatment of stages III and IV lung squamous cell carcinoma: A retrospective controlled clinical study.

Jianfei Tu, Lingqiang Lai, Dengke Zhang, Xihui Ying, Li Chen, Jiahao Wu, Jie Chen; The Fifth Affiliated Hospital of Wenzhou Medical College, Lishui, China

Background: To determine the differences in efficacy and safety between drug-eluting bead bronchial arterial chemoembolization (DEB-BACE) combined with intravenous chemotherapy and systemic chemotherapy alone for the treatment of stages III and IV lung squamous cell carcinoma (LSCC). **Methods:** 136 patients with stages III and IV LSCC were retrospectively recruited between January 2018 and August 2021 and divided into group A (chemotherapy-only, N = 95) and group B (DEB-BACE combined with intravenous chemotherapy, N = 41). The short-term efficacy, hemoptysis and dyspnea remission rates, and incidence of adverse reactions were compared between the two groups. Survival estimation was performed by Kaplan-Meier, and the Log-rank test was performed to compare survival differences between groups. **Results:** The One-month DCR (90.2% vs. 49.5%) and ORR (75.6% vs. 38.9%) were better in group B than in group A (both $P < 0.05$). Progression-free survival (PFS) was 8.0 months in Group B and 6.0 months in Group A, a statistically significant difference ($P < 0.05$). The PFS rates at 6, 12, and 24 months were 63.4%, 24.4%, 0.0%, 43.2%, 13.7%, and 0.0% in groups B and A, respectively, this difference was significant ($P < 0.05$). The median overall survival was better in group B than in group A (19.0 vs 14.0 months, $P < 0.05$). The OS rates at 6, 12, and 24 months were 100%, 85.4%, 26.8%, 78.9%, 56.8%, and 22.1% in groups B and A, respectively, with statistically significant differences ($P < 0.05$). The hemoptysis and dyspnea remission rates were better in group B than in group A within one month after treatment ($P < 0.05$), however, in terms of the incidence of adverse reactions, incidences, such as post-treatment fatigue and bone marrow suppression, were significantly lower in Group B than in Group A during the follow-up period ($P < 0.05$). **Conclusions:** DEB-BACE combined with intravenous chemotherapy is effective for the treatment of advanced LSCC, with lower adverse reactions, and significant improvement in patients' hemoptysis and dyspnea symptoms, which is worthy of clinical application. Research Sponsor: lishui Science & Technology Bureau; Zhejiang Medical Association.

8549 **Poster Session**

Prospective dynamic sampling and molecular residual disease monitoring to predict clinical outcomes for patients with unresectable, locally advanced non-small cell lung cancer undergoing radical radiotherapy.

Jia-Tao Zhang, Yi Pan, Xuan Gao, Zhi-yong Chen, Bingfa Yan, Pei-Xin Tan, Xiao-Rong Yang, Hui Lin, Hong-Hong Yan, Song Dong, Bin-Chao Wang, Jin-Ji Yang, Hai-Yan Tu, Xue-Ning Yang, Wenzhao Zhong, Xuefeng Xia, Xin Yi, Qing Zhou, Yi-Long Wu; Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China; Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, Guangdong, China; Geneplus-Beijing, Beijing, China; Geneplus-Beijing Institute, Beijing, Beijing, China; Guangdong Lung Cancer Institute, Guangzhou, China; Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China; Division 4 of Pulmonary Oncology, Cancer Center, Guangdong Lung Cancer Institut, Guangdong, China; Guangdong Lung Cancer Institute, Guangzhou, Guangdong, China; Geneplus-Beijing institute, Beijing, China; Geneplus-Beijing Institute, Beijing, China

Background: The role of molecular residual disease (MRD) detection in non-small cell lung cancer (NSCLC) patients after definitive resection has been progressively elaborated. However, the dynamic patterns of circulating tumor DNA (ctDNA) during and after radical radiotherapy (RT) remain unclear but are critical for detecting MRD in this context. **Methods:** We enrolled 139 patients with locally advanced NSCLC treated with radical RT in this prospective study. And 761 blood samples were successfully detected by ctDNA-MRD assay at different preset timepoints before, during and after RT. **Results:** There was a declining trend in ctDNA concentrations of "during RT" time point (RT reached 40 Gy) relative to those after RT. Patients with negative ctDNA of "during RT" and "after RT" time points may indicate an early response to RT, and had better progression-free survival (PFS) than those with late response to RT(ctDNA clearance only at "after RT" time point, HR = 0.30, 95%CI: 0.12-0.75, p = 0.004). Moreover, patients with both negative ctDNA of "during RT" and "after RT" time points could not benefit from consolidation therapy (HR = 0.72, 95%CI: 0.29-1.78, p = 0.478), while patients with any positive ctDNA of them could (HR = 0.59, 95%CI: 0.38-0.93, p = 0.023).The sensitivity of longitudinal MRD was 97.8% and only two patients with local progression were overlooked. The 2-year cancer-specific PFS of patients with longitudinal undetectable MRD was 88.4%, which corresponds to the potentially cured population. For patients with only blood-informed MRD detection, the sensitivity and median lead time of longitudinal MRD were 97.7% and 3.9 months, respectively, which indicating the feasibility and efficacy of blood-informed MRD detection strategy. **Conclusions:** These data shed new light on the ctDNA-MRD detection for localized NSCLC patients who received radical RT. Research Sponsor: Key Lab System Project of Guangdong Science and Technology Department, Guangdong Provincial Key Lab of Translational Medicine in Lung Cancer (Grant No. 2017B030314120).

8550 **Poster Session**

Association of circulating CD103$^+$ T cells with major pathological response in a randomized phase 2 trial of neoadjuvant durvalumab with or without stereotactic body radiotherapy in patients with early-stage non-small cell lung cancer.

Zachary Walsh, Johannes C Melms, Meri Rogava, Lindsay Caprio, Casey Ager, Amit Dipak Amin, Patricia Ho, Murtaza Malbari, Vivek Mittal, Timothy McGraw, Nasser K. Altorki, Benjamin Izar; Columbia University Medical Center, New York, NY; Weill Cornell Medical College, New York, NY

Background: We previously reported results of a randomized phase 2 study, demonstrating a higher rate of major pathological response to durvalumab in combination with stereotactic body radiotherapy (SBRT) compared to durvalumab alone in patients with localized (stage I-IIIA) non-small cell lung cancer (NSCLC). Biomarkers of response in NSCLC are poorly understood. To address this, we evaluated sequentially collected peripheral blood mononuclear cells (PBMCs) from study participants to identify easily accessible biomarkers associated with major pathological responses. **Methods:** PBMCs were obtained from study participants at defined pre-treatment, peri-operative, and post-operative timepoints. We performed 25-marker spectral flow cytometric analysis of the T cell compartment in these samples and used dimensionality reduction and clustering programs to identify populations of interest. **Results:** Our analysis of these samples revealed populations of both CD4$^+$ and CD8$^+$ T cells with hallmarks of prior antigen exposure and tissue residency (CD103$^+$, CCR7$^-$, CD45RA$^-$), suggesting tumor-experienced T cells circulating into the blood. Greater pre-treatment frequency of these T cell populations was associated with major pathological responses to neoadjuvant therapy. This observation was consistent when evaluating patients with major pathological responses across both treatment arms, and within the durvalumab plus SBRT group, where we had enough patients with major pathological responses. Maturation of disease-free survival data from this trial will enable us to evaluate the association of these biomarkers with long-term survival. **Conclusions:** Together, these data reveal an unexpected population of T cells in the peripheral blood with features of tissue-residency, which are associated with major pathological responses, and suggest that re-circulation of tumor-experienced T cells may represent a predictive biomarker for neoadjuvant treatment of NSCLC. Research Sponsor: Columbia University Herbert Irving Comprehensive Cancer Center.

8551 **Poster Session**

Association of peripheral memory B cell population maintenance and long term survival after perioperative chemoimmunotherapy in NSCLC (NADIM trial).

Belen Sierra-Rodero, Alberto Cruz Bermudez, Cristina Martinez-Toledo, Marta Molina-Alejandre, Aránzazu García-Grande, Virginia Calvo, Ernest Nadal, Rosario Garcia Campelo, Amelia Insa, Manuel Domine, Bartomeu Massuti, Alberto Garrido, Margarita Majem, Alex Martinez-Marti, Javier de Castro Carpeño, Delvys Rodriguez-Abreu, Manuel Cobo, Isidoro Barneto, Santiago Viteri, Mariano Provencio-Pulla; Instituto de Investigación Sanitaria Puerta de Hierro-Segovia de Arana, Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain; Instituto Investigacion Sanitaria Puerta de Hierro-Segovia de Arana, Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain; Fundación para la Investigación Biomédica Hospital Universitario Puerta de Hierro, Madrid, Spain; C/ Joaquín Rodrigo, 1, 28222 Majadahonda, Madrid, Madrid, Spain; Catalan Institute of Oncology, Hospital Duran i Reynals, IDIBELL. Medical Oncology, Hospitalet, Spain; Complejo Hospitalario Universitario A Coruña, A Coruña, Spain; Hospital Clinico Universitario, Valencia, Spain; Fundacion Jimenez Diaz University Hospital, Madrid, Spain; Alicante University Hospital Isabial, Alicante, Spain; Hospital Universitario de Vigo, Vigo, Spain; Santa Creu i Sant Pau, Barcelona, Spain; Vall d'Hebron University Hospital, Barcelona, Spain; La Paz University Hospital, Madrid, Spain; Hospital Universitavio Insular De Gran Canaria, Las Palmas De Gran Canaria, Spain; Hospital Regional Carlos Haya, A Gudiña, Spain; Hospital Reína Sofía, Córdoba, Spain; Dr Rosell Oncology Institute, Dexeus University Hospital, Quiron Salud Group, Barcelona, Spain; Hospital Universitario Puerta de Hierro, Madrid, Spain

Background: In the context of perioperative immunotherapy, it is crucial to personalize adjuvant treatment, identifying which patients should or should not receive post-surgical immunotherapy. Here we describe the changes in B cell peripheral blood immunophenotype during perioperative immunotherapy and its potential to predict disease progression in patients from NADIM I clinical trial (NCT03081689). **Methods:** Blood samples from 42 patients were obtained at pre-, post-neoadjuvant chemoimmunotherapy (pre-surgery) and at 6 and 12 months of adjuvant IO. Peripheral mononuclear cells were stained with CD19, CD20, CD38, CD24, CD27, CD25, CD10 antibody panel and analyzed by flow cytometry using FlowJo. Statistical analysis in paired samples was performed with Wilcoxon test and differences in parameters' fold changes between disease status groups (Progression-free at 34.2 months) were determined by Mann-Whitney U tests. Variables cutoffs were stablished using ROC curve analysis. Progression-free survival (PFS) was evaluated using Kaplan-Meier curves and long-rank test. The median follow-up was 38.0 months. **Results:** Regarding the impact of NADIM complete treatment scheme in patient's B cells, there was a reduction of memory B cells (CD19+CD20+CD38-CD24+CD27+; $p < 0.001$) and CD20 levels in total B cells (CD19+CD20+; $p = 0.001$) ($n = 17$). Importantly, this decrease occurs in all patients regardless their pathological response or disease progression. However, the magnitude of the memory B cell percentage and CD20 levels reduction was significantly more pronounced in patients whose disease progress thereafter ($p = 0.023$, $p = 0.052$ at 6 and 12 months for memory B cells; and $p = 0.002$, $p = 0.009$ at 6 and 12 months for CD20 expression). Patients with a relative drop of memory B cells greater than 90% at 6 or 12 months, showed a shorter PFS ($p = 0.028$, $p = 0.007$). Likewise, patients with a relative decrease of CD20 expression on B cells higher than 60% at 6 or 12 months had shorter PFS ($p = 0.016$, $p < 0.001$). The AUC ROCs to identify patients with disease progression, were 0.824 and 0.885 at 6 and 12 months for memory B cells; and 0.912 and 0.981 at 6 and 12 months for CD20 levels. Moreover, memory B cells percentage and CD20 levels decrease occur between surgery and the first 6 months of adjuvant therapy ($n = 21$, $p < 0.001$, $p = 0.025$). After that, these levels are maintained from 6 to 12 months of adjuvant treatment ($n = 20$, $p = 0.290$, $p = 0.682$), thus the overall reduction is also observed between surgery and 12 months samples ($n = 17$, $p < 0.001$, $p = 0.001$). **Conclusions:** Perioperative IO produces a significant reduction in memory B cells and CD20 levels. Importantly, stronger decreases might be helpful to predict progression since they are associated to shorter PFS, indicating that the maintenance of the memory B cell peripheral compartment is relevant for long-term survival of these patients. Research Sponsor: Spanish Health Ministry, ISCIII (PI19/01652, PI22/01223); Bristol Meyers Squibb; Horizon 2020 European Union Funding for Research and Innovation (CLARIFY); Spanish Ministry of Science and Innovation (RTC2017-6502-1, RTC2019-007359-1).

8552 **Poster Session**

Phase II trial of consolidation pembrolizumab (pembro) after proton reirradiation (re-RT) for thoracic recurrences of non-small cell lung cancer (NSCLC).

Nikhil Yegya-Raman, Abigail T. Berman, Christine Agnes Ciunci, Xingmei Wang, Cole Friedes, Michelle Iocolano, Ching Lai, William P. Levin, Keith A. Cengel, Roger B. Cohen, Charu Aggarwal, Melina Elpi Marmarelis, Aditi Puri Singh, Lova Sun, John Peter Plastaras, Corey J. Langer, Charles B. Simone, Steven J Feigenberg; University of Pennsylvania, Philadelphia, PA; CVS Health, Philadelphia, PA; Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; New York Proton Center, New York, NY

Background: Isolated thoracic recurrences of NSCLC in/near previously irradiated fields present a therapeutic challenge. One treatment option is re-RT with proton beam therapy (PBT) to minimize normal tissue exposure; however, distant failure is common. Herein, we report the first prospective trial of PBT re-RT followed by pembro. **Methods:** This phase II, single-arm trial (NCT03087760) enrolled patients (pts) with isolated locoregional recurrences of NSCLC in/near previously irradiated fields. Key inclusion were definitive thoracic RT $>$ 6 months (mo) prior, ECOG 0-1, and clinical target volume (CTV) $<$ 250 cc. Key exclusion were extrathoracic metastases, prior grade $\geq$3 pneumonitis, and prior immunotherapy $<$ 30 days from re-RT start. 4-12 weeks after completion of 60-70 Gy PBT re-RT, pts without progressive disease started pembro 200 mg IV q21 days for up to 12 mo. Primary endpoint was progression-free survival (PFS). Secondary endpoints were overall survival (OS) and CTCAE v5.0 toxicity. PFS and OS were measured from re-RT start and estimated using Kaplan-Meier method. **Results:** Between November 2017 and April 2021, 32 pts were consented; 10 were excluded most commonly due to CTV $\geq$250cc (N = 3) or separate primary (N = 3). 22 were eligible and initiated PBT re-RT. Trial closed early due to slow accrual. Median age was 68 years. All recurrences were biopsy-proven; 8 (36%) were squamous. Recurrences were primary tumor (N = 4), nodal (N = 8), and both (N = 10). 8 pts (36%) received prior durvalumab. Median interval from prior RT end to re-RT start was 20 mo (range 10.2-74.8). Median delivered re-RT dose and dose/fraction were 60 Gy (range 18-70) and 2 Gy (range 1.8-4), respectively; 21 pts (95%) received concurrent chemotherapy. 15 pts (68%) initiated consolidation pembro on trial and received a median of 3 cycles (range 2-17). Pembro was discontinued due to completion of 1 year (N = 3), disease progression (N = 4), toxicity (N = 5; 2 pembro-related [grade 2 pneumonitis after cycle 3 and grade 3 mucositis after cycle 13, the former also re-RT-related]), death without progression (N = 2; NSTEMI and unknown), and pt decision (N = 1). Median follow-up was 38.7 mo. Median PFS and OS were 8.8 mo (95% CI 4.2-23.7) and 22.8 mo (95% CI 6.9-not reached) for all pts, respectively, and 13.5 mo (95% CI 4.2-25.3) and 22.8 mo (95% CI 6.5-not reached) for pts who started pembro. Receipt of $>$ 3 cycles pembro (N = 7) associated with better OS (median 46.7 vs 13.8 mo, log-rank p = 0.007). 10 pts (46%) had grade $\geq$3 toxicity; 2 were pembro-related (grade 3 lymphopenia and mucositis). 1 pt had grade 5 toxicity (aortic fistula), from re-RT. **Conclusions:** In the first prospective trial of PBT re-RT + consolidation pembro, treatment proved feasible and PFS was acceptable though the capacity to administer pembro was limited. This approach may be considered in selected patients with isolated thoracic recurrences of NSCLC. Clinical trial information: NCT03087760. Research Sponsor: Merck & Co.

8553 **Poster Session**

Genomic comparison of MET exon 14 skipping and MET amplified non-small cell lung cancer.

Rachel Minne, Natalie Luo, Anne M. Traynor, Minxuan Huang, Luisina De Tullio, Jen Godden, Melissa Conrad Stoppler, Randall J. Kimple, Andrew Baschnagel; Department of Human Oncology, School of Medicine and Public Health, University of Wisconsin, Madison, WI; University of Wisconsin–Madison, Madison, WI; University of Wisconsin-Madison Carbone Cancer Center, Madison, WI; Tempus Labs, Inc., Chicago, IL; Tempus Labs, Inc., Franklin, WI; University of Wisconsin, Madison, WI; Department of Human Oncology, Madison, WI

Background: In non-small cell lung cancer (NSCLC), the MET tyrosine kinase receptor can be dysregulated by mutations and/or gene amplification. The most common MET mutation is in exon 14 (METex14), leading to impaired receptor degradation and increased MET-mediated signaling causing sustained tumor proliferation. MET amplification also leads to continued MET signaling and oncogenesis and can be a mechanism of resistance to targeted therapy. We sought to compare the genomic landscape of METex14 and high-level MET amplified tumors, both of which can be targeted with tyrosine kinase inhibitors. **Methods:** We analyzed 18,047 NSCLC tumors (any stage/subtype) sequenced with Tempus xT assay (DNA-seq of 648 genes at 500x coverage, full transcriptome RNA-seq). Tumors were queried for METex14 mutations, high MET amplification (METamp), defined as copy number gain (CNG) $\geq$10, and other MET mutations (METother). Immuno-oncology (IO) biomarkers were compared across MET-altered and MET wild-type (METwt) groups. The prevalence of somatic gene alterations was compared similarly with the false-discovery rate (FDR) adjustment. **Results:** A total of 276 (1.53%) METex14, 138 (0.76%) METamp, 27 (0.15%) METother, and 17,606 (97.56%) METwt tumors were identified. Across groups, patients with METex14 were older, more likely to be female, and nonsmokers. METex14 exhibited the lowest tumor mutational burden (TMB) and lowest neoantigen tumor burden (NTB). PD-L1 positivity rates were higher in METex14 tumors compared to METamp and METwt tumors. MET log10 gene expression was highest in METamp. METamp exhibited the lowest proportion of CD4 T cells and the highest proportion of NK cells. Compared to METex14, METamp exhibited increased prevalence of *TP53* (83% vs 37%), *TFEC* (46% vs 1.1%), *CFTR* (37% vs 1.4%), *EGFR* (31% vs. 7.6%), *WNT2* (11% vs 0.4%), *KEAP1* (14% vs 0.7%), and *STK11* (8% vs 1.4%), and decreased prevalence of *MDM2* (4.3% vs. 14%), and *FRS2* (2.9% vs. 12%). **Conclusions:** In this large population-based analysis of MET-altered NSCLC, METex14 tumors exhibited differences in IO biomarkers and the somatic landscape compared to non-METex14 NSCLC tumors. Variations in immune profiles may affect immunotherapy selection in MET-altered NSCLC and require further exploration. Research Sponsor: Tempus Labs; U.S. National Institutes of Health.

Characteristic	METex14 (N = 276)	METamp (N = 138)	METother (N = 27)	METwt (N = 17,606)	p-value
TMB[1]	2.6 (1.3, 4.2)	5.4 (3.0, 9.7)	5.0 (3.2, 6.7)	4.6 (2.7, 7.3)	<0.001
NTB[1]	1.22 (0.71, 1.95)	2.93 (1.50, 5.12)	2.44 (1.34, 3.78)	2.20 (1.22, 3.66)	<0.001
PD-L1 positivity (IHC)[2]	128 (83%)	64 (75%)	12 (86%)	6,180 (57%)	<0.001
MET log10 gene expression[1]	3.70 (3.45, 3.98)	4.43 (4.26, 4.53)	3.80 (3.69, 4.02)	3.32 (3.07, 3.57)	<0.001
%CD4 T cells of all immune cells[1]	23% (17%, 31%)	17% (11%, 25%)	23% (19%, 30%)	23% (16%, 30%)	<0.001
% NK cells of all immune cells[1]	11% (7%, 17%)	15% (9%, 24%)	14% (11%, 17%)	12% (7%, 18%)	0.013

[1]Median (Interquartile range) [2]N (%).

8554 **Poster Session**

Stereotactic ablative radiotherapy with nivolumab for early-stage operable non-small cell lung cancer: A phase 2 study.

Gustavo Schvartsman, Ana Carolina Pires de Rezende, Diogo Bugano Diniz Gomes, Ludmila De Oliveira Koch, Benoit Jacques Bibas, Oswaldo Gomes, Paulo V Campregher, Patricia Severino, Luciana Cavalheiro Marti, Vitor Ribeiro Paes, Rodrigo Caruso Chate, José Milanez Ribas, Victor Aurelio Ramos Sousa, Patricia Taranto, Fernando Moura, Ricardo Mingarini Terra, Marcos Naoyuki Samano; Hospital Israelita Albert Einstein, São Paulo, Brazil

Background: Surgery is standard of care for patients with stage I non-small cell lung cancer (NSCLC). However, 5-year mortality can reach up to 30%. For patients with contraindication to surgery, treatment with stereotactic ablative radiotherapy (SABR) leads to adequate local tumor control, but has a high rate of regional and distant failure. SABR as neoadjuvant therapy for stage I NSCLC produced a pathologic complete response (pCR) rate of only 60% when surgery was performed after 10 weeks of treatment, demanding improvement in the management of both operable and inoperable early-stage NSCLC. Immune checkpoint inhibitors (ICI) are routinely used in stages III-IV NSCLC, with recent approvals in the peri-operative setting, and may be synergistic with radiotherapy. We hypothesized that neoadjuvant nivolumab plus SABR may improve pCR rate and provide insight to its changes in the tumor microenvironment. **Methods:** This is a phase 2, single arm, open label study evaluating neoadjuvant treatment for patients with NSCLC of up to 4 cm, with no lymph node involvement (AJCC 8th edition: up to cT2aN0), and adequate surgical conditions. Treatment consisted of nivolumab 360 mg every 3 weeks for 3 doses or unacceptable toxicity. SABR started on D1 of nivolumab, with a duration of 2 to 3 weeks, depending on the lesion size and location (3 x 18 Gy; or 5 x 10 Gy; or 8 x 7.5 Gy). Standard-of-care surgery was performed at 10 (+- 2) weeks after the last radiotherapy dose. The primary endpoint of the study is pCR rate at surgery. Tissue, blood, and stool samples were collected during treatment. **Results:** We included 25 patients. All but one were cared for in the Brazilian public system. Mean age was 68 years. Mean tumor size was 2.45 cm. Only 3 patients were never-smokers. Surgery was performed as scheduled in all but one patient. pCR rate was 80% (19/24) and MPR rate was 83% (20/24) of patients who underwent surgery. Twenty-nine treatment-emergent adverse events occurred in 13 patients (23 grade 1-2 events, two grade 3 and two grade 5 events, being only one grade 3 diarrhea related to experimental treatment). The single patient who was not operated died during study treatment from relapsed acute alcoholic hepatitis. The other grade 5 event was due to a respiratory infection, both unrelated to treatment. Two patients died from surgical complications 185 and 72 days after surgery, respectively (one with pulmonary artery lesion with subsequent clinical complications and other with thromboembolic events), deemed unrelated to experimental treatment. During follow-up, two additional patients died due to comorbidities, and none relapsed to date. **Conclusions:** In this trial with patients with significant comorbidities and smoking history from the public system in Brazil, we demonstrated a pCR rate of 80% with SABR + nivolumab. Further studies are warranted to evaluate this strategy versus surgery in operable patients with stage I disease. Clinical trial information: NCT04271384. Research Sponsor: Bristol-Myers Squibb.

8555 **Poster Session**

Assessing the efficacy and safety of DEB-BACE combined with intravenous chemotherapy for the treatment of intermediate to advanced lung adenocarcinoma after progression of targeted drug resistance.

Lingqiang Lai, Jianfei Tu, Dengke Zhang, Xihui Ying, Jiahao Wu, Jie Chen, Li Chen; The Fifth Affiliated Hospital of Wenzhou Medical College, Lishui, China

Background: To compare the efficacy and safety of drug-eluting bead bronchial arterial chemoembolization (DEB-BACE) combined with intravenous chemotherapy versus systemic intravenous chemotherapy for intermediate to advanced lung adenocarcinoma with positive driver genes after progression of targeted therapy. **Methods:** A total of 131 patients with intermediate to advanced lung adenocarcinoma were retrospectively recruited from 2018-2022 and divided into Group A (standard chemotherapy regimen, N=62) and Group B (DEB-BACE and intravenous chemotherapy, N=69). The short-term efficacy, hemoptysis remission rate, dyspnea remission rate, and incidence of adverse effects were compared between the two groups using the $\chi 2$ test. Survival estimates were performed by Kaplan-Meier, and a Log-rank test was performed to examine survival differences between groups. **Results:** The three-month disease control rate (DCR: 82.6% vs 58.1%) and objective remission rate (ORR: 60.9% vs 38.7%) were better in group B than in group A (both $P<0.05$). Median progression-free survival (PFS, 10.0 vs 7.9 months) and median overall survival (OS, 33.0 vs 18.0 months) were better in group B than in group A (both $P < 0.05$). The PFS rates at 6, 12, and 24 months were 67.3%, 40.8%, and 0.0% and 54.1%, 23.2%, and 0.0% in groups B and A, respectively; and the OS rates at 6, 12, and 24 months were 100%, 95.7%, 72%, 88.6%, 66.1%, and 21.8% in group B and group A, respectively, with statistically significant differences ($P < 0.05$). Within one month after treatment, group B had better hemoptysis relief (83.3% vs. 20.0%) and dyspnea relief (57.5% vs. 30.0%) than group A (both $P < 0.05$). During the follow-up period, the incidence of adverse reactions was significantly lower in group B than in group A ($P < 0.05$). **Conclusions:** For patients with intermediate to advanced lung adenocarcinoma who have failed to progress on targeted therapy, DEB-BACE combined with intravenous chemotherapy has shown superior efficacy and survival benefit and lower adverse effects, while significantly improving patients' symptoms of hemoptysis and dyspnea, with important application prospects. Research Sponsor: lishui Science & Technology Bureau; Zhejiang Medical Association.

8556 **Poster Session**

Phase Ib study of neoadjuvant concurrent chemoradiation plus durvalumab followed by surgery and adjuvant durvalumab for resectable stage III NSCLC.

Jiyun Lee, Jaeho Cho, Chang Lee, Chang Young Lee, Jin Gu Lee, Dae Joon Kim, Hyo Sup Shim, Sun Min Lim, Hye Ryun Kim, Byoung Chul Cho, Min Hee Hong; Lung Cancer Center, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; Department of Radiation Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; Department of Radiation Oncology, Yonsei Cancer Center, Heavy Ion Research Institute, Yonsei University College of Medicine, Seoul, South Korea; Department of Thoracic and Cardiovascular Surgery, Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea; Department of Pathology, Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea; Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea; Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of (South)

Background: The use of neoadjuvant and adjuvant immunotherapy in resectable non-small cell lung cancer (NSCLC) has become a standard of care. However, the integration of immunotherapy into a trimodality treatment regimen has not been widely explored. We hypothesized that adding durvalumab to neoadjuvant concurrent chemoradiation and surgery would not increase treatment-related adverse events (TRAE) during neoadjuvant period. **Methods:** This was a prospective, single center, single-arm, open-label phase Ib study. Patients with resectable, stage III N2 NSCLC received concurrent chemoradiation [weekly paclitaxel (45mg/m2)/carboplatin (AUC 2.0) for 5 weeks with radiotherapy 45Gy] and durvalumab 1,500mg Q4W for 2 cycles followed by surgical resection and adjuvant durvalumab for 1 year. The primary endpoint was the frequency of patients who experience grade 3 or more TRAE during neoadjuvant therapy based on CTCAE 4.03. **Results:** Of 30 patients (median age 65.5 years; 67% male), 56.7% had squamous histology and 60.0% had stage IIIA. Any grade AEs and TRAEs (neoadjuvant/adjuvant) were reported in 83.3%/76.7% and 70.0%/63.3% of patients, respectively. Grade 3 or more AEs and TRAEs (neoadjuvant/adjuvant) were reported in 10.0/3.3% and 10.0%/0.0%, respectively. Grade 3 or more TRAE reported during neoadjuvant treatment were neutropenia, anemia, and nausea, one each; no Grade 5 AEs occurred. Surgical resection was not performed in three patients: two due to treatment-related adverse events (AEs) and one due to patient refusal. Among 27 patients who received complete resection, the pathologic complete response (pCR) rate and major pathologic response (MPR) rate were 40.7% (95% CI, 22.4 – 61.2) and 74.1% (95% CI, 53.7 – 88.9), respectively. Excluding four patients with EGFR, ALK, KRAS G12C, or MET ex14skipping mutations, the pCR rate was 47.8% (95% CI, 26.8 – 69.4) and MPR rate was 87.0% (95% CI, 66.4 – 97.2). Overall, pathologic downstaging was achieved in 70.4% (95% CI, 49.8 – 86.2). Objective response rate according to RECIST v1.1 was 50.0% (95% CI, 31.3 – 68.7). One patient delayed the schedule for surgical resection due to radiation pneumonitis (G2), unrelated to the drug administered. Otherwise, there were no peri-operative mortality or morbidity. All patients who underwent surgery, except one whose disease progressed immediately after resection, received at least one dose of adjuvant durvalumab; 61.5% completed 1-year treatment, 11.5% were continuing treatment, 11.5% discontinued due to AE, and 11.5% discontinued due to disease progression at the time of data cutoff. Grade 3 or more TRAE reported during adjuvant treatment were radiation pneumonitis and proteinuria, one each. **Conclusions:** This study confirms the manageable safety profile of adding durvalumab to neoadjuvant concurrent chemoradiation for treatment of resectable stage III NSCLC. Clinical trial information: NCT03694236. Research Sponsor: AstraZeneca.

8557 **Poster Session**

Development of a novel blood-based RNA gene expression platform for early-stage lung cancer diagnosis.

