**9000** **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

**Randomized phase II clinical trial of cisplatin/carboplatin and etoposide (CE) alone or in combination with nivolumab as frontline therapy for extensive-stage small cell lung cancer (ES-SCLC): ECOG-ACRIN EA5161.** *First Author: Ticiana Leal, University of Wisconsin Carbone Cancer Center, Madison, WI*

**Background:** Immune checkpoint inhibition is now given in combination with chemotherapy for first line (1L) therapy of extensive stage small cell lung cancer (ES-SCLC). We conducted a randomized phase II study of nivolumab (anti-PD1) in combination with platinum-etoposide (CE) as 1L treatment for patients with ES-SCLC (EA5161, NCT03382561). **Methods:** Patients with measurable (RECIST v1.1) ES-SCLC, ECOG performance status 0 or 1, who had not received prior systemic treatment for ES-SCLC were enrolled. Patients were randomized 1:1 to nivolumab 360 mg + CE every 21 days for 4 cycles followed by maintenance nivolumab 240 mg every 2 weeks until progression or up to 2 years (arm A) or CE every 21 days for 4 cycles followed by observation (arm B). Prophylactic cranial irradiation (PCI) was permitted at the investigator's discretion. Investigator's choice of cisplatin or carboplatin was allowed across both arms. The primary endpoint was PFS in eligible and treated patients. Secondary endpoints included OS, ORR, and safety. Adverse events (AEs) were graded per NCI-CTCAE v4.0. **Results:** This study was activated in May 2018 and completed accrual in December 2018. 160 patients were enrolled. Baseline characteristics were well balanced between arms. In the ITT population (n = 160), nivolumab + CE significantly improved the PFS compared to CE with HR 0.65 (95% CI, 0.46, 0.91; p = 0.012); mPFS 5.5 versus 4.6 months, respectively. Secondary endpoint of OS was also improved with nivolumab + CE versus CE with HR 0.67 (95% CI, 0.46, 0.98; p = 0.038); mOS 11.3 versus 8.5 months. Among patients who initiated study therapy, nivolumab + CE significantly improved the PFS compared to CE with HR 0.68 (95% CI, 0.48, 1.00; p = 0.047); mPFS 5.5 versus 4.7 months, respectively; in this population, OS was also improved with nivolumab + CE versus CE with HR 0.73 (95% CI, 0.49, 1.11; p = 0.14); mOS 11.3 versus 9.3 months. The ORR was 52.29% versus 47.71%. The incidence of treatment-related grade 3/4 AEs was 77% versus 62% and AEs leading to discontinuation 6.21% versus 2.07%. Ten patients remain on maintenance nivolumab. Lethal adverse events independent of treatment were similar between the two arms (9 in arm A; 7 in arm B). **Conclusions:** The addition of nivolumab to CE as 1L treatment for ES-SCLC significantly improved PFS and OS. No new safety signals were observed. Clinical trial information: NCT03382561. Research Sponsor: ECOG-ACRIN.

**9001** **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

**KEYNOTE-604: Pembrolizumab (pembro) or placebo plus etoposide and platinum (EP) as first-line therapy for extensive-stage (ES) small-cell lung cancer (SCLC).** *First Author: Charles M. Rudin, Memorial Sloan Kettering Cancer Center, New York, NY*

**Background:** Pembro monotherapy showed durable antitumor activity as third-line or later therapy for metastatic SCLC, leading to FDA approval in that setting. KEYNOTE-604 was a double-blind, phase 3 study of pembro + EP vs placebo + EP as first-line therapy for ES-SCLC (NCT03066778). **Methods:** Eligible patients (pts) with previously untreated ES-SCLC and no untreated CNS metastases were randomized 1:1 to pembro 200 mg Q3W or saline placebo for up to 35 cycles plus 4 cycles of standard-dose EP. Pts with CR or PR after cycle 4 could receive PCI at investigator discretion. Randomization was stratified by platinum choice (carboplatin vs cisplatin), ECOG PS (0 vs 1), and LDH (≤ULN vs > ULN). Primary endpoints were OS and PFS (RECIST v1.1, blinded central review) in the ITT population. ORR, DOR, and safety were secondary endpoints. OS and PFS treatment differences were assessed by the stratified log-rank test. The protocol specified 2 interim analyses (IAs) and a final analysis (FA). Prespecified efficacy boundaries were one-sided $P = 0.0048$ for PFS at IA2 (prespecified final PFS analysis) and 0.0128 for OS at FA. **Results:** 453 pts were randomized. 223/228 pts assigned to pembro + EP and 222/225 assigned to placebo + EP received ≥1 dose of assigned treatment; 1 pt assigned to pembro + EP received placebo + EP in error. Median age was 65 y, 74% had ECOG PS 1, and 57% had LDH > ULN; more pts in the pembro + EP arm had baseline brain metastases (14% vs 10%). At FA (median follow-up, 21.6 mo), 9% of pts in the pembro + EP arm and 1% in the placebo + EP arm remained on study treatment; 12% and 14% received PCI. At IA2 (median follow-up, 13.5 mo), pembro + EP significantly improved PFS in the ITT population (HR 0.75 [95% CI 0.61-0.91], $P = 0.0023$; median 4.5 vs 4.3 mo). At FA, pembro + EP prolonged OS in the ITT population, but the significance threshold was not met (HR 0.80 [95% CI 0.64-0.98], $P = 0.0164$; median 10.8 vs 9.7 mo). In a post hoc analysis of OS in the as-treated population, the nominal $P$ value was smaller than the significance threshold (HR 0.78 [95% CI 0.63-0.97], $P = 0.0124$). ORR at FA was 71% for pembro + EP vs 62% for placebo + EP; median DOR was 4.2 vs 3.7 mo. Observed AEs were as expected; any-cause AEs were grade 3-4 in 77% vs 75%, grade 5 in 6% vs 5%, and led to discontinuation in 15% vs 6%. **Conclusions:** Pembro + EP significantly improved PFS and prolonged OS compared with placebo + EP as first-line therapy for pts with ES-SCLC. No unexpected toxicities were seen with pembro + EP. These data support the benefit of pembro-containing regimens for ES-SCLC. Clinical trial information: NCT03066778. Research Sponsor: Merck & Co., Inc., Kenilworth, NJ, USA.

**9002** **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

**Durvalumab ± tremelimumab + platinum-etoposide in first-line extensive-stage SCLC (ES-SCLC): Updated results from the phase III CASPIAN study.** *First Author: Luis G. Paz-Ares, Hospital Universitario 12 de Octubre, Madrid, Spain*

**Background:** CASPIAN is an open-label, Phase 3 study of durvalumab (D) ± tremelimumab (T) + etoposide and either cisplatin or carboplatin (EP) for pts with 1L ES-SCLC. At the planned interim analysis (data cutoff Mar 11, 2019; 63% maturity), D + EP demonstrated a statistically significant improvement in OS compared with EP alone (HR 0.73 [95% CI 0.59–0.91]; p=0.0047). Here we present a planned updated analysis of OS for D + EP vs EP and the first results for D + T + EP vs EP. **Methods:** Treatment-naïve pts with ES-SCLC (WHO PS 0/1) were randomized 1:1:1 to D 1500 mg + EP q3w, D 1500 mg + T 75 mg + EP q3w, or EP q3w. In the IO arms, pts received 4 cycles of EP + D ± T, followed by maintenance D 1500 mg q4w until disease progression. Pts received one additional dose of T 75 mg post EP in the D + T + EP arm. In the EP arm, pts received up to 6 cycles of EP and optional PCI (investigator's discretion). The two primary endpoints were OS for D + EP vs EP and for D + T + EP vs EP. **Results:** 268, 268 and 269 pts were randomized to D + EP, D + T + EP and EP, respectively; baseline characteristics were generally well balanced across arms. As of Jan 27, 2020, the median follow-up was 25.1 mo, 82% maturity. D + EP continued to demonstrate improvement in OS vs EP, with a HR of 0.75 (95% CI 0.62–0.91; nominal p=0.0032); median OS 12.9 vs 10.5 mo, respectively. 22.2% of pts were alive at 2 y with D + EP vs 14.4% of pts with EP. D + T + EP numerically improved OS vs EP, however this did not reach statistical significance per the prespecified statistical plan: HR 0.82 (95% CI 0.68–1.00; p=0.0451 [p≤0.0418 required for stat sig]); the median OS was 10.4 mo and 23.4% of pts were alive at 2 y. Secondary endpoints of PFS and ORR remained improved with D + EP vs EP and will be presented. Confirmed investigator-assessed ORR was similar for D + T + EP vs EP (58.4% vs 58.0%). Median PFS was similar for D + T + EP vs EP (4.9 mo vs 5.4 mo), but the 12-mo PFS rate was numerically higher (16.9% vs 5.3%); PFS HR 0.84 (95% CI 0.70–1.01). In the D + EP, D + T + EP and EP arms, respectively, incidences of all-cause AEs of Grade 3/4 were 62.3%, 70.3% and 62.8%; AEs leading to discontinuation 10.2%, 21.4% and 9.4%; and AEs leading to death 4.9%, 10.2% and 5.6%. **Conclusions:** The addition of durvalumab to EP continued to demonstrate improvement in OS compared with a robust control arm, further supporting this regimen as a new standard of care for 1L ES-SCLC offering the flexibility of platinum choice. No additional benefit was observed when T was combined with D + EP in this pt population. Safety findings in all arms remained consistent with the known safety profiles of all agents. Clinical trial information: NCT03043872. Research Sponsor: AstraZeneca.

