8500 **Oral Abstract Session**

Two cycles versus three cycles of neoadjuvant sintilimab plus platinum-doublet chemotherapy in patients with resectable non-small-cell lung cancer (neoSCORE): A randomized, single center, two-arm phase II trial.

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Background: Neoadjuvant immune checkpoint inhibitors (ICIs) plus chemotherapy have a promising efficacy in resectable non-small-cell lung cancer (NSCLC), yet the period of neoadjuvant immunochemotherapy is undetermined. This phase II study compared the efficacy and safety of two cycles with three cycles of neoadjuvant sintilimab plus chemotherapy in resectable stage IB-IIIA NSCLC. **Methods:** This randomized, open-label phase II trial recruited patients aged 18 or older with histologically confirmed, treatment-naïve, American Joint Committee on Cancer-defined stage IB-IIIA, resectable NSCLC. Eligible patients were randomly assigned to two or three cycles of neoadjuvant treatment with intravenous sintilimab (200 mg) plus carboplatin (area under curve 5) and nab-paclitaxel (260mg/m^2, for squamous) or pemetrexed (500mg/m^2, for non-squamous) on day 1 of three-week cycle. After surgical resection, patients received totally four doses of perioperative immunochemotherapy, followed by one-year sintilimab maintenance under patient decision. Randomisation was stratified by tumor PD-L1 expression ($\geq$1% vs < 1%). The primary endpoint was MPR rate. Secondary endpoints included complete pathology response (pCR) rate, objective response rate (ORR), 2-year disease-free survival (DFS) rate, 2-year overall survival (OS) rate and safety. This trial is registered with ClinicalTrials.gov, number: NCT04459611. **Results:** From 6/2020 to 9/2021, 60 patients were enrolled and received neoadjuvant treatment. The patient characteristics of both arms were well balanced. Among 55 patients with successful R0 resection, we observed a higher MPR rate (41.4%, 12/29) in three-cycle group compared with two-cycle group (26.9%, 7/26) (p = 0.260), meanwhile, pCR rate achieved 24.1% (7/29) and 19.2% (5/26) respectively (p = 0.660). Patients of squamous subtype generally achieved a statistically higher MPR rate (51.6%, 16/31) compared with the non-squamous subtype (12.5%, 3/24) (p = 0.002). In squamous subgroup, three cycles neoadjuvant treatment induced a MPR rate of 60% compared with 43.8% after two cycles treatment (p = 0.366).In the meantime, the MPR rate was 21.4% versus 0% in non-squamous subgroup, respectively (p = 0.239). The ORR showed no statistical difference between three-cycle group (55.2%, 16/29) and two-cycle (50%, 13/26) (p = 0.701). Patients were well-tolerated in both groups and 5% (3/60) experienced grade 3 immune related adverse events. **Conclusions:** It is the first randomized study comparing different treatment periods of immuno-chemotherapy in the neoadjuvant setting. Three cycles neoadjuvant treatment achieved a numerically higher MPR rate compared with two cycles. Patients with squamous lung cancer obtained a better MPR rate compared with non-squamous subtype. Clinical trial information: NCT04459611. Research Sponsor: None.

8501 **Oral Abstract Session**

Nivolumab + chemotherapy versus chemotherapy as neoadjuvant treatment for resectable stage IIIA NSCLC: Primary endpoint results of pathological complete response (pCR) from phase II NADIM II trial.

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Background: Non-small cell lung cancer (NSCLC) is incurable in most patients with locally advanced stage IIIA disease. Previous results indicate that the use of neoadjuvant chemoimmunotherapy could increase the percentage of cured patients being a promising therapeutic option that has to be tested in randomized clinical trials. **Methods:** NADIM II (NCT03838159) is an open-label, randomized, two-arm, phase II, multi-center clinical trial. Patients with resectable clinical stage IIIA (per AJCC 7^{th} ed) NSCLC, ECOG PS 0-1, and no known EGFR/ALK alterations were randomized to receive Nivolumab (NIVO) 360mg + Paclitaxel 200mg/m^2 + Carboplatin AUC5 for 3 cycles every 21 days (+/- 3 days) as neoadjuvant treatment followed by surgery, or Paclitaxel 200mg/m^2 + Carboplatin AUC5 for 3 cycles every 21 days (+/- 3 days) followed by surgery. Patients with R0 resection confirmed by pathological evaluation initiated adjuvant administration of NIVO within the 3rd to 8th week (+7 days) from surgery and for 6 months. The primary endpoint was pathological complete response (pCR) by blinded independent pathological review (BIPR) in the intent-to-treat population (ITT). pCR was defined as 0% viable tumor cells in resected lung and lymph nodes; patients who did not undergo surgery were classified as non-responders. Major pathological response (MPR; ≤ 10% viable tumor) per BIPR, overall response rate (ORR), toxicity profile, and potential predictive biomarkers are secondary endpoints. **Results:** Between February 8, 2019, and November 11, 2021, 90 patients were enrolled, of whom 87 patients were valid. Neoadjuvant NIVO + chemo significantly increased the pCR rate compared to chemo in the ITT (36.2% vs 6.8%; Relative Risk (RR) 5.25 [99% CI 1.32-20.87]; P = 0.0071). NIVO + chemo also improved MPR rates vs chemo in the ITT (52 % vs 14 %), as well as ORR (74 % vs 48%). Definitive surgery occurred for 91% of pts treated with NIVO + chemo and 69% with chemo; surgery was cancelled rarely due to AEs (1 pts/experimental arm) and due to disease progression in 1 and 4 pts in the experimental and control arm respectively. Grade 3-4-related AEs were reported in 24 % vs 10% in the NIVO + chemo vs chemo arms, respectively. In the ITT experimental arm, patients with pCR had higher PD-L1 TPS (median 70%, IQR 5-90%) compared to non-responders (median 0%, IQR 0-37.5%, P = 0.0035). AUC to predict pCR was 0.734 (95% CI 0.59-0.88; P = 0.005). The pCR rate rises across increasing categories of PD-L1 TPS (< 1% 14.3%; 1-49% 41.7%; ≥50% 61.1%; P = 0.008). **Conclusions:** This study confirms the superiority of the chemo-immuno combination in patients with resectable stage IIIA NSCLC in terms of pCR, as well as the feasibility of surgery, with a moderate increase in grade 3-4 toxicity. Thus, this treatment should become the standard of care in these patients. Clinical trial information: NCT03838159. Research Sponsor: BMS.

8502 **Oral Abstract Session**

Intraoperative quality metrics and association with survival following lung cancer resection.

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Background: Surgical resection remains the preferred treatment for functionally fit patients with clinical stage I non-small cell lung cancer (NSCLC). Process-based intra-operative quality metrics (QMs) are important for optimizing long-term outcomes following curative-intent resection. We sought to characterize overall survival using a novel surgical quality score. **Methods:** We performed a retrospective cohort study using a uniquely compiled dataset of US Veterans with clinical stage I NSCLC receiving definitive surgical treatment. Based on contemporary treatment guidelines, we defined five surgical QMs: timely surgery (within 12 weeks of diagnosis), minimally invasive approach, anatomic resection via lobectomy, adequate nodal sampling (≥10 nodes), and negative margin. Using a multivariable Cox proportional hazards model, we developed a surgical quality score reflecting the relationship between these QMs and overall survival (OS). We also examined the relationship between this score and disease-free survival (DFS). **Results:** The study included 9,628 Veterans undergoing surgical treatment between 2006 and 2016. QMs were met as follows: timely surgery (n=6,633, 68.9%), minimally invasive approach (n=3,986, 41.4%), lobectomy (n=6,843, 71.1%), adequate nodal sampling (n=3,278, 34.1%), and negative surgical margin (n=9,312, 96.7%). The median (IQR) follow-up was 6.2 (2.5-11.4) years. A normalized score from 0 (no QMs met) to 100 (all QMs met) was constructed, with higher scores reflecting progressively improved risk-adjusted OS (Table). The median (IQR) OS was 86.8 (37.8-149.6) months in the highest score quintile versus 25.3 (7.1-45.8) months in the lowest score quintile. Recurrence was detected in 2,268 (23.6%) patients. Higher surgical quality score was associated with improved DFS (multivariable-adjusted hazard ratio, aHR 0.494, 95% CI 0.245-0.997). **Conclusions:** Adherence to intra-operative QMs is associated with markedly improved overall and disease-free survival. Efforts to improve adherence to surgical QMs can dramatically improve patient outcomes following curative-intent resection of early-stage lung cancer. Research Sponsor: U.S. National Institutes of Health.

Association between surgical QMs and overall survival.

Variable[a]	aHR, 95% CI	β	p-value	Score[b]
Delayed surgery (≤12 vs >12 weeks)	0.90 (0.85-0.95)	-0.11	<0.001	2
Surgical approach (minimally invasive vs open)	0.91 (0.86-0.97)	-0.09	0.002	2
Extent of resection (vs wedge)				
Lobectomy	0.79 (0.74-0.84)	-0.24	<0.001	5
Segmentectomy	0.80 (0.70-0.92)	-0.22	0.001	4
Pneumonectomy	1.18 (0.96-1.46)	0.17	0.13	0
Nodal sampling (≥10 vs <10 nodes)	0.95 (0.89-1.01)	-0.05	0.09	1
Surgical margin (R0 vs R1+)	0.54 (0.47-0.62)	-0.61	<0.001	12

[a]Also controlling for age, sex, race, BMI, smoking status, Charlson score, number of prescriptions, hospital volume, tumor location, histology, tumor size. [b]Multiply score by 4.545 to generate the normalized score (0-100).

8503 **Oral Abstract Session**

Neoadjuvant chemoradiotherapy versus neoadjuvant chemotherapy for patients with stage III-N2M0 non-small cell lung cancer (NSCLC): A population-based study.

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Background: Stage III-N2 non-small cell lung cancer (NSCLC) is a heterogeneous disease with controversial management options. Induction therapy as part of multimodal treatment is the standard of care for Stage III-N2 NSCLC. We aim to investigate the effect of adding radiotherapy to neoadjuvant chemotherapy on survival outcomes. **Methods:** All adult NSCLC patients diagnosed between 2004 and 2015 were identified in the Surveillance, Epidemiology, and End Results (SEER) database using ICD-O-3 histologic type coding. Inclusion criteria involved stage III NSCLC patients with ipsilateral lymph node involvement (N2), of any T stage, and with no known distant metastasis (M0). Our main sub-cohorts were patients who either underwent chemoradiotherapy (CRT) or chemotherapy (CT) in neoadjuvant settings. Our primary outcomes were overall survival (OS) and cancer-specific survival (CSS) in months. Cox proportional hazards model was used to analyze the effect of each treatment modality on OS and CSS in univariate and multivariate fashions. Multivariate analysis was adjusted for age, sex, marital status, T stage, resected lymph node status, tumor histology, primary site, laterality, and surgical procedure. Inverse probability treatment weighting (IPTW) was applied to create weighted samples based on study covariates. **Results:** Our analysis included 1175 patients; 799 (68.0%) underwent neoadjuvant CRT and 376 (32.0%) underwent neoadjuvant CT. Sample median age was 63 (IQR:56-69) years. T2 stage was the most prevalent (N =561, 47.7%), followed by T4 (N=243, 20.7%), T1 (N=228, 19.4%), and T3 (N=143, 12.2%). The main tumor histology was non-squamous cell carcinoma in 773 (65.8%) patients. The upper lobe was the most common primary tumor site (N =788, 67.1%). Patients underwent lobectomy (N=917, 78.0%), pneumonectomy (N=184, 15.7%), or sublobar resection (N=69, 5.9%). Adding radiotherapy to chemotherapy showed a slightly higher median OS than chemotherapy alone in neoadjuvant settings (51 vs. 47 months, respectively), and a higher median CSS (75 vs. 59 months, respectively). However, these differences were not statistically significant for OS or CSS (HR = 1.08, 95% CI: 0.91-1.28 and HR = 1.04, 95% CI: 0.89-1.21, respectively). After adjustment, age, T3-T4 stage, non-squamous histology, lower lobe primary site, positive resected lymph nodes, and pneumonectomy were all significant independent predictors for worse OS and CSS. IPTW analysis showed no remarkable survival advantage for CRT patients (HR = 1.15, 95% CI: 0.95-1.40 and HR= 1.12, 95% CI: 0.90-1.39) for OS and CSS, respectively. **Conclusions:** Adding radiotherapy to neoadjuvant CT did not result in significant survival benefits. Multiple prognostic factors should be taken into consideration when identifying the optimal choice and sequence of multimodal treatment for stage III-N2M0 NSCLC patients. Research Sponsor: None.

8504 **Oral Abstract Session**

Comparison of quality of life in patients randomized to high-dose once daily (QD) thoracic radiotherapy (TRT) with standard twice daily (BID) TRT in limited stage small cell lung cancer (LS-SCLC) on CALGB 30610 (Alliance, Sub-study CALGB 70702).

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Background: The CALGB 30610 trial demonstrated that 70Gy QD TRT was not associated with a superior overall survival compared to standard BID 45Gy TRT in limited stage small cell lung cancer. Since both arms appeared to provide similar clinical benefit, other factors such as quality of life may help oncologists decide on the best treatment approach for their patients. The present analysis was conducted to compare patients' quality of life between these regimens in terms of their physical symptoms, physical functioning and psychological state. **Methods:** In the CALGB 30610 planned sub-study CALGB 70702, patients were administered the FACT-L, FACT Trial Outcome Index-Lung Cancer (FACT-L TOI), FACT-Esophageal Cancer Eating and Swallowing Indices, ECOG Acute Esophagitis Scale, Hospital Anxiety and Depression Scale (HADS), the EQ-5D at baseline and a single item assessing difficulty swallowing at baseline, 3, 5, 7, 12, 26, and 52 weeks after starting radiation therapy. Patients were also asked to assess treatment inconvenience at these time points. The primary endpoints of CALGB 70702 were FACT-L TOI and FACT eating and swallowing subscales at 12 weeks. Mean changes from baseline were compared between arms using general linear mixed models. **Results:** 417 patients consented to participate in the patient-reported outcomes substudy. The completion rate of the questionnaires was 87% at baseline and 71% at week 52. The FACT-L total score mean worsening was significantly less in the QD arm compared to the BID arm at week 3 (-1.0 vs -7.0; P=.003), and marginally less at week 5 (-5.3 vs -11.0; P=.06). The FACT-L TOI mean worsening was significantly less in the QD arm than in the BID arm at week 3 (-2.9 vs -7.6; P=.003) and greater at week 12 (-7.6 vs -2.8; P=.03). The QD arm also had a lesser EQ-5D index mean worsening at 3 weeks (-0.04 vs 0.03; P=.002). Mean increase in the acute esophagitis score (1.06 vs 2.89; P<.001) and difficulty swallowing (0.39 vs 1.14; P<.001) were significantly greater in the BID arm at week 3. Mean worsening in HADS anxiety was significantly less in the QD arm at week 5 (-1.99 vs -0.95; P=.03). There were no other significant differences at the remaining timepoints between the two arms. Across visits on the QD arm, patients felt that treatment was inconvenient at 26% (96/376) assessments, compared to 33% (116/352) in the BID arm (chi-sq P=.03). **Conclusions:** Both radiation regimens were well tolerated. However, the QD arm had better quality of life scores at week 3 and was perceived to be less inconvenient. Clinical trial information: NCT00632853. Research Sponsor: U.S. National Institutes of Health.

8505 **Oral Abstract Session**

Serplulimab, a novel anti-PD-1 antibody, plus chemotherapy versus chemotherapy alone as first-line treatment for extensive-stage small-cell lung cancer: An international randomized phase 3 study.

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Background: Monoclonal antibodies against programmed death-ligand 1 (PD-L1) have been approved for the first-line treatment of extensive-stage small-cell lung cancer (ES-SCLC) in combination with chemotherapy. However, whether a programmed death 1 (PD-1) inhibitor provides similar survival benefit in this patient population remains unclear. In this study, the efficacy and safety of serplulimab, a novel humanized monoclonal anti-PD-1 antibody, were assessed in combination with chemotherapy in previously untreated ES-SCLC patients. **Methods:** In this international, randomized, double-blind, multicenter, phase 3 trial (NCT04063163), patients with ES-SCLC who had not received prior systemic therapy were randomized (2:1) to receive serplulimab 4.5 mg/kg or placebo intravenously every 3 weeks. All patients received intravenous carboplatin and etoposide every 3 weeks for up to 4 cycles. The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), duration of response (DoR), and safety. **Results:** Between September 12, 2019 and April 27, 2021, 585 patients were randomized (serplulimab group, $n = 389$; placebo group, $n = 196$). At interim analysis, the median follow-up duration was 12.3 months. Median OS was significantly prolonged in the serplulimab group than the placebo group (15.4 *vs.*10.9 months; hazard ratio [HR] 0.63, 95% CI 0.49–0.82; $P < 0.001$). Median PFS assessed by the independent radiology review committee (IRRC) per RECIST v1.1 was significantly longer in the serplulimab group than the placebo group (5.8 *vs.* 4.3 months; HR 0.47, 95% CI 0.38–0.59; $P < 0.001$). Efficacy improvements were also observed in ORR (80.2% *vs.* 70.4%) and DoR (5.6 *vs.* 3.2 months) as assessed by IRRC per RECIST v1.1. Grade ≥3 treatment-emergent adverse events (TEAEs) related to serplulimab or placebo were reported in 129 (33.2%) and 54 (27.6%) patients in the respective groups. Incidence of immune-related TEAEs was higher in the serplulimab group compared to the placebo group (37% *vs.* 18.4%), with the largest difference in endocrine disorders (18.3% *vs.* 4.6%), which are commonly reported with anti-PD-1/PD-L1 therapies. Four deaths (1 acute coronary syndrome, 1 pyrexia, and 1 platelet count decreased in the serplulimab group; 1 thrombocytopenia in the placebo group) that might be related to study drugs were reported. **Conclusions:** Serplulimab plus chemotherapy as first-line treatment provided significant benefits and a manageable safety profile compared with chemotherapy alone in ES-SCLC patients. For the first time, OS benefits was demonstrated with a PD-1 inhibitor in a global phase 3 study among previously untreated ES-SCLC patients. Clinical trial information: NCT04063163. Research Sponsor: Shanghai Henlius Biotech, Inc.

LBA8507 **Oral Abstract Session**

SKYSCRAPER-02: Primary results of a phase III, randomized, double-blind, placebo-controlled study of atezolizumab (atezo) + carboplatin + etoposide (CE) with or without tiragolumab (tira) in patients (pts) with untreated extensive-stage small cell lung cancer (ES-SCLC).

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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, 2022, issue of the *Journal of Clinical Oncology*. Research Sponsor: F. Hoffmann-La Roche.

8508 **Poster Discussion Session**

Two-year update from KEYNOTE-799: Pembrolizumab plus concurrent chemoradiation therapy (cCRT) for unresectable, locally advanced, stage III NSCLC.

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Background: Primary analysis (database cutoff, Oct 28, 2020) of the global KEYNOTE-799 study (NCT03631784) in patients (pts) with unresectable, locally advanced stage III NSCLC, showed that pembrolizumab (pembro; anti–PD-1) plus cCRT resulted in an ORR of 70.5% in cohort A (n = 112; squamous and nonsquamous) and 70.6% in cohort B (n = 102; nonsquamous only) and grade ≥3 pneumonitis in 9 (8.0%) and 7 (6.9%) pts, respectively. We present updated outcomes with 1 y of additional follow-up. **Methods:** In this nonrandomized, phase 2 study, eligible pts were aged ≥18 y with previously untreated, unresectable, pathologically confirmed, stage IIIA-C NSCLC with measurable disease per RECIST v1.1. Pts in cohort A (squamous and nonsquamous) received carboplatin AUC 6 plus paclitaxel 200 mg/m^2 and pembro 200 mg for one 3-wk cycle, followed by carboplatin AUC 2 plus paclitaxel 45 mg/m^2 QW for 6 wks plus 2 cycles of pembro 200 mg Q3W plus standard thoracic radiotherapy (TRT). Pts in cohort B (nonsquamous) received 3 cycles of cisplatin 75 mg/m^2, pemetrexed 500 mg/m^2, and pembro 200 mg Q3W plus standard TRT in cycles 2 and 3. All pts received 14 additional cycles of pembro 200 mg Q3W. Primary endpoints were ORR per RECIST v1.1 by blinded independent central review (BICR) and the incidence of grade ≥3 pneumonitis (per NCI CTCAE v4.0). **Results:** Of 216 pts enrolled in this study, 112 in cohort A and 102 in cohort B received treatment. Median (range) time from first dose to database cutoff (Oct 18, 2021) was 30.2 (25.3–35.5) mo in cohort A and 25.4 (14.5–35.2) mo in cohort B. ORR (95% CI) was 71.4% (62.1%–79.6%) in cohort A and 75.5% (66.0%–83.5%) in cohort B. Median duration of response (DOR) and OS were not reached (NR) in both cohorts; median PFS was 30.6 mo in cohort A, and NR in cohort B (Table). ORR was 66.7% in pts with PD-L1 TPS <1% and 77.3% in pts with PD-L1 TPS ≥1% in cohort A and 78.6% and 72.5%, respectively, in cohort B. ORR was similar by histology (squamous, 72.0%; nonsquamous, 74.1%). Grade ≥3 pneumonitis occurred in 16 pts (7.5%) overall; 9 pts (8.0%) in cohort A and 7 (6.9%) in cohort B. Treatment-related grade ≥3 AEs occurred in 64.3% and 51.0% of pts in cohort A and B, respectively. **Conclusions:** With the accrual of additional responses after >2 y of follow-up, pembro plus cCRT continues to demonstrate robust and durable responses, regardless of PD-L1 TPS and tumor histology, promising survival outcome and manageable safety in pts with previously untreated, locally advanced stage III NSCLC. Clinical trial information: NCT03631784. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	Cohort A n = 112	Cohort B n = 102
ORR, % (95% CI)	71.4 (62.1–79.6)	75.5 (66.0–83.5)
Median DOR,[a] mo (range)	NR (1.9+ to 32.5+)	NR (1.6+ to 32.5+)
DOR ≥24 mo, %	64.0	68.7
Median PFS,[a] mo (95% CI)	30.6 (16.6–NR)	NR (20.6–NR)
24-mo rate, %	55.3	60.6
Median OS,[a] mo (95% CI)	NR (26.1–NR)	NR (33.0–NR)
24-mo rate, %	64.3	71.2

"+" indicates no PD by time of last disease assessment.
[a]Kaplan-Meier estimate.

8509 **Poster Discussion Session**

Consolidation nivolumab plus ipilimumab or nivolumab alone following concurrent chemoradiation for patients with unresectable stage III non-small cell lung cancer: BTCRC LUN 16-081.

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Background: The PACIFIC trial demonstrated that a year of consolidation PD-(L)1 inhibition following concurrent chemoradiation (CRT) for unresectable stage III NSCLC improves overall survival (OS). The optimal duration of consolidation IO therapy in this setting is undefined. Studies in metastatic NSCLC demonstrate that combination PD-(L)1/CTLA-4 inhibition improves OS over chemotherapy alone. This trial evaluated the use of combination Nivolumab (N) plus Ipilimumab (IPI) or N alone for up to 6 months in unresectable stage III NSCLC after concurrent CRT. **Methods:** This is a randomized phase II, multicenter trial of 105 pts with unresectable stage IIIA/IIIB NSCLC. All pts received concurrent CRT and were then enrolled and randomized 1:1 to receive N 480mg IV q4wks (Arm A) for up to 24 weeks or N 3mg/kg IV q2 wks + IPI 1mg/kg IV q6 wks (Arm B) for up to 24 weeks. The primary endpoint is 18-month PFS compared to historical controls of CRT alone for arm A (30%) and CRT followed by Durva for arm B (44%). Secondary endpoints include OS and toxicity. **Results:** From 9/2017 to 4/2021, 105 pts were enrolled and randomized, 54 to N alone (A) and 51 to N + IPI (B). The baseline characteristics for arm A/B: median age (65/63), male (44.4%/56.9%), stage IIIA (55.6%/56.9%), stage IIIB (44.4%/43.1%), non-squamous (57.4%/54.9%), and squamous (42.6%/45.1%). The percentage of pts completing the full treatment was 70.4% on A and 56.9% on B ($p = 0.15$). Median f/u was 24.5 and 24.1 months on A and B, respectively. The 18-month PFS was 62.3% on A ($p < 0.1$) and 67% on B ($p < 0.1$), and median PFS was 25.8 months and 25.4 months, respectively. Median OS was not reached on either arm, but the 18- and 24-month OS estimates were 82.1% and 76.6% for A and 85.5% and 82.8% for B, respectively. Treatment-related adverse events (trAE) on arm A/B were 72.2%/80.4%, and grade ≥3 trAEs on arm A/B were 38.9%/52.9%. There was 1 grade 5 event on each arm (COVID19-A, Cardiac Arrest-B). The number of pts with grade ≥2 pneumonitis were 12 (22.2%) on A and 15 (29.4%) on B, with 5 (9.3%) and 8 (15.7%) grade ≥3 events, respectively. The most common (> 10%) non-pneumonitis trAEs on A were fatigue (31.5%), rash (16.7%), dyspnea (14.8%), and hypothyroidism (13%), and on B were fatigue (31.4%), diarrhea (19.6%), dyspnea (19.6%), pruritus (17.7%), hypothyroidism (15.7%), rash (15.7%), arthralgia (11.8%), and nausea (11.8%). **Conclusions:** Following concurrent CRT for unresectable stage III NSCLC, both N and N + IPI demonstrated improved 18-month PFS compared with historical controls despite a shortened interval (6 months) of treatment. OS data are still maturing but 18- and 24-month OS estimates compare favorably to prior consolidation trials. Toxicity for N alone was similar to prior single-agent trials, and the combination of N + IPI resulted in a higher incidence of trAE's, although consistent with prior reports. Clinical trial information: NCT03285321. Research Sponsor: Bristol Myers Squibb.

8510 **Poster Discussion Session**

The Selective Personalized Radio-immunotherapy for Locally Advanced NSCLC Trial (SPRINT): Initial results.

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Background: Standard therapy for unresectable locally advanced non-small cell lung cancer (LA-NSCLC) is concurrent chemoradiotherapy followed by adjuvant durvalumab. We performed a prospective trial testing sequential pembrolizumab and risk-adapted radiotherapy without chemotherapy for biomarker-selected LA-NSCLC patients. **Methods:** Patients with stage III NSCLC or unresectable stage II NSCLC, ECOG performance status 0-1, and no contraindications to protocol-specified therapy were eligible for this trial. Subjects with PD-L1 tumor proportion score (TPS) ≥ 50% underwent baseline FDG-PET/CT, received three cycles of induction pembrolizumab (200 mg, every 21 days), underwent restaging FDG-PET/CT, received risk-adapted thoracic radiotherapy (55 Gy delivered to tumors or lymph nodes with metabolic tumor volume exceeding 20 cc and 48 Gy delivered to smaller lesions, all in 20 daily fractions), and then received up to 13 cycles of additional pembrolizumab. The primary study endpoint was one-year progression-free survival (PFS). Here we report response rates following induction pembrolizumab, PFS and overall survival (OS) rates, and adverse event rates (CTCAE v. 4.03). **Results:** Twenty-five subjects with PD-L1 TPS ≥ 50% from three institutions were enrolled between August 2018 and November 2021. Median age was 71 (interquartile range [IQR] 62 to 77). One subject had stage II disease, 13 had stage IIIA disease, nine had stage IIIB disease, and two had stage IIIC disease. Median PD-L1 TPS was 75% (IQR 60 to 80%). Two subjects (8%) developed disease progression during induction pembrolizumab, and two subjects discontinued pembrolizumab after one infusion due to immune-related adverse events. Using RECIST 1.1 criteria, 12 subjects (48%) exhibited a partial (n = 11) or complete (n = 1) response following induction pembrolizumab on CT. Using PERCIST criteria, 12 subjects (48%) exhibited a partial response following induction pembrolizumab on PET. Four subjects had responses on PET but not on CT, and four had responses on CT but not on PET. With a median follow-up duration of 13 months, the actuarial 1-year PFS rate is 74%, and the actuarial 1-year OS rate is 95%. Grade 3 adverse events have been limited to single cases of anemia, arthritis, diarrhea, esophagitis, and pneumonitis, and no grade 4-5 adverse events have occurred. Exploratory analyses suggest that response to induction pembrolizumab on PET predicts efficacy of this treatment approach, with a 1-year PFS rate of 100% for responders, compared to 61% for non-responders (logrank p = 0.007). **Conclusions:** Treatment with pembrolizumab and risk-adapted radiotherapy is a promising treatment approach for LA-NSCLC patients with PD-L1 TPS ≥ 50%. Response on PET following induction pembrolizumab may be useful for identifying patients who can be treated successfully without chemotherapy. Clinical trial information: NCT03523702. Research Sponsor: Merck.

LBA8511 **Poster Discussion Session**

Neoadjuvant nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) versus chemo for resectable (IB–IIIA) non-small cell lung cancer (NSCLC): Association of pathological regression with event-free survival (EFS) in CheckMate 816.

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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, 2022, issue of the *Journal of Clinical Oncology*. Research Sponsor: Bristol Myers Squibb.

8512 **Poster Discussion Session**

EORTC-1416-LCG/ETOP 8-15 – PEARLS/KEYNOTE-091 study of pembrolizumab versus placebo for completely resected early-stage non-small cell lung cancer (NSCLC): Outcomes in subgroups related to surgery, disease burden, and adjuvant chemotherapy use.

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Background: At the second interim analysis (IA2) of the triple-blind, phase 3 PEARLS/KEYNOTE-091 study (NCT02504372), pembrolizumab significantly improved DFS compared with placebo in patients (pts) with completely resected stage IB (T ≥4 cm) to IIIA NSCLC per AJCC v7, regardless of PD-L1 expression (N = 1177, HR 0.76, 95% CI 0.63-0.91, $P = 0.0014$). We present DFS in subgroups related to surgery, disease burden, and adjuvant chemotherapy use. **Methods:** Pts had pathologically confirmed, completely resected stage IB (T ≥4 cm) to IIIA NSCLC of any PD-L1 expression and ECOG PS 0-1. Systematic complete or lobe-specific mediastinal lymph node dissection was recommended; minimally, the subcarinal and 1 lobe-specific lymph node must have been examined. Adjuvant chemotherapy of ≤4 cycles was given as indicated by local guidelines. Eligible pts were randomized 1:1 to pembrolizumab 200 mg or placebo Q3W for 18 doses (~1 y). Treatment effects on DFS were assessed in prespecified subgroups of with and without adjuvant chemotherapy and in exploratory subgroups defined by surgery type, pN stage, tumor size, no. of adjuvant chemotherapy cycles, and adjuvant regimen; only subgroups of > 50 pts were analyzed. Data cutoff for IA2 was September 20, 2021 (median time from randomization to cutoff, 35.6 mo). **Results:** By surgery type, the HR (95% CI) for DFS was 0.78 (0.64-0.96) for lobectomy (n = 925), 0.85 (0.43-1.69) for bilobectomy (n = 92), and 0.71 (0.40-1.24) for pneumonectomy (n = 127). For subgroups based on nodal status, HR (95% CI) for DFS was 0.63 (0.46-0.86) for pN0 (n = 490), 0.77 (0.57-1.03) for pN1 (n = 456), and 1.00 (0.71-1.41) for pN2 (n = 231). By tumor size, and irrespective of nodal status, the HR (95% CI) for DFS was 0.91 (0.69-1.20) for size ≤4 cm (n = 491) and 0.70 (0.55-0.89) for size > 4 cm (n = 685). The HR (95% CI) for DFS was 0.73 (0.60-0.89) in pts who received adjuvant chemotherapy (n = 1010) and 1.25 (0.76-2.05) in those who did not (n = 167). Among pts who received adjuvant chemotherapy, HR (95% CI) for DFS by number of cycles was 0.59 (0.28-1.26) for 1-2 (n = 67) and 0.74 (0.61-0.91) for 3-4 (n = 943); by regimen, it was 0.74 (0.55-0.98) for cisplatin + vinorelbine (n = 491), 0.51 (0.31-0.83) for carboplatin + vinorelbine (n = 151), 1.21 (0.73-1.98) for carboplatin + paclitaxel (n = 135), 0.65 (0.30-1.40) for cisplatin + gemcitabine (n = 57), and 0.68 (0.41-1.14) for other regimen (n = 176). **Conclusions:** Pembrolizumab generally improved DFS versus placebo regardless of type of surgery, lymph node involvement, tumor size, and type and extent of adjuvant chemotherapy in pts with completely resected stage IB (T ≥4 cm) to IIIA NSCLC. These data support the benefit of pembrolizumab as adjuvant therapy for early-stage NSCLC following complete resection and, if indicated, adjuvant chemotherapy. Clinical trial information: NCT02504372. Research Sponsor: Merck Sharp & Dohme Corp, a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

8513 **Poster Discussion Session**

Safety results of NRG-LU004: Phase I trial of accelerated or conventionally fractionated radiotherapy combined with durvalumab in PD-L1–high locally advanced non-small cell lung cancer.

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Background: In advanced non-small cell lung cancer (NSCLC), high Programmed-Death-1 Ligand (PD-L1) (>50%) expression demonstrate superior response and survival with immune checkpoint inhibitors compared to chemotherapy. We hypothesize that it is safe and feasible to substitute durvalumab instead of chemotherapy concurrently with radiotherapy (RT) in patients with Locally Advanced-NSCLC (LA-NSCLC) and high PD-L1. **Methods:** NRG-LU004 (NCT03801902) is a Phase I study for patients with stage II-III unresectable or inoperable, LA-NSCLC with PD-L1> 50% (Dako 22C3 or Ventana SP263) expression. There were safety and expansion phases with a primary endpoint of safety. Patients started with 1500 mg durvalumab Q4 weeks and thoracic RT within 2 weeks from 1st infusion. Durvalumab continued once a month up to 1 year. In the safety cohort, 6 patients in cohort 1 were treated with accelerated fractionated RT (ACRT) to 60 Gy in 15 fractions, followed by a required safety hold for 90 days. During cohort 1 safety hold, cohort 2 patients were treated with conventional RT 60 Gy in 30 fractions (CONV) followed by a 60-day safety hold. A cohort advanced to the expansion phase to enroll 6 more patients if safety criteria (0-1 patients with a dose limiting toxicity [DLT]) were met. If both cohorts were deemed safe, patients would be randomized 1:1 to ACRT or CONV with safety defined as < 4 of 12 evaluable patients per arm experiencing a DLT. Feasibility was defined as at least 80% of patients in each arm receiving at least 80% of the planned dose of durvalumab during the first 8 weeks. **Results:** 24 evaluable patients enrolled between January 2019 and June 2021. No DLTs were reported in cohort 1, and 1 (unrelated bronchopulmonary hemorrhage leading to discontinuation of durvalumab) in cohort 2. Both safety cohorts advanced to the expansion phase. All but one patient (CONV) received RT per protocol/with an acceptable variation. At the time of analysis, 24% had received all 13 cycles of durvalumab. For the ACRT cohort, there were 4 grade 3, 1 grade 4 (lymphopenia), and 1 grade 5 AE (lung infection, assessed as unrelated to therapy). For CONV, there were 8 grade 3, 0 grade 4, and 1 grade 5 AE (respiratory failure, unrelated to therapy). For feasibility, 10 of 12 (85%) patients in the ACRT cohort received the second dose of durvalumab (2 not received due to shingles and unrelated death), while 9 of 12 (75%) of the CONV cohort received the second dose (reasons for not receiving: viral hepatitis, bronchopulmonary hemorrhage, and respiratory failure, all assessed as unrelated to therapy). **Conclusions:** Chemotherapy-free thoracic RT approaches (ACRT or CONV RT) are safe, when given with concurrent durvalumab in patients with PD-L1 high LA-NSCLC. A trial to compare immunoradiotherapy and consolidation durvalumab to standard chemoradiation and consolidation durvalumab is planned. Clinical trial information: NCT03801902. Research Sponsor: U.S. National Institutes of Health.

8514 **Poster Discussion Session**

Distinct genomic and immunophenotypic features of solid-predominant versus nonsolid-predominant stage I lung adenocarcinomas and association with disease recurrence after surgical resection.