Martin J Keiser, Elizabeth Cormier-May, Matthew Alderdice, Joy N Kavanagh, Brendon Matthew Stiles; IV BioHoldings (IVBH), Newport Beach, CA; Sonrai Analytics, Belfast, United Kingdom; Albert Einstein Cancer Center, New York, NY

Background: Blood-based methods using circulating tumor DNA (ctDNA) and cell-free DNA (cfDNA) are under development for early and less invasive detection of lung cancer, although detection of the earliest stage cancers (stages 0-II) using these modalities is suboptimal. We hypothesized that a machine learning approach using RNA gene expression may offer important information on the biology of the patient, allowing for gene expression profiles to be used as a surrogate measurement of cancer disease phenotype and as a promising direction for early detection of lung cancer. In a previous study, 23 miRNA biomarkers were successfully discovered and validated for the non-invasive diagnostic classification of lung adenocarcinoma, achieving 97.7% sensitivity, 98.7% specificity in blood obtained from 383 clinical subjects. The aim of this study was to train a machine learning algorithm, from the 23 miRNA features, to test the signature for early lung cancer detection. **Methods:** A large and diverse clinical cohort was obtained from the NIH Gene Expression Omnibus database, GEO Accession Number GSE137140 (*n*=3,744), comprised of miRNA extracted from serum samples consisting of subjects with pre-operative lung cancer (*n*=1,566) and non-cancer controls (*n*=2,178). Our analytic plan leveraged machine learning methods derived from XGBoost classification, a popular supervised-learning algorithm that uses sequentially built shallow decision trees to provide accurate results and avoidance of overfitting. The algorithm was trained using XGBoost 1.4.1.1 R library programmed with R v3.6.3. **Results:** The lung cancer cohort was heavily weighted towards early-stage lung cancer (87.7% stage I/II), including representation across prevalent histologic types (adenocarcinoma 77.8%, non-adenocarcinoma 22.2%) and those who self-reported as never smokers (37.9%). The 23-miRNA signature achieved 98% sensitivity, 89% specificity in the held-out test set (Table). When incorporating age and gender, the 23-miRNA signature achieved 95.5% sensitivity, 90.3% specificity. **Conclusions:** A machine learning approach using RNA gene expression in patient serum achieved high sensitivity and specificity in a large, predominantly early-stage, lung cancer cohort. A multi-analyte, multimodal approach that leverages machine learning algorithms with RNA gene expression profiles and available demographics and clinical risk-factors, represents the possibility to accurately detect lung cancer in the earliest stages. This approach has successfully been translated from microarray to PCR instrumentation, with further validation of this machine learning method and approach currently underway. Research Sponsor: LiquidLung, Inc.; IV BioHoldings, LLC.

Results for miRNA-only XGBoost algorithm in held-out test set.

		Actual Class	
	Total *n*=748	**Control**	**Lung Cancer**
Predicted Class	**Control**	True Negative (388)	False Negative (6)
	Lung Cancer	False Positive (47)	True Positive (307)

8558 **Poster Session**

Benefit of post-operative radiation therapy for incompletely resected stage I-IIIA non-small cell lung cancer: An analysis of the National Cancer Database.

Sindu Iska, Mohamed Mohanna, Saad Sabbagh, Barbara Dominguez, Mira Itani, Hong Liang, Rafael Arteta-Bulos, Zeina A. Nahleh, Evan W. Alley; Maroone Cancer Center, Cleveland Clinic Florida, Weston, FL; Cleveland Clinic Florida, Weston, FL

Background: The presence of micro-residual (R1) or macro-residual (R2) disease in non-small cell lung cancer (NSCLC) is associated with a higher risk of recurrence. The benefits of post-operative radiation therapy (PORT) in incompletely resected NSCLC is not clear. The purpose of this study is to compare median overall survival (mOS) of treatment modalities in the post-operative setting for resected stage I-IIIA NSCLC with residual disease (R1/R2) and to determine if PORT provides benefit in this patient population using the National Cancer Database (NCDB). **Methods:** From the NCDB dataset for the years of 2006-2016, we extracted patients diagnosed with stage I-IIIA NSCLC and who had incomplete resection with residual disease (R1/R2). Kaplan-Meier analysis was performed to differentiate the effect of different post-operative treatment modalities, concurrent chemo-radiotherapy (CCRT), sequential chemo-radiotherapy (SCRT) and chemotherapy (CT) alone on mOS. Subsequently, univariate Cox regression was used to identify statistically significant variables, then multivariate Cox regression was performed to establish variables that contributed to the survival. Lastly, multinomial logistic regression was utilized to establish association of the independent factors. SAS version 9.4 was used to analyze the data. **Results:** Among the 2701 patients who met inclusion criteria, the average age was 64.1, 64.8 and 65.9 year old for CCRT, SCRT and CT, respectively. Male's constituted 53.6% and white's were 88.1%, and patient's were distributed equally across clinical stages. The majority of patients received SCRT (51.7%) followed by CT alone (39%), and CCRT (9.2%). There were no statistically significant differences in mOS between the different treatment modalities (p=0.220). Patients with R2 were 177% more likely to receive CCRT than CT compared to R1 (OR 2.77, CI 1.86-4.13 and $p<0.001$). Male's were 28% more likely to receive SCRT than CT compared to females (OR 1.28, CI 1.08-1.52 and p=0.0041). Nodal involvement was associated with decreased mOS with N2/N3 having 37% lower mOS compared to N0 (HR=1.37, CI 1.19-1.57 and $p<0.0001$). Patients who had R2 disease had a 38% lower mOS compared to those R1 (HR 1.38%, CI 1.19-1.62, $p<0.0001$). **Conclusions:** Despite the risk of unfavorable outcomes for patients with residual disease after surgery for NSCLC, the addition of radiotherapy, either concurrently or sequentially, to CT did not offer statistically significant mOS benefit compared to CT alone. Given the known toxicities of radiation, and the lack of impact on survival, the benefit of post-operative radiation is questionable among patients with residual disease after resection. Research Sponsor: Maroone Cancer Center, Cleveland Clinic Florida.

8559 **Poster Session**

Large scale evaluation of pulmonary nodule workup: A real-world study of over 150,000 patients in New York State.

Vamsidhar Velcheti, Erika Klump, Andrew Long, Hadrian Green, Tessa Williams, Tielman Van Vleck, Hesper Wong, Randall Legg, Jon Apple, Bobby Arelli, Ilker Arslan; NYU Langone-Laura and Isaac Perlmutter Cancer Center, New York, NY; Premier Inc., Charlotte, NC; Vaucluse Advisory Ltd, Betchworth, United Kingdom; Clinithink LLC, East Alpharetta, GA; Premier Inc., Ballantyne, NC; AstraZeneca Pharmaceuticals LP, Gaithersburg, MD; AstraZeneca Pharmaceuticals L.P., Gaithersburg, MD

Background: Around 1.6 million patients in the US annually have a pulmonary nodule (PN) found on imaging. Previous studies suggest 1-12% of PNs represent an underlying malignancy at a potentially curative stage. PNs ≥6mm are considered higher risk. Despite guideline availability, only about one-third of commercially insured patients with a PN receive recommended workup, which may include further investigation via imaging or surgery. In addition, patients and providers may delay workup of PNs identified during COVID-19. We aimed to describe variations in PN workup for different patient demographic and clinical characteristics at 7 healthcare institutions in New York (NY) state. **Methods:** We used a retrospective cross-sectional design in which structured demographic and unstructured clinical data were used to analyze patient documents from a NY state health information exchange from January 2018 to February 2022. Clinical features were abstracted using a clinical natural language processing platform, CLiX unlock. **Results:** 58 million documents from 5.5 million unique patients were analyzed. Of the overall 151,436 patients with PNs, workup was found in 47% (71,071). Across institutions, workup ranged between 24% and 52%; 40% (60,749) had evidence of a PN in the upper lung location. We found 52,789 patients (35%) had a maximum PN ≥6mm and of those, 55% (28,958) had a workup (Table). For patients with a PN ≥6mm, workup for non-English speaking patients was 9% lower than for English speaking patients (47% vs 56%), 17% lower for patients 18-44 years than patients 45-90 years (39% vs 56%), 47% lower for patients presenting with a chest injury rather than cancer screening (28% vs 75%), and 9% higher for patients with initial imaging via chest computed tomography (CT) rather than other CT (58% vs 49%). After the start of the COVID-19 pandemic (January 2020), overall workup decreased 3.8% and prevalence of symptoms such as dyspnea and chest pain increased. **Conclusions:** The descriptive findings of this analysis demonstrate gaps and variations in workup for patients with PNs across different demographics and clinical scenarios. A subsequent project is underway to explore strategies for improvement in adherence to guideline-recommended care to benefit patients by diagnosing lung cancer at an earlier, potentially curative stage. Research Sponsor: AstraZeneca LLC.

Workup Across Select Population Characteristics.

Characteristic	Group	Total Patients w/ PNs	Patients w/ Workup n (%)	Total Patients w/ PNs ≥6mm	Patients w/ Workup PNs ≥6mm n (%)
Age	18-44	14,296	4,213 (30)	4,059	1,571 (39)
	44-65	53,032	23,337 (44)	15,925	8,343 (52)
	65+	84,108	43,521 (52)	32,805	19,044 (58)
Language	English	112,409	54,033 (48)	39,647	22,279 (56)
	Spanish	8,990	3,389 (38)	3,045	1,360 (45)
	Chinese	1,258	571 (45)	546	269 (49)
	Other	4,227	1,995 (47)	1,623	848 (52)
Index Imaging Type	CT chest	105,037	52,503 (50)	35,504	20,517 (58)
	CT, other	37,899	14,925 (39)	12,565	6,212 (49)

8560 **Poster Session**

Mortality benefit of a blood-based biomarker panel for lung cancer and the PLCO cohort.

Johannes Fahrmann, Ehsan Irajizad, Edwin J. Ostrin, Jody Vykoukal, Jennifer Dennison, James Patrick Long, Kim-Anh Do, Ziding Feng, Samir M Hanash, Tracey Marsh; University of Texas MD Anderson Cancer Center, Houston, TX; Department of General Internal Medicine, Department of Pulmonary Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; MD Anderson Cancer Center, Houston, TX; Fred Hutchinson Cancer Research Center, Seattle, WA

Background: A 4-protein biomarker panel (4MP) combined with the validated $PLCO_{m2012}$ clinical risk model has been shown to improve lung cancer risk estimation over either metric alone. We investigated whether these panels in combination could also identify individuals at high risk of harboring a lethal lung cancer. **Methods:** We used data from an established logistic regression combining the 4MP and the $PLCO_{m2012}$ risk model, which were assessed in pre-diagnostic sera from 552 lung cancer cases and 2,193 non-cases from the Prostate Lung Colorectal and Ovarian (PLCO) cohort. Of the 552 lung cancer cases, 387 (70%) died from lung cancer. Cumulative incidence of lung cancer death as well as sub-distributional and cause-specific hazard ratios were calculated based on 4MP+$PLCO_{m2012}$ risk scores at a pre-defined 1.0% and 1.7% 6-year risk thresholds, which correspond to the 2013 and 2021 US Preventive Services Task Force lung cancer screening criteria, respectively. **Results:** When considering cases diagnosed within 1 year of blood draw and all non-cases, the AUC estimate of the 4MP+$PLCO_{m2012}$ model for risk prediction of lung cancer death was 0.88 (95% CI: 0.86-0.90). Among cases, the cumulative incidence of lung cancer death was statistically significantly higher in individuals with 4MP+$PLCO_{m2012}$ scores above the 1.0% 6-year risk threshold (modified χ^2: 5.42, *P:* 0.02). Corresponding sub-distributional and lung cancer death-specific hazard ratios for test-positive cases were 1.69 (95% CI: 1.07-2.66) and 1.80 (95% CI: 1.15-2.82), respectively. **Conclusions:** The blood-based biomarker panel in combination with $PLCO_{m2012}$ identifies individuals at high risk of a lethal lung cancer. Research Sponsor: U.S. National Institutes of Health; Cancer Prevention & Research Institute of Texas (CPRIT); MD Anderson Moon Shots Program.

8561 **Poster Session**

Incidence, outcomes, and risk factors of acute immune checkpoint inhibitor (ICI) pneumonitis post-chemoradiation with durvalumab for patients with locally advanced non-small cell lung cancer (LA-NSCLC): A population-based multicenter study.

Chloe Lim, Sunita Ghosh, Hali Morrison, Daniel E. Meyers, Igor Stukalin, Samantha Dolter, Heidi A.I. Grosjean, Marc Kerba, Desiree Hao, Aliyah Pabani; University of Calgary, Calgary, AB, Canada; Cross Cancer Institute, Edmonton, AB, Canada; Tom Baker Cancer Center, Calgary, AB, Canada; Tom Baker Cancer Centre, Calgary, AB, Canada; Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada

Background: The PACIFIC trial has drastically changed the LA-NSCLC treatment paradigm and improved survival outcomes with consolidation durvalumab post-chemoradiotherapy. Despite these promising results, real-world practice has demonstrated that ICI pneumonitis can have significant clinical complications and terminate consolidation therapy prematurely. This study aimed to identify clinical predictors, outcomes, and healthcare utilization in ICI pneumonitis in LA-NSCLC patients who received consolidation durvalumab in real-world practice. **Methods:** Using the Alberta Immunotherapy Database, we retrospectively evaluated all NSCLC patients who received durvalumab in Alberta, Canada from January 2018 to December 2021. Pneumonitis cases were identified based on radiographic changes and oncologists' clinical assessments. We examined incidence and predictive values of severe pneumonitis (≥grade 3), with secondary outcomes of overall survival (OS) and time-to-treatment failure (TTF). Exploratory multivariate analyses were performed to identify predictive values to developing severe pneumonitis and worse OS/TTF. **Results:** Of 189 total patients, most were ECOG 0-1 (91%) and had partial response from chemoradiation (85%) prior to durvalumab. 49% received full year of therapy (n = 93). Median TTF was 11.2 months, and median OS of 19.7 months with 1-year OS 64% (n = 121). 26% (n = 49) developed any grade of pneumonitis. 9% (n = 17) had severe pneumonitis. Corticosteroids were administered to 86% of the pneumonitis patients (n = 42); 53% (n = 26) required admission. 13% (n = 9) of deaths were attributed to pneumonitis. Male gender and pre-existing autoimmune condition were associated with severe pneumonitis whereas V_{20} (percentage of irradiated lung volume ≥20Gy) was associated with developing any grade pneumonitis. In multivariable analysis, male gender and V_{20} was significantly associated with worse OS whereas older age, smoking status, pneumonitis, and male gender with lower TTF. Pneumonitis development was found to be an independent risk factor for worse OS (p = 0.038) and TTF (p = 0.007). **Conclusions:** We report a pneumonitis incidence comparable to prior retrospective studies and higher rate of severe pneumonitis compared to PACIFIC trial. Our results corroborate that V_{20}, a previously established risk factor for durvalumab associated pneumonitis, is a significant predictor for developing pneumonitis and worse OS. In contrast to smaller retrospective studies, we observed male gender and pre-existing autoimmune conditions appear to predict severe durvalumab associated ICI pneumonitis. These results affirm the importance of careful patient selection for safe completion of consolidation durvalumab in real-world LA-NSCLC population. Research Sponsor: None.

8562 **Poster Session**

Impact of SARS-COV2 infection on the clinical outcomes in patients with lung cancer compared to all other cancers.

Vaishali Deenadayalan, Mona Dasgupta, Ali Shahbaz Baloch, Siri Chandana Swarna, Junglee Kim, Shweta Gupta; John H. Stroger, Jr. Hospital of Cook County, Chicago, IL; Weiss Memorial Hospital, Chicago, IL

Background: The outbreak of 2019 Novel coronavirus disease (COVID) has led to various deleterious outcomes in cancer patients. Those with lung cancer were noted to have increased morbidity and mortality when infected with COVID. We aimed to study the outcomes of COVID infection in patients with lung cancer compared to those with all other types of cancer. **Methods:** Healthcare Cost and Utilization Project-Nationwide Inpatient Sample database-2020 was queried to identify all COVID patients with lung cancer and those with all other types of cancer excluding lung cancer. The groups were compared for socio-demographic differences, medical comorbidities, inpatient mortality, length of stay (LOS), and total hospital charges (THC). Secondary outcomes included a diagnosis of thrombocytopenia (TCP), Acute Respiratory Failure (ARF), sepsis, anemia, pancytopenia and shock. Statistics were performed using t-test, univariate and multinomial logistic regression. **Results:** A total 1,050,045 COVID-19 admissions in cancer patients were identified, of which 4,625 (8.7%) had lung cancer whereas 48,840 (91.3%) had other types of cancer other than lung cancer. Lung cancer patients were older (Mean age 72 vs 69 years, $p < 0.01$). There was a higher prevalence of lung cancer compared to other cancers in whites (71 vs 58%, $p < 0.01$), hispanics had a lesser prevalence of lung cancer (7 vs 17%, $p < 0.01$). Lung cancer patients has a higher Charlson Comorbidity burden (> 2) compared to other cancers (91 vs 62%, $p < 0.01$). Lung cancer patients were less likely to have private insurance (14 vs 22%, $p < 0.01$). Among the comorbidity burden, lung cancer patients had a higher rate of dyslipidemia, COPD, Coronary artery disease, Smoking, venous thromboembolism ($p < 0.05$). A total of 8,135 cancer patients who were admitted with COVID died, among them 970 (11.9%) had lung cancer and 7,165 (88.1%) had other types of cancer making up 21% of all lung cancer admissions that died compared to 14.7% other cancer admissions ($p < 0.05$). On multivariate regression analysis, after adjusting for confounders those with lung cancer had a higher odds of all-cause mortality (aOR 1.37; 95% CI: 1.13-1.67,$p = 0.002$). Among lung cancer patients, adjusted LOS was reduced by 0.6 days (95% CI: -1.2 to -0.1, $p = 0.017$) and adjusted THC was decreased by $11,977 (95% CI: -19,010 to -4,943, $p = 0.001$). Among the secondary outcomes, lung cancer patients had lower rates of thrombocytopenia (6.5 vs 8.8%, $p = 0.01$) and anaemia (34.4 vs 38.5%, $p = 0.02$) compared to other cancer types. **Conclusions:** COVID-19 infection led to increased mortality in lung cancer patients compared to those with other types of cancer. The lower healthcare utilization was likely due to early mortality in the lung cancer cohort. This study calls attention to the increased vulnerability of lung cancer patients to the SARS COV2 infection than other cancer types. Research Sponsor: None.

8563 **Poster Session**

Development and validation of a prediction model for the recurrence of stage 1 EGFR mutation positive NSCLC in patients using machine learning with WES-based gene sets.

Akiko Tateishi, Hidehito Horinouchi, Ken Takasawa, Nobuji Kouno, Takaaki Mizuno, Yu Okubo, Yukihiro Yoshida, Shun-ichi Watanabe, Mototaka Miyake, Masahiko Kusumoto, Koji Inaba, Hiroshi Igaki, Yasushi Yatabe, Masami Mukai, Katsuya Tanaka, Naoki Mihara, Kouya Shiraishi, Takashi Kohno, Yuichiro Ohe, Ryuji Hamamoto; Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan; Division of Medical AI Research and Development, National Cancer Center Research Institute, Tokyo, Japan; Department of Experimental Therapeutics, National Cancer Center Hospital, Tokyo, Japan; Department of Thoracic Surgery, National Cancer Center Hospital, Tokyo, Japan; Division of Thoracic Surgery, National Cancer Center Hospital, Tokyo, Japan; Department of Diagnostic Radiology, National Cancer Center Hospital, Tokyo, Japan; Department of Radiation Oncology, National Cancer Center Hospital, Japan, Tokyo, Japan; Department of Radiation Oncology, National Cancer Center Hospital, Tokyo, Japan; Department of Diagnostic Pathology, National Cancer Center Hospital, Tokyo, Japan; Division of Medical Informatics, National Cancer Center Hospital, Tokyo, Japan; Division of Genome Biology, National Cancer Center Research Institute, Tokyo, Japan; National Cancer Center Hospital, Tokyo, Japan

Background: Predicting the risk of postoperative recurrence is becoming increasingly important in *EGFR* mutation positive (*EGFR*-m) non-small cell lung cancer (NSCLC). Only a few reports conducted whole exome sequencing (WES) for genomic profiling in large scale *EGFR*-m NSCLC cases. **Methods:** We conducted WES and analyzed the clinical course of patients (pts) with NSCLC who underwent surgery between 1985 and 2019 in the PRISM project of our institute. We evaluated the *EGFR*-m patients' characteristics, recurrence-free survival (RFS), and developed a prediction model using machine learning, Overlapping Group LASSO to predict whether the EGFR-m patients will recur within 5 years or not as "high-risk" and "low-risk". To develop and validate the prediction model, we divided the data from 2006 as the training cohort data set and the data before 2006 as the validation cohort data set. After the development of the prediction model, we performed a stratified Cox proportional hazards model to compare the RFS between the predicted groups. **Results:** A total of 585/1351(43.3%) pts were *EGFR*-m included in the PRISM project. Of all pts, stage I, *EGFR*-m were 205 pts. The median RFS of the stage I, *EGFR*-m 123.1 months (m). In the training cohort, the model detected 43 pts for high-risk and 88 pts for low-risk. In the validation cohort, the model predicted 29 pts for high-risk and 45 pts for low-risk. Median RFS of high-risk vs. low-risk were 52.2 m vs. 105 m (HR 2.43, p=0.01). The 1-year RFS rate, 2-year RFS rate, and 5-year RFS rates for high-risk and low-risk pts were 100% vs. 98.5%, 66.7% vs. 89.2%, and 41.7% vs. 66.1%, respectively. Twenty-eight gene set coefficients were non-zero in the prediction model. The gene sets with large positive coefficients that were considered important for prediction as "high risk" were the gene sets affected by *KRAS* gene overexpression and *p53* gene knockdown. In contrast, gene sets repressed by mTOR inhibition and genes repressed by *TBK1* gene knockdown and *KRAS* gene overexpression had large negative coefficients. **Conclusions:** We developed and validated the prediction model whether the EGFR-m patients will recur within 5 years or not. *EGFR*-m NSCLC recurrence appears to be high risk with pathways associated with *KRAS* and p53 genes, and low risk with mutations in the gene sets suppressed by the mTOR pathway and *TBK1* gene. Research Sponsor: None.

	Training cohort (n=131)		Validation cohort (n=74)	
	High risk (n=43)	Low risk (n=88)	High risk (n=29)	Low risk (n=45)
median RFS (m), 95%CI	32.8 [23.5-44.8]	NR [NR-NR]	52.2 [23.7-NR]	105 [73.1-NR]
HR, *p*-value	-		2.43, $p = 0.011$	
1-year RFS rate (%)	89 [81-98]	100 [100-100]	100 [100-100]	98.5 [95.5-100]
2-year RFS rate (%)	60 [49-75]	100 [100-100]	66.7 [44.7-99.5]	89.2 [82.0-97.1]
5-year RFS rate (%)	0	100 [100-100]	41.7 [21.3-81.4]	66.1 [55.5-78.7]

8564 **Poster Session**

Phase II trial of safety and efficacy of tislelizumab plus chemotherapy in stage II-IV non small cell lung cancer (LungMark).

Yaobin Lin, You-Hao Chen, Zhi-Chao Lin, Ming Zhou, Wen-Yu Zhai, Ze-Rui Zhao, Bing-Yu Rao, Yu-Heng Zhou, Min Huang, Hao Long; Department of Thoracic Surgery, Sun Yat-Sen University Cancer Center, Guangzhou, China; Laboratory of Drug Metabolism and Pharmacokinetics, School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou, China;, Guangzhou, China; Department of Thoracic Surgery, Jiangmen Central Hospital, Jiangmen, China; Department of Thoracic Surgery, Cancer Center of Guangzhou Medical University, Guangzhou, China; Department of Thoracic Surgery, Sun Yat-sen University Cancer Center, Guangzhou, VA, China; Institute of Clinical Pharmacology, School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou, China

Background: The current study aimed to investigate the safety and efficacy of chemotherapy with PD-1 inhibitor, tislelizumab, for stage II-IV NSCLC. Meanwhile to explore the potential biomarkers for safety and efficacy of tislelizumab plus chemotherapy in NSCLC. **Methods:** This was an open-label, multicenter, phase 2 trial conducted at 3 hospitals in China. Patients with treatment-naïve, stage II-IV NSCLC without EGFR/ALK driver mutations were enrolled. This study consisted of two cohorts, one cohort is potentially resectable disease (PRD) and the other is unresectable disease (URD). The PRD patients received 3-4 cycles of tislelizumab (200 mg Q3w) plus carboplatin-based chemotherapy. Candidates eligible for surgery underwent surgery, followed by adjuvant tislelizumab monotherapy for 1 year. The URD patients received platinum-based doublet chemotherapy plus tislelizumab for 4-6 cycles, followed by tislelizumab for squamous and tislelizumab in combination with pemetrexed for non-squamous, until disease progression or intolerable toxicity. Primary endpoint was safety. Secondary endpoints were efficacy, such as MPR/pCR(PRD cohort), ORR, PFS and OS, etc. Multi-omics analysis of baseline and post-treatment samples were conducted to explore the safety and efficacy for chemoimmunotherapy. (NCT05244837). **Results:** Between December 2020 and November 2022, a total of 100 eligible patients were enrolled and received at least one cycle of immunochemotherapy. 58 patients were with PRD, of whom 40 (68.9%) were squamous cell lung cancer. 50 (86.2%) patients were stage III disease. During neoadjuvant treatment period, 52 patients (91.2%) experienced neoadjuvant TRAEs. Most of the TRAEs were grade 1or 2. No grade 4 or 5 TRAEs was observed. The most common grade 1 or 2 TRAEs were alopecia (n = 29;50.9%), anemia (n = 25;43.9%), rash (n = 29; 50.9%). Four patients (7.0%) experienced severe TRAE of grade 3 increased ALT/AST.39 patients received surgical resection, R0 resection was performed for 38 (97.4%) patients. 29 (74.4%) achieved MPR (major pathological response), including 19 (48.7%) with a complete pathological response (pCR). 42 patients with URD were enrolled, 26 (61.9%) patients were stage IV disease. 37 patients (88.1%) experienced TRAEs. The most common grade 1 or 2 TRAEs TRAEs were anemia (n = 27; 64.3%), rash (n = 12; 57.0%). Severe TRAEs occurred in 8 (2.0%) cases, including increased ALT/AST, decreased white blood cell count etc. 29 genes were identified as differentially expressed in pretreatment tumors from patients with pCR compared to non-pCR. **Conclusions:** Neoadjuvant tislelizumab plus chemotherapy was safe and effective with high MPR and manageable TRAEs in patients with PRD. For patients with URD, tislelizumab plus chemotherapy was generally well tolerated. We have identified a differential immune landscape between pCR and non-pCR tumors. Clinical trial information: NCT05244837. Research Sponsor: None.

8565 **Poster Session**

Association of immune-related adverse events and efficacy outcomes in phase II trial of consolidation nivolumab plus ipilimumab or nivolumab alone after chemoradiation in patients with unresectable stage III non–small-cell lung cancer (NSCLC).

Cynthia Wei, Sandra K. Althouse, Hirva Mamdani, Nasser H. Hanna, Greg Andrew Durm; Indiana University School of Medicine, Indianapolis, IN; Indiana University, Indianapolis, IN; Barbara Ann Karmanos Cancer Institute, Detroit, MI; Indiana University Simon Comprehensive Cancer Center, Indianapolis, IN

Background: Immunotherapy has been widely incorporated into the treatment of patients with non-small-cell lung cancer. Many of these patients will experience immune-related adverse events (irAEs) that may lead to early discontinuation of therapy. Previous studies have reported that patients with Stage III and metastatic NSCLC who experienced irAEs receive fewer cycles of immunotherapy without decreased efficacy. Here we report a retrospective analysis of the association between irAEs and efficacy outcomes from the BTCRC LUN 16-081 randomized phase 2 trial of consolidation immunotherapy with nivolumab (N) plus ipilimumab (IPI) vs N alone following concurrent chemoradiotherapy in patients with unresectable Stage IIIA/IIIB NSCLC. **Methods:** A total of 105 eligible patients were enrolled from 9/2017 to 4/2021. Demographics, disease characteristics, and number of immunotherapy cycles received were reported in patients with and without irAEs in the two arms. Chi-square test was used for comparisons for categorical variables and Wilcoxon test for continuous variables. The Kaplan-Meier method was used to analyze progression-free survival (PFS) and overall survival (OS). A log-rank test was used to compare groups. **Results:** In treatment arm A (N alone), any grade irAEs occurred in 64.8% of patients. At a follow up of 48 months, there was no significant difference in number of N cycles started (6 vs 6, p = 0.238), progression free survival (29.4 vs 31.9 mo, p = 0.897), or overall survival (NE vs. 31.9 mo, p = 0.798) in patients with and without irAEs. Patients who discontinued N because of irAEs (n = 8 or 14.8% of patients) received significantly fewer cycles of N (2 vs 6, p = < .0001) and had a shorter PFS (8.2 vs. 31.9 months, p = < .0001) and OS (12.3 months vs. NE, p < .0001). In treatment arm B (IPI+N), any grade irAEs occurred in 84.3% of patients. At follow up of 48 months, there was no significant difference in number of IPI+N started (4 vs. 4, p = 0.260) or overall survival (NE vs. NE, p = 0.576), but there was a significantly longer PFS in those who experienced irAEs (30.9 months vs. 6.8 months, p = 0.0083). Patients who discontinued IPI+N because of irAEs (n = 18 or 35.3% of patients) received significantly fewer cycles of IPI+N (2 vs 4, p = < .0001) without a significant difference in PFS (28.1 vs. 25.3 mo, p = 0.830) or OS (NE vs NE, p = 0.755). **Conclusions:** The occurrence of irAEs alone in both arms, regardless of number, was not associated with decreased efficacy outcomes in this exploratory analysis. However, if irAEs resulted in the discontinuation of therapy, these patients did have a shorter PFS and OS in the N alone arm. This difference was not observed in the IPI+N arm and those who experienced any irAEs in the IPI+N arm had an improved PFS. Research Sponsor: Bristol Myers Squibb.

8567 **Poster Session**

EGFR tyrosine kinase inhibitors (TKIs) versus durvalumab (durva) following concurrent chemoradiation (CRT) in unresectable *EGFR*-mutant non-small-cell lung cancer (NSCLC).