**9003** **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

**PrE0505: Phase II multicenter study of anti-PD-L1, durvalumab, in combination with cisplatin and pemetrexed for the first-line treatment of unresectable malignant pleural mesothelioma (MPM)—A PrECOG LLC study.** *First Author: Patrick M. Forde, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD*

**Background:** First-line CP was FDA-approved in 2004 for unresectable MPM. Given the role of inflammation in MPM and promising responses to PD-1 pathway blockade in pretreated MPM, we conducted a phase 2 single arm study of the anti-PD-L1 antibody, durvalumab (durva), combined with CP for patients (pts) with untreated MPM of any subtype. **Methods:** Eligible pts were treatment-naïve with surgically unresectable MPM. Primary endpoint was overall survival (OS); pts received up to 6 cycles of durva-CP, followed by maintenance durva up to 1 year. Carboplatin was permitted for pts with baseline hearing or renal impairment. The first 15 pts were monitored for dose-limiting toxicities (DLTs). Secondary endpoints included toxicity, objective response by modified RECIST, progression-free survival (PFS), and correlative analyses. With a sample size of 55 patients and 32 events, the study had 90% power to detect a 58% improvement in median OS from 12 months (m) (historical control) to 19 m with durva-CP. **Results:** PrE0505 enrolled 55 patients at 15 US-based sites between 06/2017 and 06/2018. Histologic subtypes were epithelioid (75%), biphasic (11%), sarcomatoid (13%), and desmoplastic (2%). There were no DLTs during the run-in period. As of January 2020 the median follow up is 20.6 m and 29 deaths have occurred. The median OS at the time of report is 21.1 m. The 12 m OS rate was 70% with a 2 sided 95% confidence interval (56%, 81%) and two-sided 80% CI (62%, 78%). Analyses for the secondary endpoints were ongoing at abstract submission. Exome sequencing, TCR sequencing and dual PD-L1/CD8 staining have been completed on baseline tumors from at least 45 of the 55 patients enrolled as well as RNA sequencing for those with adequate tissue. Initial results show that tumors harbored an average tumor mutation burden of 22 somatic sequence alterations and varying levels of aneuploidy were detected. **Conclusions:** The combination of chemotherapy with durvalumab delivered a promising median OS for previously untreated pts with unresectable MPM. Full results from the study along with the extensive correlative analyses performed will be reported. The phase 3 PrE0506/DREAM3R trial evaluating CP-durvalumab versus CP alone will commence enrollment in the United States and Australia in 2020. Clinical trial information: NCT02899195. Research Sponsor: AstraZeneca, U.S. National Institutes of Health.

**9004** **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

**Randomized phase II study on gemcitabine with or without ramucirumab as second-line treatment for advanced malignant pleural mesothelioma (MPM): Results of Italian Rames Study.** *First Author: Maria Pagano, Oncology Unit, Clinical Cancer Center, AUSL-IRCCS Reggio Emilia, Reggio Emilia, Italy*

**Background.** The RAMES Study (EudraCT Number 2016-001132-36) is a multicenter, double-blind, randomized phase II trial exploring the efficacy and the safety of the addition of ramucirumab to gemcitabine as the second-line treatment in MPM patients (pts) after platinum/pemetrexed regimens. **Methods.** The pts were assigned (1:1) to receive Gemcitabine 1000 mg/m$^2$ i*v* on days 1 and 8 every 21 days with Placebo (Arm A) or Ramucirumab 10 mg/kg i*v* on day 1, of a 21-day cycle (Arm B), until tolerability or progressive disease. Pts was stratified by ECOG/PS (0-1 vs 2), age ($\leq$ 70 vs $>$ 70 yrs), histology (epithelioid vs non-epithelioid) and time to progression (TTP) after first-line therapy. The primary endpoint was overall survival (OS). Assuming a proportion of OS equal to 40% at 1 year in arm A, a 12% absolute improvement in OS at 1 yrs was expected in Arm B (hazard ratio = 0.70).114 events (156 subjects) are required for a one-sided log-rank test with $\alpha$ = 0.15 to have 80% power. **Results.** From December 2016 to July 2018, 164 pts were randomized, 81 pts in Arm A and 80 Arm B; 3 pts were randomized but not treated. Characteristics of pts were: median age 69 yrs (44-81), males 119 (73.9%), females 42 (26.1%); ECOG/PS0 96 (59.6%) ECOG/PS1-2 65 (40.4%); histotype epithelioid 132 (81.9%), non-epithelioid 29 (18.1%); stage III 98 (60.7%), stage IV 60 (37.3%), 3 (2.0%) missing; asbestos exposure assessed 80 (49.7%). Median of courses was 3.50 in Arm A and 7.50 in Arm B. OS was significantly longer in Arm B with median 13.8 mths (70% CI 12.7-14.4) vs Arm A with 7.5 mths (70% CI 6.9-8.9), HR 0.71 (70% CI 0.59-0.85, p = 0.057). OS at 6 and 12 mths was in Arm A 63.9% and 33.9%, and in Arm B 74.7% and 56.5%, respectively. In Arm B OS was not correlated to TTP at first-line therapy (13.6 mths in TTP $\leq$6 mths and 13.9 mths in TTP $>$ 6 mths) and histotypes (13.8 months in the epithelioid and 13.0 months in non-epithelioid). No significant differences in thromboembolism G3-4 events were observed in Arm A vs Arm B (p= 0.64). None hypertension G3-4 was reported in Arm A vs 5 pts (6.3%) in Arm B (p= 0.022). No significant differences in G3-4 haematological toxicities between the two arms were reported. **Conclusion:** In the RAMES Study the addition of Ramucirumab to Gemcitabine significantly improved OS regardless of age of pts, tumor histotype and TTP at the first-line treatment. Gemcitabine plus Ramucirumab can be considered a manageable regimen in second-line treatment of advanced MPM pts.Clinical trial information: NTC03560973. Research Sponsor: None.

**9005** **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

**CTONG1104: Adjuvant gefitinib versus chemotherapy for resected N1-N2 NSCLC with EGFR mutation—Final overall survival analysis of the randomized phase III trial 1 analysis of the randomized phase III trial.** *First Author: Yi-Long Wu, Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, School of Medicine, South China University of Technology, Guangzhou, China*