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Background: Compared to lung adenocarcinomas (LUAD) with nonsolid-predominant histology (lepidic, acinar, papillary, micropapillary), those with predominantly solid features have a higher risk of disease recurrence after surgical resection. However, little is known about the genomic landscape and immunophenotype of solid vs nonsolid stage I LUAD. **Methods:** We collected clinicopathologic data from patients with resected stage I NSCLC (AJCC 8th Edition), which underwent next-generation sequencing to identify genomic alterations and tumor mutational burden (TMB). A subset of these samples also had multiplexed immunofluorescence for CD8+, FOXP3+, PD-1+, and PD-L1 to determine differences in tumor immune cells subsets according to histologic subtype. Disease free-survival (DFS) was compared in patients based on their predominant histologic subtype (solid vs nonsolid). **Results:** Among 658 LUADs, 11.4% (N = 75) had solid-predominant and 88.6% (N = 583) nonsolid-predominant histology. After a median follow-up of 50 months from the time of surgery, 145 patients (22.0%) experienced recurrence. Compared to nonsolid-predominant LUAD, those with solid predominance had a significantly lower prevalence of activating *EGFR*, *BRAF*^{V600E}, and *METex14* mutations as well as *ALK*/*RET*/*ROS*1 rearrangements (9.3% versus 31.6%, P < 0.001), no difference in *KRAS*^{G12C} frequency (24% versus 16.8%, P = 0.14), a higher TMB (median 12.2 versus 7.2 mutations/megabase; P < 0.001), and a shorter median DFS from the time of surgical resection (43.2 months versus not reached, HR: 3.3 [95% CI: 2.2-4.9], P < 0.001). The detrimental effect of solid-predominant LUAD in DFS remained significant after adjusting for other factors such as tumor stage, surgery type, smoking status, and TMB (HR: 2.66 [95% CI: 1.71-4.11], P < 0.001]. Among LUADs profiled by multiplex immunofluorescence, compared to tumors with nonsolid-predominant subtype (N = 197), those with solid predominance (N = 23) had significantly higher numbers of CD8+, FOXP3+, PD-1+ immune cells, and PD-1+ CD8+ T cells, both intratumorally (P < 0.001) and at the tumor-stroma interface (P < 0.001). Solid-predominant subtype was also associated with a higher median PD-L1 expression level on tumor (5% versus 1%; P = 0.01) and immune cells (16% versus 7%, P = 0.02). **Conclusions:** Among patients with surgically-resected stage I LUAD, solid-predominant histology was associated with distinct genotypic and immunologic characteristics. These findings may aid in identifying patients at greater risk of recurrence after surgery. Research Sponsor: None.

8515 **Poster Discussion Session**

Surfaceome profiling to reveal unique therapeutic vulnerabilities in transcriptional subtypes of small cell lung cancer (SCLC).

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Background: Effective treatment options for SCLC remain limited and new treatment approaches are needed to improve outcome. We sought to validate the initial observation in cell lines and limited tissue samples of SCLC of a differential expression of cancer/testis (CT) antigens and TACSD2 gene that encodes surface protein, Trop2 across various subtypes of SCLC. We also tested whether overall surfaceome profile as previously described in other tumor types will show hierarchical priority of expression between transcriptionally defined SCLC subtypes. **Methods:** We conducted a comprehensive surfaceome profiling of SCLC samples using data generated by RNA sequencing (whole transcriptome) at Caris Life Sciences (Phoenix, AZ). SCLC tumors were stratified into 5 subgroups (SCLC-A/N/Y/P and -mixed) based on the relative expression of the four transcription factors. Expression values were converted to z-scores (the expression value for each gene is normalized to the average expression of that specific gene such that the z-score reflects the number of standard deviations above or below the average). The highest positive z-score among the 4 transcription factors determined subgroup. If all transcription factor z-scores for a given sample were negative, the sample was assigned to 'Mixed' subgroup. Significance was tested by Chi-square, Fisher's exact test, or Mann-Whitney U test. **Results:** We employed data generated from 674 SCLC samples; median age of 66 years and male (48.7%). The SCLC subtype distribution was 241 (35.8%), 120 (17.8%), 40 (5.9%), 143 (21.2%), 130 (19.3%) for types A, N, P, Y and mixed respectively. Supervised analysis for TACSTD2 expression showed highest levels in YAP1 subtype and was overall significantly increased in SCLC-Y (~3-fold) and SCLC-P (~2-fold) subtypes compared to A, N and mixed subtypes. Similarly, SCLC-Y subtype showed the highest median expression as well as the strongest correlation with most TACSTD2-interacting and regulatory genes. A top 10 list of candidate surface protein gene out of 3699 surfaceome genes was defined for each subtype based on the strength of correlation. The top candidate surface protein gene and CT antigen gene respectively by subtype were: SCN3A ($r = 0.7033$, $p = 1.08^{E-101}$) and NOL4, ($r = 0.574$, $p = 2.46^{E-60}$) for SCLC-A; SSTR2, ($r = 0.742$, $p = 8.18^{E-119}$) and TMEFF1, ($r = 0.3601$, $p = 4.53^{E-22}$) for SCLC-N; TMPRSS13 ($r = 0.5699$, $p = 2.64^{E-59}$) and LY6K ($r = 0.4778$, $p = 9.80^{E-40}$) for SCLC-P; and CYBRD1 ($r = 0.8559$, $p = 1.18^{E-194}$) and CTAGE5 ($r = 0.5521$, $p = 4.95^{E-55}$) for SCLC-Y. **Conclusions:** SCLC-Y subtype showed the highest expression of TACSTD2 and its interacting and regulatory genes. This subtype could serve as an enrichment factor for antibody-drug-construct targeting TROP2. Several candidate CT antigens and surfaceome genes showing strong correlation with lineage-defining transcription factors offer additional therapeutic targets in SCLC. Research Sponsor: None.

8516 **Poster Discussion Session**

Sintilimab plus anlotinib as second or further-line therapy for small cell lung cancer: An objective performance trial.

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Background: Small cell lung cancer (SCLC) tends to progress rapidly on first-line therapies, with limited subsequent-line treatment options. **Methods:** In this single-arm objective performance trial, adult patients with extensive-disease SCLC (ED-SCLC) received intravenous sintilimab 200 mg on day 1 and oral anlotinib 12 mg on days 1-14. Treatment lasted for 3 weeks per cycle and was continued until disease progression, unacceptable toxicities, or death. The primary endpoint was the superiority of progression-free survival (PFS) *versus* a PFS of 2.8 months with historical topotecan control. **Results:** Forty-two patients were enrolled, and 39 patients were evaluable for efficacy. Twenty-six patients (66.7%) had ED-SCLC, and 13 (33.3%) relapsed after concurrent chemoradiotherapy. The median follow-up was 11.9 months. The median PFS was 6.0 months (95%CI: 4.8-7.2). The 6- and 12-month PFS rate was 50.5% and 27.8%, respectively. Fourteen patients died by the data cut-off date, and overall survival (OS) was immature (16.1 months, 95%CI: 9.4-22.7). The 12- and 18-month OS rate was 56.7% and 42.5%, respectively. Three patients attained complete response and 16 achieved partial response, and 12 patients had stable disease; the objective response rate was 48.7% and the disease control rate was 79.5%. Forty patients (95.2%) had at least one treatment-related adverse event (TRAE). The most frequent TRAEs were hypothyroidism (45.2%), hypoproteinemia (40.5%) and elevated gamma-glutamyl transpeptidase (38.1%). **Conclusions:** Immunotherapy with sintilimab plus antiangiogenic drug anlotinib demonstrated promising antitumor activities as second or further-line therapy for ED-SCLC and had manageable toxicities. The findings support further development of this combination regimen for ED-SCLC. Clinical trial information: NCT04055792. Research Sponsor: None.

8517 **Poster Discussion Session**

Primary analysis from the phase 2 study of continuous talazoparib (TALA) plus intermittent low-dose temozolomide (TMZ) in patients with relapsed or refractory extensive-stage small cell lung cancer (ES-SCLC).

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Background: TALA exhibits cytotoxic effects by inhibiting poly (ADP-ribose) polymerase (PARP) proteins 1 and 2 in addition to "trapping" PARP on DNA. TMZ has been shown to increase antitumor response when combined with TALA in SCLC models (Wainberg AACR 2016). TALA plus TMZ as second-line therapy for ES-SCLC may improve disease-related outcomes. **Methods:** This is a phase 2, open-label, single-arm study of the safety and efficacy of TALA plus TMZ in patients with ES-SCLC, relapsed or refractory to a first-line platinum-based regimen. Participants receive TALA 0.75 mg (or 0.5 mg if creatinine clearance < 60 mL/min) po daily on 28-day cycles with TMZ 37.5 mg/m2 po on days 1-5. The primary endpoint is objective response rate (ORR) based on RECIST 1.1 criteria, versus a historical control of 15% ORR in second-line topotecan, with the null hypothesis rejected for 8 or more confirmed responses among 28 evaluable subjects (29% ORR). Secondary endpoints include progression-free survival, overall survival, duration of response, and time to response. Exploratory endpoints include biomarker studies such as status of DNA damage response genes (DDR) and patient reported outcomes. A Simon two-stage design was utilized to reach a total accrual of 28 evaluable patients. **Results:** Thirty-one subjects were enrolled, of which 3 were non-evaluable due to ineligibility (1) or early withdrawal of consent prior to first disease assessment (2). Eleven of 28 evaluable subjects (39.3%) achieved a confirmed partial response. The ORR was similar among platinum-refractory (3/6), -resistant (4/9), and -sensitive subgroups (4/13). The median time to response was 1.8 months (m), duration of response 5.8 m, progression free survival 4.5 m, and overall survival 11.9 m. Adverse events (AEs) were manageable, with grade ≥ 3 AEs being thrombocytopenia (61.3%), anemia (54.8%), neutropenia (41.9%), and atypical pneumonia (3.2%), which responded well to dose-hold or dose-reduction and transfusion or growth factor support as needed. Cell free DNA and tissue analysis demonstrated no germline DDR mutations among the trial subjects, but somatic DDR mutations at baseline and acquired during treatment were common. Three subjects remain on study treatment. **Conclusions:** The study exceeded its target response rate. This is the second trial to demonstrate a benefit of PARP inhibition with low-dose TMZ in SCLC (see Farago Cancer Discovery 2019). A phase 3 study is appropriate to confirm the benefit of this approach compared to currently approved options. Clinical trial information: NCT03672773. Research Sponsor: Pfizer.

8518 **Poster Discussion Session**

Targeting genomic instability in extrapulmonary small cell neuroendocrine cancers: A phase II study with ATR inhibitor berzosertib and topotecan.

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Background: Extra-pulmonary small cell neuroendocrine cancers (EP-SCNC) are rare cancers with no standard treatments at relapse that share molecular similarities with small cell lung cancer (SCLC). Concurrent inhibition of ataxia telangiectasia and Rad3 related (ATR) and topoisomerase 1, key enzymes for maintaining genomic stability, exacerbated replication stress in SCLC cells and produced durable antitumor responses in patients with relapsed SCLC (Cancer Cell 2021; PMID: 33848478). **Methods:** Combination of berzosertib and topotecan was evaluated in patients with relapsed EP-SCNC (NCT02487095). Berzosertib was administered at 210 mg/m^2 on days 2 and 5 and topotecan 1.25 mg/m^2 on days 1-5 in 21-day cycles. Whole exome sequencing (WES) and transcriptome analyses were performed to assess the genomic features associated with response. **Results:** Fifteen patients with EP-SCNC involving various primary sites were enrolled [three each: cervix, transformed SCLC; two each: bladder, breast, prostate; one each: gallbladder, ovary, rectum]. Two patients (13.3%: breast and rectum) achieved a confirmed partial response (PR; -72.2% and -48.5% tumor reduction in size) lasting 6.9 and 5.8 months. Responses occurred irrespective of platinum-sensitivity or prior treatment with topotecan or immunotherapy. Pre-treatment tumor gene expression profiles of EP-SCNC patients who achieved clinical benefit revealed enrichment of neuroendocrine differentiation (normalized enrichment score and p-value of a gene set enrichment analysis: 2.1 and 2.1 x 10^{-4}). Principal component analysis showed convergent gene expression profiles of both SCLC and EP-SCNC patients who achieved PR. Pre-treatment tumor of a breast small cell cancer patient who achieved durable response revealed amplifications of multiple genes driving replication stress such as *KRAS* and *CCND1*. Longitudinal tumor sampling of the patient through treatment course revealed increasing intra-tumor heterogeneity as a potential resistant mechanism. **Conclusions:** Combination of berzosertib and topotecan is a novel therapeutic paradigm for patients with EP-SCNCs. Both SCLCs and EP-SCNCs responding to this approach show a similar transcriptional phenotype characterized by high replication stress. Clinical trial information: NCT02487095. Research Sponsor: U.S. National Institutes of Health.

8519 **Poster Session**

Adjuvant icotinib versus observation in patients with completely resected, EGFR-mutated, stage IB non–small cell lung cancer (GASTO1003, CORIN): A randomized phase II trial.

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Background: The role of adjuvant therapy in patients with completely resected stage IB non-small-cell lung cancer (NSCLC) remains to be determined. Icotinib is standard-of-care therapy for patients with advanced NSCLC harboring epidermal growth factor receptor (EGFR) mutation. This phase II study investigated whether adjuvant therapy with icotinib improves the clinical outcome compared with observation in patients with EGFR mutation-positive resected stage IB NSCLC. **Methods:** This phase II, open-label, randomized study (GASTO1003, CORIN) was conducted at Sun Yat-sen University Cancer Center. From May 2013 to December 2020, patients with completely resected, EGFR mutation-positive, stage IB (7th TNM staging for NSCLC) NSCLC without adjuvant chemotherapy according to physician and patient choices were enrolled. The patients were assigned in a 1:1 ratio to receive adjuvant therapy with icotinib (125mg, three times daily) for 12 months or to undergo observation. Therapy continued until disease progression or intolerable toxicity. The primary endpoint was disease-free survival (DFS). Secondary endpoints included overall survival (OS) and toxicity. Survival endpoints were assessed in the intention-to-treat population. **Results:** Three patients withdrew consent and were excluded. A total of 128 patients were enrolled and randomized, with 63 patients in the icotinib group and 65 patients in the observation group. Baseline characteristics were well balanced between the groups. The median duration of follow-up was 34.9 months. A total of 13 recurrence events occurred, including 2 in the icotinib arm and 11 in the observation arm. DFS was significantly longer among those in the icotinib arm than among those in the observation arm (hazard ratio: 0.20, 95% confidence interval, 0.04-0.89; P = 0.018). The 3-year DFS for the icotinib and observation arms were 95.3% and 86.7%, respectively. The OS data were immature with 3 deaths in the observation arm. The safety profile was consistent with the known safety profile of icotinib. Icotinib was well tolerated with no unexpected adverse events. No treatment-related death occurred. **Conclusions:** Adjuvant icotinib shows prolonged DFS and acceptable toxicity in patients with completely resected EGFR-mutated stage IB NSCLC. Ajuvant icotinib provides a treatment option for these patients. Clinical trial information: NCT02264210. Research Sponsor: Betta pharmaceuticals.

8520 **Poster Session**

Patients' preferences for adjuvant osimertinib in non–small cell lung cancer (NSCLC) after complete surgical resection: What makes it worth it to patients? (PATT)—The Roswell Park (RP) Comprehensive Cancer Center experience.

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Background: There are clinical controversies surrounding the US FDA approval of Osimertinib in December 2020 as adjuvant therapy, based on disease-free survival (DFS) improvement in patients (pts) with surgically resected stage IB-IIIA EGFRm NSCLC. We initiated a survey study to investigate our hypothesis that DFS benefit alone even without significant OS maybe deemed a valuable endpoint to pts after considering trade-offs. **Methods:** Participants were recruited from pts seen at the RP Thoracic Clinic from 01/21 to 12/21. Eligible pts who were being evaluated for adjuvant systemic therapy following surgical resection were given a self-administered survey based on the validated questionnaire by Blinman et al, which was modified to provide explanation of the differences between OS and DFS and the ADAURA trial results. Survey responses were collected in an online repository. Associations between survey responses and demographics were assessed using Fisher's exact test. Changes in preference responses were assessed using McNemar's test. **Results:** A total of 524 pts with NSCLC were screened, of which 101 pts were eligible to receive the survey. 51 pts (50%) responded to the survey. Median age of respondents was 69yrs (37-83), majority were female (69%, n = 35,), married (61%, n = 31), retired (63%, n = 32), had at least some college or higher education level(54%, n = 28), with history of smoking (84%, n = 43) and with stage IIIA (43%, n = 22) adenocarcinoma (80%, n = 41). To evaluate toxicity-related tradeoffs (Q1), a ≥12 mo. improvement in OS benefit was needed for 66% of pts to consider adjuvant Osi. However, an increase of ≥ 6 mo. of DFS was enough for 66% of pts to justify taking a daily medication (Q2). One mo. increase in DFS or OS was not enough for 60% and 78% of pts respectively to justify taking the medication. A threshold 1% increase in 5-year OS was sufficient to persuade patients to take Osi for three years, even with respect to toxicity side effects (p = 0.023). (Q3). Finally, in the hypothetical cost-based scenario (Q4), there was no indication that pts were willing to pay more for each incremental increase in OS. There appears to be some association between employment status (p =.033) or educational degree (p =.049) for tolerance of side effects if there is at least 1 additional year of DFS or OS. **Conclusions:** We observed that the value patients ascribe to adjuvant Osimertinib is influenced by factors besides efficacy. Knowing pts' preferences for cancer treatments can better inform regulatory bodies in formulating cost-sharing structure for cancer therapies. Our study highlights the importance of shared decision making based on individual pts' preferences. Research Sponsor: None.

8521 **Poster Session**

Predictors of adjuvant chemotherapy refusal in lung cancer: A National Cancer Database Study.

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Background: Adjuvant chemotherapy (AC) have been shown to improve overall survival in non-small cell lung cancer (NSCLC). Despite showing significant survival benefit across various age groups, patients are known to refuse AC. However, the factors associated with such a decision remain poorly understood in lung cancer. We therefore sought to investigate the factors associated with AC refusal in a nationally representative database in the United States (US). **Methods:** From 2004 to 2017, adults (≥20 years) with histologically confirmed non-small cell lung cancer (NSCLC) who underwent complete resection and were deemed to be chemotherapy eligible (node-positive or size ≥5 cm) were identified in the National Cancer Database (NCDB). Annual trends and factors associated with refusal of AC in chemotherapy-eligible NSCLC patients were evaluated using Joinpoint regression and multivariable logistic regression. **Results:** Among the 44,957 patients who met the inclusion criteria, 18,468 (3,678 (8.2%)) were noted to refuse chemotherapy in the NCDB. Patients refusing adjuvant chemotherapy were more likely to be elderly (OR 1.08, 95% CI, 1.07-1.08; *P*<.001), uninsured when compared with government insurance (OR 1.79, 95% CI, 1.38-2.33; *P*<.001), treated in the Western region of the when compared with patients in the Northeast (OR 1.47, 95% CI, 1.28-1.68; *P*<.001). They were also more likely to have a higher Charlson score versus patients with Charlson score of zero (OR 1.31, 95% CI, 1.18-1.46; *P*<.001), have squamous cell carcinoma versus adenocarcinoma (OR 1.20, 95% CI, 1.11-1.31; *P*<.001), undergo pneumonectomy versus lobectomy (OR 1.31, 95% CI, 1.16-1.47, *P*<.001), and have ≥2 weeks hospital length of stay versus < 2 weeks (OR 2.25, 95% CI, 1.93-2.63; *P*<.001). **Conclusions:** In our analysis, we identified several sociodemographic and clinicopathologic variables that were independently associated with chemotherapy refusal. We saw the number of patients refusing AC increased sharply during the study period. Our study shows that in addition to poor post-operative recovery, underlying sociodemographic factors might predict patients at risk for refusing adjuvant chemotherapy in lung cancer. Further understanding of these factors might help devise effective interventions to motivate patients to undergo potentially life-extending chemotherapy in lung cancer. Research Sponsor: None.

8522 **Poster Session**

The Lung ART adjuvant radiotherapy phase 3 randomized trial: Impact of quality of resection in stage IIIAN2 patients.

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Background: Lung ART is an international phase 3 trial whose main objective was to evaluate the impact of post-operative conformal radiotherapy (PORT) on disease-free survival (DFS) in patients with completely resected pathologically proven N2 non-small cell lung cancer (NSCLC), with or without neo- or adjuvant chemotherapy. Previously communicated results showed no impact of PORT on DFS. However, as quality of surgical resection and extent of lymph node dissection were expected to be critically important in the interpretation of results, surgical and pathological reports were centrally reviewed by a surgical committee. **Methods:** A surgical advisory committee composed of 4 expert thoracic surgeons reviewed anonymized surgical and pathological reports of all included patients. Predefined classification rules were defined using published guidelines from the International Association for the Study of Lung Cancer and the European Society of Thoracic Surgeons. Tumor resection was defined as complete (no residual tumor and adequate lymph node assessment), uncertain (highest mediastinal nodal station involved, incomplete nodal exploration, involved N2 removed in fragments) or incomplete (presence of residual tumor). Nodal exploration was classified as sampling, selective dissection or extensive dissection. **Results:** 501 patients were included in the Lung ART trial. Before surgical committee review intervention, all patients except 2 had complete resection. 496 patients' reports were analyzed by the surgical advisory committee. The basic characteristics are specified in the following table:. **Conclusions:** Monitoring of the quality of nodal exploration and of resection should be implemented in randomized studies evaluating peri-operative strategies in NSCLC in order to provide reliable and generalizable results. Clinical trial information: NCT00410683. Research Sponsor: French National Cancer Institute, Programme Hospitalier de Recherche Clinique from the French Health Ministry, Gustave Roussy, Cancer Research UK, Swiss State Secretary for Education, Research, and Innovation, Swiss Cancer Research Foundation, Swiss Cance.

Pre-op chemotherapy (n(%))	All included patients (n = 501)	
	96 (19%)	
	Right tumors (n = 281)	Left tumors (n = 218)
Type of surgery (n(%))		
- (bi-)lobectomy	258 (92%)	176 (81%)
- pneumonectomy	19 (7%)	36 (17%)
- other	4 (1%)	6 (3%)
Mediastinal nodes examined (median n(interquartile range))	11 (6-17)	8 (5-13)
Mediastinal nodes involved (median n(interquartile range))	2 (1-3)	1 (1-2)

Nodal dissection was performed according to lobar location specific recommendations in 69% patients. Regarding nodal dissection: 28% patients had sampling, 17% selective dissection and 55% systematic dissection. Resection was considered complete (R0) in 28%, uncertain in 42%, microscopically incomplete (R1) in 30% and macroscopically incomplete (R2) in 2 patients. 3-year DFS according to R0, R(un) and R1 status was respectively, 70% (95%CI 28-not reached (NR)), 24% (17-34) and 26% (15-84) in the PORT arm, and 62% (21-NR), 24% (15-44) and 16% (10-23) in the control arm.

8523 **Poster Session**

Checkpoint inhibitor consolidation after definitive chemoradiation for stage III non–small cell lung cancer: Real-world experience in a large academic health system.

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Background: The PACIFIC trial demonstrated a 10% improvement in 5-year survival with the addition of consolidation durvalumab versus placebo after chemoradiation (CRT) in good performance status patients (pts) with stage III non-small cell lung cancer (NSCLC). However, not all patients who complete CRT go on to receive consolidation durvalumab. We sought to describe real-world use of consolidation durvalumab or other immune checkpoint inhibitors (ICI) in this setting within a single academic health system. **Methods:** We retrospectively identified pts with unresectable stage III NSCLC treated with definitive CRT between October 2017 and October 2020 within the University of Pennsylvania Health System, including two urban hospitals and two satellite centers. Pts either received consolidation ICI (ICI group) or did not (no ICI group). Baseline characteristics of the groups were compared with the Chi-squared, Fisher exact, or Wilcoxon rank-sum test as appropriate. Overall survival (OS), measured from the last day of CRT, was compared using the Kaplan-Meier method and log-rank test. **Results:** Of the 148 consecutively treated pts who completed CRT, 108 (73%) received consolidation ICI; 40 (27%) did not. Within the ICI group, 42% completed 1 year (yr) of treatment. Within the no ICI group, reasons for non-receipt included disease progression (n = 14, 35%), CRT toxicity (n = 7, 18%), comorbidity or decline unrelated to CRT (n = 7, 18%), provider choice (n = 6, 15%) due to EGFR mutation (n = 5) or atypical histology (n = 1), pt refusal (n = 3, 8%), and death without progression (n = 3, 8%). The ICI group had better performance status (ECOG 0/1/2, 46%/49%/5% ICI vs 25%/48%/28% no ICI, $p < 0.001$) lower Charlson Comorbidity Index (median, 5 [IQR 4-6] ICI vs 6 [IQR 5-8] no ICI, $p = 0.02$), and lower rates of active autoimmune disease or immunosuppression (5% ICI vs 15% no ICI, $p = 0.03$). There were no differences between groups in age (median, 68 yrs [IQR 63-73] ICI vs 71 yrs [IQR 65-73] no ICI, $p = 0.25$), sex (female, 60% ICI vs 50% no ICI, $p = 0.27$), race (Black, 19% ICI vs 20% no ICI, $p = 0.82$), stage (IIIA/B/C, 42%/48%/11% ICI vs 40%/50%/10% no ICI, $p = 0.96$), and PD-L1 expression (< 1%/1-50%/ > 50%/unknown, 36%/25%/29%/10% ICI vs 40%/25%/28%/8% no ICI, $p = 0.97$). 1- and 2-yr OS were 83% and 61% in the ICI group versus 52% and 34% in the no ICI group, respectively ($p < 0.001$). Within the no ICI group, OS was worse among those with versus those without disease progression (PD) post-CRT (1-yr OS 24% vs 74%, $p = 0.03$). **Conclusions:** In this retrospective study within a large academic health system, we found that over one-quarter of pts who completed chemoradiation for stage III NSCLC did not receive consolidation ICI, most commonly due to disease progression, CRT toxicity, or comorbidity. Survival amongst these pts is particularly poor, especially for those who experience PD shortly after CRT. Research Sponsor: None.

8524 **Poster Session**

Analysis of patients with relapsed small cell lung cancer (SCLC) receiving single-agent lurbinectedin in the phase 3 ATLANTIS trial.

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Background: Lurbinectedin, a selective inhibitor of oncogenic transcription, received accelerated approval from the US FDA in June 2020 as monotherapy (3.2 mg/m^2 IV every 21 days) for adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy. This approval was based on the overall response rate (35.2%) and duration of response (DOR; 5.3 months) observed in 105 patients from a phase 2 trial. The ATLANTIS trial (NCT02566993) investigated the combination of lurbinectedin 2.0 mg/m^2 IV + doxorubicin (DOX) 40.0 mg/m^2 IV versus topotecan or CAV. This *post hoc* analysis explored the efficacy and safety of single-agent lurbinectedin in patients who completed 10 cycles of the combination and then switched to lurbinectedin monotherapy per protocol. **Methods:** Eligible patients were ≥18 years of age with limited-stage or extensive-stage SCLC, 1 prior line of platinum-based chemotherapy (PD-1/PD-L1 inhibitors were also permitted), ECOG PS ≤2, and chemotherapy-free interval ≥30 days. Tumor assessments were per an independent review committee (IRC). **Results:** Patients who completed 10 cycles of lurbinectedin + DOX and switched to lurbinectedin monotherapy (n = 50) had a median age of 61.5 years (range: 43, 77); 62% were male; and 100% had an ECOG PS < 2. The overall median number of cycles was 15 (range: 11, 47) and included a median of 5 (1, 37) cycles on monotherapy. The majority of patients who switched to lurbinectedin monotherapy maintained or improved their tumor response (Table). All 3 patients who achieved a complete response (CR) on combination therapy maintained their CR on monotherapy. Of the 26 patients with a partial response (PR) on combination therapy, 3 (12%) achieved a CR and 15 (58%) maintained their PR. Of the 19 patients with stable disease (SD) on combination therapy, 3 (16%) improved from SD to PR (n = 2) or CR (n = 1) and 8 (42%) maintained SD. The median DOR was 8.3 months (95% CI: 7.1, 11.0). The median overall survival (OS) was 20.7 months (95% CI: 15.7, 24.8). Grade 3/4 hematologic abnormalities based on laboratory assessment included lymphopenia (36%), anemia (16%), thrombocytopenia (12%), neutropenia (12%), and leukopenia (10%). Febrile neutropenia was reported in 4% of patients. **Conclusions:** Patients with relapsed SCLC in ATLANTIS who completed 10 cycles of lurbinectedin + DOX combination and switched to lurbinectedin monotherapy tended to maintain or improve their tumor response (including an increase in CRs), with favorable OS and DOR and acceptable tolerability with no new safety signals. Clinical trial information: NCT02566993. Research Sponsor: PharmaMar.

	Best response to lurbinectedin monotherapy (3.2 mg/m^2; n = 50), n[a]				
Best response to lurbinectedin + DOX, n	CR	PR	SD	PD	Total
CR	3	–	–	–	3
PR	3	15	–	8	26
SD	1	2	8	8	19
Total	7	17	8	16	48[b]

PD, progressive disease.
[a]41 patients at 3.2 mg/m^2, 3 patients at 2.6 mg/m^2, and 6 patients at 2.0 mg/m^2.
[b]2/50 patients did not have a tumor assessment on monotherapy per IRC.

8525 **Poster Session**

A real-world (rw) evidence study quantifying the clinical value of multi-gene testing in early-stage lung adenocarcinoma (LUAD).

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Background: Resected early-stage NSCLC has high risk of recurrence, and tyrosine kinase inhibitors (TKIs) and immune checkpoint inhibitors (ICI), each requiring testing for precision biomarkers, have recently been approved in the adjuvant (adj) setting. We assessed the potential value of multi-gene testing in early NSCLC via enabling timely 1L therapy selection at recurrence and through avoidance of adj ICI in pts with driver alterations unlikely to benefit per current guidelines and the label for atezolizumab in first line (1L) NSCLC. **Methods:** Using the nationwide (~280 US cancer clinics) de-identified EHR-derived rw Flatiron Health- Foundation Medicine clinico-genomic database, we selected 6,725 evaluable pts with LUAD who underwent tissue comprehensive genomic profiling (CGP) as part of routine cancer care (01/2011 – 06/2021). We focused on alterations in 4 drivers (*EGFR*, *ALK*, *ROS1*, *RET*) and studied prevalence in early-stage specimens versus advanced (adv) specimens, as well as the rate of timely delivery of 1L therapy at recurrence for pts receiving CGP in early disease. We estimated the cost implications of adj ICI in pts with PD-L1+ LUAD and an *ALK*, *ROS1*, or *RET* fusion with a probabilistic decision tree. **Results:** CGP was performed on 1,490 specimens collected prior to adv disease (stage I 36%, II 27%, IIIA 37%) and ordered prior to adv diagnosis for 981 pts (15% of total, median 10 weeks after initial diagnosis). In specimens collected in early (n = 1,490) or adv (n = 5,130) stage LUAD, CGP identified drivers in *EGFR* (early/adv: 13%/16%), *ALK* (2.0%/4.2%), *ROS1* (0.7%/1.1%), *RET* (1.0%/1.1%), and prevalence was similar when limiting to PD-L1+ cases. Studying 596 pts with recurrence and CGP on samples collected prior to recurrence, pts with CGP results obtained before (n = 196) vs after (n = 400) recurrence had less time between recurrence and start of any 1L therapy (median 3.1 vs 5.9 weeks, $p < 0.001$). In the subset with a targetable driver detected, 32/42 (76%) with CGP before recurrence initiated matched 1L TKI while 43/67 (64%) with CGP after recurrence received matched 1L TKI ($p = 0.2$). Through avoidance of ICI in PD-L1+ early LUAD with an *ALK*/*ROS1*/*RET* driver, we estimate universal CGP (compared to *EGFR* single-gene testing) could reduce per pt expected costs by $875 (an average incremental $4,050 treatment cost reduction compared to a $3,175 increase in diagnostic cost per pt). **Conclusions:** CGP of early-stage LUAD can identify *EGFR*, *ALK*, *ROS1* and *RET* drivers and enable appropriate selection of precision therapies and timely use of effective 1L therapy at recurrence. Assuming adj ICI maintains the lack of activity in *RET*/*ROS1* as seen for *ALK*, CGP could represent a cost-effective approach for avoiding futile adj ICI and reducing the risk of subsequent TKI-associated toxicity. Additional analysis of driver+ pts receiving adj ICI is needed to help balance the risk/benefit for these high risk pts. Research Sponsor: Foundation Medicine.

8526 **Poster Session**

Racial disparities in the clinical use of durvalumab for patients with stage III unresectable non–small cell lung cancer treated at Veterans Health Administration facilities.

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Background: Evidence from the PACIFIC study and real-world data highlight the benefit of durvalumab in patients with stage III unresectable non-small cell lung cancer (UR-NSCLC). However, limited literature exists regarding disparities in durvalumab treatment patterns such as treatment initiation delays (TID), treatment interruptions (TI), number of doses, duration of therapy (DOT), adverse effects (AEs), and treatment discontinuation (TD) in minority populations. **Methods:** Patients with stage III UR-NSCLC and a self-reported racial identity of Black or White treated with durvalumab following chemoradiotherapy (CRT) at any Veterans Health Administration (VHA) facility from January 1, 2017 to June 30, 2020 were included. Patients were followed from their date of durvalumab initiation through the earliest of their last VHA visit, loss to follow up, death, or end of the study; therefore, all patients had the opportunity to be treated for 12 months. Patients were excluded if durvalumab therapy was ongoing at the end of the study. Patient charts were retrospectively reviewed for baseline characteristics and durvalumab treatment patterns including TID (>42 days from end of CRT to durvalumab start), TI (>28 days between doses), number of doses, DOT, AEs, and TD. Nominal variables were compared using chi-square/Fisher's exact tests. Continuous variables were compared using Student's t-tests/Wilcoxon Rank Sum tests. **Results:** Among 924 patients, Black patients were younger than White patients (median age 67 years [IQR, 63-71] vs. 70 years [IQR, 65-73]; p<0.01), more likely to be current smokers (54% vs. 45%; p=0.03), with more chronic liver disease (22% vs. 9%; p<0.01), but less COPD (63% vs. 72%; p=0.01). Black patients experienced more TI (25% vs. 18%; p=0.03) but TID, number of doses, DOT, and TD were similar between the groups. Black patients were less likely to have an immune-related AE (irAE) (28% vs. 36%; p=0.03) (and less pneumonitis (7% vs. 14%; p<0.01)). Toxicity was the reason for TD in 12% of Black patients vs. 20% of White patients (p=0.01), with no other significant ($\alpha < 0.05$) differences in reported reasons for TID, TI, or TD between the groups. **Conclusions:** In this real-world study, Black patients experienced similar TID, number of doses, and DOT as White patients. Black patients were less likely to experience an irAE (including pneumonitis) but experienced more TI; TD were similar but more likely to be from toxicity for White patients. Future research is needed to validate these findings. Research Sponsor: AstraZeneca.

Race and durvalumab treatment patterns.

Outcome	White (n=726)	Black (n=198)	P-value
Patients with TID	38%	45%	0.07
Patients with TI	18%	25%	0.03
Number of doses, median (IQR)	15 (7-24)	18 (7-25)	0.25
DOT (months), median (IQR)	8.7 (2.9-11.8)	9.8 (3.6-12.0)	0.08
Patients with irAEs	36%	28%	0.03
Pneumonitis	14%	7%	<0.01
Patients with TD	60%	54%	0.09

8527 **Poster Session**

PD-L1 score as a prognostic biomarker in Asian patients with early-stage, EGFR-mutated lung cancer.