Amin Nassar, Elio Adib, Jamie Feng, Jacqueline V. Aredo, Kaushal Parikh, Jeremy Phillip Harris, Ana I. Velazquez Manana, Meera Vimala Ragavan, Jessica Jiyeong Lin, Zofia Piotrowska, Bailey Gleason Fitzgerald, Christian Grohé, Kamya Sankar, Joel W. Neal, Heather A. Wakelee, Frances A. Shepherd, Roy S. Herbst, Abdul Rafeh Naqash, Sarah B. Goldberg, So Yeon Kim; Yale Cancer Center, New Haven, CT; Brigham and Women's Hospital, Boston, MA; Princess Margaret Cancer Centre, UHN, Toronto, ON, Canada; Stanford Cancer Institute, Stanford, CA; Mayo Clinic, Rochester, MN; University of California, Irvine, Orange, CA; University of California San Francisco, San Francisco, CA; University of California, San Francisco, San Francisco, CA; Massachusetts General Hospital Cancer Center, Boston, MA; Massachusetts General Hospital, Boston, MA; Icahn School of Medicine at Mount Sinai, New York, NY; Department of Respiratory Diseases, ELK Berlin, Berlin, Germany; Cedars-Sinai Medical Center, Los Angeles, CA; Stanford University Medical Center, Stanford, CA; Stanford Hospital & Clinics, Stanford, CA; Princess Margaret - University Health Network, Toronto, ON, Canada; Yale School of Medicinel, Yale Cancer Center, Smilow Cancer Hospital at Yale-New Haven, New Haven, CT; Stephenson Cancer Center, University of Oklahoma Health Sciences, Oklahoma City, OK

Background: Adjuvant osimertinib (osi) improves disease-free survival (DFS) in patients (pts) with resected, early-stage, *EGFR*-mutant (EGFRmut) NSCLC, yet the benefit of osi after CRT in pts with unresectable locally advanced NSCLC is unknown. Post-hoc analysis of the PACIFIC trial showed a lack of survival benefit with consolidation durva versus placebo in pts with *EGFR*mut NSCLC. Comparisons between consolidation durva and EGFR TKIs in unresectable *EGFR*mut NSCLC following CRT are lacking. **Methods:** We conducted a multi-institutional retrospective analysis of pts with stage III unresectable *EGFR*mut NSCLC (exon19 deletion, exon21 L858R), who received EGFR TKI or durva after $\geq$ 2 cycles of platinum-based chemotherapy plus definitive radiation therapy between 2015-2022. Baseline characteristics including age, sex, smoking history, PD-L1 status, and outcomes on DFS, overall survival (OS), and safety were collected. Multivariable (MVA) cox regression analysis was used for statistical analysis. Treatment-related adverse events (trAE) were defined using CTCAE 5.0. **Results:** Seventeen pts from 12 institutions received an EGFR TKI (osi, n=15; erlotinib, n=2), and 13 pts received consolidation durva. Median follow-up was 23 months. Median age of all pts was 61 years (IQR:52-72) and 76.7% were female. Most pts in both groups had never-smoked and had adenocarcinoma. All pts received $\geq$ 60 Gy of radiation with concurrent chemotherapy. PD-L1 expression was $\geq$ 50% in 1/10 (10%) pts treated with durva vs 6/13 (46.2%) treated with TKI, p=0.09. Median duration on treatment for EGFR TKI and durva was 12.2 months and 4.8 months, respectively. Pts treated with EGFR TKI had significantly longer 24-month DFS versus pts treated with durva after adjusting for stage (3A vs 3B vs 3C) (Table). Any grade tRAE occurred in 58.8% (10/17) of pts treated with EGFR TKI vs 38.5% (5/13) with durva. Grade $>$ 3 tRAE occurred in 15.4% (1 pneumonitis and 1 AST/ALT elevation) of pts treated with durva but in none of pts treated with EGFR TKI. Three pts within each arm came off treatment due to toxicity (EGFR TKI: 1 pneumonitis and 2 dermatitis; durva: 1 of each pneumonitis, Type 1 diabetes, AST/ALT elevation). **Conclusions:** EGFR TKI therapy after definitive CRT was associated with significantly longer DFS compared to durva in this retrospective study of pts with stage III unresectable *EGFR*mut NSCLC, without unanticipated safety signals. Follow-up is ongoing and OS outcomes will be evaluated subsequently. Further investigation is warranted to define the optimal therapy for locally advanced *EGFR*mut NSCLC. Research Sponsor: None.

Treatment	Median DFS, months (95% CI)	24-month DFS, % (95% CI)	DFS Hazard ratio (95% CI), p-value
EGFR TKI, N=17	28 (15.4-49)	88 (67-100)	0.09, 95% CI
Durva, N=13	8.5 (3.6-NR*)	31 (14-70)	(0.01-0.58), p<0.01

NR=Not reached.

8568 **Poster Session**

A combinatorial model of plasma proteins and LDCT imaging and the diagnosis of pulmonary nodules.

Meng Yang, Huan-Sha Yu, Kai-Ge Wang, Chao-Yang Liang, Jiang-Hui Duan, Hong-Liang Sun, Hong-Xiang Feng, Bei Wang, Bing Tong, Jue Wang, Ye Wang, Yong-Zhao Zhou, Xin Lu, Hong-Xia Yang, Dong-Xia Li, Wei Li, Qi-Ye He, Yun-Zhi Zhang, Rui Liu, Jian Zhou; Department of Pulmonary and Critical Care Medicine, Center of Respiratory Medicine, China-Japan Friendship Hospital, Beijing, China; Experimental Animal Center, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China; Department of Pulmonary and Critical Care Medicine, West China Hospital, Sichuan University, Chengdu, China; Department of Thoracic Surgery, Center of Respiratory Medicine, China-Japan Friendship Hospital, Beijing, China; Department of Radiology, China-Japan Friendship Hospital, Beijing, China; Department of Pathology, China-Japan Friendship Hospital, Beijing, China; Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China; Department of Rheumatology, China-Japan Friendship Hospital, Beijing, China; Beijing Changping District Hospital of Traditional Chinese Medicine, Beijing, China; Singlera Genomics Ltd., Shanghai, China; Liver Cancer Institute, Zhongshan Hospital, and Key Laboratory of Carcinogenesis and Cancer Invasion (Ministry of Education), Fudan University, Shanghai, China

Background: Low dosage computer tomography (LDCT) has been widely adopted as a sensitive method to detect early-stage lung cancer; however, debate regarding its accuracy and overdiagnosis is still ongoing. An accurate non-invasive test is needed to identify malignant nodules and reduce unnecessary invasive procedures. Studies show that plasma proteins and LDCT imaging features may be used to discriminate malignant pulmonary nodules from benign ones. We aimed to develop a combinatorial approach integrating serum protein markers and imaging features to improve the classification of pulmonary nodules. **Methods:** This study established a prospective research cohort, which enrolled 608 patients of pulmonary nodules. Plasma samples were collected to measure protein levels using Proximity Extension Assay (PEA) technology. The imaging features of the pulmonary nodules were extracted using the python 'radiomics' package. Following feature extraction, a deep learning networks model was built using training cases. The model was then tested in the testing set to evaluate its accuracy and robustness. **Results:** From the study cohort, 184 benign (BN) and 184 malignant (MT) samples matched for sex and age were chosen to have a representative training set. The rest 240 samples (81 BN and 159 MT) were used as a testing set. Image features were extracted from 448 patients (119 BN and 153 MT in training; 57 BN and 119 MT in testing) with raw LDCT image available. In the testing set, the model trained using only protein levels had an AUC of 0.83 [0.782-0.877] (sensitivity = 71.1% [95% CI 63.6-77.6]; specificity = 82.7% [73.1-89.4]) when classifying plasma samples of lung cancers from those of benign nodules. In comparison, the imaging features-only model had an AUC of 0.874 [0.821-0.916] (sensitivity = 81.5 [73.6-87.5]; specificity = 73.7 [61.0-83.4]). The combinatorial model integrating both protein and imaging features had an AUC of 0.878 [0.830-0.921] (sensitivity = 83.2% [75.5-88.8]; specificity = 77.2% [64.8-86.2]). Notably, the combinatorial model was highly sensitive for early-stage lung cancer, achieving a sensitivity of 93.1% [78.0-98.1] when classifying stage-0 lung cancer cases(n = 29) and 94.8% [85.9-98.2] for stage-I cases (N = 58). Its sensitivity for stage II-IV (n = 7) and clinically diagnosed lung cancers cases (n = 25) were 100% [64.6-100] and 40.0% [23.4-59.3], respectively. **Conclusions:** This study aimed to construct a model to distinguish malignant pulmonary nodules from benign lung diseases using protein levels and LDCT imaging features. The resulted combinatorial model showed by utilizing both types of features, it was able to accurately differentiate benign and malignant pulmonary nodules, suggesting it may provide guidance for the clinical management of these nodules. Research Sponsor: National Key Research and Development Program of China (2019YFC1315800).

8569 **Poster Session**

Cancer risk assessment in patients with persistent pulmonary nodules and its correlation with cancer-free survival.

Hui Li, Kang Qin, Zheng Zhang, Lingzhi Hong, Carol C. Wu, Myrna Cobos Barco Godoy, Mara Antonoff, Edwin J. Ostrin, Iakovos Toumazis, Don Lynn Gibbons, John Heymach, J. Jack Lee, Jia Wu, Jianjun Zhang; Department of Thoracic/Head and Neck Medical Oncology, Department of Imaging Physics, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Thoracic/Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Thoracic Imaging, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Thoracic and Cardiovascular Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of General Internal Medicine, Department of Pulmonary Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Health Services Research, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Thoracic/Head and Neck Medical Oncology, Department of Molecular and Cellular Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Imaging Physics, Department of Thoracic/Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Thoracic/Head and Neck Medical Oncology, Department of Genomic Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: With the wide use of CT for lung cancer screening and diagnosis, detection of pulmonary nodules increases drastically. Brock malignancy risk scoring is a validated risk prediction model for distinguishing malignant nodules, but it only provides a snapshot without incorporating the dynamic changes of lung nodules. Our study tested the performance of Brock malignancy risk scoring system in patients with persistent lung nodules. **Methods:** We prospectively studied a cohort of 304 patients with persistent lung nodules (at least 2 CT scans, 3 months apart with no evidence of shrinkage) who were under management at MD Anderson Cancer Center from 11/28/2018 to 12/14/2022. These lung nodules were assessed by radiologists with Brock full model. These patients were followed up routinely and subjected to biopsy as determined by treating physicians. The area under the receiver operating characteristic curve (AUC) and the optimal cut-off of Brock model was studied. Additionally, we studied another cohort with 130 patients with histologically confirmed lung cancer. We retrospectively reviewed the CT or PET/CT scans and assessed the corresponding persistent lung nodules as defined above prior to the cancer diagnosis. We explored the correlations among nodule characteristics, demographic factors and Brock cancer risk scores. Cox proportional hazards model was built for multivariate analysis. **Results:** The median follow-up time for the prospective cohort was 337 days and 40 of the 304 patients (13.16%) were diagnosed with lung cancer with a median lung cancer-free survival of 228 days. The mean risk score was 24.20% (0.12%-62.86%) for histologically confirmed malignant vs 11.01% (0.07%-61.84%) for the remaining lung nodules ($P < 0.001$). Of note, 4 of 46 (8.70%) patients with persistent lung nodules of risk scores between 5%-10% and 8 of 134 (5.97%) patients with risk score $< 5\%$ were diagnosed with lung cancer. The AUC for Brock model was 0.72 and the optimal cut-off value is 10.64% (sensitivity: 0.702, specificity:0.677). Among the retrospective cohort of 130 lung cancer patients (82.3% adenocarcinoma, 13.1% squamous cell carcinoma and 4.6% others), the predicted risk score ranged from 0.09% to 85.82%, including 33.85% of patients with risk score $< 10\%$ and 26.15% of patients with predicted risk score $< 5\%$. The risk score was not correlated with age, sex, race, ethnicity, smoking history, family history of lung cancer, emphysema, nodule types or locations. The low-risk patients had a longer median cancer-free time ($P = 0.001$). **Conclusions:** Persistency is an important risk factor for malignant lung nodules. Using Brock criteria, a substantial proportion of lung nodules with true malignant potential can be overlooked because of predicted "low risk". Improved prediction models incorporating the dynamic changes of lung nodules are warranted to guide early diagnosis of lung cancer. Research Sponsor: The University of Texas MD Anderson Lung Cancer Moon Shot Program.

8571 **Poster Session**

Optimal number of lymph node stations associated with improved survival among patients with non-small cell lung cancer (NSCLC).

Meredith Ray, Anberitha T Matthews, Olawale Akinbobola, Matthew Smeltzer, Carrie Fehnel, Nicholas R Faris, Andrea Saulsberry, Kourtney Dortch, Samuel Muhit, Raymond U. Osarogiagbon; University of Memphis, School of Public Health, Memphis, TN; Baptist Cancer Center, Multidisciplinary Thoracic Oncology Department, Memphis, TN; Baptist Memorial Health Care Corp, Memphis, TN; Baptist Memorial Healthcare System, Memphis, TN; Baptist Cancer Center, Memphis, TN; University of Memphis, Memphis, TN; Multidisciplinary Thoracic Oncology Program, Baptist Cancer Center, Memphis, TN

Background: Good quality pathologic nodal evaluation is associated with improved long-term survival in NSCLC after surgical resection. However, there is no universal definition of quality. We examined the association between number of lymph node stations (NLNS) sampled and overall survival. **Methods:** We examined the population-based Mid-South Quality of Surgical Resection (MS-QSR) cohort, excluding patients with neoadjuvant therapy, positive margins, and secondary resections. We summarized demographic and clinical characteristics with appropriate statistics. We employed four Cox regression models: 1) including NLNS as the only predictor; 2) model 1, adjusting for age, sex, histology, clinical stage, extent of resection, and surgical technique; 3) examined the impact of pathologic staging (pStage in 3 groups: IA/IB[<4cm tumor size]; IB[>4cm]/II/IIIA[pN2-]; pN2]) by modeling interaction with pStage and NLNS; 4) model 3 plus adjustments (no clinical stage). In a cut point analysis to identify the optimal NLNS for improved survival, we dichotomized the NLNS for cut points 0 to 12. Hazard ratios (HR) were calculated (as above) and plotted for each dichotomization. **Results:** The 3916 eligible patients were 21% Black, 54% male, 15% on Medicaid and 49% Medicare; 84% and 85% had clinical and pathologic stage I/II, respectively; 84% had no invasive staging; 84% had a PET-CT scan. For every additional lymph node station sampled, the HR decreased by 0.94 (95% confidence interval: 0.92, 0.96). After adjustments, the HR remained significant (Table). Our pStage cohorts comprised of 2474 (64%) IA/IB[<4cm]; 1080 (28%) IB[>4cm]/II/IIIA[pN2-]; and 290 (8%) pN2+. Once stratified, HRs remained significant among those with early stage but not for pN2+ (Table). When further adjusted, only pStage IA/IB[<4cm] patients had a significant HR, 0.94 (0.91, 0.97). The cut point analysis indicated sequential survival improvement up to ≥ 7 total stations sampled, consistently across all models/adjustments. **Conclusions:** The number of lymph node stations examined is directly associated with survival after lung cancer resection. Examination of a total of 7 intrapulmonary, hilar and mediastinal stations seems optimal. Hazard ratios (95% confidence intervals) for modeling hazards as a function of lymph node stations sampled (model 1), further adjusted for age, sex, histology, clinical stage, extent of resection, and surgical technique (model 2), including interaction with pathologic stage with no adjustments (model 3), and interaction with pathological stage with adjustments (no clinical stage) (model 4). Research Sponsor: U.S. National Institutes of Health.

	All LN Stations
Model 1:	**0.94 (0.92, 0.96)**
Model 2:	**0.97 (0.95, 1)**
Model 3: IA/IB[<4cm]	**0.9 (0.88, 0.93)**
IB>4cm/II/IIIA[pN2-]	**0.94 (0.9, 0.98)**
pN2+	1.03 (0.94, 1.12)
Model 4: IA/IB[<4cm]	**0.94 (0.91, 0.97)**
IB>4cm/II/IIIA[pN2-]	0.97 (0.93, 1.01)
pN2+	1.07 (0.98, 1.17)

8572 **Poster Session**

Reevaluating the role of adjuvant chemotherapy in early-stage, resectable NSCLC with high-risk clinical and pathologic features.

Brendan Heiden, Daniel B. Eaton, Su-Hsin Chang, Yan Yan, Martin W. Schoen, Theodore Seth Thomas, Bryan F. Meyers, Benjamin D. Kozower, Varun Puri; Washington University School of Medicine, St. Louis, MO; VA St. Louis Health Care System, St. Louis, MO; Washington University in St. Louis, St. Louis, MO; Saint Louis University School of Medicine, St. Louis, MO; Saint Louis VA Medical Center John Cochran Division, St. Louis, MO; Washington University, St. Louis, MO

Background: The preferred treatment for early-stage non-small cell lung cancer remains surgical resection with the consideration of adjuvant chemotherapy for tumors with certain high-risk features. It is commonly cited that such treatments confer a meager 5% 5-year survival benefit compared to observation alone. We sought to reassess the benefit of adjuvant chemotherapy using modern, real-world datasets. **Methods:** We performed a retrospective cohort study using a dataset from the National Cancer Database. All patients with early-stage stage NSCLC (3-5cm, node-negative) who would be eligible for adjuvant chemotherapy based on National Comprehensive Cancer Network guidelines were included (i.e., presence of at least 1 high-risk feature). High-risk clinical and pathologic features were defined as poor differentiation, tumor size (≥4cm), non-anatomic wedge resection, inadequate lymph node evaluation, vascular invasion, and visceral pleural involvement. We employed average treatment effect on the treated (ATT) weighting to match patients with similar demographic, tumor, and treatment-related variables to compare outcomes between chemotherapy versus observation groups. The primary outcome was overall survival. These findings were further validated in an independent cohort from the US Veteran Health Administration (VHA). **Results:** The study included 10,812 patients with early-stage NSCLC who had at least 1 high-risk feature. The frequencies of high-risk features were as follows: tumor size ≥4cm (n = 3,271, 30.3%), poor differentiation (n = 9,454, 87.4%), visceral-pleural invasion (n = 2,542, 23.5%), vascular invasion (n = 1,742, 16.11%), non-anatomic wedge resection (n = 781, 7.2%), and inadequate nodal sampling (n = 6,306, 58.3%). Despite the presence of high-risk features, only 1,427 (13.2%) patients received adjuvant chemotherapy. In the ATT weighted analysis, 1,261 (49.7%) patients received adjuvant chemotherapy and 1,278 (50.3%) patients received observation. The 5-year overall survival was 70.0% (95% CI 67.1-72.7) in the chemotherapy group versus 62.0% (95% CI 60.2-63.7%) in the observation group (absolute 5-year survival difference 8.0%). In the VHA cohort, 11.3% of patients received adjuvant chemotherapy. Similarly, the 5-year overall survival was 64.0% (95% CI 51.4-74.2) in the chemotherapy group versus 56.2% (95% CI 48.3-63.4) in the observation group (absolute 5-year survival difference 7.8%). **Conclusions:** These data suggest a notably larger benefit of adjuvant chemotherapy in eligible patients with high-risk clinical pathologic features compared to commonly cited statistics. With the addition of more robust treatment options in early-stage disease, adherence to adjuvant and neoadjuvant treatment guidelines may disproportionately improve early-stage NSCLC outcomes following curative-intent resection. Research Sponsor: Department of Veterans Affairs.

8573 **Poster Session**

Acute hospitalizations after proton beam therapy (PBT) versus intensity-modulated radiotherapy (IMRT) for locally advanced non–small-cell lung cancer (LA-NSCLC) in the era of immune checkpoint inhibitor (ICI) consolidation: A retrospective propensity score weighted study.

Michelle Iocolano, Nikhil Yegya-Raman, Xingmei Wang, Cole Friedes, Sang Ho Lee, Lian Duan, Bolin Li, William P. Levin, Keith A. Cengel, Corey J. Langer, Roger B. Cohen, Lova Sun, Charu Aggarwal, Abigail Doucette, Ying Xiao, Kevin Teo, Shannon O'Reilly, Jennifer Wei Zou, Charles B. Simone, Steven J Feigenberg; University of Pennsylvania, Philadelphia, PA; University of Pennsylvania Health System, Philadelphia, PA; New York Proton Center, New York, NY

Background: Prior work found that PBT is associated with fewer acute hospitalizations compared to photons for a variety of cancers. Patients (pts) with LA-NSCLC treated with concurrent chemoradiation (cCRT) and ICI consolidation are at high risk for treatment-related toxicity and acute hospitalizations. We hypothesized that PBT is associated with fewer acute unplanned hospitalizations as compared to IMRT in the era of ICI consolidation. **Methods:** This single institution, multi-site retrospective study included consecutive pts with LA-NSCLC treated with definitive cCRT with either PBT or IMRT from October 2017 to December 2021. Pts were evaluated for consolidative ICI. Primary endpoint was unplanned hospitalization within 90 days of first radiation (RT) treatment. Secondary endpoints included grade 3+ pneumonitis, grade 3+ esophagitis, PFS, and OS. Logistic regression was used to assess associations with 90-day hospitalization. Competing risk regression was used for grade 3+ pneumonitis and esophagitis and Cox regression for PFS and OS. Inverse probability treatment weighting (IPTW) was applied to adjust for differences in PBT and IMRT groups. **Results:** 316 pts were included: 117 (37%) received PBT and 199 (63%) IMRT. Median age was 68.5 yrs; median RT dose 66.6 Gy (IQR 65.9-70.0). PBT group was older (median 71.1 vs 67.2 yrs, $p < 0.005$) and had a higher Charlson comorbidity index (CCI) (median 4 vs 3, $p = 0.02$). There was no difference in receipt of ICI consolidation (66.7% vs 68.3%, $p = 0.76$). PBT group had lower mean heart dose (5.9 vs 10.8 Gy, $p < 0.001$), LAD V15 (0 vs 6%, $p = 0.001$), mean lung dose (14.7 vs 15.7 Gy, $p < 0.008$) and effective dose to immune circulating cells (median 3.7 vs 4.9 Gy, $p < 0.001$) but not mean esophagus dose. PBT was associated with fewer unplanned 90-day hospitalizations (23.9% vs 34.7%; aOR 0.52, 95% CI 0.30-0.90, $p = 0.02$). This difference persisted on IPTW analysis (OR 0.48, 95% 0.33-0.70, $p = 0.0002$) after adjusting for CCI, ECOG, smoking pack yrs, T stage, N stage, target volume, concurrent chemotherapy agent and histology. Reasons for hospitalization in PBT and IMRT groups included progression (1.4% vs 1.6%), definite/probable toxicity from cCRT (11.4% vs 18.2%), possible toxicity from cCRT (7.3% vs 12.8%) or unrelated to cCRT (2.5% vs 2.3%). There was no significant difference between PBT and IMRT groups in G3+ pneumonitis (1-year 6.0% vs 9.1%, $p = 0.49$), G3+ esophagitis (1-year 6.0% vs 6.5%, $p = 0.71$), PFS (median 14.4 vs 15.1 months, $p = 0.69$), or OS (median 34.2 vs 29.4 months, $p = 0.41$); results remained unchanged in IPTW analysis. **Conclusions:** Among pts with LA-NSCLC treated with cCRT in the era of ICI consolidation, PBT was associated with fewer acute unplanned hospitalizations compared to IMRT. Research Sponsor: None.

8574 **Poster Session**

Association of single-click radiomic classifier with response and prognosis in non-small cell lung cancers (NSCLC) treated with immune checkpoint inhibitors.

Amogh Hiremath, Haojia Li, Allison Clement, Amit Gupta, Vamsidhar Velcheti, Anant Mababhushi, Nathaniel Braman; Picture Health, Cleveland, OH; University Hospitals Cleveland Medical Center, Cleveland, OH; New York University, Laura and Isaac Perlmutter Cancer Center, New York, NY; Emory University and Georgia Institute of Technology, Atlanta, GA

Background: Radiomics has shown promise to non-invasively phenotype disease and address the limitations of extant biomarkers (e.g. PD for immune checkpoint inhibitors (ICI) in cancers, such as NSCLC. However, considerable barriers to the clinical adoption of these tools remain, such as their dependence on precise annotation of tumor extent by experienced clinical users. Here, we demonstrate a radiomic solution that requires only a single user mouse click within one or more target lesions on a baseline CT scan, to contour tumors in 3D and generate a patient-level radiomic prediction of response and outcome in ICI treated NSCLC patients. **Methods:** 1778 CT scans from 1261 patients were used to develop and validate an interactive, semi-automated tool for predicting ICI outcomes in NSCLC patients prior to therapy. A user click based deep learning contouring model was trained and validated on 1146 patients, then used to create annotations for radiomic analysis. A least absolute shrinkage and selection operator (LASSO) Cox proportional hazards model was utilized to select features associated with post-ICI overall survival (OS) and derive a radiomic risk score within a training cohort (n=74) that can separate patients into high and low risk groups. The model was tested on held out pre-treatment CTs of 41 ICI recipients from 2 institutions for association with OS, progression-free survival (PFS), and objective response (OR). **Results:** A total of 77 lesions were identified and segmented within the testing set. Average volume per lesion was 54.10 mL and per patient was 101.60 mL. OR was observed in 48.70% of patients. A threshold of -0.31 defining high and low radiomic risk groups was chosen based on optimal separation within the training set (HR=2.59 [95% 1.48~4.50], p=0.0009). Radiomic risk groups significantly stratified patients by OS (C-index=0.64, HR=3.03 [95% 1.15~8.02], p=0.03) and PFS (C-index=0.59, HR=3.20 [95% 1.13~9.10], p=0.03). Radiomic IO risk group was independently prognostic of clinical variables (Table 1) and further predicted ICI response with AUC=0.74 [95% 0.71-0.78]. **Conclusions:** From a single click in target lesions, our model was able to predict response and prognosis of ICI recipients from a baseline radiology scan. Additional multi-site validation and prospective evaluation will assess the value of the radiomics classifier as a decision support tool in the clinic. Research Sponsor: Industrial funding.

Variables	HR [95% CI]	p
Radiomic high risk	4.82 [1.41~16.53]	0.01
Gender (F vs. M)	0.81 [0.27~2.45]	0.71
Stage (per stage increase)	2.62 [0.60~11.44]	0.20
Smoking history	0.68 [0.28~1.64]	0.39
Histology	0.88 [0.54~1.45]	0.62

8575 **Poster Session**

A theranostic approach: Imaging and therapy of delta-like ligand 3–expressing small cell lung cancers.

Salomon Tendler, Tran T Hoang, David Bauer, Joshua Korsen, Alexa Michel, Roberto Degregorio, Lukas Carter, Nagavarakishore Pillarsetty, John T. Poirier, Jason Stuart Lewis, Charles M. Rudin; Memorial Sloan Kettering Cancer Center, New York, NY; NYU Medical Center-Perlmutter Cancer Center, New York, NY

Background: Small cell lung cancer (SCLC) is a highly radiosensitive tumor, with selective cell surface expression of the inhibitory Notch ligand Delta-like ligand 3 (DLL3). This facilitates targeted radionuclide therapy accompanied by complementary imaging agents to evaluate and monitor disease progression. The project aims to identify the next generation of DLL3-targeting radioimmunoconjugates to improve the clinical outcome for SCLC patients. **Methods:** In collaboration with the Tri-Institutional Therapeutics Discovery Institute, we screened and assessed >100 humanized antibodies for their binding affinities, internalization rates, and other pharmacodynamic properties. Here, we present data on two leading candidates (mAb1 and mAb2) holding highest promise in both imaging and therapy studies conducted in DLL3-expressing SCLC tumors. For in vivo imaging, antibodies were radiolabeled with Zirconium-89 (^{89}Zr), which allows for immuno-positron emission tomography (immunoPET). Therapeutic studies were performed with the same antibodies conjugated with Lutetium-177 (^{177}Lu). Human SCLC NCI-H82 xenografts were implanted in nude athymic female mice. ImmunoPET scans were acquired during multiple time points post-injection of the imaging agent, and terminal biodistribution analysis was performed. Treatment studies included administration of 400 and 600 Ci ^{177}Lu-conjugated antibodies in cohorts of mice, with appropriate positive and negative controls. **Results:** Both lead antibodies demonstrated efficient radioconjugation with either isotope. ImmunoPET imaging utilizing ^{89}Zr showed specific high-level tumor uptake for both clones with low background in non-tumor organs. *Ex vivo* gamma counting biodistribution analysis, performed 120 hours post-injection, confirmed these findings. Dosimetry estimates suggested a similar therapeutic index between the two clones, with the bone marrow being the dose-limiting organ. Preliminary results from therapy studies demonstrate a statistically significant ($p < 0.05$) prolonged overall survival for the experimental arms compared to controls, and include durable tumor responses**.** As expected for radionuclide therapy, transient hematologic suppression was observed within 7-10 days after the beginning of the treatment, with normalization of blood cell counts for all groups within three weeks. **Conclusions:** This study highlights the promise held by novel DLL3-direct radioimmunoconjugates as a diagnostic tracer, prognostic biomarker, and therapeutic agent. Both lead candidates appear promising for translation as both imaging and therapeutic agents for patients with SCLC. Research Sponsor: NIH grants; Druckemiller Lung Cancer Foundation.

8576 **Poster Session**

Reconsidering the cutoff between sensitive and refractory relapses in extensive-stage small cell lung cancer in the era of immunotherapy.

Masahiro Torasawa, Hidehito Horinouchi, Shogo Nomura, Satoshi Igawa, Maiko Asai, Hidenobu Ishii, Hiroshi Wakui, Ryota Ushio, Tetsuhiko Asao, Yukiko Namba, Ryo Koyama, Isana Katayama, Hironari Matsuda, Shinichi Sasaki, Kazuhisa Takahashi, Yukio Hosomi, Katsuhiko Naoki, Yuichiro Ohe; Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan; Department of Biostatistics and Bioinformatics, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; Department of Respiratory Medicine, Kitasato University School of Medicine, Kanagawa, Japan; Department of Thoracic Oncology and Respiratory Medicine, Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Tokyo, Japan; Division of Respirology, Neurology, and Rheumatology, Department of Internal Medicine, Kurume University School of Medicine, Kurume, Japan; Department of Internal Medicine, Division of Respiratory Diseases, The Jikei University School of Medicine, Tokyo, Japan; Department of Respiratory Medicine, Kanagawa Cancer Center, Kanagawa, Japan; Department of Respiratory Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan; Department of Respiratory Medicine, Juntendo University Urayasu Hospital, Chiba, Japan; Department of Respiratory Medicine, Juntendo University Nerima Hospital, Tokyo, Japan; Department of Respiratory Medicine, Juntendo University Shizuoka Hospital, Shizuoka, Japan; Division of Respiratory Medicine, Juntendo University Faculty of Medicine & Graduate School of Medicine, Tokyo, Japan; National Cancer Center Hospital, Tokyo, Japan

Background: The use of platinum-based doublet chemotherapy combined with immune checkpoint inhibitors (ICIs) has demonstrated promising outcomes in the first-line treatment of extensive-stage small cell lung cancer (ES-SCLC). Relapsed SCLC has been classified into "sensitive" or "refractory" relapse types according to cutoff values (60 or 90 days) of duration from the last chemotherapy administration to disease progression. However, it is unclear whether these cutoff values can be applied to ICI combination therapy. **Methods:** We retrospectively analyzed a multicenter database of ES-SCLC patients who received second-line therapy after the platinum-etoposide plus ICI (atezolizumab or durvalumab). An optimal cutoff value for the platinum-free interval (PFI) was selected, which minimized the two-sided p-value and maximized hazard ratio (HR) regarding relapse type (sensitive or refractory according to a cutoff value) calculated from a multivariable Cox regression model for overall survival (OS) including performance status (PS) and sex as covariates. The internal validity of the selected cutoff value was assessed via two-fold cross-validation (CV) manner. **Results:** A total of 101 patients (61 deaths) from 10 hospitals were included in the study. The median follow-up period was 21.1 months. The optimal cutoff value was 75 days (p=0.0002), and when applying this cutoff value, median OS was 15.9 and 5.0 months of sensitive- (n=51) and refractory- (n=50) relapsed patients, and the HR calculated from a two-fold CV was 3.13 (95% confidence interval [CI], 1.66 to 5.90). Additionally, traditional cutoff values of 60 and 90 days also predicted prognosis better, but cutoff values of 110 days or longer did not (Table). **Conclusions:** Even in the era of combined immunotherapy in ES-SCLC patients, the threshold days for classifying as sensitive- or refractory- relapse did not exhibit a significant change compared to the pre-immunotherapy era. Although further validation studies with a larger sample size would be needed, relapse type classification using the selected cutoff value of 75 days is worth considering as a new prognostic factor for relapsed ES-SCLC patients. Research Sponsor: None.