**Background:** ADJUVANT-CTONG1104, a randomized phase 3 trial showed adjuvant gefitinib treatment significantly improved disease-free survival (DFS) vs standard doublet chemotherapy in patients (pts) with epidermal growth factor receptor (*EGFR*) mutation-positive resected stage II-IIIA (N1-N2) non-small-cell lung cancer (NSCLC). 5-year survival rate of N1N2 were 38%-50% in IASLC staging system. Here, we present the final overall survival (OS) results from the study. **Methods:** From Sep 2011 to April 2014, 222 patients, aged 18-75 years, with *EGFR* activating mutation through completely resection and diagnosed as stage II-IIIA (N1-N2) NSCLC pathologically from 27 sites were enrolled. The enrolled patients were 1:1 randomized to receive adjuvant gefitinib (250 mg once per day) for 24 months (G, n=111) or vinorelbine (25 mg/m$^2$, d1 and d8) plus cisplatin (75 mg/m2, d1) every 3 weeks for 4 cycles (C, n=111). The primary endpoint was DFS in the ITT population. Secondary endpoints included OS, 3 and 5-year DFS rate, 5-year OS rate. The subsequent therapy data were collected, including crossover from C to G, re-challenge TKI and other treatment. Data cut-off date was Jan. 13, 2020. **Results:** A median follow-up was 76.9 months. The median OS (mOS) was 75.5 months based on 95 (42.8%) events in ITT whole population. The mOS was 75.5m in G arm and 79.2m in C arm (HR 0.96, 95%CI 0.64-1.43, p=0.823). The 3, 5-year OS rate were 68.6%, 53.8% in G and 67.5%, 52.4% in C respectively. DFS in 3, 5-y were 40.3%, 23.4% in G and 33.2%, 23.7% in C, respectively ($P_{3\text{-}y}$=0.395, $P_{5\text{-}y}$=891). All predefined subgroups including age, gender, lymph node, EGFR mutation type had no significant difference in statistics but in favor of G arm in trend. Subsequent treatment especially targeted therapy contributed most to OS (HR = 0.46, 95% CI 0.26 – 0.83). Median OS of patients receiving subsequent target therapy was75.5m (n=35), 36.4m in other treatment (n=33; (P$<$0.001). For G mOS were 75.5 (n=15; target therapy) and 35.0 (n=18; other, p$<$0.001), for C 62.8m (n=20) and 46.8m (n=15; p=0.251). The RR was 26.7%, DCR 66.7%, mPFS 14.1m and mOS 19.6m for patients with rechallenged EGFR TKI in G arm (n=15). No novel unexpected SAE was observed during follow up. **Conclusion** The DFS survival advantage did not translate to OS difference in ADJUVANT trial. The OS with 75.5m was the best one of survival in completely resected N1N2 NSCLC comparing with historical data and sequent TKI treatment contribute to overall survival. Clinical trial information: NCT01405079. Research Sponsor: Chinese Thoracic Oncology Group (CTONG), Chinese Thoracic Oncology Group (CTONG).

**9006** **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

**Randomized phase III study of irinotecan/cisplatin (IP) versus etoposide/cisplatin (EP) for completely resected high-grade neuroendocrine carcinoma (HGNEC) of the lung: JCOG1205/1206.** *First Author: Hirotsugu Kenmotsu, Division of Thoracic Oncology, Shizuoka Cancer Center, Shizuoka, Japan*

**Background:** In the WHO classification, small cell lung cancer (SCLC) and large cell neuroendocrine carcinoma (LCNEC) are considered as high-grade neuroendocrine carcinoma (HGNEC) of the lung. Although there were no randomized trials evaluating adjuvant chemotherapy for patients (pts) with resected HGNEC, EP was considered to be a standard regimen for this population. A phase III study showed the superiority of IP to EP in pts with extensive stage SCLC (JCOG9511). **Methods:** Pts with completely resected HGNEC were randomized in a 1:1 ratio to receive either etoposide (100 mg/m$^2$, days 1-3)/cisplatin (80 mg/m$^2$, day 1) or irinotecan (60 mg/m$^2$, days 1, 8, 15)/cisplatin (60 mg/m$^2$, day 1), using the minimization method according to sex, pathologic stage, histology and institution. The primary endpoint was changed from overall survival (OS) to relapse-free survival (RFS) during the study period. We assumed a 3-year RFS of 59% of EP arm and 72% of IP arm (hazard ratio (HR) of 0.623). Planned sample size was 220 in total to give a power of 80% with a one-sided alpha of 5%, an accrual period of 6 years and a follow-up period of 3 years. **Results:** Between April 2013 and October 2018, 221 pts with a median age of 66 years, pathological stage I (54%), SCLC (53%), were randomly assigned to the EP arm (n = 111) or the IP arm (n = 110). In the second interim analysis, the predictive probability that IP would be superior to EP at the time of the primary analysis was 15.9%, which led to early termination of the trial. With a median follow-up of 24.1 months, 3-year RFS was 65.4% versus 69.0% with HR of 1.076 (95% CI, 0.666-1.738; log-rank test, one-sided *P*= 0.619). In the subgroup analyses of histology, 3-year RFS in SCLC was 65.2% versus 66.5% with HR of 1.029 (95% CI, 0.544-1.944), and 3-year RFS in LCNEC was 66.5% versus 72.0% with HR of 1.072 (95% CI, 0.517-2.222). Overall survival at 3 years was 84.1% versus 79.0% with HR of 1.539 (95% CI, 0.760-3.117). Proportions of treatment completion were 87.4% (EP) and 72.7% (IP). Incidences (EP/IP) of grade 3 or 4 febrile neutropenia (20.2/3.7%) or neutropenia (97.2/35.8%) were more common in EP. Grade 3 or 4 diarrhea (0.9/8.3%) or anorexia (6.4/11.1%) were more common in IP. One treatment-related death due to tracheal bleeding was observed in IP. **Conclusions:** This study failed to show the superiority of IP to EP in RFS for pts with completely resected HGNEC. EP is still a standard treatment for this population. Clinical trial information: UMIN000010298. Research Sponsor: the Japan Agency for Medical Research and Development.

**9007** **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

**Randomized phase II trial comparing the efficacy of standard-dose with high-dose twice-daily thoracic radiotherapy (TRT) in limited disease small-cell lung cancer (LD SCLC).** *First Author: Bjorn Henning Gronberg, Department of Clinical and Molecular Medicine, NTNU, Norwegian University of Science and Technology and Department of Oncology, St. Olav's Hospital, Trondheim University Hospital, Trondheim, Norway*

**Background:** Concurrent chemoradiotherapy is the standard treatment of LD SCLC. Some patients are cured, but most relapse and better treatment is needed. 45 Gy in 30 fractions BID is the most recommended TRT-schedule. Studies suggest that a higher TRT-dose might prolong survival, but hitherto, this has not been confirmed in randomized trials. We aimed to investigate whether high-dose BID TRT of 60 Gy in 40 fractions was feasible, tolerated, and improved survival. **Methods:** Patients $>$ 18 years, performance status (PS) 0-2 and confirmed LD SCLC were to receive 4 courses of platinum/etoposide and were randomized to BID TRT of 60 or 45 Gy. Responders were offered prophylactic cranial irradiation of 25-30 Gy. Primary endpoint was 2-year survival; secondary endpoints were toxicity, progression free survival (PFS), and overall survival (OS). To demonstrate a 25% improvement of 2-year survival from 53% to 66% with a one-sided $\alpha$ = .10 and $\beta$ = .80, 75 patients were required on each arm. **Results:** Between 2014-2018, 176 patients were enrolled at 22 Scandinavian hospitals. 160 completed TRT per protocol and were eligible for the present analyses (60 Gy: n = 84, 45 Gy: n = 76). Median age was 65, 58% women, 90% PS 0-1. There were no significant differences in grade 3–4 esophagitis (60 Gy: 19%, 45 Gy: 18%, p = .92) or grade 3–4 pneumonitis (60 Gy: 4%, 45 Gy: 0%, p = .10). There was a trend towards more neutropenic infections on the 45 Gy arm (60 Gy: 21%, 45 Gy: 36%, p = .05). There were no significant differences in other grade 3-4 toxicity. Three patients died during the study treatment period (60 Gy: one neutropenic infection and one aortic dissection; 45 Gy: one thrombocytopenic bleeding). There were no statistically significant differences in response rates (60 Gy: 88% [95% CI 81-95], 45 Gy: 85% [95% CI 76-93], p = .52) or median PFS (60 Gy: 20 months [95% CI 11-29], 45 Gy: 14 months [95% CI 10-19], p = .31). Significantly more patients on the 60 Gy arm were alive after 2 years (60 Gy: 73% [95% CI 63-83], 45 Gy: 46% [95% CI 36-60], p = .001), and they had a significantly longer median overall survival (60 Gy: 42 months [95% CI 32-51], 45 Gy: 23 months [95% CI 17-28], HR .63 [95% CI .41-.96], p = .031). **Conclusions:** LD SCLC patients who received BID TRT of 60 Gy had a statistically significant and numerically substantial benefit in terms of 2-year survival (primary endpoint) and median overall survival compared with those who received BID TRT of 45 Gy. The higher TRT dose did not cause more toxicity than the standard dose. Clinical trial information: NCT02041845. Research Sponsor: The Norwegian Cancer Society and The Liaison Committee for Education, Research and Innovation in Central Norway.