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Background: Adjuvant Atezolizumab was recently approved in stage II-IIIA non-small cell lung cancer (NSCLC) with PD-L1 ≥1%. However, disease-free survival (DFS) benefit was mainly driven by PD-L1 ≥50% and among *EGFR*-mutated subgroup, atezolizumab did not demonstrate DFS benefit when PD-L1 0% patients were included. We sought to determine the prognostic value of PD-L1 score in early-stage *EGFR*-mutated NSCLC. **Methods:** Consecutive patients with Stage IA-IIIA NSCLC diagnosed 1/1/2010 – 31/12/2019 who underwent curative surgery at National Cancer Centre Singapore with evaluable *EGFR* and PD-L1 status were included. Co-primary endpoints were 2-year DFS and 5-year overall survival (OS) by Kaplan-Meier method. **Results:** 455 patients were included (267 *EGFR*-mutant; 188 *EGFR*-wildtype). Median age at diagnosis was 65 years, 52.3% (238/455) were males and 62.9% (286/455) were never-smokers. Adenocarcinomas comprised 92.1% (419/455) and 92.5% (421/455) had R0 resection. Stage IA comprised 42.4% (193/455), Stage IB 23.1% (105/455), Stage II 15.8% (72/455) and Stage IIIA 18.7% (85/455). Among *EGFR*-mutant, 45.3% (121/267) were Ex19del and 41.9% (112/267) were L858R. PD-L1 ≥1% among *EGFR*-mutant and *EGFR*-wildtype was 55.8% (149/267) and 60.1% (113/188) respectively (p = 0.361). PDL1 ≥50% was significantly associated with higher stage at diagnosis among *EGFR*-mutant (p < 0.001) but not *EGFR*-wildtype (p = 0.319). At median follow up of 47 months, 178 patients had relapsed. Among *EGFR*-mutant, 2-year DFS comparing PD-L1 0% and PD-L1 ≥1% was 79.0% and 68.9% (p = 0.006) while 5-year OS was 87.6% and 70.6% (p = 0.006) respectively. 2-year DFS and 5-year OS by PD-L1 tertile (as shown in table) revealed that higher PD-L1 score was prognostically worse for both DFS and OS among *EGFR*-mutant. A similar trend was observed among *EGFR*-wildtype but did not reach statistical significance, apart from PD-L1 ≥50% which had significantly inferior DFS. **Conclusions:** Higher PD-L1 score was significantly associated with worse DFS and OS among early-stage *EGFR*-mutated NSCLC, possibly due to higher stage at diagnosis among PDL1 ≥50%. Our study highlights the poor prognosis of PDL1 ≥50% *EGFR*-mutated NSCLC in a pre-osimertinib era and underscores the importance of personalised risk-stratified adjuvant strategies. Research Sponsor: Singapore National Medical Research Council (NMRC; grant No. NMRC/TCR/007-NCC/2013 and NMRC/OFLCG/002-2018).

		2-year DFS (95% CI)	HR (95% CI)	p value	5-year OS (95% CI)	HR (95% CI)	p value
***EGFR*-mutant**	PD-L1 0% (n = 118)	79.0% (70.3%-85.4%)	1		87.6% (77.4%-93.4%)	1	
	PD-L1 1-49% (n = 133)	71.9% (63.4%-78.8%)	1.58 (1.06-2.36)	0.025	70.6% (56.5%-80.9%)	2.38 (1.18-4.82)	0.016
	PD-L1 ≥50% (n = 16)	43.8% (19.8%-65.6%)	2.89 (1.51-5.53)	0.001	68.7% (34.3%-87.7%)	3.14 (1.17-8.43)	0.023
***EGFR*-wildtype**	PD-L1 0% (n = 75)	76.8% (65.3%-84.9%)	1		76.9% (62.5%-86.4%)	1	
	PD-L1 1-49% (n = 71)	70.6% (58.3%-80%)	1.41 (0.85-2.35)	0.179	61.7% (42.9%-75.9%)	1.17 (0.61-2.21)	0.639
	PD-L1 ≥50% (n = 42)	42.2% (26.8%-56.8%)	2.22 (1.30-3.81)	0.004	57.2% (39.6%-71.4%)	1.64 (0.85-3.17)	0.141

8528 **Poster Session**

Pre-existing interstitial lung abnormalities are independent risk factors for interstitial lung disease during durvalumab treatment after chemoradiotherapy in patients with locally advanced non–small lung cancer.

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Background: The standard treatment for locally advanced non-small cell lung cancer (NSCLC) is chemoradiotherapy (CRT) followed by treatment of durvalumab, one of immune checkpoint inhibitors (ICI). Interstitial lung disease (ILD) is a clinically life-threatening toxicity of CRT or durvalumab. The patient-characteristics or dose-volume histogram parameters of radiotherapy have been reported to be the risk factors for radiation-induced pneumonitis. However, the risk factors for ILD during durvalumab therapy has not been established. Interstitial lung abnormalities (ILA) are generated by aging or smoking, and manifest as minor interstitial shadow on lung computed tomography (CT). We previously reported that ILA were risk factors for ICI-induced ILD in patients with advanced NSCLC, as well as non-lung cancer. Therefore, we investigated whether ILA could be risk factors for ILD during the durvalumab therapy. **Methods:** We retrospectively enrolled NSCLC patients who received durvalumab after CRT at 10 institutions from July 2018 to June 2021. Patient-information, patient-characteristics, dose-volume histogram parameters, chest CT findings, and laboratory data, were obtained. CT findings were examined using CT obtained after CRT and prior to durvalumab therapy. **Results:** A total of 153 patients were enrolled, and the prevalence of ILA was 37.8% (56 patients) before durvalumab treatment. Among the enrolled patients, 94 (63.5%) developed ILD during durvalumab therapy. The proportion of patients with grade 1, grade 2, or grade 3 ILD was observed to be 29.7% (44 patients), 25.7% (38 patients), and 8% (12 patients), respectively. Univariate logistic regression analysis revealed that higher age, higher dose volume histogram parameters (V5, V20, mean lung dose), and the presence of ILA were significant risk factors for grade 2 or more ILD. Multivariate logistic regression analysis showed that ILA, especially ground grass attenuation in ILA, was an independent risk factor for grade 2 or more ILD (odds ratio: 7.02, 95% CI: 2.95-16.69, $p < 0.0001$). **Conclusions:** Pre-existing ILA are risk factors for ILD during durvalumab treatment after CRT. This observation is consistent with previously reported findings in patients with advanced lung cancer and non-lung cancer. Therefore, we should pay more attention to the development of grade 2 or more ILD during durvalumab treatment in patients with ILA. Research Sponsor: None.

8529 **Poster Session**

Observer performance study to examine the feasibility of the AI-powered PD-L1 analyzer to assist pathologists' assessment of PD-L1 expression using tumor proportion score in non–small cell lung cancer.

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Background: Programmed death ligand 1 (PD-L1) expression is the standard biomarker for PD-L1 inhibitors in advanced non-small cell lung cancer (NSCLC). However, evaluation of PD-L1 tumor proportion score (TPS) by pathologists causes inter-observer variation and demands time to interpret. This study aimed to evaluate the benefit of the artificial intelligence (AI) algorithm in assisting pathologists to determine TPS on PD-L1 immunohistochemistry (IHC) whole-slide images (WSIs) in NSCLC. **Methods:** Lunit SCOPE PD-L1, an AI-powered PD-L1 TPS analyzer, was developed from 393,565 tumor cells annotated by board-certified pathologists for PD-L1 expression in 802 WSIs stained by 22C3 pharmDx IHC. The AI model was developed based on a region-based convolutional neural network, and the model can detect and count PD-L1 positive or negative tumor cells from WSIs to calculate TPS. Seven independent board-certified pathologists scored ground truth (GT) of PD-L1 TPS from 199 WSI of NSCLC stained by 22C3 pharmDx IHC. TPS from each GT reader was grouped as negative (< 1%), low (1% to 49%), or high (≥ 50%). The GT of each slide was determined by the consensus of GT readers. Another twelve independent board-certified pathologists scored PD-L1 TPS from the same WSIs as observer performance testers (OPT). They scored TPS twice with a washout interval of 4 weeks, with or without AI assistance. TPS accuracy change and reading time of OPT reader according to the presence or absence of AI assistance were analyzed. **Results:** The standalone accuracy of the AI model was 0.809 (95% CI: 0.690–0.941). With AI assistance, the overall accuracy of TPS had been changed from 0.799 (95% confidence interval [CI]: 0.764–0.836) to 0.832 (95% CI: 0.796–0.869) (P = 0.004). AI assistance increased the accuracy rate in 11 out of 12 OPT readers. The result of the generalized linear mixed model revealed that AI assistance and specimen type affected the probability of correct answer, while the order of reading did not (Table). The mean time to read with AI was 195.4±506.5 (mean±standard deviation) seconds, which was significantly shorter than the mean time to read without AI (285.1±1578.4, P <0.001). **Conclusions:** This study demonstrates that an AI-powered PD-L1 TPS analyzer can assist board-certified pathologists in evaluating TPS of NSCLC by improving the accuracy of TPS group evaluation and reducing the time to read slides. Research Sponsor: Lunit Inc.

Generalized linear mixed model of various factors that can influence the result of evaluating the correct TPS group.

Factors	Odds ratio	95% confidence interval	z-value	P-value
With artificial intelligence assistance (vs. without artificial intelligence assistance)	1.241	1.071, 1.438	2.879	0.004
2nd session (vs. 1st session)	1.060	0.915, 1.228	0.774	0.439
Surgical resection (vs. Core needle biopsy)	0.661	0.566, 0.772	-5.263	<0.001

8530 **Poster Session**

Driver coexistence characteristics of ALK-fusion in Chinese patients with lung cancer.

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Background: *ALK* fusions and other driver mutations are usually mutually exclusive. With the widespread application of genetic testing techniques, the coexistence of *ALK* fusions and other driver mutations could be detected, such as *ALK* fusion and EGFR driver mutations. However, there were no systematical studies about the coexistence of *ALK* fusions and other driver mutations. Here, we retrospectively investigated the coexistence of ALK fusions and other driver mutations. **Methods:** Samples with *ALK* fusions were extracted from a Chinese lung cancer cohort, which from OncoPanscan (Genetron Health) based sequencing of tissue. Driver mutations of *EGFR*, *ROS1*, *RET*, *NTRK1/2/3*, *BRAF*, *MET*, *KRAS* and *ERBB2* could be detected. **Results:** In the cohort, 692 samples with *ALK* fusions contained the intact kinase domain. These samples could be classified into three forms: canonical fusions (only *EML4* partner, n = 601), single non-canonical fusions (only non-*EML4* partner, n = 51) and complex non-canonical fusions (two or more partners, n = 40). Among the 692 samples, only 20 samples (20/692, 2.89%) coexisted with other driver mutations, which indicated that the driver coexistence were rare. 70% (14/20) of driver coexistence were happened on canonical fusions (*EML4-ALK*) samples. They were coexisting with *EGFR* L858R (3), *EGFR* L858R plus *ROS1* fusion (1), *EGFR* L858R plus *MET* amplification (1), *KRAS* G12C/D/V (3), *MET* amplification (3), *MET* Exon14 skipping (1), *ERBB2* amplification (1), and *MET* amplification plus *ERBB2* amplification (1), respectively. 20% (4/20) of driver coexistence samples were single non-canonical ALK fusions coexisting with *EGFR* 19del (1) or 20ins (1) or L858R (1) or *MET* amplification (1). Another 10% (2/20) samples were complex non-canonical *ALK* fusions coexisting with *EGFR* G719S (1) or *RET* fusion (1). Most co-mutations have corresponding targeted inhibitors, maybe these patients can be treated by combined or sequential therapies. Among canonical fusions, single non-canonical fusions and complex non-canonical fusions of *ALK*, the frequency of the samples without coexistence of driver mutations was respectively 97.67% (587/601), 92.16% (47/51), 95.00% (38/40), without significant difference (P = 0.056). Maybe single/complex non-canonical fusions are also strong drivers as canonical fusions. **Conclusions:** In this cohort, very few of *ALK* fusion patients coexisted with other driver mutations. Among the co-existence samples, *ALK* fusion were mainly coexisting with the site mutations of *EGFR* and *KRAS*, amplifications of *MET* and *ERBB2*, fusions of *ROS1* and *RET*. These samples maybe obtain more effective outcomes by combined or sequential therapies. Research Sponsor: None.

8531 **Poster Session**

Spatial meta-transcriptomics reveal intratumor bacterial association with lung cancer cells showing a distinct oncogenic signature.

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Background: The lung intratumor microbiome influences lung cancer tumorigenesis and treatment responses, but detailed data on the extent, location, and effects of microbes within lung tumors is missing, information needed to improve treatment outcomes and prognosis. **Methods:** To address this gap, we developed a novel spatial meta-transcriptomic method simultaneously detecting the expression level of 1,811 host genes and three microbe targets (16S rRNA, 28S rRNA and CMV). After rigorous validation, we analyzed the spatial meta-transcriptomic profiles of tumor cells, T cells, macrophages, other immune cells, and stroma in tumor samples from 12 patients with early-stage lung cancer. **Results:** Bacterial burden was significantly higher in tumor cells compared to T cells, macrophages, other immune cells, and stroma. This burden increased from tumor-adjacent normal lung and tertiary lymphoid structures to tumor cells to the airways, suggesting that lung intratumor bacteria derive from the latter route of entry. Expression of oncogenic β-catenin and epithelial-mesenchymal transition pathway genes was strongly correlated with bacterial burden, as were tumor subtypes, mutation profile, histology and smoking history. **Conclusions:** Intratumor bacteria were enriched with tumor cells and associated with multiple oncogenic pathways, supporting a rationale for reducing the local intratumor microbiome in lung cancer to optimize clinical outcomes. This research was supported in part by the Intramural Research Programs of the NCI and NIAID. Other funding sources included ASCO Young Investigator Award, SITC-AstraZeneca Immunotherapy in Lung Cancer (Early Stage NSCLC) Clinical Fellowship Award, NIH Bench-to-Bedside and Back Program (BtB), NCI R00 award (CA226400), Emerson Collective Cancer Research fund, Lung Cancer Research Foundation (LCRF) pilot grant and W.W. Smith Trust Foundation award. This study was approved by NCI institutional review board (NCT00242723 and NCT02146170) and Animal Use and Care Committee at the University of Pennsylvania (#806875). Research Sponsor: U.S. National Institutes of Health, Conquer Cancer Foundation of the American Society of Clinical Oncology, Other Foundation, Other Government Agency, ASCO YIA 2019.

8532 **Poster Session**

Low skeletal muscle area and association with toxicity and hospitalization with chemotherapy in advanced non–small cell lung cancer.

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Background: Significant toxicity is common in the treatment of advanced non-small cell lung cancer (NSCLC) and can be associated with adverse events, such as unplanned hospitalization, and worse clinical outcomes. Baseline low skeletal muscle (SM) area is a marker of sarcopenia and has been associated with worse survival in other malignancies, but the association of SM area and toxicity in NSCLC is less studied. **Methods:** Patients with locally advanced or oligo-metastatic NSCLC treated with combined chemotherapy and radiotherapy with or without surgery from 2002-2013 at a single institution were reviewed. A deep-learning pipeline utilized existing pre-treatment computed tomography scans to calculate SM area at the 3rd lumbar vertebral level. Gold standard SM index (SMI) was calculated, adjusting for height, sex, and dichotomized per previously validated cutoff values. Grade 3 or higher hematologic (G3+ heme) toxicity, was assessed per NCI CTCAE v5.0, within 21-days of first chemotherapy cycle. Hospital use was defined as unplanned ED visit or inpatient hospitalization during chemotherapy. Multivariate analysis (MVA) of toxicity endpoints with SMI and baseline characteristics were analyzed by logistic regression analysis, and with overall survival (OS) using Cox regression analysis. **Results:** A total of 369 patients met inclusion criteria with median follow-up of 23.0mo (range 1-193mo), median age of 64y (range 29-88y), and were mostly male (51%). Most were clinical stage (AJCC 7th edition) IIIA (44%), IIIB (31%), or IV (10%), while 10% had upfront surgery and adjuvant chemotherapy. Most common regimen was cisplatin-based (48%). Median OS was 25.5mo and PFS was 14.0mo. Patients with low SMI were more likely to be younger (median age 70y vs 62y), ECOG performance status (PS) > 0 (74% vs 59%), lower BMI (median BMI 23.3 vs 27.7), and not receive cisplatin-based regimen (35% vs 53%). There was no difference in histology, stage, surgery, or every 3-week (q3w) chemotherapy dosing. On MVA, low SMI was associated with increased risk of G3+ heme toxicity (OR 1.74, $p = 0.04$) and increased hospital use (OR 1.79, $p = 0.04$). G3+ heme toxicity was also associated with surgery and q3w dosing, but not age, PS, BMI, or regimen. Hospital use was also associated with BMI, surgery, and cisplatin-based regimen, but not age, PS, or q3w dosing. G3+ heme toxicity (HR 1.48, $p < 0.01$), older age (HR 1.02, $p = 0.02$), and stage 4 (HR 3.32, $p < 0.01$) were associated with worse survival on MVA, but not low SMI (HR 1.25, $p = 0.11$), PS, BMI, surgery, or regimen. **Conclusions:** Low SMI predicted higher risk of G3+ toxicity during first cycle of chemotherapy. High-risk patients with low SMI experienced significant adverse events and should be considered for more aggressive symptom management or alternative treatment strategies. Research Sponsor: U.S. National Institutes of Health.

8533 **Poster Session**

Postoperative ctDNA in indicating the recurrence risk and monitoring the effect of adjuvant therapy in surgical non–small cell lung cancers.

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Background: Circulating tumor DNA (ctDNA) has emerged as a potential novel biomarker to predict molecular residue disease in lung cancer after definitive treatment. Herein, we investigated the value of ctDNA in prognosing risk of relapse and monitoring the effect of adjuvant therapy in surgical non-small cell lung cancer (NSCLC) patients. **Methods:** Forty-one surgical NSCLC patients were enrolled. Tumor tissues were collected at surgery and subjected to targeted NGS of 1021 cancer-related genes. The serial peripheral blood samples were collected at postoperative one month and then at every third or sixth month and subjected to ultra-deep targeted NGS covering 338 genes. **Results:** From 41 eligible patients including 18 patients with stage I disease, 2 with stage II and 21 with stage III, 41 tumor tissues and 137 plasma samples were enrolled and successfully tested. In tissue samples, 323 somatic variations were identified, with a median of 8 (range, 1-21) gene variations detected in each patient. *TP53* was the most common mutation (63.41%), followed by *EGFR* (58.53%), *LRP1B* (17.07%) and *KRAS* (14.63%). The first-postoperative ctDNA positive was found in 13 of 41 patients (31.71%), 9 stage III, 2 stage II and 2 stage I. During a median 9.47 months follow-up, 38.46% (5/13) patients with detectable ctDNA in the first postoperative blood sample experienced recurrence, while 3.57% (1/28) patients with undetectable ctDNA ultimately recurred. The DFS can be stratified by the first-postoperative ctDNA status, with ctDNA-positive groups having significantly reduced DFS ($p < 0.05$). We detected ctDNA in at least one time point after surgery in 17 patients (41.46%), 5 of them (29.41%) experienced recurrence. Twenty-four patients without ctDNA detection during postoperative surveillance, one (4.17%) of them ultimately recurred. Serial ctDNA detection revealed disease recurrence ahead of radiologic imaging by a median of 5.25 months (range, 0.98-14.19). Among the 41 patients, 6 patients had surgery alone, 35 patients received adjuvant therapy. For these 35 patients, ctDNA analysis can stratify patients before and after adjuvant therapy. Recurrence ratio was 33.33% (4/12) in patients with detectable and 4.34% (1/23) in patients with undetectable ctDNA before adjuvant therapy. For ctDNA analysis after adjuvant therapy, no patients (11/11) with negative ctDNA had disease-recurrence while 33.33% (1/3) patients with positive ctDNA experienced recurrence. All four patients with clearance ctDNA by adjuvant therapy remained disease free. **Conclusions:** For NSCLC patients, postoperative ctDNA is a prognostic marker, which reveals disease recurrence ahead of radiographic examination. Importantly, ctDNA-detecting may facilitate personalized adjuvant therapy, and applying adjuvant therapy to the patients with detectable ctDNA could bring clinical benefits for them. Research Sponsor: None.

8534 **Poster Session**

Analysis of circulating tumor DNA in the phase 2 BTCRC LUN 16-081 trial of consolidation nivolumab with or without ipilimumab after chemoradiation in stage III non–small cell lung cancer.

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Background: The current standard of care for patients with inoperable stage III non-small cell lung cancer (NSCLC) includes chemoradiation (CRT) followed by up to 1 year of checkpoint inhibitor (CPI) therapy. However, many patients are not able to complete 1 year of treatment and the optimal duration of consolidation therapy remains unknown. Identifying minimal residual disease (MRD) via detection of circulating tumor DNA (ctDNA) may help inform the optimal duration of treatment. Here we report the results of a preplanned correlative study evaluating the association between detectable ctDNA and survival outcomes from the BTCRC LUN 16-081 phase 2 trial of consolidation nivolumab or nivolumab plus ipilimumab following CRT in patients with unresectable Stage III NSCLC (NCT03285321). **Methods:** Following CRT, patients with unresectable stage IIIA/B NSCLC were randomized 1:1 to receive nivolumab 480 mg IV Q4weeks for up to 6 cycles or nivolumab 240 mg IV Q2weeks plus ipilimumab 1 mg/kg IV Q6weeks for up to 4 cycles. Plasma samples for ctDNA analysis were collected after completion of CRT, prior to C2D1 of CPI, and at the end of treatment or withdrawal from the study. Tumor genotyping and ctDNA analysis were performed using CAPP-Seq with a panel targeting 260 genes recurrently mutated in NSCLC. Patient-specific tumor variants were identified using tumor tissue or baseline plasma and matched leukocyte DNA samples. Tumor variants were then monitored in plasma samples using a tumor mutation-informed bioinformatic strategy. **Results:** Thirty-nine patients received either nivolumab (n = 25; cycles: median = 6, range 1-6), or nivolumab plus ipilimumab (n = 14; cycles; median = 2, range = 1-6). Patients with detectable ctDNA MRD after completion of CRT demonstrated significantly inferior progression free survival (PFS) than patients who were MRD-negative (12-month 29% vs 76%, 24-month 29% vs 68%, P = 0.003), prior to C2D1 of CPI (12-month 0% vs 85%, 24-month 0% vs 72%, P < 0.0001) and at the end of CPI (12-month 14% vs 90%, 24-month 14% vs 79%, P < 0.0001). Patients with undetectable ctDNA MRD at the end of CPI (median cycles = 5.5; range 1-6) demonstrated 24-month overall survival of 91%. Additionally, patients with decreasing or undetectable ctDNA levels after one cycle of CPI had improved outcomes compared to patients with increasing ctDNA levels (24-month PFS 73% vs 0%, P < 0.0001). Progression of disease occurred within 10.8 months of starting CPI in all patients with increasing ctDNA levels at C2D1. **Conclusions:** Detectable ctDNA before, during, and after consolidation CPI is strongly associated with inferior survival outcomes. Furthermore, less than 12 months of CPI consolidation can result in MRD negativity and high rates of long term PFS. Clinical trial information: NCT03285321. Research Sponsor: U.S. National Institutes of Health.

8535 **Poster Session**

Monitoring PD-L1 expression on circulating stromal cells in blood predicts PFS and OS in patients with metastatic NSCLC treated with PD-L1/PD-1 immunotherapy.

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Background: Cancer Associated Macrophage Like cells (CAMLs), a circulating stromal cell found in cancer patients (pts) blood, are phagocytic giant macrophages that appear to parallel the inflammatory PD-L1 state of the tumor microenvironment. Previously, we demonstrated in local non-small cell lung carcinoma (NSCLC), CAML PD-L1 expression is dynamic and predicts response to PD-L1/PD-1 immunotherapies (IMTs) following sequential sampling before and after chemotherapy (chemo) induction (~30days) based on progression free (PFS) & overall survival (OS). However this has not been tested in metastatic NSCLC (mNSCLC). Here,we report the results of monitoring PD-L1 expression in CAMLs before and after chemo induction (~30 days) to evaluate its predictive value in mNSCLC pts treated with or without IMT. **Methods:** A single blind multi-year prospective study was undertaken to test the relationship of PD-L1 expression in CAMLs to PFS & OS, pre & post chemo induction, in recurrent mNSCLC with (n = 41) or without (n = 41) additional anti-PD-L1/PD-1 IMTs. This included three IMTs: atezolizumab (n = 4), nivolumab (n = 8) or pembrolizumab (n = 29). We recruited 82 pts with pathologically confirmed recurrent mNSCLC prior to treatment for newly recurrent metastatic disease. Blood samples (15 mL) were taken at Baseline (BL), prior to chemo, and ~30 days after chemotherapy (T1). Blood was filtered by CellSieve filtration & CAMLs' expression scored as a binary high/low, to evaluate PFS & OS hazard ratios (HRs) by censored univariate & multivariate analysis at 18 months. **Results:** CAMLs were found in 97% of all tested samples, 94% at BL & 100% at T1. CAML PD-L1 at BL was found not to be associated with PFS or OS in pts treated with chemo alone (PFS p = 0.620 & OS p = 0.673) or chemo+IMT (PFS p = 0.353 & OS = 0.477) at 18 months. At T1, high CAML PD-L1 in pts treated with chemo alone had no significantly different PFS (HR = 1.3, p = 0.694) or OS (HR = 1.6 p = 0.503). However, high CAML PD-L1 at T1 in pts treated with chemo+IMT had significantly better PFS (HR = 3.1, 95%CI = 1.3-7.3, p = 0.019), and OS (HR = 3.4, 95%CI = 1.4-8.3, p = 0.014). Further subtyping & analysis is ongoing to evaluate PFS and OS at 24 months. **Conclusions:** Our data suggests that in mNSCLC, PD-L1 expression in circulating CAMLs dynamically upregulates after induction with chemotherapy and appears to predict patients with increased benefit to PD-L1/PD-1 IMTs, though additional studies are needed to validate these findings. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

8536 **Poster Session**

A phase II study of durvalumab (MEDI4736) immediately after completion of chemoradiotherapy in unresectable stage III non–small cell lung cancer: TORG1937 (DATE study).

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Background: Concurrent chemoradiotherapy followed by durvalumab maintenance for up to 12 months is the standard of care for patients with unresectable stage III non-small cell lung cancer (NSCLC). However, the best timing of starting durvalumab after completion of chemoradiation has not been identified. Progression-free survival (PFS) and overall survival (OS) were better in the subgroup of patients administered durvalumab within 14 days after last radiation to randomization according to the PACIFIC study (Antonia SJ, et al. 2017, 2018 NEJM). **Methods:** This study was a prospective, single-arm, multicenter, phase II clinical trial. Eligibility criteria included patients with unresectable stage III NSCLC, ECOG PS 0-1, age < 75 years old. Patients who did not have disease progression after definitive concurrent chemoradiotherapy (CCRT) (chemotherapy: 2 cycles of platinum-based doublet chemotherapy, radiotherapy: 60 Gy/30 Fr) received durvalumab (10 mg/kg, every 2 weeks for up to 12 months) from the next day (allowed up to 5 days) after last radiation. The primary endpoint was 1-year PFS rate from registration assessed by an independent review committee. The planned sample size was 47 with a threshold value of 50% based on results of the PACIFIC study, an expected value of 63%, one-sided alpha of 20% and power of 80% in 1-year PFS rate. **Results:** From January 2020 to August 2020, 50 patients were enrolled from 16 institutions and 47 patients were evaluable for efficacy and safety. Forty-two patients received durvalumab maintenance therapy. Patient characteristics were: male/female 41/6; median age 65 (range 42-75); ECOG PS 0/1 28/19; IIIA/IIIB/IIIC 19/21/7. The 1-year PFS rate from registration was 75.0% (60% CI: 69.0 to 80.0). The 1-year OS rate from registration was 97.7% (95%CI: 84.6 to 99.7). ORR, median PFS and median OS were 78.7%, 14.2 months (95%CI: 13.4 to not reached (NR)) and NR, respectively. Grade 3/4 adverse events were pneumonitis (4.3%), neutropenia (44.7%), febrile neutropenia (4.3%). There was no treatment-related death. **Conclusions:** Our study met the primary endpoint. Durvalumab can be safely administered immediately after completion of CCRT for patients with unresectable stage III NSCLC, no additional or unexpected toxicity occurred as a reference to the PACIFIC study. Clinical trial information: jRCTs031190117. Research Sponsor: AstraZeneca.

8537 **Poster Session**

Neoadjuvant nivolumab in early-stage non–small cell lung cancer (NSCLC): Five-year outcomes.

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Background: Neoadjuvant (neoadj) immune checkpoint blockade (ICB) with anti-PD-1 therapy has shown increasing promise for early stage NSCLC, with long-term clinical outcomes still maturing. Our group reported the first phase I/II trial of neoadj nivolumab (nivo) in resectable NSCLC, finding therapy to be safe and feasible. We now present final clinical results from this cohort, representing the longest follow up data for neoadj anti-PD-1 to date. **Methods:** Two doses of neoadj nivo (3 mg/kg) were given prior to resection in 21 patients (pts) with resectable NSCLC. 5-year (yr) follow-up data, including recurrence-free survival (RFS), overall survival (OS) and association with pathologic response were tabulated. Event time distributions were estimated with the Kaplan-Meier method. All p-values are two-sided with 0.05 significance level. **Results:** At a median follow up of 63 months, 3-, 4- and 5-yr survival rates were 85, 80, and 80% respectively. RFS rates at 3-, 4- and 5-yrs were 65, 60, and 60% respectively. As previously reported, major pathologic response (MPR: ≤10% viable tumor) was 45%, and pathologic complete response (pCR) rate was 10%. The hazard ratio (HR) for pathologic down-staging was in the direction of improved RFS, without meeting statistical significance (HR 0.36, 95% CI 0.07-1.75, p = 0.2). RFS HR estimates for MPR and an alternative pathologic cut-off of less than 50% residual tumor (RT), were 0.61, (95% CI 0.15-2.44, p = 0.48) and 0.36, (95% CI 0.09-1.51, p = 0.16) respectively. The direction of the effect of pre-treatment PD-L1 positivity (≥1%) was to improve RFS (HR 0.36, 95% CI 0.07-1.85, p = 0.22). At 5-yr follow up, 8 of 9 (89%) pts with MPR were alive and no cancer deaths have occurred. Amongst pts with MPR, 1/9 pts had a cancer recurrence in the mediastinum treated successfully with definitive chemoradiotherapy. Both pts with pCR are alive and without recurrence. Patterns of all recurrences in this cohort are summarized in table 1. No long-term immune-related adverse events have occurred other than one G3 dermatologic event. **Conclusions:** The 5-yr clinical outcomes for neoadj nivo in resectable NSCLC compare favorably to historical trends. MPR trended toward improved RFS, while definitive conclusions are limited by our cohort size and overall low recurrence rate. Thresholds of %RT beyond pCR and MPR in this setting should be explored in larger prospective studies. PD-L1 expression may play a role in predicting long-term response, but larger prospective studies are needed. Clinical trial information: NCT02259621. Research Sponsor: Cancer Research Institute and Stand Up 2 Cancer.

Pre-treatment stage	Histology	PD-L1 (%)	Notable Mutations	%RT	Adjuvant chemotherapy (Y/N)	RFS duration (months)	Local vs. Distant Recurrence (L/D)	Alive (Y/N)
IIIA	Squam	0	TP53	80	N	10.4	D	N
IIA	Adeno	0	Kras G12c, STK11	75	Y	1.8	D	Y
IIIA	Adeno	N/A	-	5	N	8.5	L	Y
IIIA	Squam	25	-	30	N	20.3	D	N
IIIA	Adeno	60	Ros1	95	N	23.1	D	Y
IIB	Adeno	0	F11R-NRG1 fusion	100	N	29.3	L	N
IA	Adeno	0	-	100	N	46.5	L	Y

8538 **Poster Session**

Prognostic role of preoperative chemosensitivity in patients with non–small cell lung cancer (NSCLC) treated with preoperative chemotherapy: A study of National Cancer Database (NCDB).

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Background: Response to preoperative systemic therapy may provide valuable information regarding tumor biology and prognosis. This is increasingly relevant nowadays considering the promising results from preoperative chemoimmunotherapy. This study aims to examine the prognostic role of preoperative chemosensitivity defined by TNM stage change in NSCLC. **Methods:** Patients with histologically confirmed clinical stage II-III NSCLC who have received preoperative chemotherapy followed by R0 curative surgery were identified in the NCDB between 2006 and 2017. Patients who have developed metastasis at the time of surgery, received any perioperative radiotherapy or single agent chemotherapy, or died within 90 days of surgery, were excluded. Preoperative chemosensitivity is categorized as ypT0N0, downstaged (pTNM < cTNM, excluding ypT0N0), and not downstaged (pTNM ≥ cTNM). Logistic regression was used to evaluate associations between chemosensitivity and demographic, clinical, and pathological factors. Log-rank was used for survival analysis and adjusted by cox regression for age, gender, race, year of diagnosis, academic center, insurance, comorbidity, histology, and clinical stage. **Results:** A total of 1266 patients were included, of whom 104 (8.2%) had ypT0N0, 575 (45.4%) were downstaged, while 587 (46.4%) were not. Female, diagnosis in recent years, treatment at academic centers, and squamous histology were significantly associated with better chemosensitivity, while clinical TNM stage, age, race, and comorbidity were not. Five-year overall survival rate is 81.2%, 57.7%, and 46.2%, respectively (log-rank $p < 0.001$). After Cox regression adjustment, compared with not downstaged, ypT0N0 (HR 0.28, 95% CI 0.17 – 0.45) and downstaged (HR 0.61, 95% CI 0.51 – 0.74) were independently associated with improved postoperative survival. **Conclusions:** Preoperative chemosensitivity defined by TNM stage change before and after chemotherapy may prognosticate NSCLC after curative surgery. It may be a useful clinical tool to identify patients with high risk of treatment failure after neoadjuvant chemoimmunotherapy in the future. Research Sponsor: U.S. National Institutes of Health.

Cox regression model of variables significantly associated with postoperative survival.

Characteristic	HR	95% CI	p-value
Age at Diagnosis	1.01	1.00, 1.02	0.003
Year of diagnosis			0.021
2010-2013 vs. 2006-2009	0.84	0.68, 1.03	
2014-2017 vs. 2006-2009	0.72	0.57, 0.91	
Comorbidity (Yes vs. No)	1.26	1.06, 1.50	0.008
Clinical stage (III vs. II)	1.45	1.19, 1.75	<0.001
Preoperative Chemosensitivity			<0.001
Downstaged vs. Not downstaged	0.61	0.51, 0.74	
ypT0N0 vs. Not downstaged	0.28	0.17, 0.45	

8539 **Poster Session**

Racial disparities in receipt of curative surgery for early-stage non–small cell lung cancer in Florida.

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Background: Lung cancer is the leading cause of cancer death in the United States. Receipt of curative-intent surgery for early-stage non–small cell lung cancer (NSCLC) is associated with disparities in race and socioeconomic status, which is subsequently related to the outcome of NSCLC. This study aimed to examine the racial disparity in receipt of curative-intent surgery among early-stage NSCLC in Florida. **Methods:** A total of 80,458 patients with early-stage NSCLC diagnosed from 2005 to 2017 were identified from the statewide cancer registry, Florida Cancer Data System (FCDS). Percentage of patients receiving curative-intent surgery was calculated for each race/ethnicity. FCDS data was linked to discharge data containing comorbidity information for each lung cancer patient. There was a 94% match between FCDS and discharge data. Multivariable logistic regression was used to determine the impact of race on receipt of curative-intent surgery for early-stage NSCLC. **Results:** Among 80,458 patients with early-stage NSCLC, 66,761 (83.0%) were White, 5,503 (6.8%) were Black and 6,981 (8.7%) were Hispanic. Of note, 69.5% Hispanic patients lived in South Florida. Asian patients (59.9%) had the highest proportion of curative surgery, followed by Hispanics (57.8%), Whites (52.9%) and Blacks (42.6%). In the multivariable model, patients with Charlson Comorbidity Index (CCI)≥3 had 34% lower odds of having curative surgery (OR, 0.66; 95% CI, 0.62 to 0.7) compared to patients who did not have any comorbidity (CCI=0). Highest poverty levels had 27% lower odds of receiving curative-intent surgery compared to lowest (OR: 0.73; 95% CI: 0.68 to 0.78). After adjusting for sociodemographic factors (i.e., age, sex, race, insurance, region) and clinical factors (i.e., histology, AJCC stage, CCI, smoking status), Blacks had 27% lower odds of receiving curative-intent surgery (OR, 0.73; 95% CI, 0.68 to 0.79), whereas Hispanics had 22% (OR, 1.22; 95% CI, 1.14 to 1.30) and Asians had 19% (OR, 1.19; 95% CI, 0.98 to 1.46) higher odds than Whites. In the stratified analysis by regions, Blacks had lower odds of receiving curative-intent surgery than Whites in all regions across Florida while Hispanics had higher odds of receiving surgery than Whites only in South Florida (OR, 1.29; 95% CI, 1.18 to 1.41). **Conclusions:** There are persistent racial disparities in receipt of curative-intent surgery for early-stage NSCLC in Florida. Specifically, Blacks are receiving less curative-intent surgery, despite adjustments for comorbidities, socio-economic status, and insurance. Ethno-regional differences within different regions of Florida are evident with Hispanics surpassing all other races in receipt of curative treatment in heavily Hispanic South Florida. Research Sponsor: This study is supported by grant 20B16 from the Bankhead Coley Research Program of the State of Florida.