PFI cutoffs related to OS in relapsed SCLC.

Cutoff (days)	p-value	significance level	Cutoff (days)	p-value	significance level	Cutoff (days)	p-value	significance level	Cutoff (days)	p-value	significance level
25	0.0443	*	65	0.0054	**	105	0.0351	*	145	0.6057	n.s
30	0.0443	*	70	0.0009	***	110	0.1251	n.s	150	0.4389	n.s
35	0.0268	*	75	0.0002	***	115	0.2073	n.s	155	0.1944	n.s
40	0.0268	*	80	0.0026	**	120	0.2968	n.s	160	0.1182	n.s
45	0.0128	*	85	0.0026	**	125	0.3107	n.s	165	0.1182	n.s
50	0.0063	**	90	0.0049	**	130	0.5647	n.s	170	0.1182	n.s
55	0.0002	***	95	0.0098	**	135	0.5647	n.s	175	0.1182	n.s
60	0.0023	**	100	0.0200	*	140	0.6057	n.s	180	0.1300	n.s

*: p<0.05, **: p<0.01, ***: p<0.001, n.s: not significant.

8577 **Poster Session**

Analysis of tumor- and circulating-free DNA methylation to identify clinically relevant small cell lung cancer subtypes.

Simon Heeke, Carl Michael Gay, Marcos Roberto Estecio, Hai T. Tran, Benjamin B. Morris, Bingnan Zhang, XiMing Tang, Maria G Raso, Pedro Rocha, Edurne Arriola, Paul Hofman, Prasad Kopparapu, Christine M. Lovly, Kyle Concannon, Yuanxin Xi, Lixia Diao, Qi Wang, Jing Wang, Lauren Averett Byers, John Heymach; University of Texas MD Anderson Cancer Center, Houston, TX; Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Epigenet & Mol Carcinogenesis, University of Texas MD Anderson Cancer Center, Houston, TX; MD Anderson Cancer Center, Houston, TX; Hospital del Mar, Barcelona, Spain; Laboratory of Clinical and Experimental Pathology, Biobank Côte d'Azur, Pasteur Hospital, FHU OncoAge, Université Côte d'Azur, CHU Nice, Nice, France; Vanderbilt University Medical Center, Nashville, TN; Bioinformatics and Comp Biology, MD Anderson Cancer Center, Houston, TX; Department of Thoracic/Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Small-cell lung cancer (SCLC) is an aggressive malignancy composed of distinct transcriptional subtypes, defined by the predominant expression of one of the three transcription factors ASCL1 (SCLC-A), NEUROD1 (SCLC-N) and POU2F3 (SCLC-P) as well as an inflamed subtype (SCLC-I; see Gay et al. Cancer Cell. 2021), each with potential therapeutic vulnerabilities. Implementing subtyping in the clinic has remained challenging due to limited tissue availability, particularly for longitudinal monitoring. Given the known epigenetic regulation of critical SCLC transcriptional programs, we hypothesized that there would be subtype-specific patterns of DNA methylation that could be detected in tumor or blood from SCLC patients. **Methods:** We included 179 patients with SCLC and performed RNA sequencing and genomic-wide reduced-representation bisulfite sequencing (RRBS). We further analyzed DNA methylation in 68 plasma samples including longitudinal samples to track SCLC subtype evolution over time. **Results:** Using machine learning approaches, we developed a highly accurate DNA methylation-based classifier (SCLC-DMC) that could distinguish SCLC subtypes using clinical tumor samples with 95.8% accuracy in the testing set compared to mRNA-based profiling. We further adjusted the classifier for circulating-free DNA (cfDNA) to subtype SCLC from plasma. Using the cfDNA classifier (cfDMC), we could demonstrate that SCLC subtypes evolve frequently during disease progression, highlighting the need for longitudinal tracking of SCLC during clinical treatment. Furthermore, methylation-based subtyping predicted response to a wide variety of drugs in preclinical models like CDK and AURK inhibitors, and clinical outcomes were indistinguishable in cohorts of patients subtyped using mRNA or SCLC-DMC ($p = 0.95$). **Conclusions:** These data establish that tumor and cfDNA methylation can be used to identify SCLC subtypes and guide precision SCLC therapy. Research Sponsor: U.S. National Institutes of Health.

8578 **Poster Session**

Pathological images machine learning and prediction of long-term efficacy for immunotherapy in small cell lung cancer.

Yuki Sato, Ryota Shibaki, Daichi Fujimoto, Tsukasa Nozawa, Satoshi Hara, Junji Uchida, Eisaku Miyauchi, Ryota Hiraoka, Haruko Daga, Takeshi Masuda, Satoshi Tanaka, Satoshi Ikeda, Go Saito, Hidekazu Suzuki, Shinya Sakata, Yoshihiko Sakata, Takashi Kijima, Nobuyuki Yamamoto, Yasuhiro Koh, Hiroaki Akamatsu; Kobe City Medical Center General Hospital, Kobe, Japan; Third Department of Internal Medicine, Wakayama Medical University, Wakayama, Japan; Wakayama Medical University/Second Dept. Surgery, Wakayama-Shi, Japan; ExaWizards Inc., Minato-Ku, Japan; Itami City Hospital, Itami-Shi, Japan; Osaka Toneyama Medical Center, Osaka-Shi, Kyoto, Japan; Tohoku University Hospital, Sendain Miyagi, IL, Japan; National Hospital Organization Himeji Medical Center, Himeji, Japan; Osaka City General Hospital, Osaka, Japan; Hiroshima University, Hiroshima, Japan; Department of Respiratory Medicine, Osaka General Medical Center, Osaka, Japan; Kanagawa Cardiovascular and Respiratory Center, Yokohama, Japan; Department of Respirology, Graduate School of Medicine, Chiba University, Chiba, Japan; Department of Thoracic Oncology, Osaka Habikino Medical Center, Habikino, Japan; Department of Respiratory Medicine, Kumamoto University Hospital, Kumamoto, Japan; Saiseikai Kumamoto Hospital, Kumamoto-Shi Minami-Ku, Japan; Hyogo Medical University, Nishinomiya, Japan; Wakayama Medical University, Wakayama, Japan, Wakayama, Japan; Wakayama Medical University, Wakayama-Shi, NA, Japan

Background: In development of effective treatment such as immune checkpoint inhibitors (ICIs) among patients with small-cell lung cancer (SCLC), the absence of biomarkers is critical. Tumor-infiltrating lymphocytes are the main activator of antitumor immunity and could be a promising biomarker if TIL can be objectively assessed throughout the whole tumor immune microenvironment (TIME). To evaluate TIME, pathological assessment is one of the easiest ways. Recently, several studies showed that machine learning analysis can assess type of lymphocytes and their localization in pathological images. Here, we aimed to develop a novel biomarker to predict efficacy of ICI in SCLC using machine learning of pathological images. **Methods:** This study was a biomarker analysis of the APOLLO study which was 32-centered, prospective cohort study of patients with extensive-stage SCLC who received chemo-immunotherapy as the first-line treatment between September 2019 and September 2020. The patient who can provide sufficient tumor tissue sample from the primary tumor were enrolled. We trained a classifier which predicts 365-day progression-free survival (PFS) by all three types of pathological images (hematoxylin and eosin, programmed death-ligand 1, and CD8_FoxP3) and patient information, and developed the patient information model, pathological image model, and combination model. We used the area under the curves (AUC) to evaluate the machine learning models. **Results:** Of 78 patients, the median age was 78 (interquartile range, 48-87), 65 patients (83%) were male, 67 patients (86%) had a performance status of 0 or 1, and three patients (3.8%) treated with steroid therapy. Among all patients, the median PFS and the 365-day PFS rates were 145 days and 10.3%. The mean AUC of these models was 0.789 (range, 0.571-0.982) in the patient information model, 0.782 (range, 0.750-0.911) in the pathological image model, and 0.868 (range, 0.786-0.929) in the combination model, respectively. According to the median precision model, the median PFS was longer for the high efficacy group than the low efficacy group (the patient information model; hazard ratio (HR) 0.468, 95% confidence intervals (CI) 0.287-0.762. the pathological image model; HR 0.334, 95%CI 0.117-0.628. the combination model; HR 0.353, 95%CI 0.195-0.637). **Conclusions:** Using machine learning by pathological images, we could predict the efficacy of immunotherapy in SCLC. This study demonstrated the potential of machine learning to help the biomarker development in SCLC by assessing TIME. Clinical trial information: UMIN000038064. Research Sponsor: Chugai Pharmaceutical Co. Ltd.

8579 **Poster Session**

Phase I/II combination study of tifcemalimab with toripalimab in patients with refractory extensive stage small cell lung cancer (ES-SCLC).

Ying Cheng, Jie Wang, Yan Yu, Qiming Wang, Runxiang Yang, Dongqing Lv, Bing Xia, Tienan Yi, Chong Li, Xicheng Wang, Wei Zhang, Liang Han, Xiaoqing Liu, Minjie Shen, Jing Xu, Peng Xue, Weihua Wang; Department of Medical Thoracic Oncology, Jilin Cancer Hospital, Changchun, China; National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China; Department of Medical Oncology, Harbin Medical University Cancer Hospital, Harbin, China; Henan Cancer Hosptal, Zhengzhou, China; Department of Medical Oncology, Yunnan Cancer Hospital, Kunming Medical University, Kunming, China; Taizhou Hospital of Zhejiang Province, Taizhou, China; Hangzhou Cancer Hospital, Hangzhou, China; Xiangyang Central Hospital, Xiangyang, China; The First People's Hospital of Changzhou, Changzhou, China; The First Affiliated Hospital/School of Clinical Medicine Guangdong Pharmaceutical University, Guangzhou, China; The First Affiliated Hospital of Nanchang University, Nanchang, China; Xuzhou Central Hospital, Xuzhou, China; The Fifth Medical Center of the Chinese People's Liberation Army General Hospital, Beijing, China; Shanghai Junshi Biosciences, Shanghai, China

Background: The B- and T-lymphocyte attenuator (BTLA) is a novel inhibitory co-signaling receptor expressed on B cell, T cells and NK cells. Co-blockade of the BTLA and PD-1 pathways improved antigen specific anti-tumor T cell response. Tifcemalimab (JS004 or TAB004) is a humanized IgG4 monoclonal antibody with a hinge mutation (S228P) that binds BTLA and blocks its interaction with its ligand HVEM. In previous phase I studies, tifcemalimab has shown preliminary anti-tumor activities as monotherapy or in combination with toripalimab (anti-PD-1) with a manageable safety profile in patients with advanced malignancies. **Methods:** Eligible ES-SCLC patients refractory to prior therapies were enrolled in this I/II study (NCT05000684). Patients received 200mg tifcemalimab and 240mg toripalimab intravenously once every three weeks until disease progression, intolerable toxicity or 2 years of treatment. Study objectives included safety, anti-tumor activity and correlative biomarkers. **Results:** As of Jan 31, 2023, a total of 43 ES-SCLC patients refractory to prior therapy were enrolled. The median age was 60.0 (range 38-75) years. The median prior line of therapy was 1 and 14 (32.6%) patients received prior anti-PD-1/L1 treatment. By the cut-off date, the median follow-up duration was 12.1 weeks. Thirty-two (74.4%) patients experienced treatment-emergent adverse events (TEAEs); 12 (27.9%) patients experienced grade $\geq$ 3 TEAEs. The most common TEAEs were hyponatraemia (16.3%), alanine aminotransferase increased (14%), aspartate aminotransferase increased (14%), and blood creatine phosphokinase increased (14%). Three (7.0%) patients experienced treatment-related adverse events (TRAEs) led to interruption of study drugs and no TRAEs led to discontinuation of study drugs were reported. Fifteen (34.9%) patients experienced immune related AE (irAEs), and 2 (4.7%) patients experienced grade $\geq$ 3 irAEs. Among 38 efficacy evaluable patients, the ORR was 26.3% and the DCR was 57.9%. The ORR was 8.3% in immunotherapy treated patients and 40.0% in immunotherapy naïve patients. By the cut-off date, 70.0% of the responses were ongoing and the median duration of response was not reached. Tumor expression of HVEM and PD-L1 was evaluated to explore the correlation with clinical response. **Conclusions:** Tifcemalimab in combination with toripalimab were well tolerated in patients with refractory ES- SCLC. Further clinical evaluation of this combination treatment in SCLC is warranted. Clinical trial information: NCT05000684. Research Sponsor: Shanghai Junshi Biosciences.

8580 **Poster Session**

Updated safety and efficacy results of SHR-1316 combined with chemotherapy and sequential chest radiotherapy as first-line therapy for extensive-stage small cell lung cancer (ES-SCLC) from a phase II trial.

Dawei Chen, Aiqin Gao, Wei Huang, Qian Shao, Xiangjiao Meng, Xiaoyong Tang, Pinliang Zhang, Xudong Hu, Yan Zhang, Jun Guo, Lei Fu, Wei Zhao, Changhong Zhao, Jiajia Yuan, Jinming Yu, Linlin Wang; Shandong Cancer Hospital, Shandong University, Jinan, China; Shandong Cancer Hospital and Institute, Jinan, China; Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Science, Jinan, Shandong, China; Jiangsu Hengrui Pharmaceuticals Co. Ltd, Shanghai, China; Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Science, Jinan, China

Background: CAPSTONE-1 study showed that SHR-1316 (PD-L1 antibody) combined with first-line chemotherapy could prolong overall survival in patients (pts) with ES-SCLC. Previous studies have shown that radiotherapy could potentially promote tumor antigen presentation and reverse immunosuppressive microenvironment in tumor. The purpose of this study was to explore the efficacy and safety of SHR-1316 combined with chemotherapy and sequential chest radiotherapy as first-line therapy for ES-SCLC. **Methods:** Key inclusion factors were 18-75 years old, histologically or cytologically confirmed ES-SCLC, ECOG performance status 0-1, no previous systematic treatment. Pts included in this study received 4~6 cycles of SHR-1316 (20mg/kg, D1, q3w) combined with EP/EC (cisplatin, 75mg/m^2, D1-3, q3w or carboplatin, AUC = 5, D1, q3w and etoposide, 100mg/m^2, D1-5, q3w), sequentially SHR-1316 combined with chest radiotherapy ($\geq$3Gy*10f or $\geq$2Gy*25f, involved-field irradiation), and then entered the maintenance treatment stage until disease progression or intolerable side effects. The main endpoints included objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS) and safety. **Results:** From October 2020 to January 2023, 63 pts with ES-SCLC were enrolled and received at least one dose of SHR-1316, 33 of them have received chest radiotherapy. The median age was 63 (range: 38-75), and most pts were male (53, 84.1%), former smokers (42, 66.7%) with an ECOG performance status 1 (60, 95.2%). At baseline, 24 (38.1%) pts were diagnosed with brain metastasis and 19 (30.2%) pts had liver metastasis. At the data cutoff date, the average number of treatment cycles was 6.9, 17 pts remained on treatment. 55 pts had at least one post-treatment tumor assessment. 41 pts achieved a confirmed partial response, and 12 pts had stable disease. The confirmed ORR and DCR were 74.5% and 96.4%, respectively. The median PFS was 7(CI: 4.3~9.7) months. Adverse events (AEs) occurred in 47 (74.6%) pts. Grade 3 or 4 AEs occurred in 35 (55.6%) pts. The most common grade 3 or 4 AEs included neutropenia (27, 42.9%), leukopenia (13, 20.6%), lymphocytopenia (5, 7.9%), pneumonia (4, 6.3%), anemia (3, 4.8%), and thrombocytopenia (2, 3.2%). **Conclusions:** SHR-1316 combined with chemotherapy and sequential chest radiotherapy as first-line therapy for ES-SCLC showed promising efficacy and acceptable safety. It is worthy of further clinical exploration. Clinical trial information: NCT04562337. Research Sponsor: None.

8581 **Poster Session**

Characteristics and outcomes of patients with small cell lung cancer (SCLC) detected with CT screening at a single health system.

Manasi Manoj Godbole, Pin Li, Kashmira Wani, Matthew Meranda, Michael J. Simoff, Shirish M. Gadgeel; Henry Ford Cancer Institute, Henry Ford Health, Detroit, MI; Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI; Henry Ford Health, Detroit, MI

Background: At diagnosis, the majority of SCLC patients have extensive-stage disease, and their median survival is only 13 months, even with the addition of checkpoint inhibitors. Previous CT screening trials did not reveal reduction in mortality for SCLC patients. The aim of our study was to analyze the baseline characteristics and clinical outcomes of SCLC patients diagnosed with low-dose CT scan as a part of lung cancer screening program. **Methods:** A retrospective chart review-based study of SCLC patients diagnosed clinically or by lung cancer screening between January 2018 and June 2022 at the Henry Ford Health System was conducted. Baseline characteristics, details of SCLC diagnosis and treatment, and outcome were recorded. Statistical analysis was performed using Chi-squared test, T-test and log-rank test. **Results:** Of the 258 patients who met eligibility criteria, 34 were diagnosed by lung cancer screening. Patients diagnosed with screening tended to be older (mean age- 70.5 years vs. 67.3 years, p=0.010). There were no differences in gender distribution, race and smoking status. Mean smoking history was 43 pack-years in both groups. Among screen-detected patients, 73.5% had limited-stage disease compared to 36.6% among clinically detected patients (p<0.001). No significant difference in the presence of brain metastases at diagnosis was observed. Among screen-detected patients, 97.1% received any therapy compared to 85.3% among the clinically detected patients (p=0.105). Overall survival (OS) was significantly better in screen-detected patients, with a 3-year survival rate of 45.5% vs. 17% (p=0.00027). By multivariable analysis, OS was better in screen-detected patients (HR=0.37, 95% CI 0.20-0.68; p=0.001) (Table). There was no significant difference in progression-free survival between the groups. **Conclusions:** Our results demonstrate that SCLC patients diagnosed through the lung cancer screening program have better overall survival rates than those diagnosed clinically. These results suggest that developing appropriate screening measures may impact SCLC-related mortality. Research Sponsor: None.

Impact on overall survival.

Variable	N (%)	Hazard Ratio (Univariable)	Hazard Ratio (Multivariable)
Screening	34 (13.2)	0.37 (0.22-0.65, p<0.001)	0.45 (0.25-0.79, p=0.005)
Age (Mean [SD])	67.7 (9.3)	1.01 (0.99-1.03, p=0.172)	1.02(1.00-1.04, p=0.024)
Female	146 (56.6)	1.09 (0.80-1.47, p=0.589)	1.38 (0.99-1.90, p=0.054)
Active smoker	77 (29.8)	Ref	Ref
Former smoker	172 (66.7)	0.90 (0.65-1.24, p=0.508)	1.08 (0.76-1.52, p=0.670)
Never smoker	9 (3.5)	1.08 (0.47-2.52, p=0.851)	1.31 (0.51-3.35, p=0.576)
Extensive stage	151 (58.5)	Ref	Ref
Limited stage	107 (41.5)	0.44 (0.32-0.61, p<0.001)	0.42 (0.29-0.61, p<0.001)
Treatment received	224 (86.8)	0.13 (0.08-0.20, p<0.001)	0.11(0.07-0.19, p<0.001)

8582 **Poster Session**

Tarlatamab in small cell lung cancer (SCLC): Safety and efficacy analyzed by baseline brain metastasis.

Stephane Champiat, Michael J. Boyer, Ramaswamy Govindan, Luis G. Paz-Ares, Taofeek K. Owonikoko, Hossein Borghaei, Hiroki Izumi, Neeltje Steeghs, Fiona Helen Blackhall, Angelika Terbuch, Melissa Lynne Johnson, Tatsuya Yoshida, Kai He, Yuyang Zhang, Simon Jones, Xi Chen, Pablo Martinez, Horst-Dieter Hummel; Gustave Roussy, Département d'Innovation Thérapeutique et d'Essais Précoces (DITEP), Villejuif, France; Department of Medical Oncology, Chris O'Brien Lifehouse, Camperdown, Australia; Divisions of Hematology and Oncology, Washington University Medical School, St. Louis, MO; Hospital Universitario 12 de Octubre, CNIO-H120 Lung Cancer Unit, Ciberonc and Universidad Complutense, Madrid, Spain; Division of Hematology/Oncology, University of Pittsburgh School of Medicine, UPMC Hillman Cancer Center, Pittsburgh, PA; Fox Chase Cancer Center, Philadelphia, PA; Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan; Department of Medical Oncology, The Netherlands Cancer Institute, Amsterdam, Netherlands; Department of Medical Oncology, The Christie NHS Foundation Trust, Division of Cancer Sciences, University of Manchester, Manchester, United Kingdom; Division of Clinical Oncology, Department of Internal Medicine, Medical University of Graz, Graz, Austria; Sarah Cannon Research Institute, Tennessee Oncology, Nashville, TN; Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan; James Thoracic Oncology Center, The Ohio State University Comprehensive Cancer Center, Columbus, OH; Amgen Inc., Thousand Oaks, CA; Translational Oncology/Early Clinical Trial Unit (ECTU), Comprehensive Cancer Center Mainfranken, University Hospital Würzburg, Würzburg, Germany

Background: Tarlatamab, a BiTE molecule targeting DLL3 and CD3, is being studied in patients (pts) with extensive stage small cell lung cancer (ES-SCLC).[1] Up to 25% of pts diagnosed with SCLC have brain metastases (BM) and 50% or more will develop BM during the course of the disease. Pts with ES-SCLC and BM have poor prognosis and quality of life. We analyzed the characteristics and outcomes of pts included in the tarlatamab phase 1 study (NCT03319940) who had baseline BM vs those who did not. **Methods:** Pts included in the phase 1 trial had SCLC that progressed after ≥1 platinum-based regimen and received tarlatamab (0.003–100 mg IV). Pts with treated BM were eligible if local therapy was delivered ≥ 2 weeks prior to first tarlatamab dose. **Results:** As of 03 January 2023, 192 pts had received tarlatamab as monotherapy. Median age was 62 (range, 32–80) y; 188 pts (98%) had ECOG PS 0–1 and median prior therapy lines was 2 (range, 1–6), with 107 pts (56%) receiving prior anti-PD1/PD-L1. 48 pts (25%) had BM at screening and 142 (74%) did not (No BM); data was missing for 2 pts (1%). Pts with BM were more likely to have received > 3 prior lines of therapy (BM, 29%; No BM, 9%) and have a record of prior brain radiation (BM, 85%; No BM, 40%); otherwise, characteristics of pts with BM were generally similar to those without. Tarlatamab delivered comparable activity in pts with BM vs. those without in terms of objective response rate (ORR; 20%, 25%) and disease control rate (DCR; 59%, 50%) (Table). Median duration of response (DoR) was 14.9 months (BM) vs. 13.0 months (no BM). Median overall survival (OS) was 13.2 months in the BM group vs 15.5 months in the no BM group. Safety outcomes were similar in terms of treatment-related AEs (TRAEs; BM, 90%; No BM, 94%) and grade (gr) ≥ 3 (BM, 38%; No BM, 39%). Groups were also comparable with respect to immune effector cell-associated neurotoxicity syndrome (ICANS) and associated neurologic events (any-grade, 6% vs 9%; gr ≥ 3, 4% vs 4%) and neutropenia (any-grade, 10% vs 15%; gr ≥ 3, 8% vs 8%). AEs numerically different in the BM vs No BM group included gr ≥ 4 TRAEs (17%, 7%) and any-grade CRS (67%, 54%). The only grade 5 TRAE (pneumonitis) occurred in the BM group. **Conclusions:** Tarlatamab continues to show promising efficacy and is generally safe in pts with ES SCLC irrespective of the presence of BM. Rates of ICANS and associated neurologic AEs were comparable between those with and without BM at baseline. Reference: 1. Paz-Ares L, et al. J Clin Oncol. DOI:10.1200/JCO.22.02823. Clinical trial information: NCT03319940. Research Sponsor: Amgen.

Efficacy in pts with and w/o BM, Interim efficacy analysis set.

	BM (n = 46)	No BM (n = 136)
ORR, n (%)	9 (19.6%)	34 (25.0%)
DCR, n (%)	27 (58.7%)	68 (50.0%)
DoR, median (95% CI)*	14.9 (3.8, NR)	13.0 (7.4, NR)
PFS, median (95% CI)	3.7 (1.9, 4.8)	3.7 (1.9, 5.3)
OS, median (95% CI)	13.2 (6.6, NR)	15.5 (10.6, NR)

*BM, n=9; No BM, n=34 CI, confidence interval; DCR, disease control rate; NR, not reached; PFS, progression-free survival.

8583 **Poster Session**

Long-term effectiveness and treatment sequences in patients with extensive stage small cell lung cancer receiving atezolizumab plus chemotherapy: Results of the IFCT-1905 CLINATEZO real-world study.

Lionel Falchero, Florian Guisier, Marie Darrason, Arnaud Boyer, Charles Dayen, Sophie Cousin, Patrick Merle, Regine Lamy, Anne Madroszyk, Josiane Otto, Pascale Tomasini, Pascale Missy, Franck Morin, Virginie Westeel, Nicolas Girard; Hôpitaux Nord-Ouest, Service de Pneumologie et Cancérologie Thoracique, Villefranche-Sur-Saone, France; Univ Rouen Normandie, LITIS Lab QuantIF team EA4108, CHU Rouen, Inserm CIC-CRB 1404, Department of Pneumology, Thoracic Oncology and Respiratory Intensive Care, F-76000, Rouen, France; URCOT, Institut de Cancérologie des Hospices Civils de Lyon, Lyon, France; Hôpital Saint Joseph, Service de Pneumologie, Marseille, France; Clinique de l'Europe, Service de Pneumologie, Amiens, France; Medical Oncology Department, Institut Bergonié, Bordeaux, France; CHU, Hôpital Gabriel Montpied, Hôpital De Jour, Service D'oncologie Thoracique, Clermont-Ferrand, France; CHBS, Hôpital Du Scorff, Oncologie Médicale, Lorient, France; Department of Medical Oncology, Institut Paoli-Calmettes, Marseille, France; Oncology, Centre Antoine Lacassagne, Nice, France; APHM, Service d'Oncologie Multidisciplinaire & Innovations Thérapeutiques, Hôpital Nord, Marseille, France; The French Cooperative Thoracic Intergroup, Paris, France; CHU Besançon, Hôpital J. MINJOZ, Service de Pneumologie, Besançon, France; Institut du Thorax Curie Montsouris, Institut Curie, Paris, France

Background: Small cell lung cancer (SCLC) is a highly aggressive type of lung cancer with a tendency towards early recurrence and limited survival. Standard-of-care in 1st-line treatment is platinum-etoposide chemotherapy plus anti-PD-L1 immune checkpoint inhibitor atezolizumab or durvalumab, based on landmark, randomized, phase 3 clinical trials. **Methods:** IFCT 1905-CLINATEZO is a nationwide, non-interventional, retrospective chart review study of patients (pts) with extensive-stage SCLC who received atezolizumab + chemotherapy as part of the French early access program between May 2019 and January 2020 (1402 pts). Inclusions were exhaustive per participating centers (65/307). Data collection run from February to November 2021. Key objectives were to assess effectiveness and safety of atezolizumab + chemotherapy and analyze subsequent treatment sequences. **Results:** The population analyzed included 518 out of the 1402 pts. There were 66% male and mean age was 65.7 years (range: 36.7-88.0); 89% had a performance status (PS) 0/1 and 27% brain metastases. Almost all the pts (96%) were smokers, with a median number of pack-years of 40. Fifty-five pts (10.6%) received at least 1 previous treatment. Median number of atezolizumab injections was 7 (range: [1-48]) for a median duration of 4.9 months (95% CI 4.5-5.1). Twenty-seven pts (5%) were under ongoing treatment at date of last news. Atezolizumab was continued beyond disease progression in 122 pts (24%) for a median duration of 1.9 months (95% CI 1.4-2.3). Best objective response was complete and partial response in 19 (3.9%) and 378 pts (77.1%) respectively; stable disease was observed in 50 pts (10.2%). After a median follow-up of 30.8 months (95% CI: [29.9-31.5]), median overall survival (OS), 12- and 24-months OS rates were 11.3 months (95% CI: [10.1-12.4]), 46.7% (95% CI 42.3-50.9) and 21.2% (95% CI 17.7-24.8) respectively. Median real world-progression free survival (based on date of the first source evidence for progression referenced by the treating physician), 6- and 12-months rates were 5.2 months (95% CI 5.0-5.4), 37.5% (95% CI 33.3-41.7) and 15.2% (95% CI 12.2-18.6) respectively. For the pts with PS 0/1, median OS was 12.2 months (95% CI 11.0-13.5). For the 55 pts with previous treatment, median OS was 14.9 months (95% CI 10.1-21.5). A total of 326 (66.4%) pts received subsequent treatment. **Conclusions:** IFCT 1905-CLINATEZO study shows the reproducibility, in a real-life setting, of the key survival outcomes of IMpower-133, that may be attributed to the selection of pts fit for this regimen, the adoption of pragmatic approaches for the management of pts receiving atezolizumab, that includes concurrent radiotherapy and treatment beyond progression, and the high proportion of pts treated with 2nd-line therapies, mostly based on chemotherapy. Research Sponsor: ROCHE.

8584 **Poster Session**

IFCT-2105 lurbiclin real-world effectiveness and treatment sequences in patients (pts) with extensive-stage small cell lung cancer (ES-SCLC) who received lurbinectedin as part of the French Early Access Program (EAP-ATU).