**9008 Poster Discussion Session; Displayed in Poster Session (Board #201), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

**Phase II study of pembrolizumab (pembro) plus platinum doublet chemotherapy and radiotherapy as first-line therapy for unresectable, locally advanced stage III NSCLC: KEYNOTE-799.** *First Author: Salma K. Jabbour, Department of Radiation Oncology, Rutgers Cancer Institute of New Jersey, Robert Wood Johnson Medical School, Rutgers University, New Brunswick, NJ*

**Background:** KEYNOTE-799 (NCT03631784) evaluates pembro plus concurrent chemoradiation therapy (CCRT) in pts with unresectable, locally advanced stage III NSCLC. **Methods:** In this phase 2, nonrandomized, open-label trial, pts with previously untreated, unresectable, pathologically confirmed stage IIIA–C NSCLC with measurable disease (RECIST 1.1) received up to 17 cycles of pembro 200 mg Q3W starting with cycle 1 plus standard thoracic radiotherapy (60 Gy in 30 daily 2-Gy fractions) in cycles 2–3 and investigator's choice of paclitaxel 200 mg/m$^2$ + carboplatin AUC 6 Q3W for cycle 1, then paclitaxel 45 mg/m$^2$ + carboplatin AUC 2 QW for cycles 2–3 (cohort A), or cisplatin 75 mg/m$^2$ + pemetrexed 500 mg/m$^2$ Q3W (nonsquamous only) in cycles 1–3 (cohort B). Primary endpoints were ORR (CR/PR per RECIST 1.1 by blinded independent central review) and rate of grade ≥3 pneumonitis (per NCI CTCAE v4.0). CIs were estimated using the Clopper-Pearson method. Safety was assessed in all treated patients; efficacy was assessed in pts with ≥15 wks follow-up. **Results:** As of Jan 3, 2020, 112 and 73 pts have been enrolled in cohorts A and B, respectively; 63 in cohort A and 52 in cohort B continue on treatment. Median (range) follow up was 8.3 (0.7–14.0) mo in cohort A and 5.8 (0.2–13.7) mo in cohort B. ORR (90% CI) was 67.0% (58.9%–74.3%) in cohort A and 56.6% (44.4%–68.2%) in cohort B (Table). Grade ≥3 pneumonitis occurred in 9 pts (8.0%; 90% CI, 4.3%–13.6%) in cohort A and 4 pts (5.5%; 90% CI, 1.9%–12.1%) in cohort B. Treatment-related grade ≥3 AEs occurred in 72 pts (64.3%) in cohort A and 30 pts (41.1%) in cohort B. 4 pts had treatment-related grade 5 pneumonitis (all in cohort A). Enrollment is complete for cohort A and ongoing in cohort B. **Conclusions:** Pembro plus CCRT shows promising antitumor activity in pts with unresectable, locally advanced stage III NSCLC. Toxicity was as anticipated with pembro plus CCRT. 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=53 |
|---|---|---|
| **ORR, % (90% CI)** | 67.0 (58.9–74.3) | 56.6 (44.4–68.2) |
| **Median (range) duration of response, mo** | NR (1.6+ to 10.5+) | NR (1.7+ to 10.5+) |
| **DOR ≥ 6 mo,† %** | 91.1 | 100 |
| **6-mo PFS rate,† %** | 81.4 | 85.2 |
| **6-mo OS rate,† %** | 87.2 | 94.8 |

*Pts with ≥15 wks follow-up.
†Kaplan-Meier estimate.

**9009 Poster Discussion Session; Displayed in Poster Session (Board #202), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

**A phase I safety and feasibility study of neoadjuvant chemoradiation plus pembrolizumab followed by consolidation pembrolizumab in resectable stage IIIA non-small cell lung cancer.** *First Author: Christopher Lemmon, Cleveland Clinic Foundation, Cleveland, OH*

**Background:** Patients (pts) with resectable stage IIIA non-small cell lung cancer (NSCLC) have high rates of recurrence despite concurrent chemoradiation (CRT) followed by surgery. Immune checkpoint inhibitor consolidation has improved outcomes in unresectable stage III pts. Here we report the addition of concurrent neoadjuvant pembrolizumab (P) to CRT in stage IIIA patients to determine the safety and feasibility of this approach. **Methods:** Pts with stage IIIA NSCLC deemed resectable by a thoracic surgeon received neoadjuvant CRT consisting of cisplatin, etoposide, and concurrent P (200mg every 3 weeks x 3) with 45 Gy in 25 fractions. Pts without progression underwent resection followed by 6 months of consolidation P. The primary objective was feasibility and safety (defined as ≤30% grade 3 or higher pulmonary toxicity or any grade 4/5 nonhematologic toxicity). Ten pts were to be enrolled in Part 1, and if 2 or fewer pts had events then an additional 10 pts were to be enrolled. Secondary objectives were progression free survival (PFS), overall response rate (ORR), and pathologic complete response rate (pCR). **Results:** The median age of 9 enrolled pts was 66 years (range 49-76). 67% were female. 8 pts were assessable for radiographic response with an ORR of 75%. One pt came off study for progression prior to surgery and one had pleural metastases found during surgery so resection was aborted. Six pts underwent complete resection with a pCR rate of 67% (4/6). Consolidation P was started on 4 pts, with 3 completing treatment and 1 declined further treatment after 3 cycles. Median follow-up is 19.6 months and median PFS has not been reached. None of the patients who underwent resection have recurred. Serious adverse events were reported in all 9 pts with most significant being 2 grade 5 events: 1 due to pneumocystis pneumonia after resection but prior to consolidation, and 1 due to cardiac arrest during the neoadjuvant phase. Grade 3 events included 1 episode each of pneumonitis, bronchopleural fistula, acute kidney injury, colon perforation, and febrile neutropenia. **Conclusions:** The addition of P to neoadjuvant CRT in resectable stage IIIA pts resulted in a high pCR rate at resection. Although the relationship between grade 5 events and the addition of P was not clear, the stopping rule for infeasibility was met. As other larger studies are underway, the trial was halted rather than amended. This investigator initiated trial was funded by Merck. Clinical trial information: NCT02987998. Research Sponsor: Merck.

**9010 Poster Discussion Session; Displayed in Poster Session (Board #203), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

**Consolidation nivolumab/ipilimumab versus nivolumab following concurrent chemoradiation in patients with unresectable stage III NSCLC: A planned interim safety analysis from the BTCRC LUN 16-081 trial.** *First Author: Melissa Yan, Indiana University Melvin and Bren Simon Cancer Center, Indianapolis, IN*

**Background:** Consolidation PD-1/PD-L1 inhibition after chemoradiation (CRT) for unresectable stage III NSCLC improves overall survival. In stage IV NSCLC, the combination of nivolumab/ipilimumab improved overall survival compared to chemotherapy in patients with PD-L1 > 1% and performed favorably in patients with PD-L1 < 1%. The safety of consolidation nivolumab/ipilimumab after CRT has not been previously assessed. **Methods:** In this randomized, multi-center, phase II study, a total of 105 planned pts with unresectable stage IIIA/IIIB NSCLC will receive chemoradiation, then randomize 1:1 to either nivolumab 480mg IV q4 wks (Arm A) or nivolumab 3mg/kg IV q2 wks + ipilimumab 1mg/kg IV q6 wks (Arm B), for up to 24 wks. In this planned interim analysis, the safety of the first 50 patients, with 25 patients treated on each arm, is assessed. **Results:** From 9/2017 to 6/2019, the first 50 patients were accrued and analyzed for this planned safety analysis. Baseline characteristics for Arm A/B: median age 64/62, stage IIIA 17/16, stage IIIB 8/9, nonsquamous 14/13, squamous 11/12. The median number of cycles completed in Arm A was 6 (range 1-6, cycle length q4 wks) and in Arm B was 4 (range 1-4, cycle length q6 wks). The rate of treatment-related adverse events leading to discontinuation of therapy was 16% in Arm A and 40% in Arm B. The percentage of patients with any > grade 3 adverse event (AE) was 32% in Arm A and 44% in Arm B. With respect to immune-related AE (irAEs), the percentage of patients with any ≥grade 2 was 44% in Arm A and 60% in Arm B; any ≥ grade 3 irAEs was 16% in Arm A and 32% in Arm B. The incidence of > grade 2 pneumonitis was 16% in Arm A and 36% in Arm B. The percentage of patients with > grade 3 pneumonitis was 4% in Arm A and 20% in Arm B. No treatment-related deaths were reported on either arm. **Conclusions:** In the post chemoradiation setting, the incidence of > grade 3 toxicity was greater in the consolidative nivolumab/ipilimumab arm, which resulted in a higher rate of treatment discontinuation than nivolumab alone. The Data and Safety Monitoring Board recommended continued enrollment without modification to the trial and the study currently remains open to accrual (66 of 105 patients have been enrolled as of 1/17/2020). Clinical trial information: NCT03285321. Research Sponsor: Bristol-Myers Squibb.