8540 **Poster Session**

Minimal residual disease (MRD) detection by ctDNA in relation to radiographic disease progression in patients with stage I-III non–small cell lung cancer (NSCLC) treated with definitive radiation therapy.

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Background: The standard of care for patients with inoperable early stage or locally advanced NSCLC is definitive stereotactic body radiotherapy (SBRT) or conventional radiation therapy (RT) with systemic therapy. Circulating tumor DNA (ctDNA) testing can be used for the assessment of MRD and predict risk of recurrence. Few studies have prospectively evaluated MRD detection and ctDNA dynamics specifically among patients with early or locally advanced NSCLC receiving definitive RT. **Methods:** In a prospective clinical cohort of patients with stage I-III NSCLC (n = 17), serial plasma samples (n = 70) were collected before and after SBRT as well as before, during, and after conventional RT with or without concurrent systemic therapy and adjuvant durvalumab. Patients were followed-up for a median of 29 months (range: 4 to 54 months) with the last serial plasma collected at a median of 5 months from completion of RT (range: 1 – 26 months). A personalized, tumor-informed multiplex PCR assay (Signatera™ bespoke mPCR NGS assay) was used for the detection and quantification of ctDNA and tracked 16 tumor variants among 16 patients and 15 tumor variants in one patient. This study evaluated the prognostic value of ctDNA, correlating MRD status with clinical outcomes, in addition to ctDNA clearance kinetics during RT. **Results:** Among 17 patients with early-stage and locally advanced NSCLC, baseline ctDNA was detected in 82% of patients (14/17). Clinical progression was confirmed radiographically for 53% (9/17). All events of clinical progression were detectable by ctDNA (sensitivity 100%, 0.63 – 1.0), with a median lead-time of 5.5 months for MRD detection compared to radiographic disease progression. Durable ctDNA clearance was observed in 29% (5/17) of patients, all of whom then remained recurrence-free until the end of follow-up (median 12 months; specificity 100%, 95% CI 0.6 – 1.0). Transient ctDNA clearance was observed in 3 patients, and recurrent ctDNA was detected before or at the time of disease progression in all 3. ctDNA status after treatment at a single time point and longitudinally were highly predictive of disease recurrence ($p < 0.0001$). **Conclusions:** ctDNA detection is feasible for patients with stage I-III NSCLC undergoing definitive chemoradiation. and can serve as a powerful predictive biomarker for disease recurrence. High baseline detection rate is essential for feasibility of a ctDNA-based MRD assay. Residual detectable ctDNA represents a powerful predictive tool to identify patients who might benefit from intensification of adjuvant therapy following definitive RT. Research Sponsor: Natera Inc.

8541 **Poster Session**

Durvalumab (durva) after chemoradiotherapy (CRT) in unresectable, stage III, EGFR mutation-positive (EGFRm) NSCLC: A post hoc subgroup analysis from PACIFIC.

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Background: Standard of care for patients (pts) with unresectable (UR) stage III NSCLC is the 'PACIFIC regimen', based on data from the phase 3 placebo (pbo)-controlled trial where consolidation durva following CRT improved overall survival (OS; hazard ratio [HR], 0.68 [95% CI, 0.53, 0.87]) and progression-free survival (PFS; HR, 0.52 [95% CI 0.42, 0.65]), in an all-comer population. However, the benefit of immunotherapy (IO) in pts with EGFRm stage III NSCLC is unclear. We report a *post hoc* exploratory efficacy and safety analysis from 35 pts with EGFRm NSCLC from the PACIFIC trial (NCT02125461). **Methods:** Pts with stage III UR-NSCLC, WHO performance status (PS) 0/1 and no progression after ≥2 cycles platinum-based concurrent CRT were randomized 2:1 (1–42 days post CRT) to receive durva (10mg/kg IV q2w for up to 1 year) or pbo, stratified by age, sex, and smoking history; enrollment was not restricted by oncogenic driver gene mutation status or PD-L1 expression. Primary endpoints: PFS (BICR; RECIST v1.1) and OS; key secondary endpoints: objective response rate (ORR) and safety. Treatment effects for the EGFRm subgroup were estimated using an unstratified Cox proportional hazard model; medians were estimated using the Kaplan–Meier method. Statistical analyses were exploratory. Data cut-off (DCO) for the EGFRm subgroup efficacy analysis was 11 January 2021. **Results:** Of 713 pts randomized, 35 had EGFRm NSCLC based on local testing (durva n = 24, pbo n = 11). In the EGFRm subgroup, more pts in the pbo vs durva arm were male (73% vs 54%), had stage IIIA disease (64% vs 46%), PS 0 (64% vs 54%) and received pre-CRT induction chemotherapy (36% vs 8%). More pts in the durva arm were Asian (63% vs 55%) and had PD-L1 on < 25% tumor cells (67% vs 36%); median age was consistent across arms. At DCO, median duration of follow-up for survival was 42.7 months (range, 3.7–74.3 months) for all randomized pts in the subgroup. Median PFS was 11.2 months (95% CI 7.3, 20.7) with durva vs 10.9 months (95% CI 1.9, not evaluable [NE]) with pbo; HR 0.91 (95% CI 0.39, 2.13). Median OS was 46.8 months (95% CI 29.9, NE) with durva vs 43.0 months (95% CI 14.9, NE) with pbo; HR 1.02 (95% CI 0.39, 2.63). ORR was 26.1% (95% CI, 10.2, 48.4) and 18.2% (95% CI 2.3, 51.8) with durva and pbo, respectively. The safety profile for durva was consistent with the overall population. In the durva and pbo subgroup arms, radiation pneumonitis was reported in 42% vs 36% of pts, and pneumonitis was reported in 17% vs 18% of pts (1 grade 3, pbo arm), respectively. **Conclusions:** In this *post hoc* exploratory analysis of 35 pts, PFS and OS outcomes with durva were similar to pbo in the EGFRm population, with wide CIs. The benefit of IO in this population remains unclear. The ongoing LAURA study (NCT03521154) is investigating the efficacy and safety of maintenance osimertinib in pts with locally advanced EGFRm stage III UR-NSCLC with no progression after CRT. Clinical trial information: NCT02125461. Research Sponsor: AstraZeneca.

8542 **Poster Session**

Multimodal prediction of response to neoadjuvant nivolumab and chemotherapy for surgically resectable stage IIIA non–small cell lung cancer.

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Background: The NADIM trial (NCT03081689), led by the Spanish Lung Cancer Group, assessed the antitumor activity and safety of neoadjuvant chemoimmunotherapy for resectable stage IIIA NSCLC. Patients received neoadjuvant nivolumab and paclitaxel-carboplatin for three cycles before surgical resection, followed by one year of adjuvant nivolumab. At 24 months, progression-free survival (PFS) was 77%, suggesting that neoadjuvant chemoimmunotherapy represents a promising option in this setting. Pathological complete response (pCR) could potentially be used as an important surrogate endpoint for survival. We present here a re-analysis of the NADIM cohort aiming to develop a machine learning algorithm to predict the pCR status based on multimodal baseline data. **Methods:** We combined baseline clinical data (e.g., age, smoking status), biological data (e.g., tumor histology, mutations), radiology reports and radiomics analysis of the baseline CT scan in a multimodal analysis. While 46 patients were enrolled in the NADIM trial, only 28 had a complete set of data available for this retrospective study. For each patient, tumors were segmented on the baseline CT-scan in 3D by a Deep Learning algorithm. Radiomics features were extracted following the IBSI standards and combined with the other data modalities. A filter-based variable selection method was applied before training several machine learning algorithms. The optimization criterion was the Area Under the ROC Curve (AUC). Due to the small size of the cohort, a leave-one-out cross-validation approach was used to properly estimate the model performance. For a sub-cohort of 20 patients for which data have been collected longitudinally during the neoadjuvant treatment, an additional Delta-radiomics model was used to predict the pCR status. **Results:** An XGBoost algorithm with a linear base learner displayed an AUC of 0.69, a precision of 75%, a sensitivity of 83% and a specificity of 50%. Features with highest weight in the algorithm were a mix of radiological, radiomics, biological and clinical features (including the neutrophils to lymphocytes ratio, mutations and histology) highlighting the importance of a truly multimodal analysis. Indeed, withdrawing a specific data modality (e.g., radiomics or biological features), led to a decrease of ~15% of the AUC. Inclusion of the Delta-radiomics analysis on the data collected longitudinally prior to surgery led to an improved AUC of 0.76 in that patient sub-cohort. **Conclusions:** This study is, to our knowledge, the first to offer a multimodal analysis of the response to neoadjuvant treatment for surgically resectable stage IIIA NSCLC and is a proof of concept that a machine learning algorithm can be used to predict the pCR in this context. These preliminary results are being confirmed in the ongoing NADIM II trial. Clinical trial information: NCT03838159. Research Sponsor: None.

8543 **Poster Session**

Identifying biomarkers associated with disease-free survival in stage I non–small cell lung cancer.

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Background: Patients with early stage, non-small cell lung cancer (NSCLC) with solitary pulmonary lesions ≤4 cm typically have favorable outcomes. However, disease recurrence impacts up to 30% of patients, leading to either additional surgical or systemic interventions. New methods to risk stratify patients based on clinical and molecular parameters may improve our ability to select cases that would benefit from more frequent surveillance or enrollment in clinical trials evaluating systemic therapy. **Methods:** We retrospectively analyzed data from 179 patients with early stage ($T_{1a\text{-}2a}N_0M_0$) NSCLC from a single institution. All patients had anatomic resection, negative margins, and systematic nodal sampling. Clinical and demographic data were abstracted from patient charts and tumor samples were molecularly profiled using the Tempus xT solid tumor assay (DNA-seq of 595-648 genes at 500x coverage, whole exome-capture RNA-seq). Pathogenic alterations (single nucleotide variants and insertion/deletions) and RNA expression were examined. Bivariate Cox-proportional Hazards models were used to assess the association of individual clinical, demographic, and molecular variables with recurrence-free survival, defined as the time from surgery until recurrence or death. **Results:** Our dataset included 166 stage IA1-3 patients and 13 stage IB patients, of which 36 patients experienced a recurrence or death event after surgery. Clinical and DNA-seq data was available for all patients, and RNA expression data was available for 172 patients. Across all patients, the most common somatically mutated genes were *TP53* (33% of tumors) and *KRAS* (16% of tumors), consistent with previous studies. Increasing $\log_{10}$-RNA expression for *NTRK1* (HR: 5.95; 95% CI, 1.16-30.4; p = 0.027) and CD274 (PD-L1) (HR: 7.88; 95% CI, 1.61-38.6; p = 0.013) and decreasing $\log_{10}$-RNA expression for *EGFR* (HR: 0.24; 95% CI, 0.05-1.21; p = 0.071) and *ERBB2* (Her2) (HR: 0.20; 95% CI, 0.04-0.97; p = 0.042) were associated with increased risk of recurrence or death. **Conclusions:** Increased expression of *NTRK1* and *CD274* (PD-L1) and decreased expression of *EGFR* and *ERBB2* (Her2) were associated with a increased risk for recurrence following surgery. This may have mechanistic implications for heightened tumor aggressiveness and/or metastatic potential. Future work will expand our cohort and validate our findings in a broader set of early-stage NSCLC patients. Research Sponsor: Swim Across America.

8544 **Poster Session**

Multi-omic and spatial dissection of immunotherapy response groups in non–small cell lung cancer (NSCLC).

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Background: Immune checkpoint inhibitors (ICI) have shown durable benefit in a subset of non-small cell lung cancer (NSCLC) patients. The composition of the tumour microenvironment (TME) is becomingly increasingly recognised as an important factor to predict response to therapy. **Methods:** Here, we applied digital spatial profiling of the tumour and stromal compartments from a 2^{nd} line NSCLC ICI-treated cohort (n = 41 patient) and standard of care (SOC), platinum treated NSCLC cohort (n = 47), to identify tissue-based signatures of response to therapy. **Results:** We demonstrate by mIHC that the interaction of $CD68^+$ macrophages with $PD1^+$, $FoxP3^+$ cells is significantly enriched in ICI refractory tumours (p = 0.012). Patients sensitive to ICI therapy expressed higher levels of IL2 receptor alpha (CD25, p = 0.028) within the tumour compartments, which corresponded with the increased expression of *IL2* mRNA (p = 0.001) within their stroma. Immuno-inhibitory markers CTLA-4 (p = 0.021) and IDO-1 (p = 0.023) were supressed in ICI-responsive patients. Tumour CD44 (p = 0.02) was depleted in the response group and corresponded inversely with significantly higher stromal expression of one of its ligands, *SPP1* (osteopontin, p = 0.008). Analysis of dysregulated transcripts indicated the potential inhibition of stromal interferon-gamma (IFNγ) activity, estrogen-receptor and Wnt-1 signalling activity within the tumour cells of ICI responsive patients. Cox survival analysis indicated tumour CD44 expression was associated with poorer prognosis (HR = 1.61, p = 0.01), consistent with its depletion in ICI sensitive patients. Similarly, stromal CTLA-4 (HR = 1.78, p = 0.003) and MDSC/M2 macrophage marker ARG1 (HR = 2.37, p = 0.01) were associated with poorer outcome while BAD (HR = 0.5, p = 0.01) appeared protective. The SOC cohort paralleled similar roles for immune checkpoints and pro-apoptotic markers, with LAG3 (HR = 3.81, p = 0.04) indicating poorer outcome, and BIM (HR = 0.16, p = 0.014) with improved outcome. Interestingly, stromal mRNA for E-selectin (HR = 652, p = 0.001), CCL17 (HR = 70, p = 0.006) and MTOR (HR = 1065, p = 0.008) were highly associated with poorer outcome in ICI treated patients, indicating pro-tumourigenic features in the tumour microenvironment that may facilitate ICI resistance. **Conclusions:** Through multi-modal approaches, we have dissected the characteristics of NSCLC treatment groups and provide evidence for the role of several markers including *IL2,* CD25, CD44 and *SPP1* in the efficacy of current generations of ICI therapy. Research Sponsor: Princess Alexandra Research Foundation.

8545 **Poster Session**

Association of the KRAS genotype and clinicopathologic findings of resected non–small cell lung cancer.

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Background: This study assessed the clinicopathological background of early-stage KRAS-mutated non-small-cell lung cancer and analyzed the biological process of KRAS-mutated tumor using an RNA sequencing procedure. **Methods:** We used a cohort of consecutive series of 179 surgically resected early-stage non-small-cell lung cancers harboring *KRAS*mutations and analyzed the clinicopathological features, including the KRAS genotypes, affecting the recurrence-free survival and prognosis. Consequently, we performed RNA sequencing to determine the gene expression profiles of nineteen *KRAS*-mutated non-small-cell cancers. **Results:** The most common *KRAS* genotype was p.G12C (57; 31.8%). A high p-stage (hazard ratio [HR], 4.181; $P < 0.0001$) and solid predominant adenocarcinoma histology (HR, 2.343; $P = 0.0076$) were significant independent prognostic factors for the recurrence-free survival. A high p-stage (HR, 3.793; $P < 0.0001$), solid predominant adenocarcinoma histology (HR, 2.373; $P = 0.0147$), and *KRAS* p.G12V genotype (HR, 1.975; $P = 0.0407$) were significant independent prognostic factors for the overall survival. A gene expression analysis of the two factors revealed the p.G12V genotype to be closer to those of stem cells, and the traits of e an enhanced fatty acid and amino acid metabolism as well as a solid predominant phenotype were shown to an acquired a trait that can withstand hypoxia and the effect of prostaglandin-endoperoxide synthase. **Conclusions:** The *KRAS* p.G12V genotype and solid predominant adenocarcinoma phenotype may be independent predictive factors of a poor clinical course in resected early-stage non-small-cell lung cancers, possibly due to the differentiation tendency observed in stem cells, the trait of an enhanced fatty acid and amino acid metabolism, and the effect of prostaglandin-endoperoxide synthase. Research Sponsor: None.

8546 **Poster Session**

Molecular characteristics of ERBB2-activating mutations in Chinese patients with NSCLC.

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Background: Activating mutations in the ERBB2 gene were shown to play an oncogenic role similar to that of ERBB2 amplification. Thus, ERBB2 mutations have emerged as therapeutic targets in non-small cell lung cancers (NSCLC). However, Activating ERBB2 mutations have not been described in detail like other driver gene mutations, such as epidermal growth factor receptor (EGFR)-activating mutations. **Methods:** In this study, we retrospectively analyzed activating ERBB2 mutations using next-generation sequencing(NGS). From May 2019 to January 2022, 21745 patients who were diagnosed with NSCLC were detected. **Results:** A total of 686 activating ERBB2 mutations were found, and 12 patients carried double ERBB2-activating mutations. In this cohort, the average age of patients was 58 years (range, 13-90 years). 59.6% of the patients were female and 88.2% were diagnosed with lung adenocarcinoma.A total of 47 ERBB2-activating mutation subtypes were defined in 674 patients. The most common activating mutations were Y772_A775dup (55.0%, 371/674), followed by G776delinsVC (8.3%, 56/674), S310F (7.7%, 52/674), G778_P780dup (5.6%, 38/674) and V659E (4.1%, 28/674). All other mutations occurred in 14 or fewer patients. ERBB2-activating mutations occurred most frequently in the tyrosine kinase domain (TKD) (80.1%), which included mutations in exon 20 (76.2%), exon 19 (3.0%), and exon 21 (1.2%),In addition, 13.2% of activating ERBB2 mutations occur in the extracellular domain, and 5.5% in the Transmembrane domain. 23.1%(156/674) patients with ERBB2 activating mutations could be evaluated for concurrent mutations, tumor mutational burden (TMB) and microsatellite instability (MSI) status. Among these patients, ERBB2-activating mutations were most frequently co-mutated with TP53(54/156) and EGFR(21/156). The frequency of EGFR mutations was much higher in non-TKD mutation patients than in TKD mutation patients (56.7% vs. 3.2%, $P < 0.001$), but no difference was observed for TP53. All these patients were microsatellite stable (MSS) and low TMB (< 10 mutations/megabase). **Conclusions:** We report mutational landscape and characteristics of ERBB2 in Chinese NSCLC patients.The prevalence of activating ERBB2 mutations was 3.1% in Chinese NSCLC patients. 80.1% of ERBB2 activating mutations were in TKD and 19.9% were in the non-TKD. The non-TKD mutations might also be used as a therapeutic target in ERBB2-directed target therapy. Research Sponsor: None.

8547 **Poster Session**

Dynamic monitoring circulating tumor DNA in plasma samples by PEAC technology for patients with early-stage non–small cell lung cancer after surgery.

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Background: Local recurrence or distant metastasis after surgery is not rare for early-stage Non-Small Cell Lung Cancer (NSCLC) patients. Present clinicopathological parameters, such as TNM stages and pathological subtype, are limited effective, as Positive Predictive Value (PPV) is low while Negative Predictive Value (NPV) is high. In recent years, circulating tumor DNA (ctDNA) has emerged as a non-invasive method for early diagnosis, prognostic stratification, disease surveillance, and treatment response evaluation. We assessed whether circulating tumor DNA (ctDNA) detected by PEAC technology could be a biomarker for minimal residual disease (MRD) and prediction of postoperative relapse in early-stage NSCLC. **Methods:** We enrolled 132 NSCLC patients with EGFR, KRAS, NRAS, BRAF and PIK3CA mutations, and obtained plasma samples at five perioperative time points (before surgery, 3-7 days, 6-months, 12-months and 18-months after surgery). Using PEAC technology, somatic mutations in plasma samples were identified and utilized for ctDNA-based MRD analysis. Clinical follow-ups were collected. **Results:** Our data showed that 32.0% (8 of 25) of patients with positive preoperative ctDNA experienced postoperative relapse, compared with 7.2% (6 of 83) in ctDNA negative patients, demonstrating that preoperative ctDNA status is an effective prognosis factor for NSCLC. In time point of 3-7 days after surgery, plasma samples were obtained from 47 patients, of which 33.3% (2 of 6) with positive ctDNA experienced postoperative relapse, while only 4.9% (2 of 41) in ctDNA negative patients. The result suggests that ctDNA positive in plasma samples of 3-7 days after surgery might be a strong biomarker for MRD detection and relapse prediction. For ctDNA surveillance, plasma samples from 6-months, 12-months and 18-months after surgery were collected and detected. At any one of the three tests ctDNA is positive, 20.0% (8 of 40) patients experienced clinical relapse, while 5.1% (3 of 59) patients with ctDNA negative status at all times relapse. A total of 14 recurrence events had occurred, ctDNA positivity precedes radiological recurrence by a median of 150.5 days (90.5 – 182, P = 0.006). **Conclusions:** Perioperative ctDNA analysis using PEAC technology is effective in early detection of MRD and relapse prediction, and hence could benefit NSCLC patient management in clinical settings. Clinical trial information: NCT03465241. Research Sponsor: Sun Yat-sen University.

8548 **Poster Session**

Optimization of treatment options for EGFR-mutant, stage III, unresectable NSCLC: A systematic review and meta-analysis.

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Background: The PACIFIC study established a new treatment standard for Stage III unresectable NSCLC, but CRT followed by durvalumab failed to bring survival benefit to patients with EGFR mutations. EGFR-TKIs have been successful in the setting of first-line treatment of advanced NSCLC and postoperative adjuvant treatment of NSCLC. We explored whether locally advanced inoperable patients with EGFR mutations can benefit from EGFR-TKIs and the possibly best treatment regimen through meta-analysis. **Methods:** Studies involving unresectable stage III NSCLC with EGFR mutations published in PubMed, Embase, Cochrane, ClinicalTrials.gov, and abstracts of important international conferences (ASCO, ESMO, WCLC) from January 1, 2000 to September 30, 2021 were screened. An integrative analysis was performed using STATA (version 16.0), and a network meta-analysis based on a Bayesian framework was performed using R (version 3.6.1) for the studies with a control group. The primary endpoints were progression-free survival (PFS) and overall survival (OS). **Results:** A total of 3291 patients were identified in 17 studies, including 5 treatment measures including concurrent chemoradiotherapy (CRT), CRT followed by durvalumab (CRT+Durva), TKI monotherapy, radiotherapy combined with TKI (RT+TKI), and CRT combined with TKI (CRT+TKI). PFS with TKI-free treatments (CRT, CRT+Durva) was significantly shorter than TKI-containing ones (TKI, RT+TKI, CRT+TKI) (HR 2.17, 95%CI 1.47-3.19), but its advantage only translated into borderline OS benefit (1.27, 0.99-1.63). In detail, the PFS with TKI-containing measures, including TKI monotherapy (0.66, 0.50-0.87), RT+TKI (0.37, 0.28-0.50), or CRT+TKI (0.14, 0.03-0.75) were all significantly longer than CRT. Furthermore, the PFS with both RT+TKI (0.40, 0.21-0.76) and CRT+TKI (0.15, 0.03-0.74) were significantly longer than CRT+Durva, while no statistical difference existed in PFS between RT+TKI and CRT+TKI. However, TKI alone had significantly shorter PFS than RT+TKI (1.78, 1.17-2.67). There was no statistical difference in OS among all the treatments, with RT+TKI ranking first in the Bayesian ranking. The integrated analysis found that RT+TKI had the longest OS (65.7 months, 55.5-76.0 months) and PFS (21.8 months, 18.0-25.7 months) and the highest response rate (77.7%, 68.8%-86.6%). Severe neutropenia was the most common with CRT+TKI, while RT+TKI brought the highest incidences of radiation pneumonitis and esophagitis. **Conclusions:** For EGFR mutant Stage III unresectable NSCLC, RT and TKI are both essential. RT+TKI and CRT+TKI have significantly longer PFS than CRT±immunotherapy, and RT+TKI has OS benefit trends. Due to the lack of sufficient studies on CRT+TKI, it is urgent to conduct large randomized clinical trials to explore the optimal treatment for these patients. Research Sponsor: None.

8549 **Poster Session**

The use of artificial intelligence with uncertainty estimation to predict lung cancer relapse from histopathology.

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Background: First-line treatment of early stage non-small cell lung cancer (NSCLC) is surgical resection, but with a 5-year survival of only 54%, rates of future relapse are high. Identifying patients at high risk of relapse can help guide adjuvant treatment decisions. Deep convolutional neural network (DCNN) AI models trained on tumor histology have shown incredible flexibility as potential biomarkers, both in lung cancer and more generally across many malignancies. While DCNN models can obtain extremely accurate results when used for routine purposes such as diagnosis, subtyping, and grading of malignancies, most models trained for prognostication or treatment response prediction do not reach performance sufficient for clinical application. Uncertainty quantification (UQ) – a family of techniques that give DCNN models the ability to report confidence alongside predictions – is an underexplored avenue in cancer AI that may help further improve performance and clinical application of models designed to provide clinicians with estimations of risk. **Methods:** To explore the potential use of UQ in clinically-oriented DCNN models, we trained models on a single-institution, retrospective digital tumor histology slide cohort from patients with Stage I-III NSCLC who underwent surgical resection to predict risk of future relapse. Estimation of uncertainty was performed using dropout as a Bayesian approximation, and uncertainty thresholds were calculated from training sets using a novel method to identify and remove low-confidence predictions. For comparison, a separate multivariate logistic regression was trained in cross-validation using known clinical risk factors. **Results:** We trained DCNN models on slides from 198 patients (40 relapsed, 158 without relapse). In this cohort, 130 patients had stage I disease (65.6%), 42 had stage II (21.2%), and 26 had stage III (13.2%). The average age was 69 years, 85% were current or previous smokers, and 38 received guideline-concordant adjuvant chemotherapy. Without UQ, a DCNN model predicted risk of future relapse with an average area under receiver operator curve (AUROC) of 0.74 across three-fold cross-validation. Using UQ estimation, 63% of slides were reported with high confidence. Relapse prediction was significantly improved in the high-confidence cohort, with an average AUROC of 0.83 in cross-validation. With a specificity of 70%, this corresponds to an average sensitivity of 86.8% across the three cross-folds (79.1%, 85.5%, and 95.7%). In comparison, a clinical-only multivariate regression model predicted relapse with a cross-validated AUROC of 0.67. **Conclusions:** This method of uncertainty quantification appears to be a powerful tool to predict lung cancer recurrence risk from digital histopathology while simultaneously providing clinicians with a measurement of algorithm trustworthiness. Research Sponsor: U.S. National Institutes of Health.

8550 **Poster Session**

Effect of durvalumab in patients with unresectable stage 3 non–small cell lung cancer post-chemoradiotherapy.

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Background: The PACIFIC study (PS) concluded that the use of durvalumab from 1 to 42 days after concurrent chemoradiotherapy (CXRT) in stage 3 unresectable non-small cell lung cancer (NSCLC) increased the median overall survival (mOS) from 29 to 48 months. It also showed a benefit in tumors with PD-L1 <25%. However, a post-hoc analysis of the PS showed no survival benefit with durvalumab in patients with PD-L1 <1% but was not statistically powered. Currently in the US, durvalumab is approved irrespective of PDL-1 percentage, whereas in Europe it is not approved for tumors with PDL-1 <1%. Also, there was no survival benefit in starting durvalumab within and after 2 weeks of CXRT. Our objectives in this study are to analyze the impact of PDL-1 expression and the date of initiation of durvalumab post CXRT on mOS. **Methods:** We conducted a retrospective observational study of stage 3 unresectable NSCLC patients who received durvalumab post CXRT at LSU Health Shreveport from 2018 to 2021. A survival analysis was done including the following variables: age, race, sex, tumor histology, tumor PD-L1 percentage, and date of initiation of durvalumab post CXRT. P-value <0.05 was considered statistically significant. **Results:** We identified 83 patients who received durvalumab after CXRT for treatment of stage 3 unresectable NSCLC. Baseline characteristics are provided in table 1. Among all the tumors, 25% had a PDL-1 <1%. 33% of the study population received durvalumab less than 30 days after CXRT and 67% received it after 30 days. The mOS was not impacted by race, sex, or tumor hisotology. Compared to higher PDL-1 percentage, patients with PD-L1 <1% had a statistically significant lower survival probability. At 14 months, 87% of patients with a PD-L1 <1% were alive compared to 100% in those with a PD-L1 1-50% or a PD-L1 >50%. Less than 35% of patients with PD-L1 <1% survived beyond 30 months compared to 45% for PD-L1 1-50% and 100% for PD-L1 >50% (p-value 0.02). Patients who received durvalumab 30-60 days after concurrent CXRT had a lower OS at 30 months compared to those who started before 30 days (44% versus 90%). However, statistical significance was not reached (p-value 0.45). **Conclusions:** This study demonstrates that patients with a PD-L1 tumor expression of <1% had a statistically significant lower survival probability compared to those with a PD-L1 expression of 1-50% and > 50% in this patient population. Time from CXRT to the start of durvalumab was not shown to affect survival outcomes. Research Sponsor: None.

Baseline characteristics of the study group.

Characteristics	
Age	63 (42 to 88)
Sex	
Male	56 (67.5%)
Female	27 (32.5%)
Race	
White	37 (45.1%)
African American	45 (54.9%)
Tumor Histology	
SCC	44 (53%)
Adenocarcinoma	32 (38.6%)
Other	7 (8.4%)
PDL-1 expression	
PDL-1 <1%	21 (25.3%)
PDL-1 1-50%	20 (24.1%)
PDL-1 >50%	20 (24.1%)
Unknown	22 (26.5%)
Start of Durvalumab post CXRT (in days)	
<30	28 (33.7%)
30-60	36 (43.4%)
>60	19 (22.9%)

8551 **Poster Session**

Equity for under-served populations in lung cancer screening and treatment: Does mobile low-dose CT scanning lead to stage shift and diagnosis with potential cures at 4 years of follow-up?

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Background: Randomized trials proved that screening high-risk patients with LDCT of chest reduces lung cancer mortality. Under-served patients have missed this benefit in most studies through access issues. We showed that mobile LDCT improves access and now assess if this translates to equity of survival. **Methods:** We used two coaches with BodyTom © portable 32 slice low-dose CT scanners (Samsung) to screen uninsured and under-served heavy smokers for lung cancer (Oncologist, 2019). All films were reviewed by central panel using LUNG RADS technique. Protocol was approved by Advarra IRB. Medicare pts were excluded as insurance covered them for LDCT (causing negative bias for diagnosis as the elderly are at high risk). **Results:** We initially screened 1200 uninsured/under-insured subjects, mean age 61 years (range 55-64), with average pack year history of 47.8 (30-150); 61% male; 18% Black, 3% Hispanic/Latino; 78% rural. We found 97 pts with LUNG RADS 4 (high risk) lesions, 30 lung cancers (2.5%), including 18 at stage I-III treated with curative intent (60%); 5 incidental non-lung cancers (renal CA 2, head & neck CA 1, pancreas CA 2); > 50% with intercurrent cardiovascular disease and COPD seen on LDCT. Of eligible first-screen subjects, 51% attended 12 month repeat LDCT and 27% attended third LDCT. One pt (6%) treated with curative intent has relapsed to date (median follow up 2.5 years, with 25% beyond 3 years). An additional 288 screened pts revealed 9 lung cancers (5 stage I-III), confirming shift to early stage disease at diagnosis. **Conclusions:** Mobile LDCT yields higher screening rate for under-served pts than prior hallmark trials, with shift to early-stage detection of lung cancer, with sustained treatment-induced remissions beyond 4 years. This approach could be applied to improve national lung cancer survival in the under-served. Research Sponsor: BMS Foundation; Leon Levine Foundation.

8552 **Poster Session**

Epidemiology and clinical impact of EGFR mutation in patients with lung cancer after radical surgical treatment.

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Background: The epidemiology of epidermal growth factor receptor (EGFR) mutation in lung adenocarcinoma and its clinical impact are well-known. However, most studies have focused on advanced-stage inoperable cancer. Data on the frequency of EGFR mutation in surgically resected lung cancer are limited. Recent studies have shown a promising effect of Osimertinib in adjuvant settings. Hence, the need to estimate the target population in the real-world data. This study aimed to assess the occurrence of EGFR mutation in patients after radical surgical treatment of lung adenocarcinoma and explore its prognostic impact compared to EGFR negative group. **Methods:** This single-center retrospective analysis included the group of 732 consecutive Caucasian patients with histopathologically confirmed lung adenocarcinoma, evaluated for EGFR mutations expression, who underwent anatomical resection between January 2016, and December 2020. EGFR status was assessed by cobas EGFR mutation test v2. The frequency of EGFR mutations, disease-free survival (DFS) and overall survival (OS) in EGFR positive and EGFR negative groups were analyzed. **Results:** EGFR mutations were found in 65 surgical patients (8.9%) and did not differ from patients with advanced stages of lung adenocarcinoma (7.9%). EGFR mutations occurred more frequently in females than males, 48 out of 344 (14%) and 17 out of 388 (4.4%), respectively. Deletions within exon 19 and the L858R mutation in exon 21 constituted 49.2% and 24.6% of all mutations, respectively, while others comprised 26.2%. One case of L858R mutation coincided with T790M in exon 20 mutation. Detailed results divided by stages are presented in the Table. The occurrence of EGFR mutation had no significant influence on DFS and OS in patients after radical resection. **Conclusions:** The frequency of EGFR mutation in postoperative lung cancer was comparable to the occurrence in the general lung cancer population. EGFR mutation did not affect DFS and OS in patients after radical resection. Research Sponsor: None.

Summary of the EGFR mutation results by stage.

Stage[1]	EGFR mutation-positive patients [n (%)]	Total numer of patients
IA	12 (7.3)	165
IB	20 (10.2)	196
IIA	5 (10.9)	46
IIB	8 (5.9)	136
IIIA	16 (10.8)	148
IIIB	4 (9.8)	41

[1]According to the 8th edition of IASLC guidelines.

8553 **Poster Session**

Lung cancer risk in persons enrolled in low-dose CT screening (LDCT) versus incidental lung nodule programs (ILNP).

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Background: LDCT screening saves lives, but <10% of eligible persons participate; eligibility criteria are imperfect; geographic, racial and socio-economic disparities have emerged. ILNP may expand access to early detection. We compared rates of lung cancer diagnosis in LDCT and ILNP population subsets. **Methods:** Prospective observational cohort study of enrollees in LDCT and ILNP in a community healthcare system in AR, MS and TN. We compared LDCT vs 4 ILNP cohorts (C) based on USPSTF 2021 LDCT eligibility criteria: <50 years (C1, too young); >80 years (C2, too old); 50 – 80 years (C3, ineligible smoking history); 50 – 80 years (C4, eligible). For certain analyses, we stratified the LDCT cohort by baseline (T0) Lung-RADS score (0-2 v 3-4). We used a Cox model to calculate crude and adjusted hazard ratios (aHR) for lung cancer diagnosis within 24 months of enrollment. **Results:** From 2015-2021, 7050 persons were in LDCT- 6073 (86%) Lung-RADS 0-2 (no/benign lesions), 977 (14%) Lung-RADS 3 or 4 (possibly malignant lesion) on T0 scan; 17,579 were in ILNP, 16%, 10%, 57% and 16% respectively in C1-4. Demographics and tobacco use history of the ILNP cohorts differed strikingly; C4 was very similar to LDCT (Table). Black persons were significantly more in C1 (too young) and C3 (insufficient tobacco use). Diagnosis of lung cancer at 36 months ranged from 1% in C1 to 15% in C4, compared to 3% in LDCT; aHR for lung cancer diagnosis within 2 years ranged from 0.23 to 5.12 (all LDCT ref), but ranged from 0.04 to 1.02 with reference to LDCT Lung-RADS 3-4. Most patients in LDCT and ILNP C2-4 had early stage. There were proportionately more Black lung cancer patients in C1-4, and 3 times more Black patients in C3 and 4 than in LDCT. **Conclusions:** ILNP provides early-detection access to a larger, more diverse population than LDCT, potentially alleviating race and socio-economics-based outcomes disparities. Research Sponsor: None.