Nicolas Girard, Florian Guisier, Aurélie Swalduz, Sylvie Van Hulst, Eric Pichon, Pernelle Lavaud, Laurent Greillier, Angelica Tiotiu, Anne Madroszyk, Olivier Bylicki, Anthony Canellas, Laure Belmont, Maeva Zysman, Pierre-Alexandre Hauss, Benoit Godbert, Clarisse Audigier-Valette, Cléa Lebreton, Franck Morin, Virginie Westeel; Institut du Thorax Curie Montsouris, Institut Curie, Paris, France; Univ Rouen Normandie, LITIS Lab QuantIF team EA4108, CHU Rouen, Inserm CIC-CRB 1404, Department of Pneumology, Thoracic Oncology and Respiratory Intensive Care, F-76000, Rouen, France; Centre Leon BERARD, Service d'Oncologie Médicale, Lyon, France; CHU, Service de Pneumologie, Nîmes, France; Service de Pneumologie, CHRU Bretonneau, Tours, France; Gustave Roussy, Villejuif, France; APHM, Hôpital Nord, Service d'Oncologie Multidisciplinaire & Innovations Thérapeutiques, Marseille, France; CHU de Brabois, Service de Pneumologie, Vandoeuvre-LES-Nancy, France; Department of Medical Oncology, Institut Paoli-Calmettes, Marseille, France; HIA SAINTE ANNE, Toulon, France; APHP Hôpital Tenon, Service de Pneumologie, Paris, France; Centre Hospitalier Victor Dupouy, Service de Pneumologie, Argentueil, France; CHU, Hôpital Haut-Lévèque, Centre François Magendie, Service des Maladies Respiratoires, Pessac, France; Centre Hospitalier Intercommunal Elbeuf Louviers, Service Pneumologie, Elbeuf, France; Hôpital Robert Schuman, Service de Pneumologie, Metz, France; CHITS Toulon Sainte Musse, Pôle de Médecine à Orientation Oncologique, Toulon, France; The French Cooperative Thoracic Intergroup, Paris, France; CHU Besançon, Hôpital J. MINJOZ, Service de Pneumologie, Besançon, France

Background: Novel options are needed for pts with ES-SCLC after the failure of first-line chemotherapy. Lurbinectedin demonstrated efficacy in a landmark phase II study [Trigo et al. Lancet Oncol. 2020 May;21(5):645], and was granted EAP-ATU in France in June 2020. **Methods:** Multicenter, retrospective cohort of consecutive pts with histologically or cytologically confirmed ES-SCLC, who received at least one dose of treatment with lurbinectedin as part of the French EAP-ATU from June 2020 until March 2021, and gave consent for the data collection, were enrolled in 47 sites. Primary and secondary endpoints were description of clinical characteristics, and exposure to treatment, response, PFS, OS, safety. **Results:** 312 pts – 64% male, median age 65 years, 72% PS0-1, 47% with brain metastasis, 58% with previous immunotherapy – were enrolled. Lurbinectedin was administered as second-line in 44% of pts; 58% were chemotherapy-refractory. Pts received a median number of 3 cycles of lurbinectedin. Concurrent radiotherapy on metastases was delivered to 38% of pts. Lurbinectedin was discontinued because of progression/death/toxicity/other reasons in 83%/8%/5%/4% of pts. Grade3/4 events were observed in 9%/5% of pts. Response rate was 22% [95%CI 17-27%], disease control rate was 38% [95%CI 32-44%]. After a median follow-up of 20.8 months, median PFS and OS were 1.9 [95%CI 1.8-2] and 4.7 [95%CI 4-5.4] months; 6-month PFS and OS were 7% [4-10%] and 42% [95%CI 37-48%]. PS≤2 and chemotherapy-free interval≥90days were associated with significantly longer OS (HR = 0.71 [95%CI 0.53-0.95] and HR = 0.58 [95% CI 0.44-076] respectively). Main sites of progression were the lung (39% of pts), the brain (39% of pts), the liver (30% of pts), and the mediastinum (30% of pts). Subsequent treatment was administered to 154 pts after discontinuation of lurbinectedin, mostly consisting of topotecan (26% of pts); response/disease control rates, and median PFS of first subsequent treatment were 11% [95%CI 6-17%], 35% [95%CI 27-44%], and 1.9 [95%CI 1.7-2.3] months. **Conclusions:** Lurbinectedin provides an additional option from second-line for ES-SCLC, with efficacy outcomes comparable to that of historical treatments. Research Sponsor: PharmaMar.

8585 **Poster Session**

Phase Ib/IIa study assessing the safety and efficacy of AL8326 monotherapy in patients with ≥3rd line small cell lung cancer (SCLC) treatment.

Xiaochun Zhang, Xingya Li, Minghong Bi, Chunxia Su, Yong Fang, Zibing WANG, Ying Yuan, Xiuping Du, Tangfeng Lv, Yingyin Li; The Affiliated Hospital of Qingdao University, Qingdao, China; Department of Oncology, First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; The First Affiliated Hospital of Bengbu Medical College, Bengbu, China; Oncology Department, Shanghai Pulmonary Hospital, Shanghai, China; Sir Run Run Shaw Hospital, College of Medicine, Zh, Hangzhou, China; Henna Cancer Hosptal, Zhengzhou, China; Department of Medical Oncology, Key Laboratory of Cancer Prevention and Intervention, Ministry of Education, The Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China; The Affiliated Hospital of Xuzhou Medical University, Xuzhou, China; General Hospital of Eastern Theater of Chinese People 's Liberation Army, Nanjing, China; Advenchen Pharmaceuticals Nanjing Ltd., Nanjing, China

Background: AL8326 is a novel, orally administered, small molecule tyrosine kinase inhibitor (TKI). The primary objective of this Phase Ib/IIa study is to evaluate the safety and efficacy of AL8326 monotherapy in patients with ≥3rd line small cell lung cancer (SCLC) treatment. **Methods:** Patients with a diagnosis of small cell lung cancer either limited or extended stage requiring third or further line treatment were eligible for enrollment. The regimen was a 28-day cycle with oral AL8326 administered at 60 mg once per day via RECISIT1.1 evaluation until disease progression (PD), or intolerable toxicity or any other reason discontinuations. **Results:** At the cut-off date Nov 30, 2022, total n = 30 patients were enrolled. The objective response rate (ORR) was 20% (6/30) (4 confirmed). The disease control rate (DCR) was 56.7% (17/30). Median progression-free survival (PFS) was 3.65 months (95% CI: 1.9 – 5.5) and median overall survival (OS) was 10.42 months (95% CI: 5.4, NE). The median duration of response (DOR) was 5.6months. All 30 subjects had reported AE at least once. Common treatment emergent adverse events (TEAE) were similar to other TKI drug and included (incidence ≥20%): thyroid stimulating hormone (TSH) increase (46.67%), proteinuria (43.33%), weight loss (40.00%), hypertension (36.67%), thrombocytopenia (33.33%), diarrhea (33.33%), positive fecal occult blood (30.00%), hypercholesterolemia (26.67%), hypertriglyceridemia (26.67%), hand- foot syndrome (HFS) (20.00%), loss of appetite (20.00%). Most of these AEs were grade 1-2 (CTCAE V5.0). **Conclusions:** AL8326 has demonstrated acceptable tolerability and positive efficacy on small cell lung cancer treatment. A US Phase 2 (NCT05363280) study is ongoing and a phase 3 study is in preparation. Clinical trial information: NCT04890795. Research Sponsor: AL8326.

8586 **Poster Session**

Tumor microenvironment-mediated immune profiles and efficacy of platinum doublet chemotherapy plus ICIs stratified by DLL3 expression in small cell lung cancer.

Masayuki Shirasawa, Tatsuya Yoshida, Kouya Shiraishi, Shigehiro Yagishita, Yuji Matsumoto, Ken Masuda, Yuki Shinno, Yusuke Okuma, Yasushi Goto, Hidehito Horinouchi, Katsuhiko Naoki, Takaaki Tsuchida, Ryuji Hamamoto, Noboru Yamamoto, Noriko Motoi, Takashi Kohno, Shun-ichi Watanabe, Yuichiro Ohe; Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan; Division of Genome Biology, National Cancer Center Research Institute, Tokyo, Japan; Department of Stem Cell Transplantation, National Cancer Center, Chuo-Ku, Tokyo, Japan; National Cancer Center Hospital, Chuo-Ku, Japan; National Cancer Center Hospital, Tokyo, Japan; Department of Respiratory Medicine, Kitasato University School of Medicine, Sagamihara, Kanagawa, Japan; Division of Medical AI Research and Development, National Cancer Center Research Institute, Tokyo, Japan; Saitama Cancer Center, Saitama, Japan; Department of Thoracic Surgery, National Cancer Center Hospital, Tokyo, Japan

Background: Delta-like ligand 3 (DLL3) frequently expressed in small cell lung cancer (SCLC) and has been emerged as a therapeutic target. However, it remains unclear how DLL3 expression status affects tumor microenvironment (TME)-mediated immune profiles and clinical outcomes of platinum doublet chemotherapy plus ICIs in SCLC patients. **Methods:** We retrospectively reviewed post-surgical limited-stage (LS)-SCLC, and extensive-stage (ES)-SCLC patients treated with platinum and etoposide (PE) plus anti-PD-L1 antibody. In LS-SCLC cohort, the transcriptome and whole-exome sequencing (WES) analysis were performed to assess the immune profiles, mutation status and neoantigen status. In ES-SCLC cohort, the association between the efficacy of immunochemotherapy and DLL3 expression by transcriptome analysis were evaluated. **Results:** Fifty-nine and 17 patients were included in the LS- and ES-SCLC cohort, respectively. In LS-SCLC cohort (n = 59), WES analysis revealed that SCLC with $DLL3_{High}$ had a significantly higher number of neoantigens (77 [95% confidence interval [CI] 65-113] vs. 48 [95% CI 17-58], p = 0.004), and a significantly higher rate of signature SBS4 associated with smoking (43% [95% CI 28-53] vs. 28% [95% CI 15-36], p = 0.02), although TMB did not differ according to DLL expression (6.6 mut/Mb [95% CI 5.3-9.6] vs. 6.5 mut/Mb [95% CI 5.2-9.9], p = 0.26). The transcriptome analysis in LS-SCLC cohort revealed that SCLC with $DLL3_{High}$ tumors had significantly suppressed immune-related pathways (IFN-γ response, inflammatory response, and TNFα signaling via nfkb), and dendritic cells (DC) function (DC Differentiation, DC Antigen Processing and Presentation, DC Migration). Profiling tumor infiltrating immune cells with CIBERSORT showed that SCLC with $DLL3_{High}$ had significantly lower proportions of T-cells, macrophages, and DCs compared with those with $DLL3_{low}$. These results suggested that $DLL3_{High}$ tumors suppressed tumor immunity by inhibiting antigen-presenting function. In ES-SCLC cohort (n = 17), the PFS of PE plus anti-PD-L1 antibody in patients with $DLL3_{High}$ was significantly worse than those in patients with $DLL3_{Low}$ (4.1 months [95% CI, 2.0-6.3] vs. 7.4 months [95% CI, 2.5-12.3]; HR 3.78 [95% CI, 1.1-12.5], p = 0.03). **Conclusions:** SCLC with high DLL3 expression was characterized by resistance to immunochemotherapy due to suppressed tumor immunity, although those tumors had higher neoantigen loads. Research Sponsor: JST AIP-PRISM, Grant Number JPMJCR18Y4; MHLW ICT infrastructure establishment and implementation of artificial intelligence for clinical and medical research program, Grant Number JP21AC5001.

8587 **Poster Session**

Efficacy and safety of high dose twice-daily thoracic radiotherapy versus standard dose for limited stage small-cell lung cancer: A multicentre, open-label randomised, phase 3 trial.

Jiayi Yu, Leilei Jiang, Lina Zhao, Xiaomin Wang, Xue Yang, Dan Yang, Minglei Zhuo, Hanxiao Chen, Yidian Zhao, Fang Zhou, Quanfu Li, Zhengfei Zhu, LI CHU, Zhanshu Ma, Qifeng Wang, Yanli Qu, Huiming Yu, Rong Yu, Jun Zhao, Anhui Shi; Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Radiation Oncology, Peking University Cancer Hospital & Institute, Beijing, China; The First Affiliated Hospital of Air Force Military Medical University (Xijing Hospital), Xian, China; Anyang Cancer Hospital, Anyang, China; Beijing University Cancer Hospital & Institute, Beijing, China; Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Thoracic Medical Oncology, Peking University Cancer Hospital and Institute, Beijing, China., Beijing, China; Peking University Cancer Hospital and Institute, Beijing, China; Yantai Yuhuangding Hospital, Yantai, China; Ordos School of Clinical Medicine I.M.M.U, Ordos, China; Department of Radiation Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; Chifeng Affiliated Hospital, Chifeng, China; Sichuan Cancer Center, Radiation Oncology Key Laboratory of Sichuan Province, Department of Radiation Oncology, Sichuan Cancer Hospital & Institute, School of Medicine, University of Electronic Science and Technology of China, Chengdu 610042, China, Chengdu, China; Liaoning cancer hospital & institute, Shenyang, China; Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Radiation Oncology, Peking University Cancer Hospital & Insti, Beijing, China; Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Radiation Oncology, Beijing, China; Peking University Cancer Hospital & Institute, Beijing, China

Background: We aimed to assess the efficacy and safety of high-dose, hyperfractionated thoracic radiotherapy of 54 Gy in 30 fractions compared with standard dose(45 Gy in 30 fractions) as a first-line treatment for LS-SCLC. **Methods:** The study was an open-label, randomised, phase 3 trial, done at 16 public hospitals in China.Key inclusion criteria were patients aged 18-70 years, with previously histologically or cytologically confirmed LS-SCLC, previously untreated or received 1-2 courses of intravenous cisplatin (75 mg/m^{2}of body-surface area, on day 1 or divided into two days of each cycle) or carboplatin (area under the curve of 5 mg/mL per min, day 1 of each cycle)and intravenous etoposide (100 mg/m^{2}of body-surface area, on days 1-3 of each cycle), and an Eastern Cooperative Oncology Group (ECOG) performance status of 0-1.Eligible patients were randomly assigned (1:1) to receive receive volumetric-modulated arc radiotherapy (VMAT) of 45 Gy in 30 fractions or the simultaneous integrated boost VMAT (SIB-VMAT) of 54 Gy in 30 fractions to the primary lung tumour and lymph node metastases starting 0-42 days after the first chemotherapy course. Both groups of patients received thoracic radiotherapy twice per day and 10 fractions per week.Prophylactic cranial radiation (PCI, 25Gy in 10 fractions) was implemented to patients with responsive disease. The primary endpoint was overall survival. Safety was analysed in the as-treated population. This study is complete and registered with ClinicalTrials.gov,NCT03214003. **Results:** Between June 30, 2017, and April 6, 2021, 224 eligible patients were enrolled and randomly assigned to 54 Gy (n = 108) or 45 Gy (n = 116).Median follow-up for the primary analysis was 45 months (IQR 41-48). Median overall survival was significantly improved in the 54 Gy group (62.4 months) compared with the 45 Gy group (43.1 months; p = 0.001). Median progression-free survival was significantly improved in the 54 Gy group (30.5 months) compared with the 45 Gy group (16.7 months; p = 0.044). The most common grade 3-4 adverse events were neutropenia (30 [28%] of 108 patients in the 54 Gy group vs 27 [23%] of 116 patients in the 45 Gy group), neutropenic infections (6 [6%] vs 2 [2%]), thrombocytopenia (13 [12%] vs 12 [10%]), anaemia (6 [6%] vs 4 [3%]), and oesophagitis (1 [1%] vs 3 [3%]). There were one treatment-related deaths in 54 Gy group (myocardial infarction). **Conclusions:** Compared with standard thoracic radiotherapy dose of 45 Gy, the high dose dose of 54 Gy improved overall survival and progression-free survival without increasing toxicities in patients with LS-SCLC, supporting twice-daily hyperfractionated thoracic radiotherapy of 54 Gy with concurrent chemotherapy is an alternative treatment option for LS-SCLC. Clinical trial information: NCT03214003. Research Sponsor: Beijing Health and Health Science Technology Achievements and Appropriate Technology Promotion Project (No. BHTPP202026); Chinese Society of Clinical Oncology (CSCO) – Linghang cancer research (No. Y-2019AZMS-0519).

8588 **Poster Session**

The effect of various social determinants of health on overall survival in the SCLC population.

Matthew M Mirsky, Chan Mi Lee, Joy Li, Carley Mitchell, Annie Zhang, Jeffrey Zhong, Pingfu Fu, Seunghee P Margevicius, Jennifer Cullen, Afshin Dowlati, Melinda Laine Hsu; University Hospitals Seidman Cancer Center and Case Western Reserve University, Cleveland, OH; Case Western Reserve University School of Medicine, Cleveland, OH

Background: Small cell lung cancer (SCLC) comprises 10-15% of all lung cancers yet little is known about the impact of social determinants of health (SDOH) on outcomes in patients with SCLC. This study aims to assess the impact of various SDOH on overall survival (OS) in patients diagnosed with SCLC at a single institution. **Methods:** We have established a large clinical/pathologic/genomic database of all patients diagnosed and treated for SCLC between 1998-2022 at our institution for retrospective study. Demographic data including sex, race, age, stage, address, and smoking status were collected. Poverty index was assessed by percent of school-aged children in poverty at the school district level based off 2021 census using the SAIPE tool and stratified as low (poverty index $<=15.1$) and high (poverty index >15.1). Water/Air carcinogens were obtained by zip code through EPA TRI Explorer database at year of SCLC diagnosis. Food desert designation was acquired through USDA low income and low access atlas at 0.5 miles for urban residences and 10 miles for rural residences respectively. Violent crime rates were obtained from the FBI Crime Data Explorer by year of diagnosis and police department jurisdiction. OS was computed from date of diagnosis to death or last known follow up date, and univariate Cox proportional hazards (PH) regression analysis was performed. Factors that were significant at significance level of 0.25 in univariate analysis were further evaluated using multivariable Cox PH model. **Results:** A total of 982 patients with SCLC were included. Univariate PH analysis demonstrated statistically significant improvement in OS with younger age (HR = 1.03, 95% CI 1.02-1.03, p <0.0001), female sex (HR = 0.8, 95% CI 0.7-0.92, p 0.001), low poverty index (HR = 1.12, 95% CI 0.98-1.12, p = 0.097), limited stage disease (HR = 3.12, 95% CI 2.66-3.66, p = <0.0001), and lack of air pollution exposure (HR = 1.09, 95% CI 0.95-1.24, p = 0.227). Multivariable PH analysis showed statistically significant OS improvement for those from lower poverty areas (HR = 1.22, 95% CI: 1.07- 1.4, p = 0.004) as well as in those without air pollution exposure (HR = 1.21, 95% CI: 1.05- 1.39, p = 0.008), controlling for age, sex, stage and smoking. Exposure to water pollution, violent crime rate, food desert designation and pack years smoked were not found to be independent predictors of OS. **Conclusions:** In this large detailed cohort of 982 patients with SCLC, there was a significantly lower OS for patients living in high poverty areas and for patients exposed to air pollutants. This effect was durable even after for controlling for age, sex, stage, and smoking status, demonstrating that these are independent risk factors associated with poorer OS. Our next research steps will be to examine the biologic basis for these disparities through genomic and transcriptomic analysis. Research Sponsor: None.

8589 **Poster Session**

Assessing inpatient outcomes for patients with small cell lung cancer presenting with superior vena cava thrombosis.

Jay Vakil, Ekrem Turk, Ayobami Gbenga Olafimihan, Vaishali Deenadayalan, Rafaella Litvin, Khaldun Obeidat, Muhammad Bilal Ibrahim, Kunnal Batra; John H. Stroger, Jr. Hospital of Cook County, Chicago, IL

Background: Superior Vena Cava Syndrome (SVCS) is a condition characterized by obstruction of the SVC that can commonly be caused by thrombus formation in the SVC. Small cell lung cancer (SCLC) frequently results in obstruction of the SVC. When severe enough, SVCS can present as a life-threatening oncological emergency. In this study we aim to explore baseline characteristics of SVC thrombosis (SVCT) in patients with SCLC, the prevalence of US hospitalizations, and disparities with regards to race and socioeconomic status. **Methods:** National Inpatient Sample was utilized to obtain pertinent data. Total hospitalizations with coexistent comorbidities of SCLC were extracted from the 2016 to 2019 database. Adult patients with a secondary diagnosis of SVC thrombosis were determined by using ICD-10 codes. We studied the racial and socioeconomic differences as well as length of stay (LOS), total hospital charges (THC), and all-cause mortality outcomes in cancer patients with and without SVC thrombosis. Statistical analysis was performed on STATA, with logistic regression analyses and chi-square tests. **Results:** A total of 480,750 patients were hospitalized for SCLC. 720 of these patients had SVC thrombosis (0.15% of SCLC patients). The mean age of those with thrombi was significantly lower compared to those without thrombi (64 vs. 69, $p < 0.001$). The SCLC with SVCT cohort had statistically higher proportion of black patients than the other cohort. Charlson index was significantly higher in SCLC with SVCT cohort (5.8 vs. 5, $p < 0.001$). Average income between the two cohort groups were similar. Medicaid and private insurance utilization were more common in SCLC with SVCT admissions compared to without SVCT. Patients presenting with SVC thrombosis had an increased hospital LOS (10 vs. 6 days, $p < 0.001$) and cost compared to other cohorts ($117,320 vs. $80,806, $p < 0.005$). All-cause mortality in patients with SCLC was 7.7% and the presence of SVC thrombosis significantly increased the odds of inpatient mortality (18.0%). Non-White races were associated with higher odds of mortality in SCLC admissions. In addition, patients with SVC thrombus also had greater odds of having a concomitant pulmonary embolism during hospitalization. **Conclusions:** In this study we found that race, insurance type, and comorbidities impacted the likelihood of developing thrombosis in the superior vena cava in patients with SCLC. Though the incidence is rare, SVC thrombosis indicates a poor prognostic factor for patients with SCLC. Further studies to evaluate these disparities in race and socioeconomic factors are warranted. The development of thrombosis and subsequent SVC syndrome is a potentially life-threatening condition; addressing potential reversible risk factors could improve mortality in a large subgroup of hospitalizations related to SCLC. Research Sponsor: None.

8590 **Poster Session**

A multicenter phase I/II trial of induction chemotherapy followed by camrelizumab, apatinib, plus chemotherapy as first-line treatment for extensive-stage small-cell lung cancer.

Chengzhi Zhou, Ming Liu, Guihuan Qiu, Xiaohong Xie, Xinqing Lin, Wenhui Guan, Zhanhong Xie, Jiexia Zhang, Yinyin Qin, Haijian Du, Xin Chen; Pulmonary and Critical Care Medicine, Guangzhou Institute of Respiratory Health, National Center for Respiratory Medicine, State Key Laboratory of Respiratory Diseases, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; Department of Oncology centre Clifford Hospital, Guangzhou, China; Department of Pulmonary and Critical Care Medicine, Zhujiang Hospital, Southern Medical University, Guangzhou, China

Background: Extensive-stage small-cell lung cancer (ES-SCLC) is a highly aggressive tumor with poor prognosis and limited treatment options. It is necessary to explore new first-line therapeutic strategies to improve patients' outcomes. This study aimed to assess the safety and efficacy of induction chemotherapy followed by camrelizumab, apatinib plus chemotherapy as first-line treatment in patients with ES-SCLC. **Methods:** Patients (pts) aged 18-75 years with histopathologically confirmed ES-SCLC and ECOG performance score of 0-1 who did not receive systemic treatment were prospectively enrolled to this study. After two 21-day cycles of induction chemotherapy (etoposide 100 mg/m^2 on days 1-3 and carboplatin AUC 5 mg/mL/min on day 1 [EC]), pts received camrelizumab (200 mg, q3w) plus apatinib (250 mg, qd) and EC for 2-4 cycles, then followed by camrelizumab and apatinib as maintenance treatment until disease progression/unacceptable toxicity/up to two years. The primary endpoint was safety. Secondary endpoints were objective response rate (ORR), PFS and OS. Targeted sequencing and whole transcriptome sequencing (WTS) were performed for pts who had sufficient tissue samples. **Results:** From Jan 28, 2021 to Aug 20, 2022, 40 eligible pts were enrolled. At the data cut-off (Jan 21, 2023), the median follow-up time was 13.6 months. Grade 3/4 treatment-related adverse events (TRAEs) were reported in 72.5% (29/40) of pts. The most common grade 3/4 TRAEs were decreased neutrophil count (35.0%, 14/40), anemia (15.0%, 6/40), decreased platelet count (12.5%, 5/40), increased serum alanine aminotransferase (12.5%, 5/40), and hyponatremia (12.5%, 5/40). Hemoptysis was observed in 15.0% of (6/40) pts, all of whom were grade 1-2. No treatment-related deaths occurred. Efficacy was evaluated in 36 pts who received two cycles of induction therapy and had at least one post-treatment efficacy evaluation. The ORR after two cycles of induction chemotherapy was 66.7% (24/36). The overall ORR and disease control rate reached 88.9% (32/36) and 97.2% (35/36), respectively. The median PFS was 7.4 months (95% CI: 6.5-8.3). The 1-year OS rate was 63.4%. Thirty and 20 pts underwent targeted sequencing and WTS, respectively. Pts with high tumor mutational burden level (TMB $\geq$ 7.0, $p < 0.001$), high homologous recombination deficiency score (HRD $\geq$ 34.0, $p = 0.012$), and altered *RB1* ($p < 0.001$) presented a longer PFS, respectively. WTS suggested that high expression of cancer-associated fibroblast signature was associated with a shorter PFS ($p = 0.001$). **Conclusions:** Induction chemotherapy followed by camrelizumab, apatinib plus EC and then maintenance therapy showed acceptable safety and encouraging efficacy, and might be a promising regimen as first-line treatment in ES-SCLC. TMB, HRD and *RB1* might be predictive biomarkers of response to the regimen. Clinical trial information: NCT05001412. Research Sponsor: 1.Beijing Xisike Clinical Oncology Research Foundation (Grant No.Y-HS202102-0118); 2.Guangzhou Science and Technology Program (Grant No.202102010371); 3.Zhijiang Laboratory-The open project (Grant No.2021PE0AC06).

8591 **Poster Session**

Efficacy and safety of lurbinectedin in elderly patients with relapsed SCLC.

Sophie Cousin, Luis G. Paz-Ares, Andrea Fülöp, Ildiko Horvath, Jose Manuel Manuel Trigo Perez, Jon Zugazagoitia, Laura Bonanno, Jose Antonio Lopez-Vilariño, Carmen Maria Kahatt, Cristian Marcelo Fernandez, Javier Gomez, Ali Hassan Zeaiter, Alejandro Navarro, Kostas N. Syrigos, Egbert Smit, Tudor-Eliade Ciuleanu, Alberto Chiappori, Rafael Lopez-Lopez, Benjamin Besse; Medical Oncology Department, Institut Bergonié, Bordeaux, France; Hospital Universitario 12 De Octubre, Madrid, Spain; Országos Korányi Pulmonológiai Intézet, Budapest, Hungary; National Koranyi Institute for Pulmonology, Budapest, Hungary; Hospital Universitario Virgen de la Victoria, IBIMA, Málaga, Spain; Hospital Universitario 12 de Octubre, Madrid, Spain; Medical Oncology 2, Istituto Oncologico Veneto IOV-IRCCS, Padua, Italy; PharmaMar, Colmenar Viejo, Spain; Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; National & Kapodistrian University of Athens, Athens, Greece; The Netherlands Cancer Institute, Amsterdam, Amsterdam, Netherlands; Institutul Oncologic Prof Dr Ion Chiricută and University of Medicine and Pharmacy Iuliu Haţieganu, Cluj-Napoca, Romania; H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; Hospital Clínico Universitario de Santiago, Santiago De Compostela, Spain; Institut Gustave Roussy, Villejuif, France

Background: Relapsed SCLC is a difficult-to-treat disease. A considerable number of SCLC patients are elderly with associated fragility and numerous comorbidities. Accelerated approval from the US FDA of lurbinectedin (Zepzelca) 3.2 mg/m^2 q3wk as second-line therapy in metastatic small cell lung cancer (SCLC) was based on results from a phase 2 basket trial (NCT02454972) showing overall response rate of 35.2% and duration of response of 5.3 months. The ATLANTIS trial (NCT02566993) assessed the combination of lurbinectedin 2mg/m^2/ doxorubicin (DOX) 40 mg/m^2 as second-line treatment for SCLC *vs.* a control arm of topotecan/CAV. **Methods:** This *post hoc* analysis explores the efficacy and safety of lurbinectedin in relapsed SCLC patients ≥65 years included in both phase 2 basket (26 patients treated with lurbinectedin) and ATLANTIS (121 patients treated with lurbinectedin/DOX and 118 patients treated in the control arm) trials. This analysis did not include patients from the phase 2 basket trial with chemotherapy-free interval (CTFI) < 30 days, as these patients were excluded in the ATLANTIS trial. **Results:** Median age was similar (72.5 in lurbinectedin basket *vs.* 69 in ATLANTIS lurbinectedin/DOX *vs.* 69 in ATLANTIS control arm), most were males (65.4% *vs.* 57.9% *vs.* 60.2%), with ECOG PS 1 (65.4% *vs.* 68.6% *vs.* 68.6%) and CNS involvement (7.7% *vs.* 10.7% *vs.* 15.3%). Median CTFI (days) was also similar (105.5 *vs.* 123 *vs.* 120). Median number of cycles was 4 *vs.* 6 *vs.* 4. Main efficacy and safety results are shown in the table. Treatment-related adverse events (AEs) were reported in 92.3%, 92.6% and 94.1% of patients, respectively (grade ≥3 in 50.0%, 59.5% and 81.4%). **Conclusions:** In elderly patients, lurbinectedin seems to be superior to the standard of care in terms of both efficacy (higher response rate and longer duration of response and overall survival) and safety (less associated hematological AEs), which reinforces its role as a treatment option in relapsed SCLC patients ≥65 years. Clinical trial information: NCT02454972, NCT02566993. Research Sponsor: PharmaMar.

	Basket (n=26)	ATLANTIS*		
		Lurbi/DOX (n=121)	Control (CAV/ topotecan) (n=118)	OR/HR (95%CI)**
ORR confirmed by IRC (%) (95% CI)	34.6 (17.2-55.7)	24.8 (17.4-33.5)	26.3 (18.6-35.2)	0.93 (0.50, 1.73)
Median DoR by IRC (mo) (95% CI)	5.1 (2.4-5.9)	6.9 (4.1-10.1)	4.2 (3.6-5.7)	0.482 (0.260-0.892)
Median PFS by IRC (mo) (95% CI)	3.4 (2.6-5.1)	4.2 (3.5-4.8)	3.0 (2.8-4.0)	0.645 (0.485-0.859)
Median OS (mo) (95% CI)	9.7 (6.2-14.9)	9.0 (7.8-10.8)	5.9 (5.3-7.6)	0.755 (0.575-0.991)
Most frequent AEs, regardless of relationship (%)	**Grade ≥3**	**Grade ≥3**	**Grade ≥3**	**p-value****
Anemia	19.2	23.1	36.4	0.0333
Febrile neutropenia	3.8	5.0	9.3	0.2161
Fatigue	15.4	13.2	15.3	0.7130
Neutropenia	65.4	43.8	73.7	<0.0001
Thrombocytopenia	7.7	16.5	33.9	0.0027

* Growth colony-stimulating factors were mandatory for both ATLANTIS treatment arms.** Nominal comparisons in ATLANTIS (small number of patients in basket trial)AEs, adverse events; CI, confidence interval; mo, months; OS, overall survival.