**9011 Poster Discussion Session; Displayed in Poster Session (Board #204), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

**Atezolizumab plus stereotactic ablative therapy for medically inoperable patients with early-stage non-small cell lung cancer.** *First Author: Karen Kelly, University of California Davis Comprehensive Cancer Center, Sacramento, CA*

**Background:** Stereotactic ablative radiation therapy (SABR) is the standard-of-care for medically inoperable, early stage non-small cell lung cancer (NSCLC), but regional and distant failures remain problematic. Based on our *in vivo* data showing synergy between radiation and immune checkpoint inhibitors (ICI) and the known efficacy and mild toxicity profile of ICI in NSCLC, we conducted a phase I study to determine the maximum tolerated dose of neoadjuvant, concurrent, and adjuvant atezolizumab with SABR for early stage NSCLC patients (pts). **Methods:** Eligible pts had histologically confirmed T1-3 NSCLC with at least one feature predictive of increased recurrence risk: diameter ≥1 cm, SUV ≥6.2 on PET, or moderately/poorly differentiated histology, were medically inoperable or refused surgery and had a Zubrod PS ≤2. Patients received 6 cycles of atezolizumab. A 3+3 dose finding design was employed with 3 dose levels: 3 mg/kg, 10 mg/kg, and 1200 mg flat dosing. SABR was delivered starting cycle 3 to 50 Gy over 4-5 fractions. Dose limiting toxicity (DLT) was assessed during the first 9 weeks. **Results:** 20 pts were enrolled, 15 pts in the dose finding and 5 pts at the recommended phase II dose (RP2D). Patient factors: Medlan age 77; 45% male, 85% smoking history, 85% PS 0-1 and 35% squamous. One pt on dose level 2 had a DLT – a grade 3 rash. Atezolizumab 1200 mg flat dosing was the RP2D. Grade 3 pneumonitis was not observed. Partial responses after 2 cycles were seen in 3/17 evaluable pts (18%) and 1 pt had a minor response. No patient progressed on treatment. PD-L1 expression was 0% 8/13 (62%), >1% - 50% 4/13 (31%), >50% 1/13 (8%) in pts with sufficient tissue. Of 5 pts with PD-L1 expression 3 (60%) were responders and 1 (12.5%) of 8 pts with 0% PD-L1 expression responded. Multi-plex Quantitative Immunofluorescence (QIF) using a T cell activation panel demonstrated to correlate with ICI response was performed on 9 samples (including 2 responders, 1 minor responder). The CD3 QIF score was > two-fold higher in the responders compared to non-responders, and the levels of proliferating and activated T cells were likewise > two-fold higher. Comprehensive stool and serial blood analyses have been completed. Correlative endpoints will be reported along with additional efficacy outcomes. **Conclusions:** Atezolizumab plus SABR is feasible, safe and shows an efficacy signal in medically inoperable early stage NSCLC. This combination will be tested in a randomized phase III trial SWOG/NRG S1914. Funding: This work was supported by the DOD CDMRP W81XWH-15-2-0063 and Genentech. Clinical trial information: NCT02599454. Research Sponsor: DEPARTMENT OF DEFENSE - CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAM, Pharmaceutical/Biotech Company.

**9012 Poster Discussion Session; Displayed in Poster Session (Board #205), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

***KEAP1/NFE2L2* mutations to predict local recurrence after radiotherapy but not surgery in localized non-small cell lung cancer.** *First Author: Michael S Binkley, Stanford University School of Medicine, Stanford, CA*

**Background:** Tumor genotyping in localized non-small cell lung cancer (NSCLC) is not broadly performed due to lack of actionable associations of mutations with treatment or outcome. We sought to identify recurrent mutations in localized NSCLC that are associated with local recurrence (LR) after radiotherapy (RT) or surgery. **Methods:** We identified consecutive patients with NSCLC treated with chemoradiotherapy (CRT), stereotactic ablative radiotherapy (SABR) or surgery from 2009-2018 at our institution with stage IA1-IIIC NSCLC who had genotyping performed on tumor tissue using a targeted gene panel. Our primary objective was to identify somatic tumor mutations that predicted LR after RT but not surgery. We also performed functional screening assays by expressing open reading frame constructs harboring patient-derived mutations in knock-out cell lines generated by CRISPR-Cas9 and evaluating effects on in vitro radioresistance. **Results:** We identified 232 consecutive patients with localized NSCLC (87.1% adenocarcinoma, 10.3% squamous, 2.3% other) who received tumor biopsy or resection specimen and underwent tumor genotyping. 47 patients with locally advanced NSCLC received CRT, 50 patients with early stage NSCLC received SABR, and 135 patients with early stage NSCLC underwent surgical resection. Of all recurrent mutations ( $>$ 5% mutation frequency), only mutations in Kelch-like ECH-associated protein 1 (*KEAP1)* or Nuclear Factor Erythroid 2-Related Factor 2 (*NFE2L2)* genes *($K/N^{MUT}$)* were significantly associated with LR after CRT or SABR, with 2-year LR in the combined RT cohort of 42.4% for $K/N^{MUT}$ versus 12.5% for wildtype (P = 0.005). Furthermore, $K/N^{MUT}$ were present in nearly half of all LR events. Strikingly, there was no significant difference in LR for $K/N^{MUT}$ tumors following CRT versus SABR (P = 0.47). Local recurrence was rare for patients who received surgery (n = 2) and was not associated with *K/N* mutation status (P = 0.60). Functional evaluation by expression of *K/N* mutations in knock-out cell lines revealed that LR only occurred in patients with mutations that induced radioresistance (i.e. pathogenic) but not passenger mutations (P = 0.04). In contrast to genotyping, NFE2L2 target gene expression analysis via RNA-seq did not predict LR (P = 0.93). **Conclusions:** Our findings suggest that *KEAP1/NFE2L2* mutations are a predictive biomarker of clinical radioresistance and a dominant cause of LR after RT. Genotyping for *KEAP1/NFE2L2* mutations could therefore facilitate treatment personalization in localized NSCLC. Research Sponsor: U.S. National Institutes of Health.

**9013 Poster Discussion Session; Displayed in Poster Session (Board #206), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

**A phase II trial of atezolizumab and bevacizumab in patients with relapsed/refractory and unresectable malignant peritoneal mesothelioma.** *First Author: Kanwal Pratap Singh Raghav, The University of Texas MD Anderson Cancer Center, Houston, TX*

**Background:** Malignant peritoneal mesothelioma (MPeM) is an orphan malignancy. No recommended/FDA approved therapies exist for salvage treatment beyond first-line platinum and pemetrexed based chemotherapy. While immune checkpoint inhibition has shown preliminary efficacy in mesotheliomas, data and efficacy is limited in MPeM patients (pts) [objective response rate (ORR) ~ 11%; median progression-free survival (mPFS) ~ 4 months (m); median overall survival (mOS) ~ 11 m]. We aimed to prospectively assess the safety and efficacy of combined anti-PD1 (atezolizumab) and VEGF (bevacizumab) blockade (AtezoBev) in pts with MPeM. **Methods:** In this phase 2 study, eligible pts with histologically confirmed MPeM, ECOG PS 0-1, and prior platinum and pemetrexed treatment were treated with 1200 mg of atezolizumab and 15 mg/kg of bevacizumab IV every 21 days until disease progression, unacceptable toxicity, or withdrawal. Primary endpoint was confirmed ORR by RECIST 1.1 by independent radiology review. Duration of response (DOR), PFS and OS were prespecified secondary endpoints. **Results:** Among 20 enrolled pts (3/2017 - 2/2019), median age was 63 (range, 33-87) years, 12 (60%) were female, 12 (60%) had PS 0, and 2 (10%) had biphasic MPeM. Among 20 evaluable pts (median cycles 14), confirmed ORR was 35% (7 pts; 95% CI: 15.4-59.2) (median DOR 8.8 m). Responses were ongoing in 5/7 (71.4%) pts at data cutoff. The median follow-up was 20.5 months. Six deaths were observed during follow-up, and the 1-year OS was 79% (95% CI: 52 – 91) (median OS ~ NR). Median PFS was estimated as 17.6 m (95% CI: 9.1 – NR). The 1-year PFS was 54% (95% CI: 28 – 74). Grade 3 (no grade 4/5) treatment-emergent adverse events occurred in 10 (50%) pts; most common being hypertension (40%) and anemia (10%). Two (10%) pts had grade 3 immune-related adverse events. Translational studies are ongoing. **Conclusions:** AtezoBev showed promising and durable efficacy in relapsed/refractory MPeM with acceptable safety profile. Ongoing multiomic analyses of pre and on-treatment tissue/liquid biopsies obtained on all these pts will provide additional insight into mechanisms and biomarkers of response and resistance. Clinical trial information: NCT03074513. Research Sponsor: Genentech Inc., MD Anderson Cancer Center