	LDCT*	LNP*			
		C1	C2	C3	C4
	N = 7050	N = 2888	N = 1824	N = 10093	N = 2774
Demographics					
Age: Median yrs (Q1-Q3)	65(60 - 70)	44(40 - 47)	85(82 - 88)	66(58 - 72)	66(60 - 71)
Female	50	59	58	55	50
Black race	**19**	**38**	**19**	**29**	**19**
Uninsured	1	18	3	9	4
Smoking history					
Former	32	13	41	29	29
Never	0	46	45	45	0
≥20 Pack years	87	19	34	14	100
Missing	10	57	48	62	0
Quit Duration <15 years	88	42	12	16	100
Missing	2	45	32	38	0
Largest lesion, median mm (Q1 - Q3)	4(2 - 6)	7(5 - 10)	8(5 - 15)	7(5 - 11)	9(5 - 15)
Cumulative # of Lung Cancer Patients (n, %)					
12 months	149(2)	19(1)	96(5)	314(3)	371(13)
24	183(3)	19(1)	102(6)	345(3)	408(15)
36	205(3)	20(1)	102(6)	364(4)	426(15)
Black race	**15**	**40**	**18**	**30**	**22**
Histology					
Adeno	45	55	48	52	47
Squamous	31	10	29	18	29
Small	16	10	5	12	12
Clinical Stage					
Stage I/II	60	30	52	57	56
Stage III	18	20	18	21	22
Stage IV	19	50	26	22	20
aHR (95% CI)					
Ref all LDCT	-	0.23 (0.14, 0.38)	1.93 (1.50, 2.48)	1.21 (1.01, 1.46)	5.12 (4.34, 6.05)
Ref Lung-RADS 3-4	-	0.04 (0.03, 0.07)	0.39 (0.30, 0.51)	0.24 (0.19, 0.29)	1.02 (0.85, 1.24)

*Numbers are column % unless otherwise stated.

8554 **Poster Session**

Treatment interruptions and discontinuations among patients with stage III unresectable non–small cell lung cancer treated with durvalumab at the Veterans Health Administration.

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Background: The PD-1/PD-L1 pathway is a mechanism of immune evasion and disruption of this pathway with immune checkpoint inhibitors (ICIs) has shown clinical benefit in multiple malignancies. Based on results from the PACIFIC trial, durvalumab is approved as consolidation therapy in patients (pts) with stage III unresectable non-small cell lung cancer (UR-NSCLC) without progression following concurrent chemoradiotherapy (cCRT). Durvalumab has been used extensively in Veterans Health Administration (VHA) facilities, providing an opportunity to evaluate durvalumab treatment interruptions (TI), treatment discontinuations (TD), and the reasons for these on a national scale. **Methods:** Patients with stage III UR-NSCLC receiving durvalumab consolidation immunotherapy at the VHA between January 1, 2017 and June 30, 2020 with a minimum follow up for 12 months were included using ICD-10, HCPCS, and J codes and followed from their durvalumab start date through the earliest of last VHA visit, loss to follow up, death, or end of study (excluded if durvalumab therapy was ongoing at the end of the study, because the full treatment course could not be determined). TI were defined as durvalumab infusions separated by >28 days. Reasons for TI and TD are presented descriptively. Durations are reported using medians and interquartile ranges (IQR). **Results:** 935 pts were included (median age = 69 years; 95% males; 96% current or former smokers; 70% with COPD; histologies [squamous (50%), non-squamous (43%), other/missing (7%)]; and 77% with carboplatin-paclitaxel as their platinum-based CRT). Durvalumab TI were experienced by 19% of pts (median [IQR] number of TI = 1 [1-1], median [IQR] TI duration = 53 days [39-90]). The main reasons for TI were toxicity (8%) and social reasons (3%) (Table). The median duration of treatment (DoT) with durvalumab (TI included) was 9.0 months (IQR 2.9-11.8). Durvalumab TD occurred in 59% of pts. Top reasons for discontinuation across all 935 pts included disease progression (24%) and toxicity (18%) (Table). **Conclusions:** In this real world analysis of national VHA data, durvalumab DoT was similar to PACIFIC despite having a patient population with worse prognostic factors (e.g. more males, squamous, COPD) with 8% of VHA pts experiencing TI and 18% TD due to toxicity. Patients could benefit from additional efforts to prevent, identify, and manage toxicities in the UR-NSCLC population Research Sponsor: Astrazeneca.

Reported reasons* for durvalumab TI and TD.

	TI % of all (N=935) patients	TD % of all (N=935) patients
Progression	<1 %	24%
Toxicity	8 %	18 %
Patient preference	1 %	6 %
Physician preference	1 %	1 %
Death		4 %
Decline in performance status	1 %	2 %
Social reasons	3 %	<1 %
Insurance & System related	<1 %	<1 %
Other	6 %	3 %

*>1 reason possible for each TI.

8555 **Poster Session**

Texture-based CT radiomics distinguishes radiation and immunotherapy induced pneumonitis in stage III NSCLC.

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Background: Recent changes to the standard of care for unresectable stage III NSCLC include chemoradiation followed by consolidative immunotherapy (IO). Pneumonitis is a well-known complication of radiotherapy (RT) and has been increasingly reported in association with IO. Although rare, pneumonitis can cause severe morbidity and possibly death in extreme cases. Differentiating RT and IO-induced pneumonitis (RTP vs IOP) is crucial for acute management and future considerations of individualized treatment. However, the clinical and radiological features of RTP and IOP may be similar and often indistinguishable on computed tomography (CT). Texture-based CT radiomics has previously been used to distinguish benign and malignant nodules on lung CT. In this study, we explore if radiomic features extracted from lung CT can distinguish between RTP and IOP. **Methods:** From 236 patients with stage III NSCLC who underwent chemoradiation followed by consolidative durvalumab, we identified 110 cases of treatment-related pneumonitis. IOP cases were identified through a retrospective review of electronic medical records and independently verified by a thoracic oncologist using features such as bilateral lung involvement, inflammatory changes outside the field of RT, temporal relationship to IO, and response to treatment. Inflammatory lesions were manually annotated using Slicer 3D. After excluding cases without discernible cause and non-identifiable lung lesions (n = 61), we included 49 cases in the study (RTP n = 20; IOP n = 29). A total of 555 features from Gabor, Laws, Laplace, and Haralick feature families were extracted on a pixel level from post-treatment CT images. A support vector machine (SVM) classifier was trained with the most discriminating features identified by Wilcoxon rank-sum test feature selection method. The classifier performance for distinguishing RTP vs. IOP was assessed by averaging the area under the receiver operating characteristic curve (AUC) values computed over 100 iterations of threefold cross-validation. **Results:** We identified the top 5 radiomic texture features distinguishing RTP from IOP including Haralick entropy, Haralick info, Laws median, and high- and low-frequency Gabor. Using 3-fold cross-validation, the SVM classifier model built on the radiomic features achieved an AUC of 0.83 (95% confidence interval, 0.78 - 0.86). **Conclusions:** Pneumonitis is a severe complication of both RT and IO that must be taken into consideration when evaluating future risks of IO-based therapies. The distinction between RTP and IOP remains challenging based on CT findings alone. Radiomic texture features analysis of post-treatment CT images can potentially differentiate RTP from IOP in stage III NSCLC patients who received RT followed by consolidative durvalumab. Additional multi-site independent validation of these quantitative image-based biomarkers is warranted. Research Sponsor: None.

8556 **Poster Session**

Durvalumab treatment initiation delays in patients with unresectable stage III non–small cell lung cancer treated at Veterans Health Administration facilities.

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Background: Durvalumab is an FDA-approved immunotherapy for the treatment of adults with UnResectable stage III non-small cell lung cancer (UR-NSCLC) without disease progression following concurrent chemoradiotherapy (CRT). There are limited real-world data regarding Durvalumab treatment initiation delays (TIDs) and reasons for them in the UR-NSCLC population. **Methods:** Patients with stage III UR-NSCLC receiving consolidation Durvalumab at the Veterans Health Administration (VHA) between January 1, 2017 and June 30, 2020 were selected from the VHA database using ICD-10, HCPCS, and J codes. All had the opportunity to be treated for 12 months and were followed from Durvalumab initiation through the earliest of their last VHA visit, loss to follow up, death, or the study's end (and excluded if Durvalumab therapy was ongoing at the study's end). Trained data abstractors determined the occurrence and reasons for TIDs (> 6 weeks from end of CRT to initiation of Durvalumab as in the PACIFIC trial) by chart review. **Results:** 935 patients were eligible for analysis (median age = 69 years; 95% males; 16% with ECOG performance status >1). TIDs occurred in 39% of the patients (Table). Durvalumab was initiated 61 days (median) from the end of CRT in TID patients vs. 31 days for those without TIDs. There were no significant (α<0.05) differences in age, race, smoking status, histology, or ECOG performance status and no comorbidity differences (except in patients with a history of cerebrovascular accident, for whom TIDs were more likely) between the TID/No-TID patients. Patients without timely post-CRT scans were more likely to have a TID. Of the 367 patients who experienced TIDs, 200 had documented reasons for the delay, consisting of other (not categorized) (28.5%), physician preference (20%), toxicity (11%), patient preference (10.5%), decline in performance status (10%), system issues (9.5%), social reasons (9%), and progression (0.5%). **Conclusions:** This is one of the largest retrospective cohort studies reporting real-world data in patients with UR-NSCLC receiving Durvalumab. TIDs were associated with increased time to post-CRT scans. This potential issue can be improved with care coordination and involvement of cancer navigators. Additional studies are needed to assess the impact of TIDs on survival outcomes. Research Sponsor: AstraZeneca.

Times to post-CRT scans and treatment patterns among TID vs. No-TID patients.

	TID (n=367)	No-TID (n=568)	P-value
Time from end of CRT to first scan, median days (IQR)	39 (25-56) n=329	28 (18-35) n=478	<0.01
Missing/unknown	n=38	n=90	
% <6 weeks	53% (174/329)	87% (416/478)	<0.01
% ≥6 weeks	47% (155/329)	13% (62/478)	<0.01
Durvalumab duration of therapy, median months (IQR)	8.7 (2.9-11.8) n=364	9.4 (3.1-11.9) n=563	0.61
Durvalumab discontinuations, %	61%	58%	0.36
Completed planned treatment, %	39%	42%	0.36

8557 **Poster Session**

Clinical activity of pembrolizumab monotherapy in diffuse malignant peritoneal mesothelioma.

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Background: Among patients with malignant mesothelioma, pembrolizumab has demonstrated activity in diffuse pleural mesothelioma (DPM), with limited data available for those with diffuse malignant peritoneal mesothelioma (DMPM). DMPM represents a clinically distinct entity from DPM and disease specific outcomes data is needed. We present real world data on the efficacy of pembrolizumab in DMPM. **Methods:** In this retrospective study, we identified patients with DMPM treated with pembrolizumab at two tertiary care cancer centers between 1/1/2009 and 1/1/2021. Clinicopathologic features were annotated. Median progression free survival (mPFS) and median overall survival (mOS) were calculated using Kaplan-Meier curves. Best overall response rate (BOR) was determined using RECIST 1.1 criteria. Association of partial response with disease characteristics was evaluated using Fisher's exact test. **Results:** We identified 24 patients with DMPM who received pembrolizumab (median age 62 years, 63% never smokers, 58% female, 75% had epithelioid histology). All patients received systemic chemotherapy prior to pembrolizumab (median prior lines of therapy: 3). BOR was 17% (3 partial responses, 10 stable disease, 5 progressive disease, 6 lost to follow-up). With a median follow up time of 29.2 months, mPFS was 4.9 months and mOS 20.9 months from pembrolizumab initiation. Three patients experienced PFS of > 2 years. Among the 14 patients who underwent next generation sequencing of tumor tissue, there were 8 somatic BAP1 alterations. Among the 17 patients tested for PDL1, 6 had positive PDL1 expression (1-80%). There was no association between partial response and presence of a BAP1 somatic alteration ($p = 0.453$), PDL1 positivity ($p = 0.7$) or non-epithelioid histology ($p = 0.55$). **Conclusions:** Pembrolizumab is active in a PDL1 unselected cohort of patients with DMPM. The overall response rate of 17% and mPFS of 4.9 months in this 75% epithelioid histology cohort warrants further investigation to identify those most likely to respond to immunotherapy, especially among epithelioid histology. Research Sponsor: This research was supported, in part, by the National Institutes of Health/National Cancer Institute (P30 CA008748).

8558 **Poster Session**

Positive impact of academic center care on overall survival in malignant pleural mesothelioma (MPM): A National Cancer Database (NCDB) socioeconomic factor analysis.

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Background: MPM is a rare cancer with a poor prognosis. Median survival for untreated patients is 4-13 months, and for treated patients is 6-18 months. Despite asbestos regulations in the United States, annual deaths from MPM rose from 2,479 in 1999 to 2,597 in 2015. Given recent treatment advances, including improvements in multimodality therapy and the introduction of immunotherapy as a treatment option in the frontline setting, the impact that patient demographics and treatment factors have on survival outcomes for MPM requires further evaluation. **Methods:** We identified all patients with MPM in the NCDB from 2004 to 2017. Differences in demographic, disease, and treatment characteristics were assessed by year of diagnosis using Chi-square test. The effect of age, race, insurance status, income, distance to treatment center, and education level on overall survival (OS) was assessed by log-rank test. **Results:** There were 15,287 MPM diagnoses in the NCDB between 2004-2010 and 17,059 diagnoses between 2011-2017. OS improved between the two time periods, with median OS of 9.46 months (95% CI: 9.23-9.63) and 5-year OS rate of 8.3% (95% CI: 7.9-8.7%) in patients from 2004-2011 and median OS of 11.33 months (95% CI: 11.01-11.7) and 5-year OS rate of 12.4% (95% CI: 11.8-13.1%) in patients after 2011, despite an increase in stage IV disease in the latter group. Older patients (≥65 years-old), males, patients with stage IV disease, patients with government primary payer insurance, and patients from urban areas all had significantly worse OS. Patients without comorbidities and those treated at an academic center had significantly better OS. OS was found to significantly increase as both income and education level increase. Patients diagnosed after 2011 were significantly older, were more frequently female, had more stage IV disease, were more frequently treated at academic centers, more commonly had government primary payer insurance, and lived significantly further away from their treatment center. Patients' time to treatment was significantly increased after 2011 (from 28 to 31 days). **Conclusions:** Socioeconomic factors play an important role in survival outcomes for patients with MPM. Many of these are linked with access to healthcare resources, which may increase the likelihood of evaluation at academic centers. For a rare malignancy such as mesothelioma, subspecialty care consisting of a comprehensive thoracic surgical evaluation and appropriate multimodality treatment are of great importance. Time to treatment increased during the study period yet OS improved, which our findings suggest are a result of an increase in evaluation and treatment at academic centers by providers skilled in delivering care to MPM patients. Research Sponsor: None.

8559 **Poster Session**

Phase I clinical safety and preliminary efficacy of PD-1-mesoCAR-T cells in the treatment of malignant pleural/peritoneal mesothelioma.

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Background: Malignant pleural/peritoneal mesothelioma (MPM) is an aggressive cancer characterized by poor therapeutic response and poor survival. Programmed cell death protein-1 (PD-1)-mediated immunosuppression is believed to be associated with T cell exhaustion and dysfunction in solid tumors. We generated chimeric antigen receptor (CAR-T) cells that can secret PD-1 nanobodies and target mesothelin (PD-1-mesoCAR-T). After identifying the anti-tumor activity and cytotoxicity of PD-1-mesoCAR-T cells by pharmacokinetics and pharmacodynamics, we conducted a proof-of-concept clinical trial in the Shanghai Tenth People's Hospital affiliated to Tongji University and the Mengchao Tumor Hospital affiliated to Shanghai University to evaluate the safety and efficacy of PD-1-mesoCAR-T cells in a dose-escalation study for malignant pleural/peritoneal mesothelioma. 6 patients received one or more infusions of the CAR-T cells with prior lymphodepletion and the longest survival is up to 18 months. **Methods:** This open-label, single-arm, multicenter, phase 1 study was enrolled patients with pathological diagnosis with malignant mesothelioma whose mesothelin expression in immunohistochemical samples was equal or greater than 50%. Immunohistochemical samples derived from surgical tissue, puncture tissue or pleural effusion. PD-1-mesoCAR-T cells were administered intravenously ranging 1×10^6–1.5×10^7/kg. Safety and efficacy were assessed in response-evaluable patients (ie, patients who received at least one dose of PD-1-mesoCAR-T and had at least one post-baseline response evaluation). **Results:** From July 20, 2020 to January 31, 2022, 9 patients were screened and enrolled and only 6 patients were evaluable. Mesothelin positive rate in the samples of these patients were from 50% to 100%. Three patients of them had PD-L1 positive staining in specimen. All patients underwent lymphodepletion before infusion. Two of patients (33.3%) had cytokine release syndrome, which were grade 1 and grade 3, respectively. Four patients (66.7%) developed fever. Two patients (25%) had grade 3 pulmonary infection. Stable disease was sustained for ≥3 months in 5 patients; 1 exhibited complete response and one partial response on PET or CT scan. The objective response rate (ORR) was 33.3%, but increased to 66.7% in the patients with PD-L1 positive. Only one patient of these patients appeared progression of disease after infusion. All enrolled patients are alive and observed continually. **Conclusions:** The clinical study of 6 patients with malignant mesothelioma shows that PD-1-mesoCAR-T cells are safe and feasible, indicating a promising curative effect. Effect of the CAR-T cells on the long term survival will be observed continually. Clinical trial information: 01722149. Research Sponsor: Shanghai Cell Therapy Group.

8560 **Poster Session**

Atezolizumab and bevacizumab in patients with relapsed mesothelioma: MIST4—a phase IIa trial with cellular and molecular correlates of efficacy.

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Background: Targeting the PD1-PDL1 axis has demonstrated significant efficacy in patients with relapsed malignant mesothelioma (MM) however the factors that determine sensitivity are unknown. Combined inhibition of vascular endothelial growth factor (VEGF) may potentiate efficacy through remodelling of the tumour microenvironment and inhibition of angiogenesis. We therefore developed a multi-centre molecularly stratified phase IIa trial to test this hypothesis and to uncover cellular and molecular determinants of efficacy as arm 4 of the Mesothelioma Stratified Therapy umbrella trial (NCT03654833, MiST4). **Methods:** Patients with any histological subtype or site of MM (pleural or peritoneal) were enrolled. Key inclusion factors: histological confirmation of MM with an available archival tissue block, ECOG performance status 0-1, prior platinum-based 1st line chemotherapy (any line allowed), evidence of disease progression with measurable disease by CT (RECIST 1.1), and adequate haematological/organ function. Patients received Atezolizumab 1200mg iv q3w with bevacizumab 15mg/kg iv q3w (AtzBev). Primary endpoint was disease control rate at 12 weeks (DCR12w). The null hypothesis was rejected if ≥ 11 patients had disease control (A'Hern design). Secondary endpoints: DCR at 24 weeks (DCR24w), best objective response rate and toxicity (NCI CTCAE 4.03). Patients could undergo an optional re-biopsy upon disease progression. Baseline BAP1, p16ink4a, PD-L1 (DAKO22C3), gut microbiome 16s RNA metagenomics, multiplex immunofluorescence, and whole exome and RNA transcriptome sequencing was conducted to explore cellular and molecular correlates of sensitivity. **Results:** Between January 2020 and February 2021, 26 patients with MM started treatment and received at least one dose of AtzBev. The median age of pts was 68 (range, 44-80) years, 69% were male, 77% epithelioid, 85% ECOG PS1, > 1 prior systemic therapy 54%. The median cycles of Atz dosing was 4.5 (IQR, 2-8) and Bev dosing was 4.5 (IQR, 2-7). DCR12w: 53.8% (95% confidence limit (CI), 33.4% – 73.4%), DCR24w: 23.1% (95%CI, 9.0% – 43.6%). Best responses (evaluable within 24w): partial – 3.8% (95%CI, 0.1- 19.6%); stable disease – 69.2% (48.2 – 85.7%); progression – 15.4% (4.4 – 34.9%). Adverse events (any cause): ≥ grade 3 toxicities affected 35% of pts. **Conclusions:** MiST4 met its primary endpoint however responses were heterogeneous. Analysis of cellular and molecular correlates are ongoing and will be presented. Clinical trial information: NCT03654833. Research Sponsor: british Lung Foundation Asthma Research UK, Victor Dahdaleh Foundation.

8561 **Poster Session**

Final survival outcomes and immune biomarker analysis of a randomized, open-label, phase I/II study combining oncolytic adenovirus ONCOS-102 with pemetrexed/cisplatin (P/C) in patients with unresectable malignant pleural mesothelioma (MPM).

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Background: MPM is an aggressive malignancy without curative treatment. ONCOS-102 is an oncolytic adenovirus expressing GM-CSF (Ad5/3-D24-GMCSF) with a clinically documented ability to stimulate local and systemic immune responses and re-modulate the tumor microenvironment, both as a monotherapy and in combination with anti-PD1 blockade. The study objectives included determining safety and tolerability, efficacy and immunological activation in repeat tumor biopsies, and correlations with clinical outcomes. **Methods:** Following a safety run-in of n = 6 pts, 25 patients were randomized to receive ONCOS-102 intratumorally under CT or US guidance at a dose of 3×10^{11} Virus Particles on Day 1, 4, 8, 36, 78 and 120, plus six cycles of P/C starting on Day 22, or control comprising six cycles of P/C only. Both treatment-naïve (1L) and previously treated patients (2L) were enrolled. Imaging was done at baseline, Day 43-64 and 127-148 and tumor biopsy were collected at baseline and at Day 36. Final survival analysis (n = 25) was performed after 30 mo follow up. Multiplex immunofluorescence for immune cell subsets, RNASeq and qPCR was performed on repeat tumor samples. **Results:** The most frequent adverse events were anaemia, neutropenia and asthenia reported by > 50% in both groups with more frequent reports of pyrexia and nausea in the experimental (exp) group. No difference in the rate of severe events (Gr 3/4 acc to NCI CTCAE vs 4.0) were observed. 30-month survival rate (n = 25) was 34.3 % vs 18.2 % (NS) with mOS of 19.3 mo (95% CI: 4.6, NA) vs 18.3 mo (95% CI: 3.1, 28.9) in the exp group vs control. For patients treated in the 1L setting, 30 mo survival was 33.3 % in the exp group (n = 8) and 0% in the control group (n = 6) with mOS of 25.0 months and 13.5 months, respectively (NS). mPFS was unchanged from prior cut-offs; 9.8 months in the exp group and 7.6 in the control (NS). ONCOS-102 + P/C induced a pronounced increase in tumor infiltration by CD4+, CD8+ and granzyme B expressing CD8+ T-cells as well as M1:M2 macrophage polarization in patients with disease control (n = 13) vs progressing patients (n = 3). The data from RNAseq and qPCR analysis will be presented. **Conclusions:** The addition of ONCOS-102 to P/C was well tolerated by MPM patients and resulted in numerically improved 30-month survival rate in the overall population, and improved mOS in chemotherapy-naïve patients, albeit not statistically significant. Substantial immunological activation in tumor associated with ONCOS-102 was demonstrated, correlating with clinical benefit. Further exploration of ONCOS-102 as a treatment option in MPM is warranted Clinical trial information: NCT02879669. Research Sponsor: Targovax ASA.

8562 **Poster Session**

PD-L1, VISTA, and CD47 expression and prognosis impact in malignant pleural mesothelioma.

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Background: Malignant Pleural Mesothelioma (MPM) has been characterized by an immune suppressive microenvironment. The immune checkpoint (IC) VISTA is notably expressed in MPM, in contrast to other IC proteins such us PD-L1. Recently, CD47 has been described as a possible diagnostic biomarker for MPM, although its impact in prognosis has not been established yet. **Methods:** This is a retrospective observational study of immunotherapy naïve MPM patients. Immunochemistry (IHC) assessment of PD-L1, VISTA and CD47 protein expression was performed on tissue microarray of 46 surgical samples. Means were compared using Mann-Whitney U test. Correlation was estimated using Pearson's coefficients. Overall survival (OS) was assessed using Kaplan–Meier curves and Cox proportional hazard models. A two-sided alpha error of 0.05 was used to assess statistical significance. Statistical analysis was conducted with Stata/SE version 16.1. **Results:** A total of 46 patients, 71.7% (33/46) male, were included in our study. Among them, 77.8% (35/45) had stage IIIB-IV, 84.8% (39/46) had received systemic therapy and 16.7% (7/42) had undergone radical-intent surgery. Asbestos exposure was confirmed in 65,7% (23/35) patients. Regarding the histological subtype, 71.7% (33/46) were epithelioid (Ep) and 13.0% (6/46) non-epithelioid (NEp), including 5 sarcomatoid and 1 biphasic. In IHC analysis, VISTA and CD47 were expressed in 63.0% (29/46) and 58.7% (27/46), respectively, whereas only 28.3% (13/46) patients had positive PD-L1 expression (≥1%). Median expression of VISTA, CD47 and PD-L1 in tumor samples was 41.8 (95% IC 0.5 - 50.7), 26.3 (95% IC 0 - 45.8) and 0 (95% IC 0-0.5), respectively. VISTA and CD47 expression were significantly higher in the Ep subgroup vs. the NEp subgroup (VISTA 39.4% vs 7.2% $p = 0.028$; CD47 37.3 vs. 0.8 $p = 0.01$). Additionally, we found a significant positive correlation between VISTA and CD47 protein expression (Pearson's $r = 0.55$, $p < 0.001$), which was consistent with the results we found in an independent MPM patient series from TCGA PanCancer Atlas ($N = 87$) based on RNA expression ($r = 0.46$; $p < 0.001$). Median OS, available in 40/46 cases, was 16.6 months (95% CI 12.03-20.43). On multivariate analysis, CD47 ≥1% expression was significantly associated with longer OS (29.7 vs 10.53 months, HR 0.35, [IC 95% 0.14-0.86]; $p = 0.02$) after adjusting for histological subtype, PDL1 and VISTA expression. In contrast, PD-L1 ≥1% showed a trend towards worse prognosis (10.3 vs 19.3 months), without reaching statistical significance (HR 2.23 [95% IC 0.95-5.23]; $p = 0.065$). No OS differences were found regarding VISTA expression. **Conclusions:** To our knowledge, this is the first study to describe VISTA and CD47 correlation in MPM. Moreover, we demonstrate CD47 expression to be an independent prognostic marker in MPM, suggesting C47 may play a key role in tumor biology of MPM, for which further validation and functional studies are necessary. Research Sponsor: None.

8563 **Poster Session**

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

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Background: Impower133 and CASPIAN studies showed that PD-L1 antibody combined with first-line chemotherapy could prolong the overall survival. 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 (PD-L1 antibody) 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. Patients (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; etoposide 100mg/m^2, D1-5, q3w), sequentially SHR-1316 combined with chest radiotherapy (≥3Gy*10f or ≥2Gy*25f, involved- field irradiation), and then entered the maintenance treatment stage until disease progression or intolerable side effects. The main endpoints included PFS, ORR and safety. **Results:** From October 2020 to December 2021, 31 pts with ES-SCLC received at least one dose of SHR-1316. The median age was 64 (range: 37-75) with 25(80.6%) male, 22(71%) former smokers and 31 (100%) ECOG performance status 1. 17 (54.8%) pts were with brain metastasis, 8 (25.8%) pts with liver metastasis, 8 (25.8%) pts with kidney/adrenal metastasis, 7(22.6%) pts with bone metastasis. At the data cutoff date, 15 pts remained on treatment, the average number of treatment cycles was 5.19. 24 pts had at least one 1 post-treatment tumor assessment. The median PFS was 7.56 months, the confirmed ORR and DCR in all pts were 50% (12/24) and 87.5% (21/24), respectively. The confirmed ORR and DCR in pts with brain metastasis were 38.5% (5/13) and 76.9% (10/13), and were 63.6% (7/11) and 100% (11/11) in pts without brain metastasis. In pts received chest radiotherapy, the confirmed ORR and DCR were 80% (8/10) and 100% (10/10). During the study period, 23 (74.2%) pts had adverse drug reactions, and 16 (51.6%) pts had grade 3 or 4 adverse drug reactions, including 12 (38.7%) neutropenia 8 (25.8%) leukopenia, 2 (6.5%) thrombocytopenia, 2 (6.5%) anemia, 1(3.2%) lymphocytopenia, 1(3.2%) amylase increased. No grade 5 adverse drug reaction was observed. **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: Jiangsu Hengrui Pharmaceuticals Co. Ltd.

8564 **Poster Session**

Preliminary safety and efficacy of camrelizumab plus nab-paclitaxel and carboplatin as frontline setting in extensive-stage small cell lung cancer (ES-SCLC) from a phase II trial.

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Background: Impower133 and CASPIAN studies showed that PD-L1 antibody combined with first-line chemotherapy could prolong the overall survival. Our previous study showed that nab-paclitaxel had a promising efficacy as later line setting in ES-SCLC. This phase II trial aimed to evaluate the efficacy and safety of camrelizumab plus nab-paclitaxel and carboplatin as front-line setting in ES-SCLC. **Methods:** Key inclusion factors were18-75 years old, histologically or cytologically confirmed ES-SCLC, ECOG performance status 0-1, no previous systematic treatment. Patients (pts) received 4 ~ 6 cycles of camrelizumab (200mg, D1, q3w) combined with nab-paclitaxel (230mg/kg, D1, q3w) plus carboplatin (AUC = 5, D1, q3w), then camrelizumab maintenance until disease progression or intolerable side effects. The primary endpoint was 6 months progression free survival rate. Secondary endpoints included PFS, ORR and safety. **Results:** From April 2021 to December 2021, 36 pts who received at least one dose of camrelizumab were included into this report. The median age was 60.5 (range: 32-73) with 30 (83.3%) males, 19 (52.8%) former smokers, and 36 (100%) ECOG performance status 1. The median drug exposure was 5 cycles, and 18 (50%) pts entered the maintenance stage. 33 pts had at least one 1 post-treatment tumor assessment. Among them, 32 partial responses (5 unconfirmed), 1 progressive disease (new lesion). The confirmed ORR was 81.8% (27/33), the unconfirmed ORR was 97% (32/33), DCR was 97% (32/33). The median PFS was 7.27 months (95% CI: 4.7 – 9.8 months). 24 (66.7%) pts had at least one adverse event, and 10 (27.8%) pts experienced grade 3 or 4 adverse events, including 10 (27.8%) neutropenia, 4 (11.1%) leukopenia, 2 (5.6%) thrombocytopenia, 2 (5.6%) anemia, 2 (5.6%) hepatic function abnormal,1(2.8%) alanine aminotransferase increased, 1(2.8%) hyperglycaemia, 1(2.8%) diabetes mellitus, and no grade 5 adverse event happened. **Conclusions:** Camrelizumab plus nab-paclitaxel and carboplatin had promising efficacy and safety profile as first-line setting in ES-SCLC, further validation is warranted. Clinical trial information: NCT04790539. Research Sponsor: Jiangsu Hengrui Pharmaceuticals Co. Ltd.

8565 **Poster Session**

Phase I/II investigator-initiated study of olaparib and temozolomide in SCLC: Updated analysis and CNS outcomes.

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Background: Temozolomide has activity in small-cell lung cancer (SCLC), including patients (pts) with brain metastases (mets; Pietanza M, Clin Cancer Res 2012). Inhibition of Poly (ADP-ribose) polymerase (PARP) is another therapeutic strategy in SCLC. We hypothesized that olaparib plus temozolomide may be safe and effective for pts with relapsed SCLC and clinically active against CNS disease (Farago A, Cancer Discovery 2019). Here, we present an updated analysis of this combination in pts with relapsed SCLC, including a second cohort testing an alternative dosing strategy and an exploratory analysis of CNS-specific outcomes. **Methods:** In this phase I/II trial of olaparib plus temozolomide in pts with recurrent SCLC, pts were sequentially enrolled into two cohorts defined by dosing schedule. In cohort 1, olaparib was dosed on D1-7 of each 21d cycle. In cohort 2, olaparib was dosed on D1-21. Temozolomide was dosed on D1-7 in both cohorts. Each cohort had a phase I portion (conventional 3+3 dose-escalation) for determination of MTD and RP2D and a phase II portion with primary endpoint of ORR. Per protocol, eligible pts could have untreated asymptomatic brain mets < 1cm and, after mandatory baseline imaging, CNS imaging was performed at investigator's discretion. A post-hoc exploratory analysis of CNS-specific outcomes was performed using modified RECIST criteria (Long GV, Lancet Oncol 2012) in which brain mets ≥5mm were considered measurable, and intracranial response was independently assessed by an attending radiologist. **Results:** 66 pts with median of 2 prior lines of therapy (range, 1-7) were enrolled, 50 pts in cohort 1 and 16 pts in cohort 2. 33/66 (50%) pts had history of brain mets, 15/66 (23%) pts had untreated brain mets at enrollment. The confirmed ORR of cohort 2 was 7% (1/14 evaluable pts, 95% CI: 0.2-33.9%), and the updated confirmed ORR of the entire study population was 34% (21/62 evaluable pts, 95% CI: 22.3-47.0%). The most common adverse events were hematologic toxicities (thrombocytopenia, anemia, and neutropenia). 22/50 (44%) of cohort 1 pts and 4/16 (25%) of cohort 2 pts required dose reduction. Of 15 pts with untreated brain mets, best overall intracranial response (including both confirmed and unconfirmed responses) was CR in 6 pts, PR in 4 pts, SD in 3 pts and PD in 1 for a CNS disease control rate of 87% (95% CI: 59.5-98.3%). Of 10 pts with CR/PR as their best intracranial response, 4 responses were confirmed. With non-CNS progression as a competing risk, the probability of CNS progression among the entire study population was 17% (95% CI: 8.8-26.7%) at 6 months and 21% (95% CI: 12.1-32.0%) at 12 months. **Conclusions:** Olaparib and temozolomide may be an effective therapy for relapsed SCLC, especially for pts with CNS disease where we observed a high rate of intracranial disease control. Ongoing analyses regarding optimal dosing schedule will inform potential for future use of this combination. Clinical trial information: NCT02446704. Research Sponsor: AstraZeneca.

8566 **Poster Session**

Interim results of an ongoing phase 1/2a study of HPN328, a tri-specific, half-life extended, DLL3-targeting, T-cell engager, in patients with small cell lung cancer and other neuroendocrine cancers.

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Background: HPN328 is a delta like canonical Notch ligand 3 (DLL3)-targeting T-cell engager (TCE) derived from the TriTAC platform, designed to minimize off-target toxicities. HPN328 contains 3 binding domains, engineered to redirect T cells to kill DLL3-expressing cancer cells: anti-DLL3 for target engagement, anti-CD3 for T-cell engagement, and anti-albumin for half-life extension. **Methods:** This ongoing Ph1/2a study is evaluating HPN328 in patients (pts) with metastatic small cell lung cancer (SCLC) and other neuroendocrine (NE) cancers associated with DLL3 expression. Eligible pts must have disease that is relapsed/refractory to standard systemic therapy. Primary endpoints are safety, tolerability, and determination of MTD/RP2D. Secondary objectives are pharmacokinetics (PK), pharmacodynamics, immunogenicity, and preliminary anti-tumor activity (RECIST 1.1). HPN328 is administered IV, once weekly. AEs are graded by CTCAE 5.0, and ASTCT for cytokine release syndrome (CRS). **Results:** As of Feb 3rd, 2022, 16 pts were enrolled in 8 dose-escalation cohorts at doses from 0.015mg to 12.0mg (SCLC n = 10 (62.5%); NE prostate cancer (NEPC) n = 2 (12.5%); other NE neoplasms (NEN) n = 4 (25%)). Median pt age was 61 (43-73) yrs. Pts received a median of 3 (1-5) prior treatments; 75% received a PD-1 blocker. At baseline, 6 pts (37.5%) had treated brain metastases and 8 (50%) had liver metastases. Median treatment duration was 10.6 (3.3-31.3 plus) weeks. Treatment is ongoing in 7 pts (44%; median 16.5 weeks). CRS was reported in 5 pts (31%); events were grade 1 or 2, occurred within 24 hrs of the 1st or 2nd dose and did not recur with rechallenge. No ≥ Grade-3 CRS occurred. No dose-limiting toxicities were observed, and no AEs led to discontinuation. HPN328 exhibited linear PK, with dose-proportional increases in exposure and a median half-life of 71 hrs. Small, transient increases in select cytokines and chemokines were observed up to 24 hrs post dose. T-cell activation and margination were observed, consistent with target engagement. DLL3 expression was confirmed on IHC analysis of most baseline biopsies. 15 pts were efficacy evaluable. 6 of 15 (40%) had decrease in sum of target lesion diameters (4 SCLC, 1 NEPC, 1 NEN). 3 of 9 (33%) SCLC pts across all doses had > 30% decrease (weeks on treatment: 17.2, 16.9 [ongoing], and 25.1 [ongoing, confirmed PR]). At doses ≥1.215mg, 2 of 4 (50%) SCLC pts had > 30% decrease and 1 had > 20% decrease. 4 pts (25%) had stable disease: 2 SCLC, 1 NEPC, 1 NEN (Thymic atypical carcinoid). **Conclusions:** HPN328 is a novel half-life extended DLL3-targeting TCE that is well tolerated and clinically active. AEs have been transient, manageable, and consistent with class. No ≥ Grade-3 CRS occurred. Tumor shrinkage has been observed, including 1 confirmed PR. Dose escalation is ongoing; updated data will be presented. Clinical trial information: NCT04471727. Research Sponsor: Harpoon Therapeutics, Inc.