8592 **Poster Session**

Dissecting small cell lung cancer subtypes with cell-free DNA fragmentomes.

Lorenzo Rinaldi, Zachary L. Skidmore, Bahar Alipanahi, Garrett Graham, Bryan Chesnick, Nobuyuki Takahashi, Rajesh Kumar, Shubhank Goyal, Melissa Lauren Abel, Justin Malin, Parth Anil Desai, Nicholas C. Dracopoli, Victor E. Velculescu, Anish Thomas, Alessandro Leal; Delfi Diagnostics, Inc., Baltimore, MD; National Cancer Center Hospital East, Shinjuku-Ku, MD, Japan; National Cancer Institute, Bethesda, MD; Delfi Diagnostics, Baltimore, MD; The Johns Hopkins University School of Medicine, Baltimore, MD

Background: Although small cell lung cancer (SCLC) is managed as a single cancer type, new evidence supports that subtypes (high vs low neuroendocrine) of SCLC acquire diverse transcriptional and epigenetic states. Furthermore, distinct SCLC subtypes acquire unique therapeutic vulnerabilities, such as the low-neuroendocrine highly inflamed SCLC subtype that has been linked to immunotherapy sensitivity. We have previously shown that DELFI (DNA evaluation of fragments for early interception) can be used to non-invasively distinguish SCLC from non-small cell lung cancer (NSCLC). Here, we report a preliminary analysis of using the DELFI approach for distinguishing among SCLC subtypes. **Methods:** Circulating cell-free DNA (cfDNA) was isolated from plasma samples of patients diagnosed with relapsed SCLC and treated with durvalumab plus olaparib in a phase II trial (NCT02484404). Over 200 cfDNA libraries were prepared for whole genome sequencing in batches with internal controls. To infer tumor gene expression profiles in cfDNA, we investigated genome-wide signals of tissue-specific transcription factors differentially regulated in SCLC, and applied a novel DELFI-based approach to inform SCLC molecular subtypes. Clinical information, patient-matched tissue transcriptome (RNA-seq), and chromatin accessibility data (ATAC-seq) were examined in orthogonal analyses. **Results:** The DELFI classifier detected SCLC cases (N = 47) with a median DELFI score of 1.0 (95% CI 0.99-1), significantly higher than previously reported scores for other lung cancer subtypes. Comparison of DELFI fragmentome signals to publicly available tumor transcriptomes shows subtype-level concordance ($r = 0.78$, $p < 0.001$, *Pearson*), particularly in pre-treatment SCLC cases separating high- vs low-neuroendocrine subtypes. High-neuroendocrine SCLCs exhibited a decrease in aggregate cfDNA fragment coverage at *ASCL1* transcription factor binding sites relative to low-neuroendocrine SCLCs ($r = 0.90$, $p < 0.001$, *Pearson*). Additionally, low-neuroendocrine SCLCs revealed a significant decrease in aggregate cfDNA fragment coverage at genomic binding sites regulated by hematopoietic transcription factors, reflecting the inflamed phenotype of this SCLC subtype. Integration of these approaches provided a cfDNA fragmentation-based machine learning model that distinguished SCLC subtypes with high performance. **Conclusions:** Genome-wide cfDNA fragmentome analyses can differentiate high- and low-neuroendocrine SCLC subtypes. Given the challenges for performing SCLC biopsies in a clinical setting, we believe this approach could be a viable method of subtyping SCLC in a non-invasive manner. Research Sponsor: Delfi Diagnostics; U.S. National Institutes of Health.

8593 **Poster Session**

Phase 2 small cell lung cancer (SCLC) cohort of a phase 1b/2 trial of a liposomal formulation of eribulin in combination with nivolumab.

Koichi Azuma, Shuji Murakami, Hisato Kawakami, Kyoichi Okishio, Motohiro Tamiya, Haruki Kobayashi, Daichi Fujimoto, Shunichi Sugawara, Toshiyuki Kozuki, Yuko Oya, Hiroki Izumi, Takayuki Shiroyama, Rie Tohnai, Noboru Yamamoto, Shota Kaname, Daiko Matsuoka, Yohei Otake, Takao Takase, Taro Semba, Makoto Nishio; Kurume University Hospital, Kurume, Japan; Kanagawa Cancer Center, Yokohama, Japan; Kindai University Faculty of Medicine, Osakasayama, Japan; National Hospital Organization Kinki-Chuo Medical Center, Osaka, Japan; Osaka International Cancer Institute, Osaka, Japan; Shizuoka Cancer Center, Shizuoka, Japan; Wakayama Medical University Hospital, Wakayama, Japan; Sendai Kousei Hospital, Sendai, Japan; National Hospital Organization Shikoku Cancer Center, Matsuyama, Japan; Fujita Health University Hospital, Toyoake, Japan; National Cancer Center Hospital East, Kashiwa, Japan; Osaka University Hospital, Osaka, Japan; Hyogo Prefectural Cancer Center, Hyogo, Japan; National Cancer Center Hospital, Tokyo, Japan; Ono Pharmaceutical Co., Ltd., Osaka, Japan; Eisai Co., Ltd., Tokyo, Japan; Eisai Co., Ltd., Ibaraki, Japan; Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan

Background: E7389-LF is a liposomal formulation of the microtubule dynamics inhibitor eribulin. Combining E7389-LF with an immune checkpoint inhibitor (ICI; eg, nivolumab) may improve antitumor response via vascular remodeling. The phase 1b part of the open-label Study 120 evaluated the dosing and safety of E7389-LF in combination with nivolumab in patients (pts) with solid tumors. The phase 2 part assessed efficacy and safety in disease cohorts; herein, we report results from the SCLC cohort. **Methods:** Pts with unresectable and measurable SCLC who had progression during or after 1st-line (1L) platinum-based chemotherapy with/without an ICI were enrolled to the SCLC cohort of the phase 2 part of Study 120. Pts received E7389-LF 2.1 mg/m^2 in combination with nivolumab 360 mg IV Q3W. The primary objective of the phase 2 part was to assess the objective response rate (ORR). Secondary objectives included assessments of safety and progression-free survival (PFS); exploratory objectives included the disease control rate (DCR), overall survival (OS), and biomarker analysis. Tumor response was assessed by investigators per RECIST v1.1 Q6W. All adverse events (AEs) were monitored and recorded. **Results:** In the SCLC cohort, 34 pts were enrolled; the median age was 66.0 years (range 46–81). At data cutoff (May 31, 2022), 5 pts (14.7%) were undergoing treatment. Discontinuations occurred in 29 pts (85.3%)—26 (76.5%) primarily due to disease progression, 3 (8.8%) due to an AE. Efficacy analyses included 33 pts, as 1 pt had their diagnosis of SCLC changed to a different cancer type after being enrolled. Of the 33 evaluable pts, 27 (81.8%) had an ICI as part of their prior 1L therapy. The ORR of E7389-LF in combination with nivolumab was 24.2% (95% CI 11.1–42.3) in the evaluable population; the DCR was 75.8% (95% CI 57.7–88.9). Median PFS was 3.98 mos (95% CI 2.63–4.40); the 6-mo PFS rate was 27.7% (95% CI 13.0–44.6). At a median follow-up period of 10.6 mos, median OS was not reached (95% CI not estimable); the 6-mo OS rate was 90.9% (95% CI 74.4–97.0). Treatment-related, treatment-emergent (TE)AEs of any grade and of grade ≥3 severity occurred in 97.1% (n = 33) and 82.4% (n = 28) of the 34 enrolled pts, respectively; the most common treatment-related TEAE was neutropenia (any grade: 58.8% [n = 20]; grade ≥3: 52.9% [n = 18]). The neutrophil count nadir occurred around cycle 1 day 8. TEAEs led to dose reduction of E7389-LF in 19 pts (55.9%). Withdrawal of E7389-LF or nivolumab occurred in 5 pts (14.7%): acute kidney injury, cough, myocarditis, pneumonitis, and radiation pneumonitis (n = 1 each). Changes in vascular and immune-related plasma markers were observed. **Conclusions:** E7389-LF in combination with nivolumab showed notable antitumor activity as 2L therapy in pts with SCLC, as evidenced by the notable ORR of 24.2%. No new safety signals were observed for this combination. Clinical trial information: NCT04078295. Research Sponsor: This trial was sponsored by Eisai Co., Ltd., Tokyo, Japan. Nivolumab was provided by Ono Pharmaceutical Co., Ltd., Osaka, Japan.

8594 **Poster Session**

Spatially resolved multi-region transcriptomic subtyping and assessment of gene expression profiles associated with long-term benefit from chemo-immunotherapy in patients with extensive-stage small cell lung cancer (ES-SCLC).

Melina Peressini, Rosario Garcia Campelo, Manuel Cobo-Dols, Manuel Domine, Javier de Castro Carpeño, Jose Fuentes Pradera, Juan Felipe Cordoba, Emilio Esteban, Enric Carcereny, Laia Vilà, Alberto Moreno, Silverio Ros Martinez, Gerardo Huidobro Vence, Bartomeu Massuti, Magdalena Molero, Vera Adradas, Esther Conde, Santiago Ponce Aix, Luis G. Paz-Ares, Jon Zugazagoitia; Hospital Universitario 12 de Octubre, Madrid, Spain; Complejo Hospitalario Universitario A Coruna Hospital Teresa Herrera-Materno Infantil, A Coruna, Spain; Hospital Universitario Regional Málaga, Málaga, Spain; Fundacion Jimenez Diaz University Hospital, Madrid, Spain; Hospital Universitario La Paz, Madrid, Spain; Virgin de Valme University Hospital, Sevilla, Spain; Hospital Universitario Arnau de Vilanova, Lleida, Spain; Hospital Universitario Central de Asturias, Oviedo, Spain; Hospital Germans Trias i Pujol. ICO Badalona, Badalona, Spain; Hospital Parc Taulí Sabadell, Sabadell, Spain; Hospital Universitario Reina Sofía, Cordoba, Spain; Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain; Hospital Universitario de Vigo Alvaro Cunqueiro, Vigo, Spain; Alicante University Hospital Isabial, Alicante, Spain; Pathology Department, Hospital Universitario 12 de Octubre. Universidad Complutense de Madrid. Research Institute Hospital 12 de Octubre (i+12). CIBERONC, Madrid, Spain; Gustave Roussy, Villejuif, France; Hospital Universitario 12 De Octubre, Madrid, Spain; Department of Medical Oncology, Hospital Universitario 12 de Octubre, Madrid, Spain

Background: Transcriptomic subtyping holds promise for personalized therapy in SCLC, but intra-tumoral transcriptomic heterogeneity and its clinical significance remain poorly defined. In this study, we aimed to assess transcription factor defined subtypes within multiple regions of intact tissues and identify gen sets associated with long-term chemo-immunotherapy benefit. **Methods:** We assessed baseline FFPE tumors from 32 ES-SCLC patients enrolled in the IMfirst clinical trial (EudraCT: 2019-002784-10). We used GeoMx DSP to perform transcriptomic analysis from multiple intratumoral regions of interest (ROIs). We used an assay with +1800 genes (GeoMx CTA) plus custom-designed mRNA probes targeting subtype-defining transcription factors not included in the CTA assay (POU2F3, NEUROD1, and YAP1). Custom probes were quantitatively validated using FFPE cell lines. **Results:** We profiled 175 ROIs from 32 tumors. Cluster analysis based on the expression of ASCL1, NEUROD1, POU2F3, and YAP1 showed that all samples clustered within 4 groups: SCLC-A (76 ROIs [43%]), SCLC-N (31 ROIs [18%]), SCLC-P (18 ROIs [10%]), and SCLC-Y (50 ROIs [29%]). ASCL1 was the most abundantly expressed transcription factor, prevailed in the SCLC-A subtype, and showed inverse correlation with POU2F3 ($r=-0.55$, $p<0.0001$) and YAP1($r=-0.70$, $p<0.0001$). YAP1 was expressed at low levels and was more broadly distributed across all 4 subtypes. Differential expression and gene set enrichment analysis (GSEA) using linear mixed models revealed that SCLC-A subtype was enriched in cell cycle and DNA damage repair genes, and showed repression of multiple gene sets associated with anti-tumor immune response. In contrast, SCLC-Y subtype showed the opposite pattern. The SCLC-P subtype was also enriched in genes related to cancer antigens and T-cell checkpoints. Most patients (n=18, 56%) had tumors with coexistence of more than one subtype, not evident through morphological inspection. Combined SCLC-A and SCLC-Y subtypes was the most common mixed phenotype (n=8, 25%). Four patients (13%) had tumors with co-existence of three subtypes. Transcriptional subtypes, subtype-defining transcription factors as single genes, or the presence of subtype heterogeneity, were not associated with outcomes. Gene sets involved in mitochondrial metabolism and MHC class I antigen presentation were the highest enriched pathways in tumors from patients with sustained benefit (time to progression ^{3} 12 months). **Conclusions:** This study reveals substantial intratumoral transcriptomic subtype heterogeneity in human SCLC. In this limited sample set, we did not observe outcome association for transcriptional subtypes. Our findings related to long-term chemo-immunotherapy benefit require validation in independent cohorts. Research Sponsor: Roche Pharma SA.

8595 **Poster Session**

Role of consolidative thoracic and prophylactic cranial radiation in extensive stage small cell lung cancer in chemo-immunotherapy era.

Jai Kumar Khatri, Rick Voland, John Charles Flickinger, Maria Tria Tirona, Toni Pacioles, Jennifer Dotson, Muhammad Omer Jamil, Khurram Anwar, Vivek Yadala, Thomas Wright, Malcolm DeCamp, Yousef Shweihat, Zani S Zander, Mark Hayden Cooper, John M. Varlotto; Marshall University School of Medicine, Edwards Cancer Center, Huntington, WV; School of Nursing, University of Wisconsin, Madison, WI; Presbyterian University Hospital, Pittsburgh, PA; Edwards Comprehensive Cancer Center, Marshall University School of Medicine, Huntington, WV; Marshall University Joan C. School of Medicine, Huntington, WV; University of Wisconsin, Madison, WI; Marshall University Joan C. Edwards School of Medicine, Huntington, WV; Pathology & Laboratory Medicine | College of Medicine, University of Cincinnati, Cincinnati, OH; Edwards Comprehensive Cancer Center, Huntington, WV

Background: The role of consolidative thoracic and prophylactic brain radiation in extensive stage small cell lung cancer patients is controversial. We investigated the factors associated with the use of any radiation therapy (RT) and whether Radiation has a benefit to overall survival (OS) in the total patient group and whether this benefit is the same if Chemotherapy (CT) only is used, or chemo-immunotherapy (CT-IO) is used. **Methods:** The NCDB database was queried from years 2017-2019. Patients receiving systemic therapy- STX (CT or CT-IO) had to have at least 6 months of follow-up and have no brain metastases at diagnosis. All RT patients had to receive upfront systemic therapy, were treated 2 to 6 months from diagnosis, and if treated to the brain received 25Gy in 10 fractions only. Multi-variate analyses (MVA) were used to determine factors associated with OS and selection for any radiation. Propensity matching for factors affecting OS were used to generate Kaplan-Meier OS curves. Log-rank tests were used to determine differences in Kaplan Meier survival curves for the effects of RT on OS. **Results:** The total number of patients receiving RT or systemic therapy alone as well as their median follow-ups(months(mn) were (981, 33.02mn) and (8909, 30.59mn). The median time to the start of STX and RT were 22days and 135 days respectively. MVA noted that RT had a greater effect on OS (Thoracic, Brain, Both – HRs = 0.78, 0.75, and 0.68) than other interventions including IO (HR 0.87) and palliative care without RT (HR 1.07). Selection for radiation depended significantly upon factors affecting OS(HR) including liver metastases (0.59), females (1.21), age/10yr(0.78) and Charlson co-morbidity index of $>$ 3(0.66), but did not depend upon insurance status, race, or county income/high school graduation rates. Propensity score matched OS curves noted the same effects of RT on OS whether CT or CT-IO was given. The lowest HRs were noted when both thoracic and brain RT were given (see table). **Conclusions:** The patient with extensive stage small cell lung cancer who reach candidacy and receive RT may have a significant improvement in OS compared to the patients treated only with CT or CT-IO. Combined thoracic and prophylactic brain RT seems to be better than either one alone. The impact of radiation whether given to one or two sites may be more beneficial than immunotherapy added to chemotherapy. Research Sponsor: None.

Regimen	HR	p-value	N	18Month OS-KM
CT only	REF	REF	5783	15%
CT + Thoracic RT vs CT with no RT (Ref)	0.68(0.59,0.77)	$<$ 0.0001	256	28%
CT + Brain RT vs Ref	0.67(0.60,0.76)	$<$ 0.0001	305	33%
CT + Both Brain and Thoracic RT vs Ref	0.59(0.49,0.70)	$<$ 0.0001	112	39%
CT-IO	REF	REF	3126	19%
CT-IO with thoracic RT vs CT-IO (Ref)	0.68 (0.56,0.83)	$<$ 0.0001	119	38%
CT-IO with brain RT vs REF	0.73(0.60,0.88)	$<$ 0.0001	132	38%
CT-IO with Thoracic + brain RT vs Ref	0.62(0.46,0.82)	$<$ 0.0001	57	44%

8596 **Poster Session**

Brain metastasis burden and management in small cell lung cancer: An analysis of 8705 patients.

Karolina Gaebe, Anders W. Erickson, Natasha B. Leighl, Kelvin K. Chan, Benjamin H. Lok, Sunit Das; University of Toronto, Toronto, ON, Canada; Princess Margaret Cancer Centre, Toronto, ON, Canada; Sunnybrook Odette Cancer Centre, Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; St. Michael's Hospital, University of Toronto, Toronto, ON, Canada

Background: Patients with small cell lung cancer (SCLC) have historically been characterised by poor overall survival (OS) and high risk for intracranial metastatic disease (IMD), but large-scale real-world evidence on clinical presentation and treatment in this population is lacking. These patients traditionally receive whole brain radiation therapy (WBRT) for IMD, however, a recent systematic review has indicated that OS following stereotactic radiosurgery (SRS) may be non-inferior compared with WBRT. We aim to describe the clinical characteristics and outcomes of patients with SCLC and IMD in Ontario, Canada. **Methods:** We included all patients diagnosed with SCLC between April 2007 and March 2018 identified through a provincial health administrative database. Information on patient and treatment characteristics, incidence and time to IMD, and OS from time of SCLC diagnosis were collected and analyzed using R. **Results:** A total of 8705 patients were included. Median age was 68 years (range 18-103). Most patients presented with extensive disease (n = 5625) and were diagnosed after 2011 (n = 5768). Patients who received chemotherapy (n = 5563) had significantly longer OS than those who did not (median 10.64 vs 1.58 months (mo), hazard ratio (HR) 0.36, 95% confidence interval (CI) 0.34-0.37). 6662 patients received brain imaging at the time of primary diagnosis (CT: 5126, MRI: 1536), and 88% of patients surviving longer than 6 mo received more than one follow-up brain scan. 31% developed IMD (synchronous: 1175, asynchronous: 1511) with median intracranial progression-free survival of 5.65 mo. Median OS of patients with IMD was 9.76 mo, 29 and 1300 received SRS and WBRT as first treatment for their IMD, respectively. OS was in favour of SRS over WBRT (median 20.47 vs 8.74 mo, HR 0.57, 95% CI 0.39-0.84), which remained significant in multivariate analysis ($p < 0.001$). **Conclusions:** OS for patients with SCLC remains poor, and many patients present with IMD. With careful selection, patients with SCLC may benefit from SRS treatment. Research Sponsor: None.

8597 **Poster Session**

Molecular predictors and immunomodulatory role of dual checkpoint inhibitor blockade using ipilimumab/nivolumab in patients with extensive stage small cell lung cancer.

Anne C. Chiang, Hossein Asghari, Kerryan Ashley, Scott N. Gettinger, Sarah B. Goldberg, Roy S. Herbst, Frederick Hugh Wilson, Benjamin Robert Newton, Michael Keith Cohenuram, Kert D. Sabbath, Ashita D. Talsania, Armand Vincent Russo, Eric Schultz, Stan Skrzypczak, Carl Kingsford, Kurt A. Schalper; Yale University School of Medicine, New Haven, CT; Ocean Genomics, Pittsburgh, PA; Yale University Dept of Pathology, New Haven, CT; Yale School of Medicine, New Haven, CT; Yale Cancer Center, New Haven, CT; Yale School of Medicinel, Yale Cancer Center, Smilow Cancer Hospital at Yale-New Haven, New Haven, CT; Yale University, New Haven, CT

Background: Small cell lung cancer (SCLC) is an aggressive neuroendocrine carcinoma with poor prognosis. In extensive stage patients, frontline treatment with chemoimmunotherapy shows modest clinical benefit. However, the biological impact of immunotherapy in SCLC is poorly understood with no clear predictive biomarkers to guide patient selection in this setting. **Methods:** We collected paired baseline (pre-treatment), on-treatment (week 4), and progression biopsies from patients with relapsed advanced-stage SCLC treated with combination nivolumab (nivo) and ipilimumab (ipi) in a single-arm, phase 2 clinical trial (NCT03670056). Nivo 1 mg/kg and ipi 3 mg/kg were administered every 3 weeks for 4 cycles, followed by nivo maintenance until progressive disease (PD) by RECIST 1.1 or treatment-limiting toxicity. Paired pre/on-treatment samples were available from 16/22 patients, as well as 3 biopsies at progression. The tumor samples were studied using whole exome DNA sequencing (including germline DNA) and RNA-sequencing coupled to Ocean Genomics TxomeAI data analysis pipeline. **Results:** 6/11 evaluable patients had PD; 5 patients showed clinical activity of treatment (3 with stable disease, 2 with partial response). The frequency of deleterious mutations in *TP53* and *RB1* was 91% and 64%, respectively. Mutations in *HLA-A* were more common in baseline samples from patients with PD than those with clinical activity. New *TP53* and *PLEC* mutations were found 4 of 6 patients with PD in week 4 samples vs baseline. The baseline tumor mutational burden was not associated with treatment sensitivity and prominently increased in week 4 biopsies of PD patients. All four molecular SCLC transcriptomic subtypes based on the expression of *ASCL1*, *NEUROD1*, and *POU2F3* were present in the trial with SCLC-A being the most common (9/16 cases). All patients with clinical activity to ipi/nivo were of SCLC-A subtype. 2/16 of cases showed a different molecular subtype after 4 weeks of treatment: one case with SCLC-N switched to SCLC-A and another case converted from SCLC-A to SCLC-N. Comparison of baseline and on-treatment samples showed upregulation of transcripts associated with T-cell activation and PD-1 signaling. In the 3 biopsies at progression, transcriptomic changes included reduction of neutrophil degranulation, type 1/2 interferon and signatures, as well as down-regulation of β-2 microglobulin, while cell cycle and mitotic prophase pathways were overexpressed. **Conclusions:** Dual checkpoint blockade using nivo/ipi has a prominent immunomodulatory role in extensive stage SCLC characterized by increased local adaptive immune responses, reduced HLA class-I antigen presentation and change in the molecular subtype in a subset of cases. We identified genomic features associated with treatment sensitivity/resistance. Clinical trial information: NCT03670056. Research Sponsor: Bristol-Myers Squibb.

8598 **Poster Session**

Utilization of circulating tumor DNA (ctDNA) analysis to detect minimal residual disease post-surgery and disease progression in metastatic thymic tumors.

Fatemeh Ardeshir-Larijani, Karthik Raja Ravichandran, Bryan P. Schneider, Milan Radovich, Rohan Maniar, Ashiq Masood, Kenneth Kesler, Patrick J. Loehrer; Indiana University, Melvin and Bren Simon Cancer Center, Indianapolis, IN; Indiana University School of Medicine, Indianapolis, IN; Indiana University Melvin and Bren Simon Comprehensive Cancer Center, Indianapolis, IN; Melvin and Bren Simon Cancer Center, Indianapolis, IN; Indiana University Dept of Cardiosurgery, Indianapolis, IN

Background: Thymic epithelial tumors (TETs) are rare and tend to have an indolent disease course. Follow-up consists of physical examinations and routine imaging (CT scans) with no currently available biomarkers to complement surveillance. This study aimed to assess the utility of ctDNA in MRD detection and disease monitoring in TETs. **Methods:** From Nov 2020 till Feb 2022, ctDNA analysis using a tumor-informed mPCR-NGS (Signatera) assay was performed on 29 patients (pts) with primary (pTETs) or metastatic TETs (mTETs). For pts with early-stage disease, the baseline ctDNA was measured 4-8 w post-surgery and repeated q3m. For mTETs, ctDNA was measured at the first visit, and then q3m with interval CT scan q3-4 m. ctDNA was quantified as mean tumor molecules (MTM)/mL of plasma. All pts had at least one measurement (up to 4). GraphPad was used for statistical analysis. **Results:** Of 29 pts overall, 9 pts were excluded at the time of analysis for various reasons; a) insufficient specimen (n=5), b) presence of concurrent active cancer (n=2), and c) final report delay (n=2). Of 20 evaluable pts, 7 pts had pTETs and 13 mTETs. The median age was 50 yrs (range, 17-72), and WHO histology distribution of AB=3, B1=5, B2=9, B3=12, TC=3. History of autoimmune disease and second malignancy (not active at the time of obtaining ctDNA) was reported in 33% (n=9) and 40% (n=8) of evaluable pts, respectively. Of 13 metastatic pts, 6 had stage IVA with pleural-only metastasis, 7 pts had Stage IVB with 2 extra-thoracic (liver, adrenal), and 5 with intrathoracic (lung, chest wall, and LNs) involvement. From 7 pTETs, 6 pts had R0 resection with undetectable post-operative ctDNA, while R1 resection with detectable ctDNA was reported (0.47 MTM/mL) in one pt. In mTETs, the mean level of ctDNA in pts with the stable disease was 0.18 MTM/mL (0.1-0.2), pleural-only progression 1.26 MTM/mL (0.1-1.9), and progressive disease (primary and/or pleural) 7.67 MTM/mL(5.04-9.5). Comparing the mean level of ctDNA in clinically stable metastatic pts with those who had progression, pts with pleural-only progression did not have a significantly higher level of ctDNA (p=0.51). In contrast, pts with primary and/or pleural progression had significantly higher levels of ctDNA (p=0.02). The level of ctDNA correlated with tumor size. An increase of 4-6mm in tumor size was associated with an approximate 0.2 MTM/mL increase in ctDNA or making the undetectable status detectable. **Conclusions:** The ctDNA level correlates well with the tumor volume in mTETs. In pTETs, ctDNA was negative following R0 resection but not in the R1, supporting its potential use as a surrogate biomarker for MRD. This is a pilot study, and the expansion of these data is ongoing to validate the utility of ctDNA testing in these settings. If validated, ctDNA may augment or minimize the routine use of CT scans for disease monitoring in resected and mTETs. Research Sponsor: Alumni award hematology/ oncology fellowship/ Indiana University.

TPS8599 **Poster Session**

Durvalumab with chemotherapy as first line treatment in advanced pleural mesothelioma: A phase 3, randomised trial (DREAM3R).

Patrick M. Forde, Anna K. Nowak, Brett Gordon Maxwell Hughes, Peey Sei Kok, Chris Brown, Zhuoxin Sun, Valsamo Anagnostou, Ken O'Byrne, Sonia Yip, Alistair Cook, Willem Joost Lesterhuis, Nick Pavlakis, Julie R. Brahmer, Hedy L. Kindler, Anne S. Tsao, Marjorie Glass Zauderer, Suresh S. Ramalingam, Martin R. Stockler; Bloomberg–Kimmel Institute for Cancer Immunotherapy, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD; University of Western Australia, Nedlands, Australia; The Prince Charles Hospital, Brisbane, Australia; NHMRC Clinical Trials Centre, The University of Sydney, Sydney, NSW, Australia; Dana-Farber Cancer Institute, Boston, MA; Johns Hopkins Kimmel Cancer Center, Baltimore, MD; Princess Alexandra Hospital, Queensland University of Technology, Translational Research Institute, Brisbane, Australia; NHMRC Clinical Trials Centre, The University of Sydney, Camperdown, NSW, Australia; Medical School and National Centre for Asbestos Related Diseases, University of Western Australia, Perth, Australia; National Centre for Asbestos Related Diseases, University of Western Australia, Nedlands, Australia; Genesis Care, North Shore Health Hub, Sydney, NSW, Australia; Bloomberg-Kimmel Institute for Cancer Immunotherapy, Johns Hopkins Kimmel Cancer Center, Baltimore, MD; University of Chicago, Chicago, IL; University of Texas MD Anderson Cancer Center, Houston, TX; Memorial Sloan Kettering Cancer Center, New York, NY; Winship Cancer Institute, Emory University Hospital, Atlanta, GA

Background: Two phase 2 trials of durvalumab plus chemotherapy in advanced pleural mesothelioma exceeded pre-specified efficacy criteria. The recent CM 743 trial showed overall survival (OS) was longer in those assigned ipilimumab and nivolumab (ipi nivo) than standard chemotherapy, however the benefits were primarily in the subgroup with non-epithelioid histology. DREAM3R will determine the effectiveness of durvalumab plus chemotherapy as first line treatment for advanced pleural mesothelioma. The DREAM3R protocol was recently amended to allow treatment with ipi nivo as per CM 743 in the control group, and to confine further accrual to epithelioid subtype. **Methods:** Treatment-naïve patients with advanced, epitheloid pleural mesothelioma will be randomized (1:1) to either experimental group treatment: durvalumab 1500 mg every 3 weeks plus chemotherapy (pemetrexed 500 mg/m^2 plus either cisplatin 75 mg/m^2 or carboplatin AUC 5) every 3 weeks for 4-6 cycles, followed by durvalumab 1500 mg every 4 weeks until disease progression, unacceptable toxicity or patient withdrawal, or control group treatment: physician's choice of either chemotherapy or ipi nivo (up to 2 years). The target sample size of 480 recruited over 33 months, with follow up for another 18 months provides over 85% power if the true hazard ratio for OS is 0.70, with 2-sided alpha of 0.05, assuming a median OS of 18 months in the control group. Key eligibility criteria: Epithelioid pleural mesothelioma; measurable disease per RECIST 1.1 modified for mesothelioma; ECOG PS 0-1; and adequate hematologic, renal, and liver function. Exclusions: Prior systemic anticancer treatment for pleural mesothelioma, diagnosis based solely on cytology or fine needle aspiration biopsy, contraindication to immunotherapy or conditions requiring immunosuppressive agents or corticosteroids. Participants are stratified at randomization for: age (18-70 years vs. $>$ 70), sex, planned control regimen (chemotherapy or ipi nivo), platinum (cisplatin vs. carboplatin) and geographic region (USA vs. ANZ). The primary endpoint is OS. Secondary endpoints include progression-free survival; objective tumor response; adverse events; health-related quality of life; and use of healthcare resources in ANZ. Tertiary objectives are to identify potential prognostic and/or predictive biomarkers (including those identified in prior phase 2 studies, PD-L1 expression, tumor mutation burden, genomic characteristics, and HLA subtypes), validation of radiological measures of response, and studies of possible radiomic biomarkers in mesothelioma. The study is active and enrolling in both ANZ and in the US. Clinical trial information: NCT04334759 and ACTRN12620001199909. Research Sponsor: AstraZeneca.