**9014 Poster Discussion Session; Displayed in Poster Session (Board #207), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

**PIT-1: Randomized phase II trail of pemetrexed-cisplatin plus bevacizumab or concurrent thoracic radiation therapy followed by surgery in stage IIIA (N2) nonsquamous non-small cell lung cancer.** *First Author: Kazuya Takamochi, Department of General Thoracic Surgery, Juntendo University School of Medicine, Tokyo, Japan*

**Background:** PIT-1 (Personized Induction Therapy-1) is a multicenter, open-label, randomized phase II study using selection design of platinum doublet chemotherapy plus angiogenesis inhibitor or concurrent thoracic radiation therapy (TRT) as induction therapy followed by surgery in patients with stage IIIA (N2) nonsquamous non-small cell lung cancer (NSCLC) to investigate the efficacy and safety of these treatment strategies. **Methods:** Patients with stage IIIA (pathologically proven N2) nonsquamous NSCLC randomly received (1:1) induction therapy consisting of pemetrexed (500 mg/m$^2$) and cisplatin (75 mg/m$^2$) plus bevacizumab (15 mg/kg) intravenously every 3 weeks for three cycles (arm A) or concurrent TRT (45 Gy in 25 fractions) (arm B) followed by surgery. The primary endpoint was 2-year progression-free survival (PFS) rate and key secondary endpoints included overall survival (OS), the objective response rate (ORR) as defined by the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, the pathological complete remission (pCR) rate, feasibility and toxicity. **Results:** Eighty-eight patients were randomly assigned (each arm, n = 44) between October 2013 and June 2017 and 82 (arm A, n = 42; arm B, n = 40) were treated. Patient demographics were balanced between the two arms. The percentage of patients who received induction therapy followed by surgery was 88.1% (37/42) in arm A and 92.5% (37/40) in arm B. The complete resection rate was 81.1% (30/37) in arm A, and 91.9% (34/37) in arm B. The 2-year PFS rate was 36.8% (95% CI: 22.4-51.2) in arm A, and 50.0% (95% CI: 33.8-64.2) in arm B. The 2-year OS rate was 80.5% (95% CI: 64.7-89.7) in arm A, and 80.0% (95% CI: 64.0-89.5) in arm B. The ORR was 50.0% (21/42) in arm A and 60.0% (24/40) in arm B. The pCR rate was 8.1% (3/37) in arm A and 10.8% (4/37) in arm B. Grade 3 or 4 toxicities occurred during induction therapy in 35.7% of the patients in arm A and 22.5% of the patients in arm B. Grade 3 or 4 surgical complications occurred in 21.4% of the patients in arm A and 20.0% of the patients in arm B. Although no fatal toxicity was observed during induction therapy in either arm, two patients in arm A died after surgery due to bronchopleural fistula. **Conclusions:** The 2-year PFS rate in arm B was higher than that in arm A. Fatal surgical complications were only observed in arm A. Therefore, we chose pemetrexed-cisplatin plus concurrent thoracic radiation therapy as the investigational induction treatment strategy for a future phase III study. Clinical trial information: 000011941. Research Sponsor: None.

**9016 Poster Discussion Session; Displayed in Poster Session (Board #209), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

**SAKK 16/14: Anti-PD-L1 antibody durvalumab in addition to neoadjuvant chemotherapy in patients with stage IIIA(N2) non-small cell lung cancer (NSCLC)—A multicenter single-arm phase II trial.** *First Author: Sacha Rothschild, Department of Medical Oncology, University Hospital Basel, Basel, Switzerland*

**Background:** For patients (pts) with resectable stage IIIA(N2) non-small cell lung cancer (NSCLC) neoadjuvant chemotherapy (chemo) with 3 cycles cisplatin (cis)/docetaxel (doc) followed by surgery is an accepted standard of care leading to a 1-year (yr) event-free survival (EFS) of 48% and a 5-yr overall survival (OS) of 37%. PD-1/PD-L1 inhibitors have recently shown to lead to high response rates in resectable NSCLC. **Methods:** SAKK 16/14 is an open-label single-arm phase II study including 68 pts with resectable NSCLC stage IIIA(N2) (T1-3 N2 M0), irrespective of histological subtype, genomic aberrations or PD-L1 expression status. Neoadjuvant treatment consisted of 3 cycles of cis 100 mg/m$^2$ and doc 85 mg/m$^2$ q3w followed by 2 cycles of durvalumab 750 mg q2w. Durvalumab was continued after surgery q2w for 1 yr. The primary endpoint is EFS at 1 yr. The statistical hypothesis is to improve EFS at 1 yr from 48% based on the SAKK 16/00 study to 65%. Here, we report the primary endpoint and response data from 67 evaluable pts included in the study. **Results:** 68 pts were included from 06/16 to 01/19 and 67 pts (35 males, 32 females) were evaluable. Median age was 61 yrs (range, 41-74). 52 pts (77.6%) had a WHO PS of 0. 95.5% were current or former smokers. The majority of tumors were adenocarcinoma (55.2%) followed by squamous cell histology (32.8%). Clinical stage T1, T2 and T3 were present at diagnosis in 22.4%, 49.3% and 28.4%, respectively. 81.1% of pts underwent resection. The main reason for not undergoing surgery was disease progression (33.3%). Pneumonectomy was performed in 5 pts (9.1%), 43 pts underwent lobectomy and 7 pts bilobectomy. 30-day postoperative mortality was observed in one patient (1.8%). One patient died due to a bleeding complication after surgery most likely not related to neoadjuvant therapy. Radiographic response was 44.8% (95%CI: 32.6-57.4) after neoadjuvant chemo and 59.7% (95%CI: 46.4-71.9) after additional neoadjuvant immunotherapy. 1-yr EFS was 73.3% (90%CI: 62.5-81.4). Results for pathologic remission rate as well as correlation with PD-L1 status will be presented during the meeting. **Conclusions:** We report on treatment outcomes of the largest cohort of pts with resectable stage IIIA(N2) NSCLC receiving perioperative immune checkpoint inhibitor therapy. The addition of perioperative durvalumab to standard of care cis/doc is safe and leads to a high response rate and a very encouraging 1-yr EFS rate that appears substantially higher than with chemo alone. Clinical trial information: NCT 02572843. Research Sponsor: AstraZeneca, Other Foundation.

**9017 Poster Discussion Session; Displayed in Poster Session (Board #210), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

**The anti-disialoganglioside (GD2) antibody dinutuximab (D) for second-line treatment (2LT) of patients (pts) with relapsed/refractory small cell lung cancer (RR SCLC): Results from part II of the open-label, randomized, phase II/III distinct study.** *First Author: Martin Edelman, Fox Chase Cancer Center, Philadelphia, PA*

**Background:** Although SCLC is highly responsive to initial therapy, most pts relapse < 1 y. Topotecan (T) and irinotecan (I) are used in 2LT of SCLC; however, treatment response is low: ≤10-25% and median survival is ~4-5 months. Preclinical studies support GD2 as an SCLC target. This study evaluated the combination of D+I vs. I alone or T alone in 2LT of SCLC pts. **Methods:** Pts with RR SCLC, Eastern Cooperative Oncology Group 0-1, were randomized 2:2:1 to receive D 16-17.5 mg/m$^2$ intravenously (IV) plus I 350 mg/m$^2$ IV (Day 1 q21d), I 350 mg/m$^2$ IV (Day 1 q21d), or T 1.5 mg/m$^2$ IV (Days 1-5 q21d). Randomization was stratified by duration of response to prior platinum therapy. Primary endpoint was overall survival (OS) in pts treated with D+I vs. I alone and was analyzed using stratified log-rank test and COX regression. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), and clinical benefit rate, ORR + stable disease (CBR). Safety was assessed. **Results:** 471 pts were randomized to D+I (n = 187), I (n = 190), or T (n = 94). Baseline characteristics were balanced (24.2% women; mean ± SD age 61.6 ± 8.7 y). Median OS was similar in pts receiving D+I (6.9 [3.5,10.9] months) vs. I alone (7 [3.6,13.1] months) (HR [95% CI]: 1.12 [0.9,1.4]; P = 0.3132) or T alone (7.4 [3.8,12.8] months) (HR [95% CI]: 1.05 [0.8,1.37]; P = 0.7233). Median PFS was similar in pts receiving D+I (3.5 [1.5,6.2] months) vs. I (3 [1.4,5.7] months) or T (3.4 [1.6, 6.1] months) alone. ORR was similar in pts receiving D+I (17.1%) vs. I (18.9%) or T (20.1%) alone. CBR was similar in pts receiving D+I (67.4%) vs. I (58.9%) or T (68.1%) alone. Grade 3 or higher adverse events were experienced by 77% D+I, 69.5% I, and 86.4% T pts. **Conclusions:** Treatment with D+I was not superior to established 2LT for RR SCLC. Exploratory analyses are ongoing to evaluate GD2 expression in circulating tumor cells, select protein biomarkers, and any correlative impact on observed response. Clinical trial information: NCT03098030. Research Sponsor: United Therapeutics.