8567 **Poster Session**

Impact of underrepresented populations on clinical outcomes of chemo-immunotherapy for extensive-stage small cell lung cancer: Real-world prospective cohort study.

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Background: Chemo-immunotherapy is the standard 1st-line therapy for patients with extensive-stage small cell lung cancer (ES-SCLC). Prospective data about underrepresented populations outside the clinical trial such as elderly or poor risk has not been revealed. **Methods:** We conducted a 32-hospitals prospective cohort study of consecutive patients with ES-SCLC who received carboplatin and etoposide with atezolizumab as 1st-line therapy between September 2019 and September 2020. The primary outcome was 6-months progression-free survival (PFS) probability of all patients. The secondary outcomes were overall survival (OS), PFS, time to treatment failure, objective response rate, safety, and differences in efficacy and safety depending on whether or not the key eligible study criteria of previous trials are met. **Results:** In total, 207 patients with ES-SCLC were analyzed. The median age was 72 years, and 64 patients (31%) were elderly (≥75 years). Most patients (89%) had a performance status (PS) of 0 or 1. As a result, 132 (64%) was categorized as eligible patients. The 6-months PFS probability of all patients was 38.8 % (95%CI:32.4-45.7%). Between eligible and ineligible patients, there was significant difference of patients who attained disease control (93% versus 77%, p = 0.002). Median PFS was significantly longer in eligible patients than ineligible patients (5.1 vs. 4.7 months; P =.03, HR 0.72 (95% CI 0.53–0.97)), and median OS was longer in eligible patients than ineligible patients, without any significant difference (15.8 vs. 13.1 months; P =.10, HR 0.73 (95% CI 0.51–1.07)). Survival analysis identified a PS score of 0-1 (HR: 0.60, 95% CI: 0.39-0.97, p = 0.03) as a significant predictor of better PFS, while PS score of 0-1 (HR: 0.51, 95% CI: 0.31-0.89, p = 0.01) and younger patients (< 75 years) (HR: 0.66, 95% CI: 0.45-0.97, p = 0.03) as significant-good predictor of OS. The rate of severe AEs was higher in ineligible patients than in eligible (39% vs. 27%, respectively; p = 0.07), although the difference was not significant. Older age was significantly associated with severe AEs (p = 0.049). **Conclusions:** The real-world efficacy of chemo-immunotherapy for ES-SCLC was similar to that of pivotal clinical trials. However, trial-ineligible patients with ES-SCLC had poor treatment outcome and the higher rates of severe adverse events in this prospective cohort study. Our study suggests that positive results among the trial eligible patients may not translate to ineligible patients. Clinical trial information: UMIN000038064. Research Sponsor: Chugai pharmaceutical.

8568 **Poster Session**

Impact of trilaciclib on multilineage chemotherapy-induced myelosuppression events in patients with extensive-stage small cell lung cancer: Post-hoc analyses of data from randomized clinical trials.

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Background: Trilaciclib is a short-acting CDK4/6 inhibitor administered prior to chemotherapy for multilineage myeloprotection. Reduced occurrence of chemotherapy-induced myelosuppression (CIM) events across neutrophil, red blood cell, and platelet lineages was reported in 3 Phase 2 clinical trials of trilaciclib versus placebo in patients with extensive-stage small cell lung cancer (ES-SCLC). In this post-hoc trial analysis, we further assessed the impact of trilaciclib on the occurrence of single and concurrent multilineage CIM events. **Methods:** Analyses were conducted separately by line of chemotherapy. In the first-line (1L) setting, pooled data from the G1T28-05 and G1T28-02 trials, in which trilaciclib or placebo was administered prior to etoposide, carboplatin, and atezolizumab [E/P/A] and E/P, respectively, were used. In the 2/3L setting, analyses were based on data from the G1T28-03 trial where patients received trilaciclib or placebo prior to topotecan. The proportion of patients with single and concurrent multilineage CIM events and incidence rate were estimated per cycle and during the first 4 cycles of chemotherapy. Severe (grade $\geq$ 3 per CTCAE definition) CIM events of neutropenia (SN), anemia (SA), and thrombocytopenia (ST) were assessed. Concurrent CIM events were defined as having 2 or 3 lineage-specific CIM events overlap for $\geq$ 1 day. As sensitivity analyses, the occurrence of CIM events in patients with ES-SCLC receiving 1L treatment in the G1T28-05 and G1T28-02 studies was analyzed separately. **Results:** Compared with placebo, fewer patients receiving trilaciclib had single-lineage CIM events and concurrent events in 2 or 3 lineages during cycles 1–4 of 1L chemotherapy using pooled data from G1T28-05 and G1T28-02 (Table). A similar trend was observed in the 2/3L setting. Generally, SN occurred more frequently in earlier cycles, whereas SA and ST tended to occur later. The sensitivity analysis in each individual 1L trial yielded consistent results with the pooled analysis. **Conclusions:** Patients with ES-SCLC receiving trilaciclib prior to chemotherapy had fewer single and concurrent multilineage CIM events than patients receiving placebo. Clinical trial information: NCT03041311, NCT02499770, NCT02514447. Research Sponsor: G1 Therapeutics, Inc.

CIM events per 21-day cycle among 1L and 2/3L patients with ES-SCLC during cycles 1–4.

	1L Pooled (G1T28-05 and G1T28-02)		2/3L (G1T28-03)	
Proportion of patients with events (%) Incidence rate per cycle	Trilaciclib (n = 90)	Placebo (n = 90)	Trilaciclib (n = 32)	Placebo (n = 28)
SN	14.4	56.7	40.6	46.4
	0.047	0.211	0.157	0.206
SA	8.9	17.8	6.3	25.0
	0.027	0.053	0.018	0.078
ST	0.0	12.2	25.0	14.3
	0.000	0.038	0.069	0.058
Concurrent SN and SA	2.2	4.4	6.3	10.7
	0.006	0.009	0.018	0.030
Concurrent SN and ST	0.0	13.3	37.5	35.7
	0.000	0.035	0.118	0.105
Concurrent SA and ST	2.2	3.3	3.1	3.6
	0.009	0.009	0.018	0.009
Concurrent SN, SA, and ST	0.0	2.2	15.6	32.1
	0.000	0.009	0.044	0.113

8569 **Poster Session**

Exploratory analysis using cfDNA-based fragmentomics to predict disease recurrence in limited disease small cell lung cancer.

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Background: The current standard of care (SOC) for limited disease (LD) small cell lung cancer (SCLC) is definitive concurrent chemoradiotherapy (CCRT). Despite the high response rate to SOC, up to 70% of the patients potentially experience disease recurrence and fail to show the prolonged clinical benefit. We investigated the feasibility of cell-free DNA (cfDNA) based genomic alteration and fragmentomic analysis using pre-and post-treatment samples to investigate the predictive value of disease recurrence in LD-SCLC. **Methods:** The blood sample from fifty LD-SCLC who were treated with definitive CCRT were collected before and after the treatment. Target sequencing, AlphaLiquid scan (IMBdx, Korea), composed of 106 target genes, was conducted using cfDNA and peripheral blood mononuclear cells. Based on the recurrence-free survival (RFS) interval of 12 months, patients were categorized into group with persistent response (PeR, n = 29) and non-PeR (n = 21). Fragmentomics analyses were collected using the proportion of cfDNA fragments sized in P1 (100 – 155 bp) and P2 (160 – 180 bp) ranges. **Results:** Initial analysis was conducted based on the gene of interest. Patients with *RB1* mutation (n = 11) detected in follow-up sample demonstrated significant shorter RFS compared to the *RB1* wild type (WT) patients (n = 39) (7.9 mon. vs. NR, $P = 0.002$). Among the patients who were available for our fragmentomics analysis in follow up samples (n = 19), non-PeR (n = 9) group were significantly high in P1 range ($P = 0.003$) and low in P2 range ($P = 0.002$) compared to PeR group (n = 10). AUCs using the fragment proportion in P1, proportion in P2, and the fragmentation ratio (proportion in P1 / proportion in P2), were 0.889, 0.911, and 0.889, respectively. The survival analysis using fragmentation ratio showed significantly longer RFS in fragmentation ratio low group compared to the high group (7.6 mon. vs. NR, $P = 0.002$). Integrating *RB1* mutation status with fragmentation ratio, patients with both *RB1* WT and fragmentation ratio low (n = 9) showed the most favorable outcomes ($P = 0.006$). On the contrary, patients with either *RB1* mutated or high in fragmentation ratio (n = 10) showed median RFS of rest than 12 months. **Conclusions:** In this study, we investigated the clinical feasibility of cfDNA detected mutation and size of the fragment in disease recurrence of LD-SCLC using the sample collected before and after definitive CCRT. It is observed that patients with either *RB1* mutation or high fragmentation ratio detected from cfDNA after the completion of CCRT are likely to experience early disease recurrence. Our findings suggest that cfDNA could provide supplementary information in predicting early treatment failure and support the clinical decision in selecting high-risk patients who might need intense monitoring and additional consolidative treatment. Research Sponsor: None.

8570 **Poster Session**

Stereotactic radiosurgery (SRS) versus whole brain radiation therapy (WBRT) in patients with small cell lung cancer (SCLC) and intracranial metastatic disease (IMD): A systematic review and meta-analysis.

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Background: Patients with SCLC are at high risk for the development of IMD and, subsequently, rapid intracranial progression. SRS has supplanted WBRT as first-line treatment for IMD in most solid cancers, but WBRT remains first-line treatment for IMD in SCLC patients. Data on SRS in SCLC are limited to small retrospective studies. **Methods:** Studies reporting on SRS in SCLC patients with IMD were collected from EMBASE, MEDLINE, CENTRAL, and grey literature sources (n = 3,732 studies). Random-effects meta-analysis pooled hazard ratios (HR) for overall survival (OS) between SRS and WBRT ± SRS boost, as well as medians for OS in months (mo) and risk rates for intracranial local (LC) and intracranial distant control (DC) in single-arm SRS studies. **Results:** OS following SRS was non-inferior compared with WBRT ± SRS boost (HR 0.90; 95% confidence interval (95CI), 0.73-1.10; n = 7 studies; n = 18,130 patients), and superior compared with WBRT alone (HR 0.80; 95CI, 0.66-0.96; n = 7 studies; n = 16,961 patients). Pooled median OS from single-arm studies following SRS was 8.99 mo (95CI, 7.86-10.15; n = 14 studies; n = 1,682 patients). Pooled LC and DC estimates following SRS were 81% (95CI, 67%-99%) and 66% (95CI, 50%- 86%), respectively, at 6 mo, and 78% (95CI, 61%-98%) and 58% (95CI, 46%-75%), respectively, at 12 mo. **Conclusions:** This systematic review and meta-analysis provides evidence that SRS may achieve analogous survival outcomes compared with WBRT in patients with SCLC and IMD, indicating that a subset of SCLC patients may benefit from first-line SRS treatment. Prospective trials should investigate the impact of metastatic burden as well as LC and DC differences between WBRT- and SRS-treated SCLC patients. Research Sponsor: None.

8571 **Poster Session**

Adverse events self-reported by patients (pts) with extensive-stage small cell lung cancer (ES-SCLC) treated with durvalumab (D) plus platinum-etoposide (EP) or EP in the CASPIAN study.

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Background: The CASPIAN phase 3 study established D+EP as a global standard of care in ES-SCLC. Patient-Reported Outcomes - Common Terminology Criteria for Adverse Events (PRO-CTCAE) was developed to complement standard adverse event (AE) reporting in oncology trials. Here we describe patient-reported symptomatic AEs using PRO-CTCAE in CASPIAN, the first time the PRO-CTCAE tool has been piloted in SCLC research. **Methods:** In CASPIAN, treatment-naïve pts (WHO PS 0/1) with ES-SCLC received 4 cycles of D+EP q3w followed by maintenance D q4w until progressive disease (PD), or up to 6 cycles of EP q3w. As part of exploratory analyses, where validated local language versions were available (in English, German, Japanese or Spanish), pts were asked to complete the PRO-CTCAE by e-device at baseline, q3w during EP (in both arms), then q4w until PD, followed by day 28 post-PD, 2 months post-PD, and q8w until second progression/death. Presence/absence, frequency or severity were examined during the first 24 weeks after starting treatment across 11 AEs selected as being relevant to pts with ES-SCLC (Table). **Results:** In total, 164 of the 537 pts randomized to D+EP and EP in CASPIAN (31%; D+EP: 83; EP: 81) were asked to complete the PRO-CTCAE. At baseline, the PRO-CTCAE was completed by 84% of these pts in the D+EP arm and 81% in the EP arm; compliance rates > 60% were achieved up to cycle 32 for D+EP and cycle 6 for EP. Examined AEs were reported by a minority of pts before starting treatment in both arms (range D+EP vs EP: 4% vs 3% for hand-foot syndrome to 34% vs 41% for dry mouth). Baseline AE rates were generally maintained in both arms up to 24 weeks after starting treatment, except for itchy skin, which showed a numerical increase from 13% at baseline to a peak of 34% at cycle 6 in the D+EP arm and 12% at baseline to a peak of 42% at cycle 8 in the EP arm; and dizziness, which showed a numerical increase from 16% at baseline to a peak of 40% at cycle 5 in the D+EP arm, while rates were maintained vs baseline in the EP arm. Most pts reporting these AEs indicated that they occurred rarely or occasionally, or were mild or moderate in severity. **Conclusions:** Self-reported data from pts in CASPIAN showed that the 11 AEs examined during the 24 weeks after starting treatment were reported by a minority of pts, mostly with rare or occasional occurrence, and mild to moderate severity. Rates and patterns of AEs over time were broadly similar in the D+EP and EP arms. These results complement the CASPIAN safety profile and give insight into pts' experience of treatment. Clinical trial information: NCT03043872. Research Sponsor: AstraZeneca.

Primary attribute examined	AEs
Presence/absence	Rash; pain, swelling, or redness at a site of drug injection or IV
Frequency	Arm or leg swelling; pain in the abdomen; shivering or shaking chills
Severity	Itchy skin; numbness or tingling in hands or feet; dizziness; mouth and throat sores; hand-foot syndrome; dry mouth

8572 **Poster Session**

The efficacy and safety of taletrectinib in patients with TKI-naïve or crizotinib-pretreated ROS1-positive non–small cell lung cancer (NSCLC).

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Background: Taletrectinib (AB-106 / DS-6051b) is a next-generation, potent, CNS- penetrant, selective ROS1 tyrosine kinase inhibitor. The ongoing TRUST study (NCT04395677) is a multicenter, open-label, single-arm, Phase 2 study of taletrectinib in Chinese ROS1-positive NSCLC patients who are TKI -naïve or crizotinib-pretreated. Here we present the updated efficacy and safety results of the study. **Methods:** The eligible ROS1-positive NSCLC patients were enrolled into either TKI-naïve or crizotinib-pretreated cohorts, and treated with taletrectinib 600mg once daily. The study endpoints included overall response rate (ORR), duration of response (DOR), disease control rate (DCR), overall intracranial response rate (IC-ORR), progression-free survival (PFS), and safety profile. **Results:** As of the data cutoff date of September 7, 2021, 61 of the 86 stage IV patients enrolled in the study have at least three postbaseline tumor assessment of which 40 patients in the TKI-naïve cohort, and 21 patients in the crizotinib-pretreated cohort (50% patients having at least one prior chemotherapy). In the TKI -naïve cohort, the confirmed ORR by investigators per RECIST 1.1 was 90.0%: [95%CI: 76.3%; 97.2%] (36/40); and the DCR was 95% [95%CI: 83.1%; 99.4%] (38/40). In the crizotinib-pretreated cohort, the confirmed ORR by investigators was 47.6% [95%CI: 25.7%; 70.2%] (10/21); and DCR was 76.2%: [52.8%; 91.8%] (16/21). The mDOR and mPFS are not reached yet for both cohorts. Of 6 patients having brain metastasis and measurable target brain lesions at baseline, the intracranial ORR and IC-DCR were 83.3% and 100%, respectively. Of 4 patients with ROS1 G2032R mutation, 3 patients achieved partial response (PR), and 1 patient achieved stable disease (SD). The most common treatment-related adverse events (TRAEs) include diarrhea, nausea, vomiting, transaminase elevation, anemia, neutrophil count decrease, etc. were Grade 1 or 2, and the most common AEs (below 10%) were ALT/AST increased but reversible. **Conclusions:** Taletrectinib demonstrated meaningful clinical efficacy in both TKI-naïve and crizotinib-pretreated ROS1 positive NSCLC patients. In particular, taletrectinib showed clinical effectiveness in patients with ROS1 secondary G2032 mutations and patients with brain metastasis. Taletrectinib was well tolerated in this patient population. Clinical trial information: NCT04395677. Research Sponsor: AnHeart Therapeutics Inc.

8573 **Poster Session**

Efficacy and safety of camrelizumab combined with chemotherapy (irinotecan combined with platinum) followed by camrelizumab combined with apatinib in the first-line treatment of advanced small cell lung cancer: A phase II study.

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Background: The treatment mode of small cell lung cancer (SCLC) is mainly based on the comprehensive treatment of chemotherapy and radiotherapy. IMpower133 study, suggesting that immune checkpoint inhibitors combined with chemotherapy first-line treatment for advanced SCLC may bring new research directions of clinical benefit. Previous study suggested that the combination of anti-PD-1 antibody camrelizumab and VEGFR-2 inhibitor apatinib significantly improved antitumor effects. The aim of this study was to evaluate the efficacy and safety of camrelizumab combined with chemotherapy (irinotecan combined with platinum) followed by camrelizumab combined with apatinib in the first-line treatment of SCLC. **Methods:** Extensive-stage small cell lung cancer patients were enrolled in this single-center, single-arm study. During the induction treatment phase, Patients received camrelizumab (200mg q3w), irinotecan (65 mg/m2, q3w) and platinum (cisplatin: 30 mg/m2, carboplatin: AUC=4~5), after 4-6 cycles, the patient entered the maintenance phase, and then patients received camrelizumab combined with apatinib until disease progression or unacceptable toxicity. Treatment efficacy was assessed every 3 cycles (6 weeks). The primary endpoint is progression-free survival (PFS). Secondary endpoints are objective response rate (ORR), disease control rate (DCR), duration of response (DoR) and overall survival (OS), which are based on RECIST 1.1. **Results:** At data cut-off (Jan 10, 2022), 20 extensive-stage SCLC patients were enrolled in the study, of which 18 patients were evaluable. Median age was 64 years, male accounts for 85.0% (17/20). Median follow-up was 5.0 months (range 0.4~17.6 months). Of 18 evaluable patients, no one achieved complete response Partial response was achieved by 17 (94.4%) patients and stable disease exhibited by 1 (5.6%) patient. The ORR and DCR were 94.4% and 100%, respectively. mPFS and mDoR have not been reached. In terms of adverse events (AEs), reactive cutaneous capillary hyperplasia (RCCEP) was observed in 10 (47.6%) patients 10 patients. Grade III-IV AEs were observed in 7 (35.0%) patients with neutropenia, thrombocytopenia, hemoglobin reduction, leukopenia, rash. The rest were grade I-II AEs. **Conclusions:** The treatment in this study showed impressive ORR and DCR, and acceptable toxicity, and may be a promising method as a first line treatment. Clinical trial information: NCT04453930. Research Sponsor: Jiangsu Hengrui Medicine Co.,Ltd.

8574 **Poster Session**

Total metabolic tumor volume on 18F-fluorodeoxyglucose-positron emission tomography ([18F]-FDG-PET) scan: A potential prognostic factor in extensive-stage small cell lung cancer.

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Background: Small-cell lung cancer (SCLC) is a highly aggressive neuroendocrine lung cancer, accounting for 10-15% of all lung cancers, commonly classified in limited stage (LS-SCLC) and extensive stage (ES-SCLC). Despite the introduction of chemoimmunotherapy as new standard first-line therapy for ES-SCLC, the benefit of addition of the programmed-death ligand 1 (PD-L1) inhibitors is limited to a subset of patients, suggesting the importance to identify predictive biomarkers of response. [18F]FDG-PET/CT is commonly used for the staging and therapeutic planning of SCLC patients. Metabolic parameters derived from [18F]FDG-PET could predict patient outcomes by measuring the extension of metabolically active tumor (metabolic tumor volume [MTV]) or its metabolic heterogeneity (total lesion glycolysis [TLG]). **Methods:** We retrospectively collected patients with pathologically confirmed diagnosis of SCLC, who had undergone an [18F]FDG PET/CT scan within 30 days from the start of first-line treatment for ES-SCLC. Patients with LS-SCLC at diagnosis were included if presenting relapse at pre-treatment scans performed at least 90 days from the end of treatment with radical intent. We calculated metabolic parameters, MTV and TLG, by summing each single lesion's MTV and TLD respectively. The primary endpoint of the study was overall survival (OS), defined as the time from [18F]FDG PET/CT scan acquisition to death from any cause. **Results:** A total of 86 SCLC patients ES-SCLC were included. Patients with hyponatremia, hypoalbuminemia and elevated LDH levels were associated with greater number of lesions, greater total MTV, and higher total TLG at [18F]FDG-PET/CT/CT scan. At a median follow-up of 20.9 months, the median OS was 11.1 months. Median survival was longer among patients with Na + $\geq$135 mEq/L, with normal albumin levels and in those with normal LDH levels and without bone metastases. Patients with low total MTV had longer OS compared with those with high total MTV (11.9 months vs 4.8 months, respectively). High total MTV was independently associated with the risk of death ($p < 0.001$) but not with the risk of progression. **Conclusions:** Our preliminary data showed that total MTV could provide prognostic information in patients with ES-SCLC, suggesting a potential role as stratification factor in immunotherapy-based clinical trials. Research Sponsor: None.

8576 **Poster Session**

Nab-PTX and nab-PTX combined with immune checkpoint inhibitors for relapsed small cell lung cancer.

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Background: Despite sensitivity to first-line chemotherapy, most small cell lung cancer (SCLC) patients experience disease progression after initial treatment. Nab-PTX showed comparable anti-tumor activity for relapsed SCLC. Whether immune checkpoint inhibitors (ICIs) combined with nab-PTX could improve clinical outcome for relapsed SCLC has not been fully evaluated. The aim of this study is to evaluate efficacy and safety of nab-PTX and nab-PTX combined with ICIs for relapsed SCLC. **Methods:** We retrospectively reviewed relapsed SCLC patients who were given nab-PTX (130mg/m2, day1,8 /Q3 weeks) or nab-PTX combined with ICIs (PD-1 or PD-L1), from Feb 2017 to Sep 2021. Clinical data were collected from electronic medical records. The clinical outcome, including progression-free survival (PFS) and overall survival (OS) were assessed using the Kaplan-Meier method and standard Log-rank test. **Results:** A total of 56 patients with relapsed SCLC were included, 29 and 27 patients received nab-PTX (group A) and nab-PTX combined with ICIs (group B), respectively. Baseline characteristics were well balanced between the groups. Patient characteristics (group A: group B) were as follows; median age 57: 59, male 25(86.2%): 24(88.9%), heavy smoking 23(79.3%): 18(66.7%), ECOG-PS 1 19(65.5%) :19(70.4%), extensive disease 28(96.6%) :25(92.6%), liver metastasis 10(34.5%) :12(44.4%), brain metastasis 8(27.6%) :10(37%), refractory relapse 10(34.5%) :11(40.7%). ORR in group A and B were 17.2% vs 40.7%, and DCR in group A and B were 72.4% vs 66.7%, respectively. The median PFS and median OS were similar between group A and B (median PFS, 2.8months vs 3.2months; median OS, 9.3 months vs 11.0months). PFS and OS according baseline characteristics were showed in the table. Toxicity profile of group B was tolerable as well as group A. **Conclusions:** This retrospective study indicated nab-PTX combined with ICIs failure to improve clinical outcome for relapsed SCLC when compared with nab-PTX monotherapy. Research Sponsor: None.

Progression-free survival and overall survival according to baseline characteristics.

Subgroup	Treatment	median PFS (months)	*p* value	median OS (months)	*p* value
Liver metastasis	Group A(n=10)	1.6		7.6	
	Group B(n=12)	1.5	0.255	6.1	0.664
Brain metastasis	Group A(n=8)	1.6		12.8	
	Group B(n=10)	2.6	0.755	10.5	0.24
Sensitive relapse	Group A(n=19)	2.9		10.8	
	Group B(n=16)	3.2	0.872	10.5	0.289
Refractory relapse	Group A(n=10)	1.6		9.1	
	Group B(n=11)	3.2	0.749	11	0.862

8577 **Poster Session**

Genomic analysis and prediction of therapeutic vulnerabilities of small cell lung cancer from rovalpituzumab tesirine phase III trial (MERU).

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Background: Predicting variable therapeutic responses that are driven by the genetic and transcriptomic heterogeneity of Small Cell Lung Cancer (SCLC) offers an opportunity for implementing precision therapies within the cancer cells and tumor microenvironment (TME). MERU was a Phase III study of Rovalpituzumab Tesirine (Rova-T) as maintenance therapy following first-line platinum-based chemotherapy in participants with extensive stage SCLC. In this study, we comprehensively analyzed the baseline genomic data in the MERU cohort to interrogate SCLC's heterogeneous TME and tumor-intrinsic molecular and genetic drivers for therapeutic vulnerabilities. **Methods:** RNA-seq and Whole-Exome-Sequencing (WES) data were collected from archival tumor samples of 306 of 740 subjects enrolled in MERU. RNA-seq reads were aligned with STAR and quantified for gene expression by HTSeq. WES reads were analyzed for somatic mutation and copy number variation using AbbVie's tumor-only WES pipeline. TME heterogeneity was evaluated using gene-set variation analysis of pan-cancer TME gene signatures. SCLC subtyping was performed using expression of 4 transcriptional factors (TF): ASCL1, NEUROD1, POU2F3, and YAP1. A computational framework of mapping MERU transcriptome expression profile to Cancer Dependency Map (DepMap) dataset was developed to synthetically screen MERU samples' drug sensitivity. **Results:** TF subtyping reveals high prevalence of SCLC-A and -N subtypes in the MERU cohort, consistent with high expression of DLL3 in these two neuroendocrine subtypes. Correlation of TME gene signature scores identified two distinct clusters in the MERU cohort with correspondingly polarized immune-suppressive and -inflamed phenotypes. The pro-inflammatory score combining IFN-gamma and TGF-beta signatures, predicted prognosis in the MERU cohort better than the previously reported SCLC-I signature (Hazard Ratio: 0.71 [95% CI 0.38-1.3] vs. 1.29 [95% CI 0.65-2.6]). WES analysis identified high prevalence of TP53 and RB1 mutations, in line with the reported prevalence of these genetic drivers in SCLC. The clinical characteristics including gender, smoking status, and prior treatment, are not significantly associated with either TF or TME subgroup. The computational drug screen framework maps 83% of MERU samples to DepMap SCLC cell lines. The correlation of subtype TF expression with drug sensitivity was highly concordant between MERU and DepMap. Collectively, this approach demonstrated that molecular subtyping can be leveraged to broadly predict drug response in SCLC patients. **Conclusions:** Our comprehensive genomic analysis of the MERU cohort provides new insights into SCLC heterogeneity from both tumor-intrinsic and tumor-immune interaction perspectives and shall contribute to the development of predictive biomarkers and therapeutic opportunities for SCLC. Research Sponsor: AbbVie Inc.

8578 **Poster Session**

The predictive value of YAP-1 for efficacy of immunotherapy among patients with ES-SCLC.

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Background: IMpower133 showed benefits in both progression-free survival (PFS) and overall survival (OS) of etoposide/carboplatin plus atezolizumab (ECT) regimen in extensive-stage small-cell lung cancer (ES-SCLC), but the absolute benefit was limited. Previous studies have classified SCLC patients by RNA-seq clustering analysis to explore the dominant population for treatment, but was difficult for clinical application. We aimed to explore whether expressive status of Yes-Associated Protein 1 (YAP-1) can screen dominant population of immunotherapy among ES-SCLC patients. **Methods:** We selected ES-SCLC patients treated in our hospital from Jan, 2018 to Jul, 2021, and enrolled 21 patients with ES-SCLC received ECT regimen whose formaldehyde-fixed, paraffin-embedded sample was reachable. Assessments of complete remission (CR), partial remission (PR), disease stable (SD) and progressive disease (PD) were according to the efficacy evaluation criteria of solid tumor (RECIST) version 1.1. Immunohistochemistry (IHC) of YAP-1 (ET1608-30, 1/100) was conducted. The H-score was calculated by IHC Profiler. All statistical analyses were evaluated using SPSS 22.0, X-tile 3.6.1, and Excel. P values < 0.05 were considered statistically significant. **Results:** Baseline information was provided in table. The median H-score of responders (CR/PR patients) and non-responders were 13.97 (95%CI: 8.97-16.30) and 23.72 (95%CI: 8.13-75.40) that were significantly different ($P < 0.05$). H-score and PFS showed negative correlation by spearman ($r = -0.603$). Patients were divided into two groups as low expression group (H-score ≤ 25.00, $n = 16$) and high expression group (H-score > 25.00, $n = 5$) according to the cut-off value of H-score. The median PFS of these two groups were 7.1m (95%CI: 2.6-11.6m) and 3.4m (95%CI: 0.9-5.9m), respectively. K-M curves of PFS were significantly different ($P < 0.05$). **Conclusions:** Our preliminary results have indicated a potential efficacy predictive value of YAP-1 protein. And the expression level of YAP-1 protein was negatively correlated with efficacy of ECT in ES-SCLC patients. Research Sponsor: None.

		Responders n = 13	Non-responders n = 8	Total	P-value
Age(years)	Median(range)	64(55-72)	62(54-68)	62(54-72)	
	≤65	9(69.23%)	7(87.50%)	16(76.19%)	0.30
	> 65	4(30.77%)	1(12.50%)	5(23.81%)	
Gender	Male	11(84.62%)	8(100.00%)	19(90.48%)	0.27
	Female	2(15.38%)	0(0.00%)	2(9.52%)	
Smoke	Smoker	10(76.92%)	8(100.00%)	18(85.71%)	0.16
	Non-smoker	3(23.08%)	0(0.00%)	3(14.29%)	
Type	Pure SCLC	12(92.31%)	6(75.00%)	18(85.71%)	0.29
	Combined SCLC	1(7.69%)	2(25.00%)	3(14.29%)	
Therapy(line)	1st(ECT)	10(76.92%)	7(87.50%)	17(80.95%)	0.57
	2nd(ECT)	3(23.08%)	1(12.50%)	4(19.05%)	
Ki-67 index	< 90	2(15.38%)	2(25.00%)	4(19.05%)	0.54
	≥90	11(84.62%)	6(75.00%)	17(80.95%)	
NSE	< 22.69	4(30.77%)	1(12.50%)	5(23.81%)	0.99
	22.69-36.16	4(30.77%)	2(25.00%)	6(28.57%)	
	37.00-57.59	0(0.00%)	3(37.50%)	3(14.29%)	
	> 57.59	5(38.46%)	2(25.00%)	7(33.33%)	

8579 **Poster Session**

A phase I study of anlotinib with concurrent chemoradiotherapy for limited-stage small cell lung cancer.

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Background: Concurrent chemoradiotherapy (CCRT) is the standard treatment for limited-stage small-cell lung cancer (LS-SCLC). However, LS-SCLC remains an area of high unmet medical need. Anlotinib is an antiangiogenic multi-target tyrosine kinase inhibitor. In the phase II ALTER-1202 trial, anlotinib significantly improved clinical outcomes in advanced small-cell lung cancer. We report here a phase 1 trial of anlotinib with CCRT for LS-SCLC. **Methods:** This is a prospective, single-arm, phase I clinical trial using a 3+3 design. Patients aged between 18 and 75 with previously untreated LS-SCLC, PS 0-1 and adequate organ function are eligible. Patients received anlotinib (12mg, qd, d1-14, q3w) and chemotherapy (etoposide, 100 mg/m^2, d1-3, q3w and cisplatin, 25 mg/m^2, d1-3, q3w) for cycle 1, then anlotinib [dose escalation at 3 levels (DL1-3) 8mg, 10mg and 12mg, qd, d1-14, q3w], chemotherapy (etoposide, 50 mg/m^2, d1-5, q4w and cisplatin, 25 mg/m^2, d1-3, q4w) and thoracic radiotherapy (60-66 Gy in 30-33 daily 2-Gy fractions starting on day 1 of cycle 2) for cycles 2–3, then anlotinib (12mg, qd, d1-14, q3w) and chemotherapy (etoposide, 100 mg/m2, d1-3, q3w and cisplatin, 25 mg/m^2, d1-3, q3w) for cycles 4-6. Cycles 5-6 were given as appropriate according to the patient's physical condition. Prophylactic cranial radiation was given according to the judgment of the investigator after CCRT. The purpose of this study is to determine the maximum tolerated dose (MTD) of anlotinib when combination with CCRT. **Results:** Twelve patients were enrolled from May 2020 to September 2021. No DLTs were observed in DL1 (3 patients) or DL2 (3 patients). At DL3 (6 patients), 1 patient had a DLT of grade 3 pulmonary embolism. Grade 3 adverse events were white blood cell count decreased, neutrophil count decreased, lymphocyte count decreased, hypertension, albumin decreased and pulmonary embolism. One patient had grade 3 pulmonary embolism and grade 4 neutrophil count decreased in DL3 at cycle 1. One patient had grade 2 radiation pneumonitis after cycle 5 and grade 1 radiation esophagitis at cycle 3 in DL3. One patient had grade 2 radiation esophagitis at cycle 3 in DL2. The MTD was not reached. **Conclusions:** Combined treatment with anlotinib and CCRT for limited-stage small cell lung cancer is well tolerated and further clinical investigation is warranted. Clinical trial information: NCT04882033. Research Sponsor: None.

8580 **Poster Session**

Efficacy and safety of lurbinectedin as second-line therapy in Chinese patients with small cell lung cancer: Preliminary results of a phase 1 study.