TPS8600 **Poster Session**

A randomised phase II trial of niraparib versus active symptom control in patients with previously treated mesothelioma: NERO.

Gareth Owen Griffiths, Daniel Griffiths, Zina Eminton, Kayleigh Hill, Charlotte Poile, Mavis Nye, Judith Cave, Sarah Danson, Elizabeth Toy, Pooja Jain, Nicola Steele, Paul Shaw, Paul Taylor, Peter Wojciech Szlosarek, Dionysis Papadatos-Pastos, Liz Darlison, Dean Anthony Fennell; Cancer Research UK Clinical Trials Unit, University of Southampton, Southampton, United Kingdom; University of Southampton, Southampton, United Kingdom; University of Leicester, Leicester, United Kingdom; c/o Southampton Clinical Trials Unit, University of Southampton, Southampton, United Kingdom; University Hospital Southampton, Southampton, United Kingdom; Weston Park Hospital, Sheffield, Sheffield, United Kingdom; Somerset NHS Foundation Trust, Taunton, United Kingdom; Leeds Cancer Centre, Leeds, United Kingdom; Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; Velindre Cancer Centre, Cardiff, United Kingdom; Wythenshawe Hospital, Manchester, United Kingdom; Barts Cancer Institute, London, United Kingdom; The Princess Alexandra Hospital NHS Trust, Harlow, United Kingdom; University Hospitals Leicester, Leicester, United Kingdom; University of Leicester and Leicester University Hospitals, Leicester, United Kingdom

Background: Malignant mesothelioma is a universally lethal cancer that has been increasing over the last three decades. No treatment has been licenced for patients with relapsed mesothelioma after receipt of licenced systemic anti-cancer therapy in the UK. A previous single-arm phase IIa trial (MiST1) evaluated the efficacy of Poly (ADP-ribose) polymerase (PARP) inhibition in mesothelioma, which met its primary endpoint with 15% of patients having durable responses exceeding 1 year. Therefore, there is a need to evaluate PARP inhibitors in a randomised trial in relapsed mesothelioma patients. NERO is currently in progress in this setting. **Methods:** Co-ordinated by the CRUK Southampton Clinical Trials Unit, NERO is a multicentre, two arm, open-label UK randomised phase II trial comparing niraparib + Active Symptom Control (ASC) versus ASC alone in mesothelioma patients who have relapsed after previously receiving platinum-based systemic therapy. NERO is not restricted by line of therapy and treatment allocation ratio is 2:1 (niraparib + ASC:ASC), stratified by histology and response to prior platinum-based therapy. Participants will receive either niraparib + ASC or ASC alone for a period of 24 weeks. Participants will be treated until disease progression, withdrawal, death or development of significant treatment limiting toxicity. Participants randomised to niraparib will receive 200/300 mg every day in a 21-day cycle. The primary endpoint is progression-free survival, where progression is determined by modified RECIST or RECIST 1.1; investigator reported progression; or death from any cause, whichever comes first. Time to event data will be analysed and presented using Kaplan-Meier curves according to the intention to treat principle, with treatment-related intercurrent events handled using the treatment strategy policy, and study withdrawal following the "while on study" strategy. A Cox proportional hazards model will be used to calculate the Hazard Ratio, 95% CIs and p-value adjusted for stratification factors. Median PFS and 6 and 12 month PFS will also be reported. Secondary endpoints include overall survival, best overall response, 12 and 24 week disease control, duration of response, treatment compliance and safety/tolerability. Patients consent to provide mandatory diagnostic tissue blocks, blood samples and an optional stool sample for translational research. These will be used to interrogate homologous recombination deficiency and its association with response in NERO, translational research comprising multi-omic analysis with multiplex immune landscape phenotyping will be analysed and correlated with clinical outcome using machine learning. NERO opened in July 2022 and will be run in approximately 10 UK secondary care hospitals with the aim of recruiting 84 evaluable patients (recruitment is currently 24 on 11-Jan-2023). Clinical trial information: NCT05455424. Research Sponsor: Asthma and Lung UK; GSK.

TPS8601 **Poster Session**

Nivolumab with chemotherapy in pleural mesothelioma after surgery: The NICITA trial.

Rajiv Shah, Laura V. Klotz, Daniel Christian Christoph, Karsten Schulmann, Hans-Georg Kopp, Niels Reinmuth, Michael Ried, Maike de Wit, Eva Lotte Buchmeier, Claas Wesseler, Martin Reck, Andre Bethge, Cornelius Waller, Petra Hoffknecht, Bjoern Hackanson, Marc A. Schneider, Rouven Behnisch, Petros Christopoulos, Martin E. Eichhorn, Michael Thomas; Department of Thoracic Oncology/Internal Medicine, Thoraxklinik, Heidelberg University Hospital and Translational Lung Research Center Heidelberg (TLRC), German Center for Lung Research (DZL), Heidelberg, Germany; Department of Thoracic Surgery, Thoraxklinik, Heidelberg University Hospital and Translational Lung Research Center Heidelberg (TLRC), German Center for Lung Research (DZL), Heidelberg, Germany; Department of Medical Oncology, Evang. Kliniken Essen-Mitte, Essen, Germany; Thorakale Onkologie und onkologische Palliativmedizin, Lungenkrebszentrum der Ruhr-Universität Bochum, Lungenklinik Hemer, Bochum, Germany; Robert Bosch Centrum für Tumorerkrankungen, Klinik Schillerhöhe, Stuttgart, Germany; Thoracic Oncology, Asklepios Clinics Munich-Gauting, Gauting, Germany; Department of Thoracic Surgery, University Medical Center Regensburg, Regensburg, Germany; Department of Hematology, Oncology and Palliative Care, Vivantes Klinikum Neukölln, Berlin, Germany; Lungenklinik, Kliniken der Stadt Köln gGmbH, Cologne, Germany; Lungenheilkunde und Thoraxzentrum, Asklepios Klinikum Harburg, Hamburg, Germany; Lungen Clinic Grosshansdorf, Airway Research Center North (ARCN), German Center of Lung Research (DZL), Grosshansdorf, Germany; Department of Pneumology, Clinic Bremen-Ost, Bremen, Germany; Department of Hematology, Oncology and Stem Cell Transplantation, University Medical Center Freiburg and Faculty of Medicine, University of Freiburg, Freiburg, Germany; Department of Thoracic Oncology, Franziskus-Hospital Harderberg, Georgsmarienhütte, Germany; Interdisciplinary cancer centers Augsburg, University Hospital Augsburg, Augsburg, Germany; Translational Research Unit, Thoraxklinik, Heidelberg University Hospital and Translational Lung Research Center Heidelberg (TLRC), German Center for Lung Research (DZL), Heidelberg, Germany; Institute for Medical Biometry, Heidelberg University, Heidelberg, Germany; Department of Thoracic Oncology, Thoraxklinik and National Center for Tumor Diseases at Heidelberg University Hospital, Heidelberg, Germany; Translational Lung Research Center Heidelberg (TLRC-H), Member of the German Center for Lung Research (DZL), Heidelberg, Germany

Background: Pleural mesothelioma (PM) is a highly aggressive cancer of the pleura, predominantly caused by prior asbestos exposure. Currently, there is no approved standard therapy for the treatment of early-stage PM. In most cases a multimodal therapy is recommended consisting of locoregional treatment by surgical cytoreduction via extended pleurectomy/decortication (eP/D), which, if feasible, can be combined with hyperthermic intrathoracic chemoperfusion (HITOC), together with inductive or adjuvant chemotherapy. Considering the immunogenic effects of chemotherapy on the tumor microenvironment, synergistic effects are expected when such a treatment is combined with immune checkpoint inhibitor therapy. In addition, interactions between immune infiltrates and mesothelioma cells play a role in the advent of PM, also implying a beneficial role for immunotherapy in this entity. This is also supported by recent clinical data that demonstrated beneficial effects of immune checkpoint inhibitors in patients with advanced PM. The NICITA trial is an investigator-initiated trial, investigating the combination of adjuvant chemotherapy with immune checkpoint inhibitor compared to chemotherapy alone in radically resected patients with early stage PM. **Methods:** The NICITA trial is a randomized, open-label, phase II clinical trial that is conducted in 14 centers across Germany. Eligible patients have been diagnosed with PM in tumor stages I-III (UICC 8th edition) and epithelioid subtype, and must have undergone cytoreductive surgery by eP/D with or without HITOC. Patients will be randomized 1:1 to receive either a combination of 4 cycles of pemetrexed/platinum-based adjuvant chemotherapy and nivolumab (480 mg q4w) followed by nivolumab maintenance therapy (12 cycles, 480 mg q4w) or 4 cycles of adjuvant chemotherapy only. Stratification will take place according to previous HITOC treatment (yes vs. no), ECOG status (0,1 vs. 2), and achievement of macroscopic complete resection (yes vs. no). The primary endpoint of this trial is time-to-next-treatment. Secondary endpoints include additional measures of efficacy (progression-free survival, overall survival, measures of treatment-beyond-progression) and quality of life, as well as the assessment of safety. Furthermore, a comprehensive longitudinal collection of biomarker samples, including tumor tissue, blood, and stool samples, for an accompanying translational research project is implemented in this clinical trial. Sample size justification: the recruitment of 46 patients to each arm with a low drop-out rate of 13% appears feasible resulting in 40 patients to be analyzed per arm. This sample size will permit a descriptive comparison and adequately describe the tested treatment options as deduced from the precision of the median TNT confidence interval estimate. As of February 2nd 2023, 85 of planned 92 patients have been enrolled into the NICITA trial. Clinical trial information: NCT04177953. Research Sponsor: Bristol Myers Squibb GmbH & Co.KGaA (BMS).

TPS8602 **Poster Session**

Neoadjuvant immunotherapy in sarcomatoid mesothelioma (Alliance A082101).

Aaron Scott Mansfield, Xiaofei F. Wang, Dennis A. Wigle, Colleen Watt, Gregory A. Masters, Kathryn Kelley, David E. Kozono, Tom Stinchcombe; Mayo Clinic, Rochester, MN; Duke University Medical Center, Durham, NC; Alliance for Clinical Trials in Oncology, Chicago, IL; Helen F. Graham Cancer Center and Research Institute, Newark, DE; Alliance Protocol Operations Office, Chicago, IL; Dana-Farber Cancer Institute, Boston, MA; Duke Cancer Institute, Durham, NC

Background: Sarcomatoid mesothelioma is the most aggressive form of pleural mesothelioma and is associated with the worst prognosis of the histologic variants of this disease. In the Checkmate 743 clinical trial the patients with sarcomatoid mesothelioma who received ipilimumab and nivolumab had survival outcomes that were similar to those of patients with epithelioid mesothelioma. In comparison, the patients with sarcomatoid mesothelioma who received chemotherapy had the worst outcomes in this trial, highlighting the known limited efficacy of chemotherapy against this histologic variant. Checkmate 743 demonstrated that ipilimumab and nivolumab is a new standard of care for non-epithelioid mesothelioma. Surgery typically has not been offered to this group of patients given their historically poor outcomes. With the significant survival gains seen patients with sarcomatoid mesothelioma treated with immunotherapy, we hypothesized that surgery may extend the benefits seen with immunotherapy. **Methods:** Alliance for Clinical Trials in Oncology A082101 is a prospective, phase 2 nonrandomized clinical trial for patients with sarcomatoid mesothelioma. The co-primary objectives are to determine the percentage of patients with potentially resectable sarcomatoid mesothelioma able to proceed with surgery after neoadjuvant ipilimumab and nivolumab, and the progression-free survival (PFS) at 12 months (12-month PFS). For sample size determination, we assumed that if the true rate of surgery is 75% or greater, it would indicate that neoadjuvant immunotherapy is feasible to be given prior to surgery. On the other hand, if the true rate of surgery is 50% or less it would indicate that neoadjuvant immunotherapy is not worthy of further investigation. Twenty-six (26) eligible patients will be needed to receive neoadjuvant immunotherapy. If 16 or fewer of the 26 eligible patients proceed to surgery, it will be concluded that the experimental therapy is not worthy of further investigation. Otherwise, it will be concluded that the experimental therapy is worthy of further investigation. Safety monitoring will be done through a 6-week run-in for the first 10 patients to assess for pre-operative and post-operative toxicities and complications. Sequential boundaries will be used to monitor severe toxicity and complication rates. Accrual will be halted if excessive numbers of severe toxicity and complications in pre-operative and post-operative phases are seen. Tumor and blood-based biomarkers will be included as exploratory biomarkers. Clinical trial information: NCT05647265. Research Sponsor: U.S. National Institutes of Health; Alliance.

TPS8603 **Poster Session**

Phase 2 randomized trial of neoadjuvant or palliative chemotherapy with or without immunotherapy for peritoneal mesothelioma (Alliance A092001).

Aaron Scott Mansfield, Austin Goodrich, Nathan R. Foster, Panos Savvides, Liza C Villaruz, Patrick M. Forde, Kanwal Pratap Singh Raghav, Paul Bernard Romesser, Diane Feldman, Liang Cao, Mary M. Salvatore, Anja C. Roden, Steven Francis Powell, Ardaman Shergill, Pamela N. Munster, Gary K. Schwartz, Travis Edward Grotz; Mayo Clinic, Rochester, MN; Alliance Statistics and Data Management Center, Mayo Clinic, Rochester, MN; Mayo Clinic Arizona, Phoenix, AZ; University of Pittsburgh Medical Center, Pittsburgh, PA; Johns Hopkins Medicine, The Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; The University of Texas MD Anderson Cancer Center, Houston, TX; Memorial Sloan Kettering Cancer Center, New York, NY; Alliance Protocol Operations Office, Chicago, IL; NCI, Bethesda, MD; Department of Radiology, Columbia University Irving Medical Center, New York, NY; Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN; Sanford Health, Sioux Falls, SD; Department of Medicine, Section of Hematology & Oncology, University of Chicago Medical Center, Chicago, IL; University of California, San Francisco, San Francisco, CA; Columbia University Irving Medical Center, New York, NY

Background: Peritoneal mesothelioma is a rare and poorly studied disease with few treatment options. For patients (pts) who are not surgical candidates, treatment recommendations for systemic therapy have been extrapolated from clinical trials for pleural mesothelioma that commonly exclude pts with peritoneal mesothelioma. Recently, the combination of the PD-1 inhibitor nivolumab and the CTLA-4 inhibitor ipilimumab received FDA-approval for the frontline treatment of non-resectable pleural mesothelioma. Additionally, a prospective, non-randomized phase 2 trial demonstrated activity with combined PD-L1 (atezolizumab) and VEGF (bevacizumab) blockade in peritoneal mesothelioma. In parallel, encouraging activity with combined chemo-immunotherapy has been reported in pleural mesothelioma. Given the benefits observed with immunotherapy, and the potential to improve upon those with chemotherapy and VEGF inhibition, we seek to determine whether the addition of the PD-L1 inhibitor atezolizumab improves outcomes with chemotherapy and bevacizumab in pts with newly diagnosed peritoneal mesothelioma. **Methods:** Alliance for Clinical Trials in Oncology A092001 is a prospective, randomized phase 2 clinical trial. All pts with newly diagnosed peritoneal mesothelioma will be randomized 1:1 using a dynamic allocation Pocock-Simon procedure to receive carboplatin, pemetrexed and bevacizumab, with or without atezolizumab, every 21 days for four cycles. Patients who are eligible to proceed with surgery after four cycles of therapy will then do so. Pts who are not eligible to proceed with surgery may receive maintenance bevacizumab and atezolizumab, or second-line atezolizumab with bevacizumab until progression of disease or toxicity. The primary objective is to determine if frontline treatment with carboplatin, pemetrexed, bevacizumab and atezolizumab results in a superior best response rate (RR) to carboplatin, pemetrexed and bevacizumab as determined by RECIST. With 31 eligible pts per arm (62 eligible total), this randomized design has 80% power to detect an improvement in the RR from 20% to 45%, with a 1-sided significance level of 0.10 where an interim futility analysis will be conducted after 32 pts are enrolled. Stratification factors include eligibility for cytoreductive surgery at diagnosis and histologic subtype. Secondary endpoints include progression-free survival, overall survival and adverse events. As integrated biomarkers, we will determine if soluble mesothelin-related peptides and megakaryocyte potentiating factor correlate with responses. This trial was recently approved by the National Cancer Institute Central IRB and is activating at sites across the country. Clinical trial information: NCT05001880. Research Sponsor: U.S. National Institutes of Health; Alliance.

TPS8604 **Poster Session**

NeoCOAST-2: A phase 2 study of neoadjuvant durvalumab plus novel immunotherapies (IO) and chemotherapy (CT) or MEDI5752 (volrustomig) plus CT, followed by surgery and adjuvant durvalumab plus novel IO or volrustomig alone in patients with resectable non-small-cell lung cancer (NSCLC).

Florian Guisier, Jaafar Bennouna, Alexander I. Spira, Dong-Wan Kim, Byoung Yong Shim, Houssein Abdul Sater, Italia Grenga, Swapnil S Parmar, Agata A. Bielska, Alula Yohannes, Raymond Mager, Oday Hamid, Lara McGrath, Yun He, Yee Soo-Hoo, Rakesh Kumar, Jonathan Spicer, Patrick M. Forde, Tina Cascone; Department of Pneumology, Rouen University Hospital, Rouen, France; Department of Medical Oncology, University Hospital of Nantes, Nantes, France; Virginia Cancer Specialists, Fairfax, VA; Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea; Department of Internal Medicine, St. Vincent's Hospital, The Catholic University of Korea, Gyeonggi-Do, Korea, Republic of (South); Department of Hematology and Medical Oncology, Cleveland Clinic, Cleveland, FL; AstraZeneca, Waltham, MA; AstraZeneca, Gaithersburg, MD; Department of Thoracic Surgery, McGill University, Montreal, QC, Canada; Bloomberg–Kimmel Institute for Cancer Immunotherapy, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD; Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Neoadjuvant platinum-based CT plus IO prolongs event-free survival (EFS) and increases pathological complete response (pCR) rate in patients with resectable NSCLC vs CT alone (Forde et al. N Engl J Med 2022). IO+IO+CT combinations have the potential to further improve pCR and survival outcomes. The phase 2 NeoCOAST-2 study (NCT05061550) is evaluating multiple neoadjuvant IO+IO+CT combinations in patients with resectable, early stage NSCLC. Novel IO molecules being evaluated include the anti-CD73 monoclonal antibody (mAb), oleclumab; the anti-NKG2A mAb, monalizumab; and the PD-1/CTLA-4 bispecific mAb, volrustomig. The latter recently demonstrated durable responses vs a PD-1 inhibitor plus CT as first-line treatment for patients with metastatic NSCLC (ESMO 2022; LBA56). Here we describe the NeoCOAST-2 study design. **Methods:** This randomized, open-label, multicenter study will enrol approximately 210 patients with previously untreated, histologically/cytologically confirmed, resectable Stage IIA–IIIB (AJCC 8th edition) NSCLC. Patients will be stratified by PD-L1 expression ($< 1\%$ vs $\geq 1\%$) and receive treatment with durvalumab + oleclumab + CT, durvalumab + monalizumab + CT, or volrustomig + CT every 3 weeks for 4 cycles prior to surgery, followed by adjuvant durvalumab + oleclumab, durvalumab + monalizumab, or volrustomig for up to 1 year or until disease progression per RECIST v1.1. Surgery should occur within 40 days after the last dose of neoadjuvant therapy and adjuvant therapy should commence within 10 weeks after surgery. The primary endpoints are pCR rate (per blinded independent pathologist review) and safety and tolerability. Secondary endpoints include investigator-assessed EFS, disease-free survival and overall survival, feasibility to surgery, major pathological response rate, objective response rate following neoadjuvant therapy, pharmacokinetics, immunogenicity, and changes in circulating tumor DNA. The study is currently recruiting patients across the US, Europe, Canada, and Asia. Clinical trial information: NCT05061550. Research Sponsor: AstraZeneca.

TPS8605 **Poster Session**

A phase I-III platform study evaluating the safety and efficacy of multiple therapies in patients with biomarker-defined locally advanced, unresectable stage III non–small-cell lung cancer (NSCLC).

Luis G. Paz-Ares, Carl Michael Gay, Caicun Zhou, Terufumi Kato, Luis Corrales, Karl Redhead, Ahmadur Rahman, Denise Bradley, Elizabeth Theogaraj, Katherine E. Hutchinson, Sarah M. Shagan, Benjamin J. Solomon; Hospital Universitario, 12 de Octubre, Universidad Complutense de Madrid, Madrid, Spain; Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Oncology, Shanghai Pulmonary Hospital, Shanghai, China; Kanagawa Cancer Center, Yokohama, Japan; Centro de Investigación y Manejo del Cáncer (CIMCA), San José, Costa Rica; Roche Products Ltd, Welwyn Garden City, United Kingdom; F. Hoffmann-La Roche Ltd, Basel, Switzerland; Genentech, Inc., South San Francisco, CA; Peter MacCallum Cancer Centre, Melbourne, Australia

Background: Durvalumab following chemoradiation (CRT) is a standard of care for unresectable stage III NSCLC, but there remains an unmet need for improved therapeutic options among patients with driver-mutated tumors that are unresponsive to immunotherapy. As targeting of specific driver mutations (e.g. *ALK*, *RET*, *ROS1*) has proven effective in the metastatic setting, it is hypothesized that outcomes could also be improved for patients with driver-mutated stage III NSCLC. **Methods:** BO42777 (NCT05170204) is a phase I–III platform study evaluating the safety and efficacy of multiple targeted therapies versus durvalumab following CRT in patients with locally advanced, unresectable stage III NSCLC. Biomarker eligibility is determined via local tissue testing or central testing within the BX43361 master screening study (NCT05419375). Biomarker-eligible patients are enrolled into the relevant cohort and randomized 1:1 to receive durvalumab or targeted therapy (alectinib [*ALK*+], entrectinib [*ROS1*+], or pralsetinib [*RET* fusion+]). New cohorts may be added in the future. Key inclusion criteria: locally advanced, unresectable stage III NSCLC, age $\geq$18 years, $\geq$2 prior cycles of concurrent or sequential CRT (cCRT or sCRT), and ECOG PS 0–2. Patients are stratified based on staging (IIIA vs IIIB or IIIC), CRT type (cCRT vs sCRT), and PD-L1 status (tumor cell score $<$ 1% vs $\geq$1% vs unknown) and will receive investigational treatment for three years or durvalumab for one year, until progression or maximum duration of treatment, unacceptable toxicity, consent withdrawal, or death. Primary endpoint: progression-free survival (RECIST v1.1) by blinded independent central review. Key secondary endpoints: distant metastasis-free survival, time to CNS progression, objective response rate, duration of response, overall survival, and safety (adverse events). Time to confirmed deterioration and patient-reported outcomes will be assessed through questionnaires. Tumor response will be assessed by CT/MRI imaging at regular intervals. Enrolment is ongoing (target of 320 patients) across 200 sites in 11 countries. As of 7 February 2023, five patients have been randomized. This trial in progress was previously presented at ELCC, Luis Paz-Ares *et al.* (#744), and reused with permission. Clinical trial information: NCT05170204. Research Sponsor: These trials are sponsored by F. Hoffmann-La Roche Ltd.

TPS8606 **Poster Session**

A randomized, double blinded, multicenter phase 3 study of platinum-based chemotherapy with or without QL1706 as adjuvant therapy in completely resected stage II-IIIb NSCLC.

Yuming Zhu, Tao Jiang, Lianghua Fang, Tao Zhang, Xiaoyan Kang, Caicun Zhou; Department of Medical Oncology,Shanghai Pulmonary Hospital, Shanghai, China; Department of Thoracic Surgery, The Second Hospital Affiliated to Air Force Medical University, Xi'an, Shannxi, China; Medicine Department, Qilu Pharmaceutical Co., Ltd., Jinan, China; Statistics and Statistical Programming Department, Qilu Pharmaceutical Co., Ltd., Jinan, China; Department of Medical Oncology, Shanghai Pulmonary Hospital, Shanghai, China

Background: Adjuvant atezolizumab is approved for PD-L1 positive stage II-IIIA NSCLC in USA and China. To date, there are few clinical studies on dual immune checkpoint inhibitors in adjuvant settings of NSCLC. QL1706, a MabPair product, is a novel bifunctional antibody containing a mixture of anti-PD-1 IgG4 and anti-CTLA-4 IgG1 antibodies. QL1706 monotherapy has demonstrated good safety and promising antitumor activity in advanced solid tumors in a phase Ia/Ib study with 518 patients, including 146 NSCLC patients. Meanwhile, in NSCLC patients with negative oncogene drivers, QL1706 plus 2 cycles of chemotherapy as first line treatment resulted in an ORR of 58.6% (17/29) and the mPFS was 6.97 months. Furthermore, in the *EGFR* mutant NSCLC patients who previously were treated with EGFR-TKI, QL1706 plus platinum-based chemotherapy and bevacizumab showed promising efficacy with an ORR of 64.5% (20/31). This study is designed to investigate the efficacy and safety of QL1706 or placebo plus platinum doublet chemotherapy as adjuvant treatment in stage II-IIIB NSCLC. **Methods:** In this phase **III**, randomized, double-blind, placebo-controlled, multicenter study, 632 eligible pts, who is completely resected stage **II-III$_B$** NSCLC (AJCC 8th) with negative *EGFR, ALK* etc, will be enrolled. Pts will be randomized 1:1 to receive QL1706 (5 mg/kg) or placebo plus chemotherapy, administered every 3 weeks (Q3W). The regimen of vinorelbine/paclitaxel plus cisplatin/carboplatin is chosen for squamous NSCLC, while pemetrexed/vinorelbine plus cisplatin/carboplatin for non-squamous NSCLC. Randomization will be stratified by PD-L1 TPS (ie, $< 1\%$, $\geq 1\%$), disease stage (stage II, III) and predominant tumor histology (ie, squamous vs non-squamous). The primary endpoint is disease-free survival (DFS) per investigators in PD-L1 TPS $\geq 1\%$ pts and in all randomized pts, which will be tested hierarchically. An interim analysis is to occur when about 70% DFS events achieved in pts with PD-L1$\geq 1\%$. Enrollment began in Nov, 2022. ClinicalTrials.gov NCT05487391. Clinical trial information: NCT05487391. Research Sponsor: Qilu Pharmaceutical Co., Ltd.

TPS8607 **Poster Session**

Phase 3 study of durvalumab with SBRT for unresected stage I/II, lymph-node negative NSCLC (PACIFIC-4/RTOG3515).

Clifford Grant Robinson, Ligang Xing, Hiroshi Tanaka, Sadatomo Tasaka, Shahed N Badiyan, Haitam Nasrallah, Tithi Biswas, Mikhail Shtivelband, Wolfgang Schuette, Anhui Shi, Adriana Hepner, Karen Barrett, James R. Rigas, Haiyi Jiang, Steven H. Lin; Department of Radiation Oncology, Washington University in St. Louis/Siteman Cancer Center, St. Louis, MO; Department of Radiation Oncology, Shandong Cancer Hospital, Shandong First Medical University, Jinan, China; Niigata Cancer Center Hospital, Niigata, Japan; Hirosaki University School of Medicine and Hospital, Hirosaki, Japan; Rambam Health Care Campus, Haifa, Israel; Department of Radiation Oncology, University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, OH; Ironwood Cancer and Research Centers, Chandler, AZ; Städtisches Krankenhaus Martha-Maria Halle-Dölau gGmbH, Halle, Germany; Beijing Cancer Hospital, Beijing, China; AstraZeneca, Gaithersburg, MD; AstraZeneca, Cambridge, United Kingdom; Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Stereotactic body radiation therapy (SBRT) is a standard treatment for patients with unresectable (UR) stage I/II, lymph-node negative NSCLC, with excellent safety and high rates of primary tumor control. Despite predominant regional and distant failure that increases with tumor size, no adjuvant therapy is approved for these patients. Durvalumab is a selective, high-affinity, human IgG1 monoclonal antibody that blocks PD-L1 binding to PD-1/CD80. In the placebo-controlled, phase 3 PACIFIC trial of patients with stage III UR-NSCLC without disease progression on/after concurrent chemoradiotherapy, durvalumab improved progression-free survival (PFS) and overall survival (OS) with manageable safety (Antonia, et al. 2017; 2018), leading to its approval in stage III UR-NSCLC. Osimertinib is a 3rd-generation, irreversible CNS-active EGFR tyrosine kinase inhibitor that selectively inhibits NSCLC tumors with EGFR-sensitizing mutations (EGFRm). In the recent placebo-controlled, phase 3 ADAURA trial, osimertinib demonstrated statistically significant and clinically meaningful improvement in disease-free survival (DFS) (HR, 0.20 [99.12% CI, 0.14–0.30], $P < 0.001$) in patients with resected stage IB-IIIA EGFRm NSCLC (Wu, et al. 2020), leading to its approval in an adjuvant setting. Based on data for durvalumab and osimertinib in the early-stage setting, PACIFIC-4 is designed to assess the efficacy and safety of durvalumab combined with SBRT in patients with stage I/II UR-NSCLC and osimertinib after SBRT in patients with stage I/II EGFRm UR-NSCLC. **Methods:** PACIFIC-4 (NCT03833154) is an international, phase 3 study with two independent cohorts. Eligible patients are $\geq$18 years of age with stage T1-T3, N0, M0 unresected NSCLC and ECOG PS 0–2. The main cohort of approximately 630 patients will be randomized (1:1) in a double-blind manner, stratified by tumor size and location, to receive durvalumab (1500 mg IV) or placebo every 4 weeks for up to 26 cycles with concurrent standard of care (SoC) SBRT. The primary endpoint in this cohort is PFS (RECIST v1.1) by blinded independent central review; other endpoints include OS, health-related quality of life, and safety. The protocol was amended (v4) to exclude patients with an identified EGFRm from the main cohort and add a separate cohort of approximately 60 patients with EGFRm (L858R or Ex19del) who will receive osimertinib 80 mg PO QD, following SoC SBRT, for up to 36 months. The primary endpoint in this cohort is 4-year PFS (RECIST v1.1) by independent central review; secondary endpoints include PFS, OS, and safety. Trial recruitment is ongoing. *Previously presented at the European Lung Cancer Congress (ELCC) 2022, FPN (Final Publication Number): 122TiP, Clifford Robinson et al. – Reused with permission.* Clinical trial information: NCT03833154. Research Sponsor: AstraZeneca.