**9018 Poster Discussion Session; Displayed in Poster Session (Board #211), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

**Molecular subtypes and clinical outcomes to initial systemic treatment in patients with small cell lung cancer.** *First Author: Wei-Chu Victoria Lai, Memorial Sloan Kettering Cancer Center, New York, NY*

**Background:** Investigators have proposed that differential expression of the transcription regulators ASCL1 and NeuroD1 can be used to define molecular subtypes of small cell lung cancers (SCLCs). Here we evaluate SCLC subtypes based on ASCL1 and NeuroD1 expression in patients (pts) treated with first-line (1L) chemotherapy profiled with targeted next-generation sequencing (NGS). **Methods:** We used NGS (MSK-IMPACT) to profile tumors from pts with SCLCs. We performed IHC to assess ASCL1 (A) or NeuroD1 (N). Objective response rate (ORR) to therapy was determined using RECIST. PFS and OS were analyzed using Kaplan-Meier. **Results:** 281 pts with SCLCs were profiled with NGS (102 LS-SCLC; 179 ES-SCLC). Most frequently mutated genes were *TP53* (90%), *RB1* (68%), *KMT2D* (22%), *NOTCH1* (15%), *FAT1* (14%), *PTPRD* (12%). Mutations in *BIRC3*, *FOXL2*, *TENT5C*, *TET1*, *NRAS*, *KIT*, *TSHR*, *ESR1* were enriched in ASCL1-/NeuroD1+ (A-/N+), and mutations in *KMT2D* and *EP300* were enriched in A-/N- ($p<0.05$). Copy number alterations in *WWTR1*, *ATR*, *IKZF1*, *PALB2*, *PIK3CB* were enriched in A-/N+ ($p<0.05$). IHC for ASCL1 and NeuroD1 was performed on 78 samples: 11 A-/N-, 32 A+/N-, 4 A-/N+, 31 A+/N+. Overall survival at 1 year based on subtype was 25% in A-/N- (2/9), 60% in A-/N+ or A+/N- (13/32), and 55% in A+/N+ (10/25). For the 10 pts who survived 2 years, 5 were A+/N- and 5 were A+/N+. 146 pts treated with 1L platinum had RECIST-evaluable disease. ORR was 75% (110/146; 95% CI 68-82%). Median PFS was 7 months with CR/PR and 3.5 months with SD/PD (HR 0.32; 95% CI 0.18-0.56). Median OS was 17 months with CR/PR and 11 months with SD/PD (HR 0.55; 95% CI 0.34-0.9). Mutations in *RUNX1*, *EPHA7*, *CDKN2A*, *FLT1* and copy number alterations in *FGFR1*, *CCND1* were enriched in patients with SD/PD ($p<0.05$). PFS rate at 6 months was 25% in A-N- (1/4), 60% in A-/N+ or A+/N- (9/15), and 55% in A+/N+ (6/11). For the 7 pts who survived 2 years, 3 were A+/N- and 4 were A+/N+. **Conclusions:** Molecular subtypes defined by ASCL1 and NeuroD1 encompass molecular characteristics that may predict patient outcomes. Further investigation is needed to delineate the underlying biological differences among the various subtypes to help define therapeutic vulnerabilities of each subtype of SCLC. Completion of IHC for ASCL1, NeuroD1 and additional key transcription factors POU2F3 and YAP1 are in progress for the entire cohort. WES and RNA sequencing are occurring in parallel and will be correlated with IHC results and clinical outcomes. Research Sponsor: None.

**9019 Poster Discussion Session; Displayed in Poster Session (Board #212), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

**YAP1 positive small-cell lung cancer subtype is associated with the T-cell inflamed gene expression profile and confers good prognosis and long term survival.** *First Author: Taofeek Kunle Owonikoko, Winship Cancer Institute of Emory University, Atlanta, GA*

**Background:** The dominant expression of transcription factors ASCL1, NeuroD1, YAP1 or POU2F3 characteristically defines four small cell lung cancer (SCLC) subtypes (SCLC-A, SCLC-N, SCLC-Y and SCLC-P). The clinical validation and biological relevance of these emerging SCLC subtypes is currently lacking. **Methods:** Using the Illumina TruSeq RNA Exome Kit, we generated RNA-Seq data from 61 cases of SCLC and pulmonary carcinoid to interrogate gene expression differences in SCLC subtypes as well as in survival outliers (top and bottom decile) matched for clinically relevant prognostic factors and treatment. We also assessed YAP1 protein expression in a blinded fashion by immunohistochemistry in 130 SCLC cases. **Results:** We successfully classified 68% of SCLC into one of the four SCLC subtypes whereas 81.5% of carcinoids did not fit into any of these categories. GSEA for differentially expressed genes between outlier subgroups showed significant upregulation of interferon gamma and interferon alpha response genes in late survivors. Moreover, a previously validated 18-gene T-cell inflamed gene expression profile was upregulated in late survivors and in the SCLC-Y subtype. Furthermore, the SCLC-Y subtype and late survivors showed higher expression of HLA gene family and reduced expression of cancer testis antigens. The median (95% CI) OS was 14 (4.3, 28.8), 16.7 (0.9, NA), 8.1 (2, 9.7) and 20.1 (0.6, 39.5) months respectively, for SCLC-A, N, P and Y subtypes. YAP-1 protein expression was positive in 17 of 130 (13%) SCLC cases. The majority of cases with positive YAP1 expression by immunohistochemistry, 12 of 17 cases (70.6%), were limited stage SCLC at the time of original diagnosis. **Conclusions:** SCLC subtypes have clinical implication as predictive and prognostic biomarker. SCLC-Y subtype is enriched for T-cell inflamed phenotype and long term survival, and may predict for clinical benefit of immunotherapy. Research Sponsor: Novartis Oncology.

**9020 Poster Session (Board #213), Fri, 8:00 AM-11:00 AM**

**Validation of tumor DNA in bronchial lavage as a diagnostic tool in lung cancer.** *First Author: Sara Witting Christensen Witting Christensen Wen, Department of Oncology, Vejle Hospital, University Hospital of Southern Denmark, and Institute of Regional Health Research, University of Southern Denmark, Vejle, Denmark*

**Background:** Diagnosing lung cancer requires invasive procedures with risk of complications for the patient. The HOXA9 gene is highly methylated in lung cancer, and methylated tumor DNA (meth-tDNA) in bronchial lavage has previously shown potential as a diagnostic biomarker. The aim of the present study was to validate these preliminary results. **Methods:** Patients were referred by the general practitioner on suspicion of lung cancer. The Danish diagnostic package includes chest and abdominal CT scan, bronchoscopy, blood tests, and histopathological or cytological verification. Twelve ml lavage fluid was collected at bronchoscopy for analysis of meth-tDNA based on droplet digital PCR according to our published method. A positive test was defined as ≥ 4 droplets containing meth-tDNA and a ratio between HOXA9 and Albumin of > 0.15%. The analysis was performed blinded to clinical data and meth-tDNA status was compared with the final diagnosis. **Results:** The study population was 204 consecutively enrolled patients. The material consisted of a discovery cohort (n = 105, presented at ASCO 2019) used for establishing the cut-points, and a validation cohort (n = 99). Six were excluded from analysis due to malignancy other than lung cancer and one due to failed analysis. In the discovery cohort, the sensitivity was 68.7% (95% CI 56.2-79.4%), specificity 88.2% (95% CI 72.6-96.7%), and positive predictive value (PPV) 92.0% (95% CI 80.8-97.8%). In the validation cohort, the same values were 76.9% (95% CI 63.2-87.5%), 77.3% (95% CI 62.2-88.5%), and 80.0% (95% CI 66.3-90.0%), respectively. Analyzing the entire patient material (n = 197) the sensitivity, specificity, and PPV were 72.3% (95% CI 63.3-80.1%), 82.1% (95% CI 71.7-89.8%), and 86.0% (95% CI 77.6-92.1%), respectively. The false positive samples were equally distributed among patients with cryptogenic organizing pneumonia, granulomatous inflammation, and acute inflammatory disease. The false negative samples were mainly from patients with peripheral tumor, no radiologically detectable tumor, and mesothelioma. **Conclusions:** Meth-tDNA in bronchial lavage holds potential as a supplementary tool in the diagnosis of lung cancer with a clinically relevant sensitivity and specificity. Routine clinical application awaits further validation in a clinical trial. Research Sponsor: The grant for early detection of cancer, Region of Southern Denmark, Denmark.