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Background: Lurbinectedin (Zepzelca), a selective inhibitor of oncogenic transcription, was granted accelerated approval on June 15, 2020, by the FDA for adult patients (pts) with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy, based on the results from SCLC cohort in PM1183-B-005-14 trial. Here we report the preliminary results of a phase 1 study (LY01017/CT-CHN-101) which aimed to evaluate the safety, tolerability, pharmacokinetics (PK) characters and preliminary efficacy of lurbinectedin in Chinese pts with advanced solid tumors including relapsed SCLC. **Methods:** In the dose-escalation stage, 10 pts with advanced solid tumors received lurbinectedin (2.5-3.2 mg/m^2) as 1-hour i.v. infusion q3wk in a classical 3+3 design, without primary granulocyte colony-stimulating factor (G-CSF) prophylaxis during Cycle 1. In the dose-expansion stage, 22 pts with relapsed SCLC after first-line platinum-based chemotherapy were treated with single-agent lurbinectedin at the recommended dose (RD) defined in the dose-escalation stage, with or without G-CSF support. Endpoints included safety (CTCAE v5.0), tolerability, PK, and confirmed objective response rate (ORR; RECIST v1.1). The data cutoff was January 13, 2022. **Results:** No dose-limiting toxicity (DLT) was observed in the first 3 pts treated at 2.5 mg/m^2, while 1/7 pts treated at 3.2 mg/m^2 had DLT (grade 4 neutropenia lasting $\geq$3 days) in Cycle 1, thus 3.2mg/m^2 without G-CSF prophylaxis was defined as the RD of the dose-expansion stage. At cutoff, 22 SCLC pts treated in the dose-expansion stage were still ongoing, with 21 and 22 pts evaluable for efficacy and safety, respectively. The investigator-assessed confirmed ORR was 42.9% (9/21, partial responses). The duration of response (DOR) is pending. The most common grade 3-4 treatment-related adverse events (TRAEs) were neutropenia (16 [72.7%]), leukopenia (13 [59.1%]), thrombocytopenia (9 [40.9%]), increased ALT (4 [18.2%]), anemia (3 [13.6%]), and increased AST (2 [9.1%]). Serious treatment-related adverse events, including neutropenia (5 [22.7%]), leukopenia (4 [18.2%]), thrombocytopenia (3 [13.6%]), increased ALT (2 [9.1%]), increased AST (2 [9.1%]), vomiting (2 [9.1%]), febrile neutropenia (1 [4.5%]), and edema (1 [4.5%]), were reported in 10 pts (45.5%). No cases of infection, sepsis and Hy's law were reported. A total of 40.9% (9/22) had dose delay and 31.8% (7/22) had dose reduction, mainly attributed to hematological toxicities. No discontinuations occurred due to AEs. No treatment-related deaths were reported. **Conclusions:** Lurbinectedin at the RD (3.2mg/m^2) shows promising efficacy as second-line therapy in Chinese pts with SCLC, with acceptable tolerability and manageable safety profile. Clinical trial information: NCT04638491. Research Sponsor: Pharma Mar, S.A, Pharmaceutical/Biotech Company.

8581 **Poster Session**

A phase 1/2 trial of lurbinectedin (L) in combination with pembrolizumab (P) in relapsed small cell lung cancer (SCLC): The LUPER study.

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Background: L is a novel anticancer agent that inhibits trans-activated transcription and modulates the tumor microenvironment. L is approved by the FDA for metastatic SCLC patients (pts) with progressive disease (PD) on or after platinum-based chemotherapy (CT). The LUPER study is assessing the safety, tolerability, and preliminary efficacy of L+P as second-line regimen for SCLC pts after failure of platinum-based CT. Phase 1 data are presented here. **Methods:** In this phase 1/2 trial (NCT04358237), adult pts with histologically confirmed SCLC, PD to a previous CT-containing regimen (≥4 weeks before study initiation), no prior exposure to immunotherapy, ECOG PS of 0-1, and measurable disease as per RECIST 1.1 are eligible. Pts with treated, stable, and asymptomatic brain metastases (BMs) are allowed. A 3+3 dose-escalation was done to determine the recommended phase 2 dose (RP2D) of L+P. L was dosed at 2.4 mg/m^2 and 3.2 mg/m^2 IV Q3W in the dose level (DL)1 and 2, respectively, in combination with fixed dose of P (200 mg IV Q3W). The RP2D was the highest DL at which 0/3 pts or ≤1/6 pts experienced dose-limiting toxicities (DLTs) during the first cycle. Treatment was administered until PD, unacceptable toxicity, or consent withdrawal. Secondary endpoints include safety as per CTCAE 5.0, preliminary efficacy, and pharmacokinetics. **Results:** Thirteen pts were enrolled across 3 hospitals in Spain (DL1, n = 7; DL2, n = 6). Median age was 66 (range 43–78) years, 46.2% were female, 61.5% had ECOG PS of 1, 38.5% had platinum-free interval < 90 days, 30.8% had LDH > upper normal limit, and 15.4% had BMs. One DLT (G3 asthenia) and one G4 neutropenia lasting > 3 days (controlled with G-CSF prophylaxis upon C2, without requiring dose delay or modification) occurred in the DL1. No DLT were reported in the DL2. The RP2D was identified as 3.2 mg/m^2 L and 200 mg P IV Q3W. At data cutoff (Jan 21, 2022), 5 (38.4%) pts remained on treatment (1 pt in DL1 discontinued due to COVID-19 in cycle 1). Median duration of treatment was 2.1 (0–11.8) months, 5 (38.5%) pts had ≥8 cycles, and median relative dose intensity of L and P were 91.1% and 95.7%, respectively. Immune-related AEs (G2 pneumonitis; G3 ALT increased) led to P discontinuation in 2 (15.4%) pts. Responses were shown in both DLs, with ORR of 30.8% (1 confirmed complete response and 3 partial responses); 3 pts had stable disease (SD; including 1 patient with SD > 12 weeks) and 5 (38.5%) pts experienced PD. **Conclusions:** This is the first report to demonstrate a manageable safety profile and preliminary efficacy of second-line L+P for relapsed SCLC pts. This combination warrants further confirmation in the ongoing expansion phase 2. Clinical trial information: NCT04358237. Research Sponsor: PharmaMar, MSD.

8582 **Poster Session**

Circulating tumor DNA (ctDNA) mutations associate with response in patients (pts) with extensive-stage small cell lung cancer (ES-SCLC) treated with talazoparib (TALA) and temozolomide (TMZ).

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Background: Poly (ADP-ribose) polymerase (PARP) inhibition in combination with TMZ is a promising treatment strategy for ES-SCLC. In SCLC models, TALA, a potent PARP inhibitor, exhibits cytotoxic effects by impairing PARP proteins 1/2 and trapping PARP on DNA while TMZ potentiates antitumor response by contributing to genomic instability (Wainberg 2016). A prior analysis of ctDNA in 15 pts treated on trial with TALA and TMZ suggested that mutations in DNA damage repair (DDR) genes occurred with this combination and may associate with response (Mulroy ASCO 2021). **Methods:** Pts with relapsed or refractory ES-SCLC were treated with TALA 0.75 mg po daily with TMZ 37.5 mg/m2 po on days 1-5 of 28-day cycles in a phase 2 clinical trial (UCLA/TRIO-US L-07, NCT03672773). ctDNA was collected and assessed based on allele frequency and plasma copy number at baseline and every 8 weeks during treatment with the Guardant360 assay (Redwood City, CA). DDR status was defined as a mutation known or likely to result in aberrant expression of *ATM* or *BRCA1/2* (other DDR genes not detected by assay) (Pearl 2015). Germline DDR mutations were evaluated with matched-normal (PBMC) whole exome sequencing (WES) with archival specimens by Tempus (Chicago, IL). Response to treatment was defined by RECIST 1.1 criteria. Fisher s exact tests were used to compare proportions of patients, with P-values <0.05 considered statistically significant (www.r-project.org, Vienna, AU). **Results:** For 27 pts with evaluable response, 78 ctDNA samples were collected. The most common baseline somatic alterations were mutations in *TP53* (23 pts), *RB1* (8 pts), *ATM* (5 pts), and *BRCA2* (5 pts). There were no patients with germline DDR mutations. Overall, 22/27 (81.5%) had disease control (DC), including 11 with confirmed partial responses (PR) and 11 with stable disease while 5 had progressive disease. All those with PRs and ctDNA burden >0.2% at baseline experienced a ctDNA decrease at 8 weeks of treatment. DDR mutations were found in 18/27 (66.7%) pts. Of those with ≥ 1 follow-up ctDNA time point collected, 13/17 (76.4%) pts had at least one new mutation detected while on treatment, most commonly in *ATM* (6 pts). The appearance of new mutations associated with DC (P=0.042) and with a trend towards improved progression free survival (PFS, 5.9 m vs 3.6 m, P=0.099). All 5 pts with DDR mutations present at baseline had DC with TALA and TMZ, and 9/11 (81.8%) of those with PR had DDR mutations detected at some point during the trial, although the trend toward DC enrichment with DDR mutations did not maintain statistical significance (P=0.24). **Conclusions:** Mutations in DDR genes occur on treatment with TALA and TMZ and may associate with disease control. Validation in a larger cohort will be pursued. Research Sponsor: Pfizer.

8583 **Poster Session**

A pilot study of ipilimumab and nivolumab in recurrent extensive-stage small cell lung cancer after platinum-based chemotherapy.

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Background: Immunotherapy has shown efficacy in the treatment of recurrent, extensive-stage small cell lung cancer (ES-SCLC). In the Checkmate 032 trial, ipilimumab and nivolumab combination therapy resulted in a 21% objective response rate in relapsed SCLC. At present, there are no biomarkers used in clinical practice to predict treatment responsiveness in SCLC. Ipilimumab and nivolumab act by blocking key co-inhibitory immune pathways of CTLA-4 and PD-1/PD-L1, respectively, leading to reinvigoration of anti-tumor cytotoxic T cell responses and a decrease in immune suppressive tumor infiltrating leukocytes. The ratio of intratumor Teff (CD8+) cells to Treg (CD4+/Foxp3+) cells (Teff/Treg) could be a more reliable biomarker than effector cell infiltration alone. **Methods:** In this open-label, single arm trial, we enrolled patients with ES-SCLC who previously received platinum-based chemotherapy; prior anti-PD-1 /PD-L1 therapy was allowed. Patients were treated with nivolumab 1 mg/kg and ipilimumab 3 mg/kg, for a total of 4 doses each and received nivolumab 480 mg beginning with cycle 5, every 4 weeks until progression, unacceptable toxicity or study discontinuation. On-study biopsies were performed prior to initiation of therapy and during week 4 for the biomarker primary objective—to correlate disease response with intratumor Teff/Treg changes. Secondary objectives include determining ORR, DOR, PFS, and OS. **Results:** Twenty-two patients (median age 63.5 [range 54-80] years, ECOG 0/1/2 [41%/50%/9%], sex M/F [45%/55%]) were enrolled and received treatment. Fourteen (64%) had paired biopsies while on treatment. Fifteen patients were evaluable per RECIST with an ORR of 13% (2/15, 2 partial responses [13%]) and DCR was 40% (6/15, 4 stable disease [27%]). Grade 3 treatment-related adverse events (TRAEs) occurred in 9/22 [40%]. Grade 4 TRAEs occurred in 2/22 [9%] (elevated lipase and elevated bilirubin) and Grade 5 TRAEs occurred in 1/22 patients (hepatic failure). Out of the 9 patients previously treated with anti- PD-1/PD-L1 therapy, 1 had a partial response and 2 had stable disease. Multiplexed quantitative immunofluorescence analysis revealed changes of both CD8+ effector T cells and Tregs in the tumor micro-environment associated with clinical benefit to immunotherapy. **Conclusions:** Combination immunotherapy with ipilimumab and nivolumab shows clinical efficacy in relapsed extensive-stage SCLC, including those previously treated with anti-PD-1/PDL-1 therapy. Obtaining paired biopsies was shown to be successful in this prospective trial to study the tumor microenvironment in SCLC tumors treated with checkpoint inhibitors. Early biomarker evaluation during week 4 shows local immunomodulatory effect of treatment and supports exploration as predictive biomarker in this population. Clinical trial information: 03670056. Research Sponsor: Bristol Myers Squibb.

8584 **Poster Session**

Trends in treatment patterns associated with small cell lung cancer in a U.S. Medicare population.

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Background: Characterizing changes in the incident small cell lung cancer (SCLC) patient population and SCLC treatment landscape is essential for understanding drivers of outcomes among patients diagnosed with SCLC. The objective of this study was to examine trends in patient characteristics and treatment patterns for SCLC in a Medicare population. **Methods:** A retrospective analysis was conducted using the Surveillance, Epidemiology, and End Results (SEER)–Medicare linked data. Patients were included if they had a record with a diagnosis of SCLC in the database from 1/1/2007 – 12/31/2017 and were ≥65 years of age at diagnosis. Patients also had continuous enrollment for ≥180 days pre-SCLC diagnosis. Characteristics and treatment patterns were stratified by year of SCLC diagnosis. **Results:** 13,516 patients met the study criteria. Overall, 57.7% were female, mean age was 74 years, 89.5% were white, and 45.6% had a history of tobacco use. The majority (73.1%) were diagnosed with stage IV disease. Just over half (55.4%) of patients initiated first line (1L) treatment and mean time from diagnosis to 1L treatment was 6 weeks. Only 36.7% of those initiating 1L went on to second line (2L). Platinum-based chemotherapy (carboplatin or cisplatin + etoposide) was by far the most common 1L regimen (91.3%). 44.7% of patients received monotherapy in 2L, with topotecan being the most common (28.4%) regimen. Carboplatin + etoposide was used for approximately 20% of 2L patients. Over time, the demographic characteristics of patients diagnosed with SCLC was fairly stable with the exception of patients reporting a history of tobacco use, which more than tripled, increasing from 19.3% to 67.7% between 2007 and 2017. Between 2007 and 2017 the share of SCLC patients initiating 1L treatment increased 8.2% from 53.8% to 58.2% and the share initiating 2L fluctuated between 35% and 39%. Platinum-based chemotherapy was consistently used by the vast majority (88.7%–96.6%) of patients in 1L during the study period. Other chemo monotherapy (e.g., topotecan) and platinum-based chemotherapy with or without irinotecan were the most common 2L regimens from 2007-2014. Use of checkpoint inhibitors (CPIs) in 2L began in 2015 and became the most common 2L treatment following platinum-based chemotherapy by 2017 with 41.5% of patients receiving a CPI in 2L. **Conclusions:** While an increasing share of SCLC patients are pursuing treatment, less than 60% of SCLC patients receive any anticancer therapy. Fewer still receive more than one line of treatment, highlighting the ongoing need for effective therapies for SCLC. Research Sponsor: Ipsen.

8585 **Poster Session**

Lenvatinib for the treatment of thymic epithelial tumors (TETs): A real-life multicenter experience.

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Background: TETs are rare malignancies of the anterior mediastinum being thymoma (T) B3 and thymic carcinoma (TC) the most aggressive subtypes. There is no standard treatment after platinum-based chemotherapy in refractory or metastatic setting. A phase 2 trial has reported clinical benefit for lenvatinib 24mg (objective response rate [ORR] of 38%), a novel multi-targeted inhibitor of VEGFR, FGFR, RET, c-Kit, and other kinases; significant toxicity grade 3 hypertension was 64%. No real-life data exists. **Methods:** We selected patients (pts) under lenvatinib as a second-line or beyond for refractory TETs from 8 International centers from France (belonging to the nationwide network RYTHMIC) and United States. We analyzed epidemiologic, clinical and pathological characteristics of patients with TET's. The toxicity was evaluated according to CTCAE v4, with a local evaluation of efficacy and we assessed toxicity profile and survival outcomes. **Results:** From March 2020 to December 2021, 29 pts were enrolled. Median age at diagnosis was 49 (24-71), 51.7% were women, 6/29 (20.7%) reported auto-immune disorders (AIDs). TC was the most frequent subtype (n=18, 62.1%), followed by B3 and B2. Lenvatinib was used as a second line for 52% of pts, mainly starting from 14 mg/daily (n=20, 69%) and one pts with concomitant pembrolizumab. The ORR was 17% (95%CI 3.0-32.0) with partial responses only seen in TC, and the disease control rate was 76% (95%CI 59.0-92.0). Response was observed with the dose of 24mg in 3 pts and 14mg in 2 pts, with a median follow-up period of 5 months (m) (95%CI 3.2-6.7), PFS at 6 and 12 m was 64% and 30%, respectively. Toxicity is summarized in table 1. Dose de-escalations were needed in 27.5% of pts. **Conclusions:** We confirm the activity of lenvatinib in pts with advanced or metastatic T and TC, despite the use of lower doses than the phase 2 study. Research Sponsor: None.

Toxicity profile of the cohort later to starting lenvatinib.

	TOXICITY			
Syndrome	**Any grade**	**%**	**Grade ≥3**	**%**
High blood pressure	12	41,3	0	0
Asthenia	7	24,2	1	3,4
Diarrhea	4	13,7	0	0
Mucositis	4	13,7	2	6,9
Hypothyroidism	3	10,3	0	0
Liver toxicity	2	6,9	2	6,9
Abdominal pain	2	6,9	0	0
Neuropathy	2	6,9	0	0
Palmo-plantar SD	1	3,4	0	0
Anemia	2	6,9	0	0
Thrombopenia	1	3,4	0	0
Neutropenia	1	3,4	0	0
Headache	1	3,4	0	0
Edema	1	3,4	0	0
Fever	1	3,4	0	0
Alopecia	1	3,4	0	0

8586 **Poster Session**

CD47 expression patterns in thymic epithelial tumors.

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Background: Blockade of CD47, an immunoglobulin overexpressed on solid tumor cells that inhibits macrophage phagocytosis, is a promising anti-cancer immunotherapy which has not yet been explored in thymic epithelial tumors (TETs). TETs, including thymomas and thymic carcinomas, are rare tumors with limited immunotherapy treatment options due to the high rates of immune-related adverse effects observed with PD-1/PD-L1 checkpoint inhibitors. This study aimed to examine CD47 protein expression in TETs. **Methods:** A clinically annotated tissue microarray of 67 TETs consisting of 64 thymomas and 3 thymic carcinomas, as well as 14 thymic controls were included. Each sample with an average of 3 cores was stained for CD47 epithelial expression (rabbit monoclonal antibody SP279, Abcam, USA). Samples were scored for intensity as follows: 0 = none, 1 = weak, 2 = moderate, and 3 = strong. An H-score, defined as intensity x percentage of tumor involved, was also assigned and ranged from 0 to 300. Samples with an intensity score of < 2 or an H-score of < 150 were categorized as $CD47^{low}$, while the rest as $CD47^{high}$. Multivariate linear regression analysis accounted for WHO subtype, stage, resection status and presence of paraneoplastic syndrome (Prism 9, Graphpad). **Results:** Compared to normal thymic tissue, TETs were more frequently CD47 positive and had significantly higher levels of CD47 expression. CD47 was present in 91% of TETs, compared to 64.3% of normal thymus. Importantly, the level of expression was significantly higher in TETs by 16-fold (mean H-score 75.0 vs 4.6, $p = 0.003$). Among tumors, univariate analyses showed that higher CD47 expression was correlated with a lower stage ($p = 0.032$) and more complete resection ($p = 0.058$). A multivariate analysis accounting for these factors showed that CD47 expression by both H-score and intensity were each highly correlated with WHO histology subtype ($p = 0.0005$; $p = 0.0017$ respectively) with lower grade subtypes more frequently found in $CD47^{high}$ tumors. The most frequent subtype in $CD47^{high}$, when compared to $CD47^{low}$ tumors, was AB (61.5% vs 13.7%) and the least frequent was B2 (0% vs 37.3%). Tumors with the highest grade (subtype C, thymic carcinomas) were exclusively $CD47^{low}$. $CD47^{high}$ tumors were associated with an increased incidence of paraneoplastic syndromes (52.4% vs 12.0%, $p = 0.0014$). **Conclusions:** CD47 expression was found in the vast majority of TETs, and in significantly higher levels than normal thymic tissue. Among tumors, those with higher CD47 expression tended to have lower grade and stage, as well as higher frequency of paraneoplastic syndromes. This study is the first to examine CD47 expression in TETs. Given the prevalent expression of CD47 found in TETs and current available CD47 targeted agents, this study lends support for further investigation of this novel therapeutic approach. Research Sponsor: None.

8587 **Poster Session**

Genomic characterization of thymic epithelial tumor from real-world data.

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Background: Thymic epithelial tumors (TETs), including thymic carcinomas and thymomas, are rare neoplasms arising in the mediastinum. Chemotherapy is still the mainstay of treatment and few therapeutic options are available for patients with advanced or metastatic TETs. Due to their rarity, the sample size in the previous reports about the genomic profiles of TETs was small and the results varied from study to study, which hinders the development of treatment. Herein, we investigated the comprehensive genomic characteristics of TETs evaluated in a large genomic database profiled in a real-world setting. **Methods:** Tissue biopsy-based comprehensive genomic profiling was performed in the course of routine clinical care. We included data from two different cohorts: Foundation Medicine Inc. (FMI) in the US (Frampton GM, et al. Nat Biotechnol 2013) and the Center for Cancer Genomics and Advanced Therapeutics (C-CAT) in Japan, which is engaged in a national project for collecting genomic analysis and clinical results from patients. Samples profiled at Foundation Medicine were examined for all classes of alterations in 253 genes targeted across all assays. Tumor mutational burden (TMB) and microsatellite instability (MSI) were calculated as previously described (Chalmers ZR, et al. Genome Med 2017. Trabucco, et al. J Mol Diagn 2019). Patients' background including histology, age, and sex were also investigated, and genetic alteration, TMB, and MSI were stratified by them. **Results:** A total of 794 patients were collected for our study, including 722 cases from FMI and 72 cases from C-CAT. In the FMI data, 414 cases of thymic carcinoma and 308 cases of thymoma were included. *CDKN2A* (39.9%), *TP53* (30.2%) and *CDKN2B* (24.6%) were frequently altered in thymic carcinoma, versus *TP53* (7.8%), *DNMT3A* (6.8%), *CDKN2A* (5.8%) and *CDKN2B* (4.6%) in thymoma. TMB-High ($\geq$ 10muts/Mb) and MSI-High were present in 7.0% and 2.3% of thymic carcinomas, and 1.6% and 0.3% of thymomas, respectively. Comparison of the thymic carcinoma cohort based on age $<$ 60 vs 60+ years found a significant difference in prevalence of *NFKBIA* alterations (2.7% age $<$ 60 vs 11.7% age $\geq$ 60, $p = 0.034$), while a similar comparison of the thymoma cohort found no significant differences between age groups. An analysis based on sex did not find any significant differences between groups. 55 cases of thymic carcinoma and 17 cases of thymoma were included from C-CAT data. In thymic carcinoma, *CDKN2A* (27.3%), *TP53* (23.6%) and *CDKN2B* (20.0%) were also frequently altered, while alterations of *TSC1* (23.5%) and *CD22*, *LTK*, *NOTCH1*, *KMT2A*, *SETD2*, *ATM* (17.6% each) were found in thymoma. **Conclusions:** To the best of our knowledge, this is the largest cohort in which genomic alterations, TMB, and MSI status of TETs were investigated. We suggest that several gene mutations, TMB, and MSI status might be potential targets for treatment and lead to therapeutic development opportunities, especially in thymic carcinoma. Research Sponsor: None.

8588 **Poster Session**

Impaired seroconversion after SARS-COV-2 mRNA vaccine in patients with thymic epithelial tumors.

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Background: Thymic epithelial tumors (TET) are rare malignancies associated with dysregulation of the immune system and humoral and cell mediated immunity abnormalities. Anti-syndrome coronavirus type 2 (SARS-CoV-2) vaccine is effective at preventing COVID-19 morbidity and mortality. No published data are available regarding the immunization in TET patients (pts). The aim of this study was to evaluate the immunization in TET pts who received two doses of mRNA vaccine, by longitudinal serological detection of SARS-COV-2 spike-binding IgG antibody. **Methods:** Starting from April 2021 to October 2021, consecutive TET pts referred to the Rare Tumors Coordinating Center of Campania Region (CRCTR - Naples, Italy) were enrolled. All study subjects received two doses of COVID-19 mRNA vaccine (BNT162b2 by Pfizer-BioNTech). SARS-CoV-2 spike-binding IgG antibody (Ab) serological levels were analyzed by centralized chemiluminescent immunoassay (CLIA) at different time-points, including before 1^{st} vaccine dose (T0) and 1 month after 2^{nd} dose (T2). Cut-off for Ab titers positivity was > 25 AU/mL. **Results:** Forty pts were enrolled; 23 (57.5%) were female and 17 (42.5%) male. Eleven pts (27.5%) suffered from thymic carcinoma, 28 (70%) thymoma, and 1 (2.5%) thymic hyperplasia. At the time of study enrollment, 20 pts (50%) had no evidence of disease (NED) and were in follow-up; the remaining 20 pts had evidence of disease (ED) by imaging and were receiving systemic treatment (55% oral low-dose etoposide-based therapy, 40% somatostatin analogs + prednisone, 5% supportive care). Immune system disorders were diagnosed in 29 TET pts (72.5%): 19 pts (47.5%) had Good's Syndrome (GS) and 10 (25%) other immune disorders. At T0, all enrolled pts had negative Ab titers and no prior SARS-CoV-2 infection. At T2, Ab data were available for 37 pts (92.5%): 18 pts (48.7%) had positive Ab titers, whereas 19 (51.3%) did not achieve seroconversion. Among pts with ED, seroconversion was achieved only in 2 cases (11.8%). Lack of seroconversion at T2 was significantly associated with ED (Fisher's exact test p: 0.0001) and with the presence of GS (Fisher's exact test p: 0.0489). No significant association of seroconversion with other immune disorders and disease features was found. **Conclusions:** Our data showed that TET pts with ED had substantially higher probability of impaired seroconversion after SARS-COV-2 vaccine as compared with NED pts. We warrant further studies to evaluate the role of disease status, anti-tumor treatments and immune disorders in post-vaccine immunization of TET pts. Research Sponsor: None.

8589 **Poster Session**

Immunological signature of patients with thymic epithelial tumors.

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Background: Thymic epithelial tumors (TETs) are complex diseases frequently associated with immune disorders, including Good Syndrome (GS). Etiopathogenesis of immune dysregulations in TETs patients is still not totally explained. The aim of this study was to evaluate differences in immune cell phenotype, as well as in the serum expression levels of a panel of cytokines, chemokines, and growth factors in patients with TETs and GS with or without autoimmune disorders (AD). **Methods:** From May 2019 to June 2020, consecutive patients with TETs and GS were recruited at Rare Tumors Coordinating Center of Campania Region (CRCTR – Naples, Italy). We analyzed the immunophenotype from peripheral blood focusing on selected immune cell subsets (monocytes, neutrophils, eosinophils, CD4+T cells, CD8+T cells, B-cells, NK cells and NKT- cells, T regulatory cells) processed for blood cell count and immunophenotyping, according to the 8-color immunophenotyping kit and Treg detection kit (CD4/CD25/CD127), and a panel of cytokines, chemokines, and growth factors from peripheral blood serum screened with pre-formed kits by Bioplex multiplex. D'Agostino-Pearson normality test was used to evaluate whether the continuous data were normally distributed, and a two-tailed t-test for independent samples was used. p-values < 0.05 were considered statistically significant. **Results:** Overall, 29 patients were enrolled [17 (58.6%) with and 12 (41.4%) without AD]. Sixteen patients (55.2%) were female and 13 patients (44.8%) were male. Tumor histology included thymoma in all the patients with AD, whereas there were 10 cases of thymoma and 2 of thymic carcinoma in the group of patients without AD. The analysis of leucocytes by blood cell count showed a statistically significant higher number of leucocytes, ascribable to T lymphocytes ($p = 0.023$), B lymphopenia ($p = 0.003$) and decrease of T regulatory cells ($p = 0.009$) in TET patients with AD, as compared with TET patients without AD. Moreover, TET patients with AD showed significantly higher circulating levels of IL-15 ($p = 0.032$), VEGF ($p = 0.007$), IP-10 ($p = 0.013$), GM-CSF ($p = 0.042$), IL-6 ($p = 0.031$), and MIP-1α ($p = 0.017$) with respect to TET patients without AD. **Conclusions:** To our knowledge, this is the first report describing a profound alteration in B and T lymphocytes in TET patients associated with AD. The observed differences may be potentially important in the clinical management of this complex disease. Additional studies are needed to better understand the immunophenotypic alterations in TETs patients. Research Sponsor: None.

TPS8590 **Poster Session**

Neoadjuvant and adjuvant capmatinib in resectable non–small cell lung cancer with *MET* exon 14 skipping mutation or high *MET* amplification: GEOMETRY-N trial.

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Background: Neoadjuvant therapy is the earliest opportunity to eliminate micrometastatic disease. Emerging data suggest that neoadjuvant therapy in non-small cell lung cancer (NSCLC) can elicit major pathological responses (MPRs) that translate into prolonged survival outcomes, serving as an early surrogate for efficacy. Adjuvant therapy can improve overall and disease-free survival (DFS) in patients with completely resected NSCLC. DFS observed with osimertinib in patients with early-stage *EGFR*-mutated tumors supports evaluation of other tyrosine kinase inhibitors (TKIs) in the neoadjuvant and adjuvant settings. In early-stage NSCLC, *MET* exon 14 skipping mutation (*MET*ex14) and de novo *MET* amplification (*MET*amp) are estimated to occur in up to 2.8% and 1.7% of patients, respectively. Capmatinib, a selective MET TKI, is FDA approved for patients with metastatic *MET*ex14 NSCLC. It was studied in GEOMETRY mono-1 in patients with advanced/metastatic NSCLC with *MET*ex14 or *MET*amp. In 2 treatment-naive *MET*ex14 cohorts, overall response rate (ORR) was 68% and 66%. In a treatment-naive high-level *MET*amp cohort, ORR was 40%. Capmatinib had a tolerable safety profile; most adverse events were reversible with dose adjustments. Based on the ORRs and safety profile observed in treatment-naive patients with advanced/metastatic *MET*-dysregulated NSCLC, GEOMETRY-N (NCT04926831), a Phase II, 2-cohort, 2-stage study, is evaluating the efficacy and safety of neoadjuvant and adjuvant capmatinib therapy in improving the MPR rate and outcomes in patients with *MET*ex14 or high-level *MET*amp NSCLC. **Methods:** Adults with resectable, histologically confirmed NSCLC stage IB-IIIA, N2 and select IIIB (T3N2 or T4N2) with either *MET*ex14 (cohort A) or high-level *MET*amp (gene copy number $\geq$10; cohort B) are eligible. *MET*ex14 must be determined by a Clinical Laboratory Improvement Amendments (CLIA)-certified lab. *MET*amp must be determined by fluorescence in situ hybridization at a CLIA-certified lab or by FoundationOne CDx next-generation sequencing. Prior systemic anticancer therapy is prohibited. Patients will receive capmatinib 400 mg twice daily for 8 weeks before surgical resection, followed by 3 years of adjuvant capmatinib. In the 2-stage design, stage 1 will enroll 9 patients per cohort, with MPR evaluated in each cohort after 9 patients have completed neoadjuvant therapy; stage 2, enrolling 10 more patients in a cohort, will proceed only if $\geq$1 of 9 participants has an MPR. About 42 patients will be enrolled, with 19 evaluable patients per cohort. Primary endpoint is MPR rate (local assessment). Secondary endpoints are complete pathological response rate (central and local review), ORR (local assessment), DFS, and safety. Following treatment, there will be a 2-year survival follow-up. Enrollment has started; expected first patient first visit: March 31, 2022. Clinical trial information: NCT04926831. Research Sponsor: Novartis Pharmaceuticals.

TPS8591 **Poster Session**

Phase III study with atezolizumab versus placebo in patients with malignant pleural mesothelioma after pleurectomy/decortication (AtezoMeso study).

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Background: Surgery for malignant pleural mesothelioma (MPM) is indicated mainly in multimodal approaches and in clinical trial settings. Different studies have shown significantly lower complication rates, lower peri-operative morbidity and mortality with pleural/decortication (P/D), with similar overall survival rates. The biology of mesothelioma shows significant heterogeneity. Surgical tumor reduction may create a host environment more amenable to immunotherapy by reducing the ratio of tumor cells versus antitumor effector T lymphocytes, reducing the quantities of intratumor and/or systemic immunosuppressive cells, and ablating tumor-derived paracrine factors that promote local recruitment of immunosuppressive cells. Encouraging clinical data emerging in the field of tumor immunotherapy have demonstrated that therapies focused on enhancing T-cell responses against cancer can result in a significant survival benefit. The AtezoMeso Study evaluates the introduction of atezolizumab-ATEZO in MPM, patients (pts) after P/D and platinum/pemetrexed perioperative therapy. **Methods:** This is a double-blind, placebo controlled, phase III trial, in 20 Italian centers. Main inclusion criteria are P/D without macroscopic residual and ECOG-PS 0-1. Pts who underwent to P/D without macroscopic residual disease and have received at least 4 cycles of perioperative therapy with cisplatin/carboplatin and pemetrexed, will be randomized (2:1) to receive ATEZO or placebo. Therapy will be administered at dose of 1,200 mg iv, every 21 days, for 12 months or until recurrence, unacceptable toxicity or patient/physician decision. Randomization will be done through a centralized system, using histology (epithelioid vs nonepithelioid) and stage (I vs > I) as stratification factors. Pts will be radiologically evaluated after surgical before starting therapy and then every 12 weeks for 24 months or until recurrence. Quality of life (QoL) will be evaluated with the EQ-5D questionnaire administered at baseline and every 12 weeks. Tissue tumor samples will be centrally analyzed to determinate the genomic profile using FoundationOne CDx platform. The primary endpoint is the evaluation of the atezolizumab efficacy in terms of disease free survival (DFS). Secondary endpoints include the safety and efficacy in terms of overall survivall and QoL. Assuming a median DFS equal to 9 months in placebo arm, an accrual time of 24 months and a follow-up time of 24 months, a sample size of 162 pts will allow to detect true hazard ratios of 0.62 with power 0.8, at a confidence level of 95%. At February 14th, 2022, 3 pts have been enrolled. Clinical trial information: 2020-003762-39; GOIRC-02-2019. Research Sponsor: Roche.

TPS8592 **Poster Session**

Assessing the predictive value of ctDNA on relapse in patients with resected stage IB-IIIA NSCLC treated with adjuvant chemotherapy plus concomitant atezolizumab followed by atezolizumab: BTCRC LUN 19-396.

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Background: A standard of care treatment for most patients with stage II and III non-small cell lung cancer (NSCLC) and a PD-L1 > 1% is surgery followed by adjuvant (adj) histology-specific chemotherapy followed by 1 year of atezolizumab. The benefit of adding atezolizumab concomitantly to chemotherapy in the adj setting has not been reported. In addition, the optimal duration of adjuvant therapy is undefined. Emerging data have demonstrated the potential for ctDNA to predict clinical recurrence in patients with surgically resected lung, breast, and colon cancer. The current study explores the predictive value of ctDNA for early relapse in patients treated with adj chemotherapy plus atezolizumab. **Methods:** The LUN19-396 is a phase II biomarker study that enrolls pts with resected NSCLC stage IB (tumors ≥ 4cm), IIA, IIB, and select IIIA (T3N1-2, T4N0-2). The ctDNA will be assessed within 60 days post-surgery and then every 3 months up to 12 months. All pts will receive treatment with 4 cycles of Cisplatin 60-75mg/m2 + Docetaxel 60-75mg/m2 + Atezolizumab 1200mg IV on day 1 q 3w (for patients with squamous cell cancer) or Cisplatin 60-75mg/m2 + Pemetrexed 500mg/m2 + Atezolizumab 1200mg on day 1 IV q 3w (for patients with non-squamous cell), followed by up to 13 additional cycles of Atezolizumab 1200mg IV every 3w. This trial will enroll a total of 100 pts to achieve more than 80% power. The primary objective is to estimate the percentage of pts with detectable ctDNA after surgery who have clearance of ctDNA at designated time points during adjuvant therapy. The key secondary objective is to estimate the 1-year disease-free survival in pts with undetectable ctDNA after 4 cycles of adj chemotherapy plus atezolizumab who had detectable ctDNA after surgery. This trial has enrolled 17 pts as of February 8, 2022. Clinical trial information: NCT04367311. Research Sponsor: Genentech.

TPS8593 **Poster Session**

A phase 1/2 study of REGN5093-M114, a METxMET antibody-drug conjugate, in patients with mesenchymal epithelial transition factor (MET)-overexpressing NSCLC.