TPS8608 **Poster Session**

A master screening study to determine biomarker status and trial eligibility for patients with malignant tumors.

Benjamin J. Solomon, Ahmadur Rahman, Denise Bradley, Elizabeth Theogaraj, Andrés Cardona, Sarah M. Shagan, Venice Rosalie Archer, Luis Corrales; Peter MacCallum Cancer Centre, Melbourne, Australia; Roche Products Ltd, Welwyn Garden City, United Kingdom; F. Hoffmann-La Roche Ltd, Basel, Switzerland; Genentech, Inc., South San Francisco, CA; F. Hoffmann-La Roche Ltd, Welwyn Garden City, United Kingdom; Centro de Investigación y Manejo del Cáncer (CIMCA), San José, Costa Rica

Background: Targeting of oncogenic driver alterations has proven to be an effective clinical approach across many tumor types. As a result of the approval of targeted therapies against oncogenic driver alterations, molecular biomarker testing is commonly recommended for patients with advanced/metastatic non-small cell lung cancer (NSCLC) before initiation of first-line treatment. Although there are emerging clinical trial data using targeted therapies in patients with early-stage NSCLC, currently molecular biomarker testing is not universally performed as part of routine clinical practice in the early-stage setting. Screening platforms can be utilized to provide comprehensive, validated biomarker testing to facilitate access to clinical trials for appropriate investigational therapies, based on biomarker status. This type of approach aims to be more efficient and to streamline patient recruitment and improve patient access to clinical trials where biomarker testing is not currently performed as part of routine care, especially when the biomarkers of interest are at low prevalence. **Methods:** This global, non-Investigational Medicinal Product (non-IMP), multicenter master screening study (NCT05419375) provides centralized tissue-based testing to determine patients' biomarker eligibility for linked Roche clinical trials. Currently this study is only open to screening patients for a linked platform study in unresectable stage III NSCLC (NCT05170204). However, it is envisaged that this screening study will be expanded to support additional clinical trials and indications in the future. Eligible patients must be aged ≥18 years with locally advanced, unresectable stage III NSCLC (according to AJCC 8th edition), an ECOG PS of 0–2, confirmed availability of a formalin-fixed paraffin-embedded tumor specimen obtained prior to chemoradiation, and adequate hematologic and end-organ function. If a patient is found to have an oncogenic driver mutation and is considered a good candidate for a linked clinical trial, the investigator may propose that they be screened into the respective study. Tumor tissue samples will be centrally tested by validated molecular tests for the presence of specific genetic alterations: *EGFR*, *ALK*, *ROS1*, *KRAS*, *BRAF*, *HER2*, *RET*, *MET*, and *NTRK1*/2/3. Immunohistochemistry may also be performed to determine PD-L1 expression as required by the linked trial eligibility criteria. The primary objective of this screening trial is to determine the biomarker status of patients and their eligibility to participate in a linked clinical trial. Exploratory objectives include characterization of biomarker profiles and patients' subsequent treatment. No therapeutic intervention will be administered in this study. Enrolment is ongoing across 51 sites in ten countries, with a target enrolment of 15,000 patients. As of 9 February 2023, 27 patients have been enrolled. Clinical trial information: NCT05419375. Research Sponsor: This study is sponsored by F. Hoffmann-La Roche Ltd. Third-party medical writing assistance, under the direction of the authors, was provided by Vanessa Poon, BSc of Ashfield MedComms, an Inizio company, and was funded by F. Hoffmann-La Roche Ltd.

TPS8609 **Poster Session**

Phase 3 trial of durvalumab combined with domvanalimab following concurrent chemoradiotherapy (cCRT) in patients with unresectable stage III NSCLC (PACIFIC-8).

Mustafa Özgüroğlu, Benjamin Philip Levy, Hidehito Horinouchi, Jinming Yu, Ellie Grainger, Patrick Hoang Phuong, Daniel Peterson, Michael David Newton, Alexander I. Spira; Istanbul University—Cerrahpaşa, Cerrahpaşa School of Medicine, Istanbul, Turkey; Johns Hopkins Sidney Kimmel Cancer Center at Sibley Memorial Hospital, Washington, DC; Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan; Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Science, Jinan, China; AstraZeneca, Cambridge, United Kingdom; Arcus Biosciences, Hayward, CA; AstraZeneca, Waltham, MA; AstraZeneca, Gaithersburg, MD; Virginia Cancer Specialists, Fairfax, VA

Background: The PACIFIC trial (NCT02125461) established up to 12 months of consolidation therapy with durvalumab as standard of care (SoC) for patients with unresectable stage III non-small-cell lung cancer (NSCLC) and no disease progression after platinum-based cCRT. To improve outcomes further in this population, novel immunotherapy combinations that build on the backbone of PD-L1 inhibition with durvalumab are being explored. Domvanalimab (AB154) is a Fc-silent humanized IgG1 monoclonal antibody that blocks interaction of the T cell immunoreceptor with Ig and ITIM domains (TIGIT; upregulated by immune cells) with CD112 and CD155 (expressed by tumor and antigen-presenting cells), reducing inhibition of T cells and natural killer cells and, thereby, promoting antitumor activity. The combination of TIGIT inhibition with PD-(L)1 inhibition has shown encouraging activity in phase 1 and 2 trials in metastatic NSCLC, with enriched benefit observed among patients with PD-L1 positive tumors (Rodriguez-Abreu, et al. 2020; Niu, et al. 2020). In ARC-7 (NCT04262856), a randomized, phase 2 trial, the combination of domvanalimab and PD-1 inhibition was associated with improvement in progression-free survival (PFS) versus PD-1 inhibition alone (HR, 0.55; 95% CI, 0.31–1.0) in treatment-naïve patients with metastatic NSCLC and high PD-L1 expression (tumor proportion score ≥50%) (Johnson, et al. 2022). PACIFIC-8 (NCT05211895) is assessing the efficacy and safety of durvalumab combined with domvanalimab as consolidation therapy in patients with PD-L1 positive, unresectable stage III NSCLC and no disease progression after platinum-based cCRT. **Methods:** PACIFIC-8 is a phase 3, double-blind, placebo-controlled, randomized, global trial. Eligible patients (aged ≥18 years) must have PD-L1 positive, unresectable stage III NSCLC (tumor cell [TC] expression ≥1% by central lab; VENTANA SP263 IHC assay), WHO performance status 0/1, documented EGFR/ALK wild-type tumor status, and not have progressed following definitive, platinum-based cCRT (≥2 cycles). Approximately 860 patients will be randomized (1:1) to receive SoC durvalumab (1500 mg IV) combined with either domvanalimab (20 mg/kg IV) or placebo, every 4 weeks for up to 12 months. The primary endpoint is PFS (RECIST v1.1) by blinded independent central review (BICR) in patients with PD-L1 TC ≥50%. Secondary endpoints include PFS (RECIST v1.1; BICR) in patients with PD-L1 TC ≥1%, overall survival, objective response rate and duration of response (RECIST v1.1; BICR), safety/tolerability, and patient-reported outcomes. Trial enrollment is ongoing. *Previously presented at the European Society for Medical Oncology (ESMO) Congress 2022, FPN (Final Publication Number): 971TiP, Mustafa Özgüroğlu et al. – Reused with permission.* Clinical trial information: NCT05211895. Research Sponsor: AstraZeneca.

TPS8610 **Poster Session**

Phase 3 study of durvalumab combined with oleclumab or monalizumab in patients with unresectable stage III NSCLC (PACIFIC-9).

Fabrice Barlesi, Sarah B. Goldberg, Helen Mann, Aarthi Gopinathan, Michael David Newton, Charu Aggarwal; Gustave Roussy and Paris Saclay University, Faculty of Medicine, Villejuif / Kremlin-Bicêtre, France; Yale Cancer Center, Yale School of Medicine, New Haven, CT; AstraZeneca, Cambridge, United Kingdom; AstraZeneca, Gaithersburg, MD; Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA

Background: Based on the findings of the phase 3 PACIFIC trial, durvalumab as consolidation therapy is the standard of care for patients with unresectable Stage III NSCLC and no disease progression following chemoradiotherapy (CRT; the PACIFIC regimen). However, further improvements in outcomes are needed for this population and, to build upon the backbone of PD-L1 inhibition with durvalumab, immunotherapy combinations including anti-TIGIT, anti-CD73, and anti-NKG2a monoclonal antibodies (mAbs) are now being explored. Two potential candidates, oleclumab and monalizumab, have demonstrated encouraging clinical activity in a randomized, phase 2 trial when combined with durvalumab in this setting. Oleclumab (MEDI9447) is a human IgG1λ mAb that inhibits the function of CD73, to reduce extracellular adenosine production and thus promote antitumor immunity. Monalizumab (IPH2201) is a first-in-class, humanized, IgG4 mAb that prevents NKG2A from binding to HLA-E, which reduces inhibition of natural killer and CD8+ T cells. The combination of each of these molecules with durvalumab consolidation therapy was evaluated in the phase 2 COAST study (NCT03822351). In COAST (n = 189), patients receiving combination therapy reported numerically higher objective response rates (durvalumab plus oleclumab: 30.0%; durvalumab plus monalizumab: 35.5%; durvalumab monotherapy: 17.9%) and prolonged progression-free survival versus durvalumab alone, with no new/significant safety signals (Herbst, et al. 2022). Thus, the combination of oleclumab or monalizumab with consolidative durvalumab warrants further evaluation in a phase 3 trial. **Methods:** PACIFIC-9 (NCT05221840) is a phase 3, double-blind, placebo-controlled, randomized, international trial. Eligible patients (age ≥18 years) must have EGFR/ALK wild-type unresectable Stage III NSCLC, a WHO performance status of 0/1, documented PD-L1 status, and must not have progressed following ≥2 cycles of definitive, platinum-based concurrent CRT. Approximately 999 patients will be randomized (1:1:1) to receive up to 12 months of treatment (in 28-day cycles) with durvalumab plus either oleclumab (Arm A); monalizumab (Arm B); or placebo (Arm C). The primary endpoint is progression-free survival (RECIST v1.1) by blinded independent central review (BICR). Overall survival is a key secondary endpoint. Other secondary endpoints include objective response rate and duration of response (RECIST v1.1; BICR), patient-reported outcomes, PD-L1 expression on tumor cells relative to efficacy outcomes, and safety/tolerability (CTCAE v5.0). Trial enrollment is ongoing. *Previously presented at the World Conference on Lung Cancer (WCLC) 2022, FPN (Final Publication Number): P1.10-01, Fabrice Barlesi et al.* Clinical trial information: NCT05221840. Research Sponsor: AstraZeneca.

TPS8611 **Poster Session**

Randomized phase 3 study of tarlatamab, a DLL3-targeting bispecific T-cell engager (BiTE), compared to standard of care in patients with relapsed small cell lung cancer (DeLLphi-304).

Luis G. Paz-Ares, Enriqueta Felip, Myung-Ju Ahn, Fiona Helen Blackhall, Hossein Borghaei, Byoung Chul Cho, Melissa Lynne Johnson, Suresh S. Ramalingam, Martin Reck, Alicia Zhang, Chia-Hsin Ju, Mukul Minocha, Sujoy Mukherjee, Gaurav Suri, Danielle Jandial, D Gwyn Bebb; Hospital Universitario 12 de Octubre, CNIO-H120 Lung Cancer Unit, Ciberonc and Universidad Complutense, Madrid, Spain; Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of (South); The Christie NHS Foundation Trust, Division of Cancer Sciences, Manchester, United Kingdom; Fox Chase Cancer Center, Philadelphia, PA; Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Korea, Republic of (South); Sarah Cannon Research Institute, Tennessee Oncology, Nashville, TN; Winship Cancer Institute, Emory University Hospital, Atlanta, GA; LungenClinic, Airway Research Center North, German Center for Lung Research, Grosshansdorf, Germany; Amgen Inc., Thousand Oaks, CA; Amgen Limited, Uxbridge, United Kingdom

Background: Small cell lung cancer (SCLC) is an aggressive malignancy for which very few patients achieve long term disease control; response to most treatments is transient and second line treatment options are limited. Delta-like ligand 3 (DLL3) is a Notch ligand aberrantly expressed on the surface of up to 85% of SCLC cells and minimally expressed in normal tissues, making it an attractive therapeutic target. Tarlatamab is a bispecific T cell engager (BiTE) molecule designed to bind DLL3 on target cancer cells and CD3 on T cells, thereby driving T cell-dependent killing of tumor cells. Results from the first-in-human study in patients with relapsed/refractory SCLC (DeLLphi-300; NCT03319940) demonstrate tarlatamab efficacy in pretreated patients with confirmed responses in 23% of patients and median duration of response $>$ 12 months.[1] Median overall survival (OS) was 13.2 months. Grade $\geq$ 3 treatment-related AEs (TRAEs) occurred in 31% of patients and TRAEs resulted in discontinuation in 4% of patients. This promising efficacy/safety profile is being evaluated further in a phase 2, open-label study in patients with relapsed/refractory SCLC after $\geq$2 lines of prior treatment (DeLLphi-301; NCT05060016). **Methods:** NCT05740566 is a randomized, open-label, phase 3 study of tarlatamab compared with standard of care (SOC) in ~700 patients with relapsed SCLC after platinum-based first-line chemotherapy. Patients will be randomized 1:1 to receive tarlatamab or SOC therapy (lurbinectedin or topotecan in US, Canada, Australia, Singapore, Korea; amrubicin in Japan; topotecan in all countries except Japan), stratified by prior anti-programmed cell death 1 (PD-1) or anti-programmed cell death ligand 1 (PD-L1) exposure, chemotherapy-free interval, presence of brain metastases, and SOC (topotecan/amrubicin vs lurbinectedin). The primary objective is to compare the efficacy of tarlatamab with SOC on prolonging OS. Key secondary endpoints include comparison of progression free survival (PFS) based on investigator assessment per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) and patient-reported outcomes (PRO) including disease-related symptoms, physical function, and global health status of quality of life. Key eligibility criteria include adults with histologically or cytologically confirmed relapsed SCLC who progressed following 1 platinum-based regimen. Patients must have measurable lesions as defined per RECIST 1.1 within the 21-day screening period and must have adequate organ function. Exclusions include untreated or symptomatic central nervous system metastases, history of immune checkpoint inhibitor use resulting in severe immune-mediated adverse event, and previous history of NSCLC. Enrollment is ongoing. References 1. Paz-Ares L, et al. *J Clin Oncol*. DOI:1200/JCO.22.02823. Clinical trial information: NCT05740566. Research Sponsor: Amgen.

TPS8612 **Poster Session**

A phase II study to evaluate the efficacy and safety of combination therapy of durvalumab (MEDI4736) and amrubicin in patients with recurrent small cell lung cancer (SCLC): Aphrodite trial, in progress.

Yuka Kato, Kadoaki Ohashi, Toshiyuki Kozuki, Shoichi Kuyama, Kakuhiro Yamaguchi, Toshihide Yokoyama, Hideki Uno, Michihiro Yoshida, Noboru Hattori, Katsuyuki Hotta, Katsuyuki Kiura; Department of Thoracic oncology and Medicine, National Hospital Organization Shikoku Cancer Center, Matsuyama-City, Ehime, Japan; Department of Allergy and Respiratory Medicine (Thoracic Oncology), Okayama University Hospital, Okayama, Japan; Department of Thoracic Oncology and Medicine, National Hospital Organization Shikoku Cancer Center, Matsuyama, Japan; Department of Respiratory Medicine, National Hospital Organization Iwakuni Clinical Center, Iwakuni City, Yamaguchi, Japan; Department of Respiratory Medicine, Hiroshima University Hospital, Hiroshima, Japan; Department of Respiratory Medicine, Kurashiki Central Hospital, Kurashiki, Japan; Center for Innovative Clinical Medicine, Okayama University Hospital, Okayama, Japan; Department of Allergy and Respiratory Medicine (Thoracic Oncology), Okayama university hospital, Okayama-Shi Kita-Ku, Japan

Background: Immunochemotherapy (ICT) is the standard first-line treatment for extensive stage (ES)-SCLC. However, progression-free survival for patients (pts) treated with ICT as first-line therapy is approximately 5 months, and half of the pts will relapse within 6 months. Several drugs have been approved for the treatment after relapse, and amrubicin has been used as a second-line treatment in Japan for 20 years. However, the efficacy of pts treated with amrubicin is unsatisfactory, the median survival was 9.2 months (pts with sensitive relapse (SR-pts)) and 2.6 months (pts with refractory relapse (RR-pts)), indicating an urgent need for new therapeutic strategies in the treatment of post-relapse SCLC pts. A retrospective study showed significant improvement in survival for patients who progress on immunochemotherapy, treated with same ICI plus chemotherapy as second-line therapy (Trans Lung Cancer Rec. 2020). Cytotoxic chemotherapy introduced immunogenic cell death and the addition of chemotherapy to ICI might have a synergistic effect. Based on these assumptions, the combination of amrubicin with ICI may provide additional benefit for post-progression pts and we are therefore initiating this study. **Methods:** This is an open-label, single-arm, multicenter, physician-initiated Phase 2 study of amrubicin plus durvalumab in Japanese pts with relapsed SCLC. The study is divided into a lead-in cohort (LIC) and a Phase 2 part; the LIC will use a 3+3 design to ensure safety and will proceed to the Phase 2 part if the first 3 pts have no dose limiting toxicity (DLT) or the first 6 pts have only 1 DLT. Eligibility criteria include pts with ES-SCLC who relapse after platinum-containing chemotherapy with durvalumab as first-line therapy, age ≥20, ECOG 0-1. The primary endpoint is 1-year survival. Patients were treated with intravenous amrubicin 40 mg/m2 on day 1-3 and durvalumab 1500 mg/body on day 1 every 3 weeks until PD or unacceptable toxicity. The planned number of pts was 18 each with sensitive relapse (SR-pts) and refractory relapse (RR-pts) which was calculated based on the results of a previous randomized controlled trial (J Clin Oncol. 2008). In this trial, the point estimates and two-sided 90% confidence intervals (Clopper Peason method) for 1-year survival corresponding to the expected 1-year survival were: SR-pts (11/18 patients): 0.611 (90% CI: 0.392-0.801), RR-pts (8/18 0.444 (90% CI: 0.244-0.659). Enrollment began in October 2022, and will be completed by March 2025. Clinical trial information: jRCT2061220036. Research Sponsor: AstraZeneca.

TPS8613 **Poster Session**

A phase III study of lurbinectedin alone or in combination with irinotecan vs investigator's choice (topotecan or irinotecan) in patients with relapsed small cell lung cancer (SCLC; LAGOON trial).

Benjamin Besse, Luis G. Paz-Ares, Solange Peters, Federico Cappuzzo, Martin Reck, Antonio Calles, Raffaele Califano, Jose Antonio Lopez-Vilariño, Susie Veramendi, Carmen Maria Kahatt, Ali Hassan Zeaiter, Jacob Sands; Institut Gustave Roussy, Villejuif, France; Hospital Universitario 12 De Octubre, Madrid, Spain; CHUV University Hospital of Lausanne, Lausanne, Switzerland; Istituto Nazionale Tumori "Regina Elena", Roma, Italy; Lungen Clinic, Grosshansdorf, Germany; Hospital General Universitario Gregorio Marañon, Madrid, MA, Spain; The Christie NHS Foundation Trust and Division of Cancer Sciences, The University of Manchester, Manchester, United Kingdom; PharmaMar, Colmenar Viejo, Spain; Dana-Farber Cancer Institute, Boston, MA

Background: Lurbinectedin is a novel synthetic chemical entity that acts as an inhibitor of oncogenic transcription and is active in tumors addicted to transcription. A phase II Basket trial (NCT02454972) in patients with small cell lung cancer (SCLC) treated with lurbinectedin in the second-line setting showed overall response rate (ORR) of 35.2% and median duration of response (DoR) of 5.3 months, with durable responses (43.0% $\geq$ 6 months). Based on these results, lurbinectedin was granted accelerated approval by the US FDA. An ongoing phase I/II trial (NCT02611024) is evaluating the lurbinectedin/irinotecan combination. Preliminary results showed ORR of 62% and median DoR of 5.7 months (2020 World Conference on Lung Cancer) warranting expansion to 100 patients. These results have supported the conduction of a phase III trial (LAGOON - NCT05153239). **Methods:** LAGOON is a randomized phase III clinical trial evaluating two experimental arms (lurbinectedin alone, 3.2 mg/m^2 D1 q3wk, or lurbinectedin 2 mg/m^2 D1 plus irinotecan D1, D8 q3wk) *versus* Investigator's Choice (topotecan D1-5 q3wk or irinotecan D1 q3wk according to label) as control arm in relapsed SCLC patients. Approximately 705 patients will be enrolled. Central randomization will be implemented (1:1:1 ratio). Stratification will be done according to chemotherapy-free interval (CTFI) after first line (sensitive *vs.* resistant); prior anti-PD-(L)1; baseline central nervous system (CNS) involvement; lactate dehydrogenase value, and Investigator's preference for the Control Arm. Main inclusion criteria include age $\geq$ 18 years, confirmed SCLC diagnosis, one prior line of platinum-containing chemotherapy with/without anti-PD-(L)1, and CTFI $\geq$ 30 days. Patients with CNS metastases can participate if pretreated and radiologically stable for at least 4 weeks. Main exclusion criteria include platinum-naïve patients, patients pretreated with more than one prior chemotherapy regimen (including platinum re-challenge), and prior treatment with lurbinectedin, trabectedin, PM14, or topoisomerase I inhibitors. An Independent Data Monitoring Committee will oversee the conduct of the study. An Independent Review Committee will provide the patient's response at each tumor assessment endpoint to determine the best patient's response and the date of objective response or progression/censoring according to RECIST v.1.1. Clinical trial information: NCT05153239. Research Sponsor: PharmaMar.

TPS8614 **Poster Session**

Prophylactic cerebral irradiation or active brain magnetic resonance imaging surveillance in small-cell lung cancer patients (EORTC-1901: PRIMALung).

Antonin Levy, Thierry Berghmans, Nicolaus Andratschke, Giulia Leonetti, Michael Koller, Corinne Faivre-Finn, EORTC Lung Cancer Group; Gustave Roussy, Villejuif, France; Jules Bordet Institute, Hôpitaux Universitaires de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium; Department of Radiation Oncology, University Hospital Zurich, Zurich, Switzerland; EORTC, Brussels, Belgium; Center for Clinical Studies, University Hospital Regensburg, Regensburg, Germany; Christie Hospital, Withington Manchester, United Kingdom

Background: PRIMALung is an EORTC-sponsored study. Primary objective is to show that overall survival with brain MRI surveillance alone is non-inferior to brain MRI surveillance combined with PCI in patients with SCLC. PCI is currently SOC in most institutions, but can be associated with neurocognitive toxicity and impact quality of life. 600 patients will be recruited from 50 EORTC centres in 10 countries. This study is currently recruiting and will play an important role in clarifying whether MRI surveillance is a viable strategy in SCLC. Furthermore, it will answer important questions about the role of PCI in the era of immunotherapy, particularly in ES-SCLC. **Methods:** Key eligibility: ECOG performance status $\leq$ 2 patients with SCLC (Limited or Extensive-Stage, stage I-IV) who did not progress after ($\leq$ 16 weeks from day 1 of last cycle of chemotherapy to randomisation) completed standard therapy. Absence of progression, brain metastases or leptomeningeal disease after completing therapy. Trial Interventions: Patients will be randomised 1:1 to receive brain MRI surveillance with or without PCI (25Gy in 10 fractions). Primary objective - to show that overall survival with brain MRI surveillance alone is non-inferior to brain MRI surveillance combined with PCI. Secondary objectives - cognitive failure-free survival, quality of life and acute/late toxicities according to CTCAE v5.0. The trial was open to recruitment on 27/10/2022. Three countries open to date (Belgium, Switzerland, UK). Further sites in France, Poland and Austria will be open to recruitment Q1 2023. The first patient has been randomized on the 4th of January 2023. Further information: https://clinicaltrials.gov/ct2/show/NCT04790253 contact: 1901@EORTC.org. Clinical trial information: NCT04790253. Research Sponsor: Astra Zeneca; EORTC LCG, PHRC-K (France), Ligue contre le Cancer (France), CE (Belgium), Swiss Cancer League (Switzerland).

TPS8615 **Poster Session**

Dares: A phase II trial of durvalumab and ablative radiation in extensive stage small cell lung cancer.

Aditya Juloori, Gregory Gan, Jun Zhang, Mohamed E. Abazeed, Jared H Hara, Andrew Baschnagel, Anne M. Traynor, Michael F. Bassetti, Marina Chiara Garassino, Jyoti D. Patel, Steven J. Chmura, Christine M. Bestvina; University of Chicago Medical Center, Chicago, IL; University of Kansas Medical Center, Kansas City, KS; University of Kansas Medical Center (KUMC), Westwood, KS; Northwestern University, Chicago, IL; University of Chicago, Chicago, IL; Department of Human Oncology, Madison, WI; University of Wisconsin-Madison Carbone Cancer Center, Madison, WI; University of Wisconsin Carbone Cancer Center, Madison, WI; Department of Medicine, Section of Hematology/Oncology, Knapp Center for Biomedical Discovery, The University of Chicago, Chicago, IL; Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL

Background: Most patients diagnosed with small cell lung cancer have extensive stage disease (ES-SCLC) at presentation, portending a poor prognosis with median survival rate of 9 - 11 months and a 2-year overall survival (OS) of less than 5%. Checkpoint inhibitors have recently transformed the landscape for first-line treatment for ES-SCLC patients with the CASPIAN and IMpower133 trials demonstrating an OS benefit with the addition of Durvalumab and Atezolizumab to chemotherapy, respectively. Hypofractionated ablative radiation therapy (RT) provides effective local metastasis control. Increasing evidence suggests that apart from its direct effects, ablative RT can trigger the innate and adaptive immune system. Beyond synergistic mechanisms of modulating the immune response, direct tumor debulking by radiation may also be particularly well suited as an adjunct to immunotherapy. Such upfront cytoreduction can relieve tumor-related immunosuppression and prevent early treatment failure at sites of initial involvement. Prior studies have demonstrated OS and PFS benefits to the addition of local therapy in metastatic non-small cell lung cancer. Multi-site ablative RT has also been shown to be safe in the setting of immunotherapy in multiple published prospective trials. We hypothesize that the addition of RT to chemotherapy and Durvalumab for newly diagnosed ES-SCLC patients will improve PFS. **Methods:** 49 patients will be enrolled across four institutions in this phase II clinical trial. Treatment naive ES-SCLC patients with PS 0-2 who have at least one RECIST measurable lesion meeting criteria for ablative radiation will be eligible for enrollment. Patients with symptomatic brain metastasis will undergo cranial radiotherapy prior to starting on trial. Patients will be treated with four cycles of platinum/etoposide and Durvalumab. During cycle 2, patients will undergo ablative radiation therapy to 1 – 4 sites of extracranial disease. Radiation dose and organ at risk (OAR) constraints are consistent with NRG BR001. During planning, OAR constraints will be prioritized over tumor coverage. Following four cycles of chemotherapy and Durvalumab, patients will continue with maintenance Durvalumab 1500 mg q28 days until progression, toxicity, or study withdrawal. The primary endpoint is PFS. Using a historic control of 5 month median PFS with chemo/immunotherapy from CASPIAN and IMpower133, we hypothesized that the addition of ablative RT would improve the PFS from 5 months to 8 months. sample size of 49 patients was calculated for 80% power with alpha of 0.1. Secondary endpoints include overall survival, time to second line therapy, response rate, and rate of grade 3+ adverse events. Peripheral blood, stool, nasal, and buccal samples will be obtained at baseline, after RT, and at the time of progression and/or immune-related toxicity and will be used for exploratory analysis. NCT05068232. Clinical trial information: NCT05068232. Research Sponsor: AstraZeneca.

TPS8616 **Poster Session**

Phase II study of hemithoracic intensity-modulated pleural radiation therapy (IMPRINT) for patients with pleural metastases from thymic malignancies.

Andreas Rimner, James Huang, Andrew Pagano, Michelle S. Ginsberg, Jason C. Chang, Gregory J. Riely, Charles B. Simone, Daniel Richard Gomez, Annemarie Shepherd; Memorial Sloan Kettering Cancer Center, New York, NY; MSKCC, New York, NY; New York Proton Center, New York, NY; Memorial Sloan Kettering Cancer Center at Basking Ridge New Jersey, Bernards, NJ

Background: Pleural metastases are common sites for recurrence and progression in patients with thymic malignancies. The management of pleural metastases typically involves surgical resection with or without neoadjuvant or adjuvant systemic therapy. After surgical resection of pleural metastases, the 5-year progression-free survival (PFS) rate is about 29-45%. While radiation therapy (RT) is standardly used in the management of locally-advanced thymic malignancies, the role of RT in patients with pleural metastases in unclear. Intensity-modulated pleural radiation therapy (IMPRINT) is a RT technique currently being used to treat malignant pleural mesothelioma (MPM) patients with 2 intact lungs at centers that specialize in MPM treatment. This IMPRINT technique can potentially be extrapolated to thymic patients with pleural metastases. Because the risk of toxicity is of greater concern for thymic patients given their overall relatively favorable prognosis, the rate of toxicity, particularly radiation pneumonitis, needs to be established in the thymic patient population. **Methods:** This is a single-arm, single institution Phase II study of hemithoracic IMPRINT for patients with pleural metastases from thymic malignancies. The primary endpoint of this study is grade 3 or higher radiation pneumonitis within 4 months of completing RT. Secondary endpoints include any toxicity, progression-free survival, patterns of failure and overall survival. Patients must have a pathologically confirmed diagnosis of a thymic malignancy with radiologic or pathologic evidence of pleural metastases. Thymoma or thymic carcinoma are allowed. Patients may have de novo stage IVA disease or recurrent disease in the pleura. There must be no evidence of extrathoracic metastatic disease or contralateral pleural/pericardial disease. Surgical resection of the pleural nodules (ex: pleurectomy/decortication, debulking/metastasectomy) are allowed. Extrapleural pneumonectomy is not allowed. Patients are excluded if they have undergone prior thoracic radiation therapy preventing hemithoracic pleural IMRT, whereas prior thymic bed radiation and/or prior pleural SBRT are allowed. RT will be administered to the ipsilateral pleura to 50.4 Gy in 28 fractions. An optional dose-painting boost to gross disease up to 60 Gy while respecting normal tissue constraints is allowed. Patients can be treated with photon or proton therapy. Simulation, contouring and RT planning guidelines have been developed. Patients will be followed per protocol at regular intervals for at least 12 months following RT. The expected accrual is 36 patients over 4 years. Further information can be found on clinicaltrials.gov (NCT05354570). Clinical trial information: NCT05354570. Research Sponsor: Memorial Sloan Kettering Cancer Center.