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Background: MET, also called hepatocyte growth factor receptor (HGFR), is a high-affinity transmembrane protein receptor for HGF. MET is overexpressed in various malignancies, including non-small cell lung cancer (NSCLC). MET overexpression can accompany *MET* exon 14 alteration or de novo/acquired *MET* amplification. REGN5093-M114 is an antibody drug conjugate composed of a novel linker-payload (M114, carrying the maytansine derivative M24, a potent inhibitor of microtubule assembly) covalently bound to lysine residues on a MET-targeting human IgG4p bispecific antibody, REGN5093. In preclinical models of MET overexpressing cancers, REGN5093-M114 demonstrated significant dose-dependent antitumor activity. **Methods:** This is an open label, phase 1/2, first-in-human, multicenter dose-escalation study with cohort expansion evaluating REGN5093-M114 in patients with MET-overexpressing NSCLC (NCT04982224). Patients must have advanced stage NSCLC for which there are no approved therapies available expected to confer clinical benefit, with tumor overexpressing MET (≥75% tumor cell staining at 2+) as centrally confirmed by immunohistochemistry. For the expansion phase, patients must have at least one lesion that is measurable by RECIST 1.1. REGN5093-M114 will be administered intravenously once every 3 weeks over 30 minutes until disease progression, intolerable adverse events, withdrawal of consent, or study withdrawal. The primary objectives in dose escalation are to evaluate safety, tolerability, PK, and maximum tolerated dose and/or recommended phase 2 dosing regimen of REGN5093-M114. PKs will include the assessment of REGN5093-M114, total antibody, and payload M24 concentrations. The primary objective in dose expansion is to assess preliminary anti-tumor activity of REGN5093-M114 in MET-overexpressing NSCLC as measured by the objective response rate. The secondary objectives of both phases of the study include an evaluation of treatment durability, and the immunogenicity of REGN5093-M114. This study is currently open to enrollment. Clinical trial information: NCT04982224. Research Sponsor: Regeneron Pharmaceuticals, Inc.

TPS8594 **Poster Session**

LIBRETTO-001 cohort 7: A single-arm, phase 2 study of neoadjuvant selpercatinib in patients with resectable stage IB-IIIA *RET* fusion-positive NSCLC.

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Background: Despite definitive surgery and perioperative chemotherapy, many patients with locoregional non-small cell lung cancer (NSCLC) continue to experience recurrent disease and limited survival. Although targeted therapies are standard treatment for metastatic NSCLC with genomic alterations, their use in the early-stage setting is still being characterized. Initial studies examining targeted therapy in neoadjuvant setting for early-stage epidermal growth factor receptor positive NSCLC has shown promise. Selpercatinib is a highly selective, potent, and central nervous system active rearranged during transfection (RET) inhibitor with demonstrated robust and sustained antitumor activity and manageable toxicity in patients with *RET* fusion-positive advanced NSCLC. Cohort 7 of the Phase 2, open-label, single arm LIBRETTO-001 study evaluates efficacy and safety of neoadjuvant selpercatinib in patients with resectable stage IB-IIIA *RET* fusion-positive NSCLC (NCT03157128). **Methods:** Key eligibility criteria include age ≥18 years; histologically confirmed stage IB–IIIA NSCLC (AJCC, version 8); presence of *RET* fusion in tumor (by PCR or NGS) or blood (by NGS) (pre-treatment biopsy confirmed); resectable and operable tumor; measurable disease (RECIST 1.1); and ECOG performance status 0-1. Key exclusion criteria include presence of other known oncogenic drivers; and concurrent investigational anticancer therapy. Eligible patients will undergo full staging including radiographic tumor measurements using CT, PET, and brain MRI at baseline and after two 28-day cycles of neoadjuvant selpercatinib, followed by surgery. Dosing regimen is 160 mg twice daily. Resected tumor specimens will be sent to an Independent Pathology Review Committee (IPRC) for evaluation. Patients may then be treated with stage-appropriate adjuvant therapy/surveillance, based on the treating physician's decision, followed by selpercatinib until disease recurrence, unacceptable toxicity, withdrawal, or death, for a maximum treatment duration of 3 years. The primary endpoint is to determine the rate of major pathologic response (MPR) by IPRC, defined as ≤ 10% residual viable tumor cells in the surgically resected specimen. Efficacy based on the MPR will be assessed using the Simon's 2-stage design. In Stage I, 9 patients will be enrolled; if ≤1 patient achieves an MPR, the study will be stopped. Otherwise, at least 10 additional patients will be enrolled, with a total of 19 patients undergoing surgery. The rate of pathologic complete response (pCR) by IPRC, disease-free survival, and overall survival will be assessed as secondary endpoints. pCR rate will be determined at the time of surgery, indicating no remaining viable tumor cells. Safety of peri-operative treatment will be assessed, including 30- and 90-day post-operative readmission and mortality rates. Clinical trial information: NCT03157128. Research Sponsor: Eli Lilly and Company.

TPS8595 **Poster Session**

A first-in-human phase 1 study of the next-generation RET inhibitor, LOXO-260, in RET inhibitor refractory patients with RET-altered cancers (trial in progress).

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Background: *RET* fusions are found in 1-2% of lung adenocarcinomas and 10-20% of papillary thyroid carcinomas. Activating *RET* mutations occur in 50-60% of medullary thyroid cancers (MTCs). Selpercatinib was the first selective RET inhibitor approved by the FDA and is indicated for patients (pts) with *RET* fusion-positive NSCLC and thyroid cancer, and *RET* mutant MTC. Despite marked and durable activity, acquired resistance can eventually develop through a variety of mechanisms. These include acquisition of RET G810X mutations at the solvent front of the ATP pocket. LOXO-260 is a highly potent and selective inhibitor of RET designed to have activity against both solvent front and gatekeeper mutations, expressed alone or together, while maintaining potency against *RET* fusions or mutations (Kolakowski GR. et al. 2021 *Cancer Research* 81 (13 Suppl) 1464). **Methods:** LOXO-NGR-21001 is a global, open-label, first-in-human phase 1 study of LOXO-260 in pts with *RET* fusion-positive advanced solid tumors and *RET* mutant MTC who received a prior selective RET inhibitor. Phase 1a dose escalation will utilize a modified i3+3 design, allowing for pt backfill to previously cleared dose levels. Phase 1b dose expansion will evaluate LOXO-260 in specific expansion cohorts: *RET* fusion-positive NSCLC or thyroid cancers and *RET* mutant MTC. The primary objectives in dose escalation are to determine the MTD/RP2D and safety of LOXO-260. Key secondary objectives include characterization of PK and preliminary antitumor activity of LOXO-260 per RECIST v1.1. The primary objective of dose expansion is to assess the antitumor activity of LOXO-260 based on investigator-assessed overall response rate (ORR). Key secondary objectives are to characterize the PK and antitumor activity of LOXO-260 based on progression-free survival (PFS), time to response (TTR), and duration of response (DOR). Eligible pts must have received a prior selective RET inhibitor, have a documented *RET* fusion or *RET* mutation and a diagnosis of locally advanced, unresectable and/or metastatic cancer per disease-specific criteria, and must have progressed or be intolerant to standard therapies or must have refused such a therapy. Pts must be ≥18 years old and have an ECOG PS of 0-2. Key exclusion criteria include presence of serious cardiac conditions, interstitial lung disease, symptomatic CNS metastases, or carcinomatous meningitis. Clinical trial information: NCT05241834. Research Sponsor: Loxo Oncology.

TPS8596 **Poster Session**

LCMC LEADER neoadjuvant screening trial: LCMC4 evaluation of actionable drivers in early-stage lung cancers.

Boris Sepesi, David Randolph Jones, Bryan F. Meyers, Jamie E. Chaft, Lynette M. Sholl, Yu Shyr, Karen Kelly, Jules Lin, Paul A. Bunn, John D. Minna, Valerie W. Rusch, Ignacio Ivan Wistuba, David J. Kwiatkowski, David Paul Carbone, Lynne D. Berry, Jay M. Lee, Khaled Tolba, Mark G. Kris; Thoracic and Cardiovascular Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX; Memorial Sloan Kettering Cancer Center, New York, NY; Washington University School of Medicine, St. Louis, MO; Department of Pathology, Brigham and Women's Hospital, Boston, MA; Vanderbilt University Medical Center, Nashville, TN; University of California Davis Comprehensive Cancer Center, Sacramento, CA; University of Michigan, Ann Arbor, MI; University of Colorado Denver, Aurora, CO; The University of Texas Southwestern Medical Center, Dallas, TX; Department of Translational Molecular Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX; Cancer Genetics Laboratory, Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA; The Ohio State University Comprehensive Cancer Center, Columbus, OH; Vanderbilt University, Nashville, TN; David Geffen School of Medicine at UCLA, Los Angeles, CA; Foundation Medicine, Inc., Cambridge, MA

Background: Comprehensive genomic profiling (CGP) has transformed the care of patients with advanced non-small cell lung cancer (NSCLC), giving many patients access to precision targeted treatment and immunotherapy with remarkable improvements in outcomes. Studies show that patients with lung cancers with oncogenic drivers are the least likely group to benefit from checkpoint inhibitors and are better served by enrollment in studies of targeted therapies. Early-stage NSCLC is now poised to benefit from these precision approaches with the regulatory approval of the first tyrosine kinase inhibitors and checkpoint inhibitors for the adjuvant treatment of resected NSCLC, each requiring testing for precision biomarkers. Neoadjuvant precision therapy for NSCLC has the potential to further improve treatment outcomes. **Methods:** The LCMC4 Evaluation of Actionable Drivers in EaRly Stage Lung Cancer (LEADER) Neoadjuvant Screening Trial (NCT04712877) is a collaborative diagnostic study developed by the Lung Cancer Mutation Consortium (LCMC), supported by the Thoracic Surgery Oncology Group and the Lung Cancer Research Foundation. The primary objective is to determine the proportion of patients with stage IA2-III lung cancers who possess actionable oncogenic drivers, defined as 1 of 11 actionable genomic alterations: mutations in *EGFR*, *BRAF*^{V600E}, *MET* exon 14, *KRAS* G12C, and *HER2*, rearrangements in *ALK, RET, NTRK, and ROS1,* and amplification of *MET* and *HER2*. The study will also assess the feasibility of CGP to detect actionable oncogenic drivers in patients with suspected early-stage lung cancers scheduled to undergo biopsies to establish the diagnosis of lung cancer. The protocol will enroll 1000 patients with operable stage IA2-III (TNM 8th edition) lung cancer who will undergo CGP utilizing the Foundation Medicine 324 gene assay as well as paired liquid biopsy analysis. Results will enable selection of neoadjuvant therapy and enrollment onto independent therapeutic trials with genomically matched neoadjuvant treatment, standard therapies, or other trials if no driver is detected. The approach will be considered feasible if >35% of non-squamous NSCLCs have 1 of the 11 actionable alterations. Tumor mutational burden and PD-L1 IHC will be assessed. Plasma specimens collected pre- and post neoadjuvant treatment and post-surgery will be used for research to study the ability of circulating tumor DNA to assess neoadjuvant treatment response and minimal residual disease. 26 academic sites in the US plan to enroll patients. Clinical trial information: NCT04712877. Research Sponsor: Genentech, Other Foundation, Pharmaceutical/Biotech Company.

TPS8597 **Poster Session**

Phase 3, randomized, placebo-controlled study of stereotactic body radiotherapy (SBRT) with or without pembrolizumab in patients with unresected stage I or II non–small cell lung cancer (NSCLC): KEYNOTE-867.

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Background: Anti–PD-(L)1-directed therapy following radiotherapy or following concurrent chemoradiation is associated with significantly longer PFS and OS in patients with advanced or metastatic NSCLC, including those with locally advanced inoperable tumors. KEYNOTE-867 (NCT03924869) evaluates the efficacy and safety of SBRT with or without pembrolizumab in patients with unresected stage I or II NSCLC. **Methods:** In this phase 3, randomized, placebo-controlled study, approximately 530 adult patients with previously untreated, unresected, histologically/cytologically confirmed stage I or II (T1 to limited T3, N0, M0) NSCLC are randomized 1:1 to receive thoracic SBRT to primary tumors for ≤2 wk (Table) and either pembrolizumab 200 mg or placebo every 3 wk for 17 cycles (approximately 1 year) or until disease recurrence, development of unacceptable AEs, SBRT not started for any reason, or study withdrawal. Randomization is stratified by disease stage (I vs II), ECOG PS (0 or 1 vs 2), geographic region (East Asia vs non-East Asia), and reason for not receiving surgery (medically inoperable vs refused surgery). Imaging assessment by blinded independent central review (BICR) occurs at 12 wk (≥10 wk after SBRT completion), followed by every 16 wk for 3 y, and then every 6 mo. Primary endpoints are event-free survival (EFS) by BICR and OS. Secondary endpoints include time to death or distant metastases and safety; exploratory endpoints are time to subsequent treatment, disease-specific survival, and time to recurrence/progression on subsequent line of therapy. AEs are monitored throughout the trial until 30 d after last dose (90 for serious AEs) and graded according to NCI CTCAE version 4.0. EFS and OS are analyzed by the nonparametric Kaplan-Meier method, treatment differences by stratified log-rank test, and hazard ratios by stratified Cox proportional hazard model with Efron's method of tie handling. Enrollment started on June 17, 2019, and is ongoing at 168 sites around the world. Clinical trial information: NCT03924869. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Stereotactic body radiotherapy regimen.[a]

Unit Dose Strength(s)	
Peripheral tumors	45–60 Gy in 3 fractions (preferred regimen); 48–50 Gy in 4 fractions or 50–55 Gy in 5 fractions (acceptable regimens)
Tumors abutting the chest wall	48–50 Gy in 4 fractions; 50–55 Gy in 5 fractions
Central tumors	50–55 Gy in 5 fractions; 60–70 Gy in 8 fractions

[a]Regimens have been amended since the original protocol.

TPS8598 **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, Vinicius Ernani, Patrick M. Forde, Liza C Villaruz, Kanwal Pratap Singh Raghav, Paul Bernard Romesser, Krista Garbacz, Liang Cao, Mary M. Salvatore, Anja Roden, Steven Francis Powell, Ardaman Shergill, Pamela N. Munster, Gary K. Schwartz, Travis Edward Grotz; Mayo Clinic, Rochester, MN; Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN; Emory Univ, Atlanta, GA; The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD; University of Pittsburgh Medical Center, Hillman Cancer Center, Pittsburgh, PA; The University of Texas MD Anderson Cancer Center, Houston, TX; Memorial Sloan Kettering Cancer Center, New York, NY; University of Chicago Comprehensive Cancer Center, Chicago, IL; Genetics Branch Center for Cancer Research National Cancer Institute, Bethesda, MD; Department of Radiology, Columbia University Irving Medical Center, New York, NY; Department of Laboratory Medicine & Pathology, Mayo Clinic, Rochester, MN; Sanford Health, Sioux Falls, SD; The University of Chicago, Medical and Biological Sciences, Chicago, IL; University of California San Francisco, San Francisco, CA; Columbia University Irving Medical Center, New York, NY; Division of Hepatobiliary and Pancreas Surgery, Mayo Clinic, Rochester, MN

Background: Peritoneal mesothelioma is a rare and poorly studied disease with few treatment options. For patients who are not surgical candidates, treatment recommendations for systemic therapy have been extrapolated from clinical trials for pleural mesothelioma that commonly exclude patients 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 patients with newly diagnosed peritoneal mesothelioma. **Methods:** A092001 is a prospective, randomized phase 2 clinical trial. All patients 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. Patients 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 whether 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 patients 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 patients are enrolled. As stratification factors we have included eligibility for cytoreductive surgery at diagnosis, and histologic subtype. Secondary endpoints include assessment of 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. Support: U10CA180821, U10CA180882. Clinical trial information: NCT05001880. Research Sponsor: U.S. National Institutes of Health.

TPS8599 **Poster Session**

DREAM3R: Durvalumab with chemotherapy as first-line treatment in advanced pleural mesothelioma—A phase 3 randomized trial.

Patrick M. Forde, Anna K. Nowak, Peey-Sei Kok, Chris Brown, Zhuoxin Sun, Valsamo Anagnostou, Kenneth John O'Byrne, Sonia Yip, Alistair Cook, Willem Joost Lesterhuis, Brett Gordon Maxwell Hughes, Nick Pavlakis, Julie R. Brahmer, Hedy L. Kindler, Anne S. Tsao, Marjorie Glass Zauderer, Suresh S. Ramalingam, Martin R. Stockler; The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD; Sir Charles Gairdner Hospital, Perth, Australia; NHMRC Clinical Trials Centre, The University of Sydney, Sydney, NSW, Australia; NHMRC Clinical Trials Centre, University of Sydney, Sydney, Australia; Dana-Farber Cancer Institute, Boston, MA; Johns Hopkins University School of Medicine, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD; St. James's Hospital, Dublin, Ireland; NHMRC Clinical Trials Centre, University of Sydney, Sydney, NSW, Australia; University of Western Australia, Perth, Australia; National Centre for Asbestos Related Diseases, University of Western Australia, Nedlands, Australia; Department of Medical Oncology, Royal Brisbane & Women's Hospital, and School of Medicine, University of Queensland, Brisbane, QLD, Australia; Northern Cancer Institute, St. Leonards, Sydney, Australia; Johns Hopkins University School of Medicine, Baltimore, MD; University of Chicago, Chicago, IL; The University of Texas MD Anderson Cancer Center, Houston, TX; Memorial Sloan Kettering Cancer Center, New York, NY; Winship Cancer Institute of Emory University, Atlanta, GA

Background: Combination PD1/CTLA4 immune checkpoint blockade and platinum-pemetrexed (CP) chemotherapy are standard first-line options for the treatment of unresectable malignant pleural mesothelioma (MPM). Two recent, single-arm, phase 2 trials (DREAM and PrE0505) combining the PD-L1 inhibitor durvalumab and standard first line CP both exceeded pre-specified efficacy criteria. The Phase 3 DREAM3R trial aims to determine the effectiveness of including durvalumab with first line CP chemotherapy in advanced MPM. **Methods:** Treatment-naïve patients with advanced MPM will be randomized (2:1) to either durvalumab 1500 mg every 3 weeks plus chemotherapy (cisplatin 75 mg/m2 or carboplatin AUC 5 and pemetrexed 500 mg/m2) every 3 weeks for 4-6 cycles (Arm A), followed by durvalumab 1500 mg every 4 weeks until disease progression, unacceptable toxicity or patient withdrawal, versus doublet chemotherapy alone for 4-6 cycles with all patients monitored for progression. The target sample size is 480 patients recruited over 27 months, with follow up for an additional 24 months. This provides over 85% power if the true hazard ratio for overall survival (OS) is 0.70, with 2-sided alpha of 0.05, assuming a median OS of 15 months in the control group. Key eligibility criteria include: MPM of any histological subtype; measurable disease per RECIST 1.1 modified for mesothelioma (mRECIST 1.1); ECOG PS 0-1; and adequate hematologic, renal, and liver function. Exclusions: Prior systemic anticancer treatment for MPM, diagnosis based solely on cytology or fine needle aspiration biopsy, contraindication to immunotherapy or conditions requiring immunosuppressive agents or corticosteroids. Patients will be further stratified at randomization by: Age (18-70 years vs. > 70), sex, histology (epithelioid vs. non-epithelioid), planned 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 healthcare resource use in ANZ. Tertiary correlative objectives aim to further explore and validate potential prognostic and/or predictive biomarkers (including those identified in the DREAM and PrE0505 studies, PD-L1 expression, tumor mutation burden, genomic characteristics, and HLA subtypes) via tissue and serial blood samples. An imaging databank will be assembled for 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 ACTRN 12620001199909. Research Sponsor: AstraZeneca.

TPS8600 **Poster Session**

An open-label, multicenter, phase 2 study of the safety and efficacy of navtemadlin (KRT-232) in patients with *TP53* wild-type relapsed/refractory small cell lung cancer.

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Background: Small cell lung cancer (SCLC) is a highly aggressive neuroendocrine tumor characterized by early metastasis and a high recurrence rate with currently available treatment options. Although SCLC is generally sensitive to initial chemotherapy, responses are not durable and most patients eventually relapse. Prognosis is poorer in the relapsed/refractory (R/R) setting and currently available treatment options, including checkpoint inhibitors, are associated with a median overall survival of 2-9 months (Chauhan 2020; Trigo 2020; Chung 2020). Approximately 15% of patients have a *TP53* wild-type ($TP53^{WT}$) gene. In patients with extensive-stage SCLC, $TP53^{WT}$ is paradoxically associated with an inferior response to chemotherapy (Dowlati 2016). Thus, the presence of $TP53^{WT}$ may help identify a small subset of patients with an even greater unmet need. Murine double minute 2 (MDM2) is the key negative regulator of the tumor suppressor protein, p53, which can induce apoptosis of malignant cells by shifting the balance between prosurvival and proapoptotic BCL-2 family members. In SCLC cell lines, MDM2 inhibition restored p53 function leading to downregulation of prosurvival Bcl-2 and Mcl-1 proteins, and upregulation of the proapoptotic Bim protein, thereby inducing cancer cell death (Yu 2019). Navtemadlin (KRT-232) is a potent, selective, orally available MDM2 inhibitor that restores p53 function to drive apoptosis of $TP53^{WT}$ malignancies. Treatment with navtemadlin may be an effective strategy for patients with $TP53^{WT}$ SCLC. **Methods:** The open-label, multicenter Phase 2 KRT-232-112 study (NCT05027867) is evaluating navtemadlin in $TP53^{WT}$ patients with R/R SCLC. Eligibility criteria include age $\geq$18 years, ECOG performance status $\leq$2, presence of measurable disease and demonstrated radiographic progression after $\geq$1 prior platinum-containing therapy with no curative therapy available. Patients must have received a checkpoint inhibitor if available and not contraindicated. Patients with symptomatic or uncontrolled central nervous system metastases or those with prior MDM2 inhibitor treatment will be excluded. In part 1 of the study, approximately 20 patients will be randomly assigned to receive oral navtemadlin once daily in 21-day cycles at 240 mg 7 days (D) on/14D off (Arm A) or 180 mg 7D on/14D off (Arm B) until disease progression or unacceptable toxicity. In part 2, an additional 18 patients will be enrolled in each arm selected for expansion. The primary endpoint is objective response rate per RECIST v1.1. Secondary endpoints include duration of response, progression-free survival, overall survival, disease control rate, and safety. This trial is ongoing and will enroll patients at approximately 40 global sites. Clinical trial information: NCT05027867. Research Sponsor: Kartos Therapeutics, Inc.

TPS8601 **Poster Session**

TRUST-II: A global phase II study for taletrectinib in *ROS1* fusion–positive lung cancer and other solid tumors.

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Background: Taletrectinib (AB-106/DS-6051b) is a next-generation, brain-penetrant, ROS1/ NTRK tyrosine kinase inhibitor (TKI) and has shown clinically meaningful effect and safety profile in ROS1+ Non-Small Cell Lung Cancer (NSCLC) patients in phase 1 studies (Fujiwara et al, Oncotarget 2018; 9(34): 23729-23737; Ou et al, JTO Clin Res Rep. 2020 Oct 21;2(1):100108). Taletrectinib has also demonstrated activity against ROS1 G2032R resistance mutation and CNS metastases in the ongoing phase 2 TRUST study (NCT04395677) in China. Also, taletrectinib has shown preliminary efficacy against NTRK positive solid tumors in an ongoing phase 2 study (NCT04617054). **Methods:** TRUST-II study (NCT04919811) is a phase 2, global, multicenter, open-label, single-arm multi-cohort study evaluating the efficacy and safety of taletrectinib for *ROS1* fusion-positive advanced metastatic NSCLC and other solid tumors. Taletrectinib will be given at 600 mg once daily in 21-day cycle. The patients with ROS1 fusions detected by local tests are eligible to enroll with retrospective confirmation by a central laboratory. The study consists of four cohorts: cohort 1: systemic chemotherapy naïve or $\leq$ one prior line and ROS1 TKI naïve NSCLC (N = 53); cohort 2: previously treated with one ROS1 TKI (crizotinib or entrectinib) and with progression who are either chemotherapy naïve or $\leq$ one line of platinum and/or pemetrexed based therapy for NSCLC (N = 46); cohort 3: $\leq$ 2 prior ROS1 TKIs and with progression who are either chemotherapy naïve or $\leq$ 2 lines of platinum and/or pemetrexed based therapy for NSCLC (N = 10); and cohort 4: systemic chemotherapy naïve or $\leq$ 2 prior lines of chemotherapy, but ROS1-TKI naïve ROS1 positive solid tumor other than NSCLC (N = 10). The primary endpoint is objective response rate (ORR) (RECIST v1.1) by independent review committee (IRC) assessment for cohorts 1 and 2. Key secondary endpoints include IRC-assessed duration of response, IRC-assessed intra-cranial ORR, progression free survival (PFS), overall survival (OS), and safety. This study is currently recruiting in Japan, Republic of Korea, and USA. Additional accrual is planned in Canada, China, and European Union. Clinical trial information: NCT04919811. Research Sponsor: AnHeart Therapeutics Inc.

TPS8603 **Poster Session**

Phase 2 study of tarlatamab, a DLL3-targeting, half life–extended, bispecific T-cell engager (HLE BiTE) immuno-oncology therapy, in relapsed/refractory small cell lung cancer (SCLC).

Suresh S. Ramalingam, Myung-Ju Ahn, Hiroaki Akamatsu, Fiona Helen Blackhall, Hossein Borghaei, Horst-Dieter Hummel, Melissa Lynne Johnson, Martin Reck, Yiran Zhang, Danielle Jandial, Sunfa Cheng, Luis G. Paz-Ares; Winship Cancer Institute of Emory University, Atlanta, GA; Samsung Medical Center Sungkyunkwan University School of Medicine, Seoul, South Korea; Wakayama Medical University Hospital, Wakayama, Japan; The Christie NHS Foundation Trust, Manchester, United Kingdom; Fox Chase Cancer Center, Philadelphia, PA; University Hospital Würzburg, Comprehensive Cancer Center Mainfranken, Translational Oncology/Early Clinical Trial Unit, Würzburg, Germany; Sarah Cannon Research Institute, Nashville, TN; LungenClinic, Airway Research Center North, German Center for Lung Research, Grosshansdorf, Germany; Amgen Inc., Thousand Oaks, CA; Hospital Universitario 12 de Octubre, Madrid, Spain

Background: SCLC is characterized by rapid growth and early development of metastases. Platinum-based first-line chemotherapy is associated with a high initial response rate; however, disease recurrence is common. Delta-like ligand 3 (DLL3) is a Notch ligand that is upregulated and aberrantly expressed on the cell surface in most SCLC, making it a compelling therapeutic target. Tarlatamab is an HLE BiTE immuno-oncology therapy designed to bind DLL3 on target cancer cells and CD3 on T cells, forming a cytolytic synapse inducing T cell activation and expansion and T cell-dependent killing of tumor cells. Interim results of an ongoing first-in-human study in patients with relapsed/refractory SCLC (NCT03319940) show preliminary evidence for tarlatamab efficacy in pretreated patients with confirmed partial responses in 20% of patients and duration of response of 8.7 months (Owonikoko TK, et al. Abstract 8510. Presented at: ASCO Annual Meeting, June 4–8, 2021; Virtual). Grade ≥ 3 treatment-related AEs (TRAEs) occurred in 27% of patients and TRAEs resulted in discontinuation in 5% of patients. This promising efficacy/safety profile supports further study of tarlatamab in SCLC. **Methods:** NCT05060016 is a phase 2, open-label study evaluating tarlatamab in patients with relapsed/refractory SCLC after two or more lines of prior treatment. Part 1 is a dose characterization phase in which subjects will be randomized 1:1 to two active doses of tarlatamab. Part 2 will continue enrollment for the selected target dose only based on interim analysis of Part 1. Key eligibility criteria include adults with histologically or cytologically confirmed SCLC whose disease progressed/recurred after two or more lines of prior treatment including at least 1 platinum-based regimen (including a PD-L1 inhibitor, if standard of care, with certain exceptions per protocol), treated brain metastases, ECOG performance status ≤1, and life expectancy ≥ 12 weeks in the opinion of the investigator. The primary endpoint for the primary analysis is ORR per RECIST 1.1 as assessed by blinded independent central review. Secondary objectives are to evaluate antitumor activity by additional measures (duration of response, progression-free survival, disease control rate and duration, overall survival), safety and tolerability, immunogenicity, and pharmacokinetics. Sites in North America, Asia and Europe are participating in the trial with subjects already enrolled and enrollment ongoing. Clinical trial information: NCT05060016. Research Sponsor: Amgen Inc.

TPS8604 **Poster Session**

MC1923 phase II clinical trial of durvalumab (MEDI4736) and topotecan or lurbinectedin in patients with relapsed extensive-stage small cell lung cancer previously treated with chemotherapy and immunotherapy.

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Background: Chemoimmunotherapy followed by durvalumab maintenance yields a median overall survival of 12.9 months in patients with extensive stage Small Cell Lung Cancer (ES SCLC), which is an improvement over chemotherapy alone. However, 90% of these patients will have progressive disease. While topotecan and lurbinectedin have established modest activity in the second line, it is unknown whether continuing immunotherapy in this setting confers additional benefit. In preclinical studies lurbinectedin, a DNA minor groove binder, used with immune checkpoint inhibitors has synergistic effects. **Methods:** This phase 2 trial is enrolling patients with ES SCLC who have progressed on platinum based chemoimmunotherapy, to three treatment groups. Group 1 includes patients with platinum sensitive SCLC who will receive durvalumab (1500 mg given as an intravenous [IV] infusion once every 3 weeks) and topotecan (1.25 mg/m^2/day IV for 5 consecutive days every 3 weeks). In Groups 2A and 2B, patients with platinum sensitive and platinum resistant disease respectively, receive durvalumab and lurbinectedin (3.2 mg/m^2 IV on Day 1 of every 21-day cycle). Patients with platinum sensitive disease are assigned to Groups 1 or 2A based on the preferences of the treating physician and the patient. Patients with treated/stable CNS metastases are eligible. The primary endpoint is the proportion of patients who are alive at 6 months (6OS) for Group 1 and the proportion of patients who are alive and progression-free at 6 months (6PFS) in Groups 2A and 2B. Secondary endpoints include safety, adverse event profile, response rate, PFS, and OS. The sample size is based on a 2-stage Simon Optimal Design. For Treatment Group 1, with 22 eligible patients there is 80% power to detect a true 6-month OS rate (6OS) of 75%, with 10% alpha under the null hypothesis that the true 6OS is at most 50%. For Treatment Group 2A, with 20 eligible patients this design has 80% power to detect a true 6-month PFS rate (6PFS) of 65%, with 10% alpha under the null hypothesis that the true 6PFS is at most 40%. For Treatment Group 2B, with 22 eligible patients this design has 80% power to detect a true 6-month PFS rate (6PFS) of 40%, with 10% alpha under the null hypothesis that the true 6PFS is at most 19%. To account for possible drop-outs, accrual targets will be 24, 22, and 24 patients to Groups 1, 2A, and 2B respectively. For the safety analyses, 6 patients will be enrolled at the starting dose level for each treatment group (1, 2) and then briefly closed to accrual to assess adverse events. If we observe 2+ DLTs in these 6 treated patients during Cycle 1 within a treatment group (1 vs. 2), we will declare the combination treatment too toxic and lower the starting dose of chemotherapy for the next 6 patients. The study was open for all 3 groups as of January 2022 and has accrued 2 patients. Clinical trial information: NCT04607954. Research Sponsor: AstraZeneca.

TPS8606 **Poster Session**

KeyVibe-008: Randomized, phase 3 study of first-line vibostolimab plus pembrolizumab plus etoposide/platinum versus atezolizumab plus EP in extensive-stage small cell lung cancer.

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Background: Current standard of care immunotherapy plus chemotherapy options for first-line extensive-stage small-cell lung cancer (ES-SCLC) are associated with modest improvements in median OS and PFS. In the KEYNOTE-604 study, first-line pembrolizumab plus etoposide/platinum (EP) significantly improved PFS (HR 0.75; 95% CI, 0.61–0.91; $P = 0.0023$) compared with placebo plus EP in ES-SCLC; OS was also longer with pembrolizumab plus EP vs placebo plus EP but did not reach statistical significance (HR 0.80; 95% CI, 0.64–0.98; $P = 0.0164$). Preclinical and clinical data suggest that blocking the interaction between the T-cell immunoreceptor with immunoglobulin and ITIM domains (TIGIT) and its ligands CD112 and CD155 with the anti-TIGIT humanized monoclonal antibody vibostolimab (MK-7684) yields promising antitumor activity when combined with pembrolizumab, with or without chemotherapy, including in patients with lung cancer. The current phase 3 study, KeyVibe-008 (NCT05224141), is comparing the efficacy and safety of first-line treatment with MK-7684A, a co-formulation of vibostolimab plus pembrolizumab, in combination with EP vs atezolizumab plus EP in patients with ES-SCLC. **Methods:** This multicenter, randomized, double-blind, phase 3 study is enrolling patients aged ≥18 years with histologically or cytologically confirmed, previously untreated ES-SCLC. Patients must have measurable disease per RECIST v1.1; ECOG PS of 0 or 1; no active CNS metastases/carcinomatous meningitis, autoimmune disease, neurologic paraneoplastic syndromes, pneumonitis, or interstitial lung disease; and must provide a pretreatment tumor sample. Patients are randomized 1:1 to receive up to 4 cycles of EP (cisplatin or carboplatin) in combination with MK-7684A (vibostolimab 200 mg + pembrolizumab 200 mg) Q3W or atezolizumab (1200 mg) Q3W, followed by MK-7684A or atezolizumab, respectively, until disease progression, unacceptable AEs, intercurrent illness, protocol violation, or investigator/patient decision. Randomization is stratified by ECOG PS (0 vs 1), LDH (≤ULN vs > ULN), liver metastases (yes vs no), and brain metastases (yes vs no). The primary endpoint is OS. Secondary endpoints include PFS, ORR, and duration of response per RECIST v1.1 by blinded independent central review; safety; and patient-reported outcomes (PROs). Tumor imaging occurs at baseline, every 6 weeks until 48 weeks, and every 9 weeks thereafter until disease progression, start of new anticancer treatment, withdrawal of consent, or death. PROs are assessed using validated instruments including the EORTC quality of life and EuroQol questionnaires. AEs are graded according to NCI CTCAE v5.0. Enrollment is ongoing worldwide. Clinical trial information: NCT05224141. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

TPS8607 **Poster Session**

Phase II study of KN046 in patients with thymic carcinoma who failed immune checkpoint inhibitors.

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Background: Thymic carcinomas are the most aggressive form of thymic epithelial tumors. They are often not operable and are more resistant to chemotherapy than thymomas. Thymic carcinoma is sensitive to pembrolizumab. However, most patients who respond to pembrolizumab eventually recur. Recently, molecules that combine PD(L)1 and CTLA-4 have been developed for solid tumor patients, with the hope that targeted therapy will be more effective than standard of care. KN046 is a bi-specific antibody against PD-L1 and CTLA-4 with a much higher affinity of the anti-PD-L1 portion and a weaker affinity for anti-CTLA-4, potentially leading to less autoimmune disorders and toxicities. We developed a Phase II study to test the hypothesis that dual PD-L1 and CTLA-4 inhibition with KN046 may represent a safe and tolerable option for patients with advanced thymic carcinoma who have progressed on prior treatment with immune checkpoint inhibitors. **Methods:** Key eligibility criteria include thymic carcinoma with progression after treatment with an immune checkpoint inhibitor with no limit to prior lines of therapy, adequate organ function and performance status. History of prior or current autoimmune disorders are not allowed and history of baseline positive anti-acetylcholine receptor (AChR) autoantibody are not allowed. KN046 will be administered intravenously at 5 mg/kg every 2 weeks until progression or excessive toxicity for up to 2 years. A cycle is defined as 2 treatments (28 days). The primary objective is to evaluate the antitumor activity of KN046 in patients with thymic carcinoma as measured by overall response rate defined by RECIST 1.1 criteria. The secondary objectives are to assess the safety and tolerability of KN046 including safety as measured by the number of adverse events (CTCAE 5.0), duration of response (RECIST 1.1) from first documented response to the date of first documented disease progression, progression-free survival, and overall survival. Exploratory objectives include the association of biomarkers (PD-L1 expression, tumor immune microenvironment determined by multiplex IHC, tumor mutational burden, T-cell inflamed gene expression profile) and clinical efficacy parameters. We will also characterize the safety laboratory results (AChR autoantibodies and creatinine kinase) and the occurrence of adverse events of interest. Simon's two-stage design will be used. The null hypothesis that the true response rate is 5% will be tested against a one-sided alternative of target response rate ≥20%. In the first stage, 10 patients will be accrued. If there are no responses in the first stage, then the study will be stopped. Otherwise, 19 additional patients will be accrued for a total of 29 patients. The null hypothesis will be rejected if ≥4 responses are observed in 29 patients, with a type 1 error rate of 0.05 and power of 80%. The study was activated at Weill Cornell Medicine in December 2021. Clinical trial information: NCT04925947. Research Sponsor: Jiangsu Alphamab Biopharmaceuticals.