| meth-tDNA status | Lung cancer | No lung cancer |
|---|---|---|
| **Discovery: Positive** | 46 | 4 |
| **Discovery: Negative** | 21 | 30 |
| **Validation: Positive** | 40 | 10 |
| **Validation: Negative** | 12 | 34 |
| **Total: Positive** | 86 | 14 |
| **Total: Negative** | 33 | 64 |

**9022 Poster Session (Board #215), Fri, 8:00 AM-11:00 AM**

**Role of adjuvant chemotherapy in patients with pathological stage I NSCLC with high-risk features.** *First Author: Lubina Arjyal, Gundersen Health System, La Crosse, WI*

**Background:** Lobectomy is the current standard of care for patients with stage I non-small cell lung cancer (NSCLC). There is a lack of prospective data on the benefit of adjuvant chemotherapy (CT) in patients with negative margins but with high-risk features: lympho-vascular invasion (LVI) or visceral pleural invasion (VPI). We aimed to investigate the benefit of adjuvant CT in patients with pathological stage I NSCLC with high-risk features. **Methods:** The 2016 National Cancer Database was queried to identify patients with pathological stage I NSCLC ($8^{th}$ edition AJCC staging) diagnosed from 2010-2015 who received lobectomy/pneumonectomy with clear surgical margins. Patients were stratified into high risk (tumor size ≥2 cm with LVI and/or VPI) or low risk group. Multivariate Cox proportional hazards regression and propensity score matched Kaplan-Meier survival analysis were used to compare overall survival between those who received adjuvant CT and those who did not. **Results:** 34,556 patients were identified with 1114 (3.2%) receiving adjuvant CT. On multivariate Cox regression analysis, high risk tumors (hazard ratio [95% confidence interval] = 1.31 [1.25-1.38]) and lack of adjuvant chemotherapy (1.25 [1.09-1.44]) were associated with worse overall survival (OS). Additionally, male sex, age ≥ 60 years, higher comorbidity burden, lack of insurance, low facility volume, low median income, non-squamous histology were associated with worse OS. After propensity score matching, Kaplan-Meier survival analysis of the high risk subgroup (n = 2923) showed a significant difference in overall survival (OS) between those who received adjuvant CT (n = 1032, 5 year OS, 74.7%; 95% CI, 70.9%-78.0%) and those who did not (n = 1891, 5 year OS, 66.9%; CI, 63.9%-69.6%; p = 0.0002). In patients with no high risk factors for recurrence (n = 384), OS was not significantly different between the patients who received adjuvant CT (n = 78, 5 year OS, 75.8%; CI, 61.3%-85.5%) and those who did not receive adjuvant CT (n = 306, 5 year OS, 77.1%; CI, 70.0%-82.7%; p = 0.3). **Conclusions:** Our study showed better survival with adjuvant CT in patients with pathological stage I NSCLC who have tumor size greater than 2 cm, LVI and/or VPI. Research Sponsor: None.

**9023 Poster Session (Board #216), Fri, 8:00 AM-11:00 AM**

**Circulating tumor DNA (ctDNA) analysis predicts recurrence following surgery in patients with stage I-IIIA non-small-cell lung cancer (NSCLC): Results of GASTO1035 and GASTO1018.** *First Author: Si-Yu Wang, Sun Yat-sen University Cancer Center, Guangzhou, China*

**Background:** Circulating tumor DNA can be detected in the plasma and serum of patients with solid tumors and has emerged as a noninvasive biomarker for dynamically monitoring tumor. Postsurgical ctDNA analysis of early-stage NSCLC may identify patients at high risk of recurrence and facilitate early intervention and personalized cancer therapy. **Methods:** These studies recruited 123 patients with newly diagnosed resectable stage I-IIIA NSCLC. Preoperative and postoperative plasma and postoperative tissue samples were subjected to next-generation sequencing (Nanjing Shihe Jiyin Biotechnology Inc.) using a 425 cancer-related genes panel. Peripheral blood samples were collected before surgery, postoperatively within 1 month, and every 3-6 months for up to 3 years. Plasma samples with at least 1 variants detected in tissue samples were defined as ctDNA positive. **Results:** After 4 exclusions, 119 eligible patients were enrolled from June 2016 to February 2019. Presurgical ctDNA was detectable in 31 of 117 (26.5%) patients and was associated with inferior recurrence-free survival (HR, 3.90, 95% CI, 1.44-10.58, P = 0.004). Similarly, ctDNA was detected in 13 of 116 (11.2%) of the first postsurgical samples and was associated with shorter RFS (HR, 3.54, 95% CI, 1.22-10.23, P = 0.002). During surveillance after surgery, ctDNA-positive patients (38/119, 31.9%) were more than 9 times more likely to experience disease recurrence than ctDNA-negative patients (HR, 9.17, 95% CI, 2.60-32.42, P < 0.001). Serial ctDNA detection preceded radiologic disease recurrence by a median lead time of 4.23 months (95% CI, 0.91-7.54 months). We also observed a positive correlation between the ctDNA detection rate and the disease stage. **Conclusions:** These results suggest that detection of ctDNA before and after surgery is associated with the identification of a high risk of disease recurrence of resectable NSCLC. Perioperative ctDNA analyses identify disease recurrence earlier than standard-of-care radiologic imaging, and thus could facilitate personalized cancer treatment at early time points. Clinical trial information: NCT03465241 and NCT03172156. Research Sponsor: None.

**9024 Poster Session (Board #217), Fri, 8:00 AM-11:00 AM**

**Validation of 4-marker protein panel for the early detection of lung cancer using PLCO samples.** *First Author: Johannes Fahrmann, University of Texas MD Anderson Cancer Center, Houston, TX*

**Background:** We have previously demonstrated that a protein panel consisting of ProSFTPB, CEA, CA125 and CYFRA21.1 may improve lung cancer risk assessment and has potential to define eligibility for computed tomography screening. Herein, we aimed to validate the classifier performance of the 4-marker protein panel using pre-diagnostic serum samples from the PLCO cohort. We additionally explored the additive value of diacetylspermine (DAS) with the 4-marker protein panel for identifying lung cancer cases. **Methods:** ProSFTPB, CEA, CA125 and CYFRA21.1 levels were measured in baseline sera of 537 lung cancer cases (76 SCLC/461 NSCLC) diagnosed within 6 years of baseline blood draw and 3772 cancer-free controls using bead-based immunoassays. DAS was measured using ultrahigh performance liquid chromatography mass spectrometry. Samples were analyzed in a double-blinded randomized fashion. **Results:** Overall classification performance (receiver operating characteristic area under the curve (ROAUC)) of the 4-marker panel for delineating lung cases diagnosed within 1 year and 1 to 2 years of baseline blood draw from cancer-free controls was 0.78 (95% CI: 0.74-0.82) and 0.73 (95% CI: 0.68-0.78), respectively. Classification performances of the 4-marker panel amongst lung cancer cases diagnosed within 1 year of baseline blood draw stratified into adenocarcinoma, squamous cell carcinoma and small cell lung cancer subtypes yielded ROAUCS of 0.78 (95% CI: 0.72-0.85), 0.76 (95% CI: 0.69-0.83) and 0.79 (95% CI: 0.68-0.90), respectively. Sub-analyses adjusting for smoking status yielded comparable ROAUC point estimates. Comparison of the 4-marker performance amongst non-NLST and NLST eligible lung cancer patients diagnosed within 1 year of baseline blood draw in comparison to matched cancer-free controls resulted in ROAUCs of 0.71 (95% CI: 0.63-0.79) and 0.74 (95% CI: 0.69-0.80), respectively. Analyses evaluating the additive classifier performance of serum DAS with that of the 4-marker protein panel revealed statistically significant improvement (McNemar Exact Test 2-sided $p < 0.05$) in sensitivity at high specificity derived from youden index for SCLC and squamous cell carcinoma cases diagnosed within 2 years from baseline blood draw, respectively, in comparison to the 4-marker protein panel alone. **Conclusions:** We have validated the performance of the 4-marker panel for early detection of lung cancer in the PLCO pre-diagnostic cohort. We further demonstrate that DAS can complement the 4-marker protein panel and identify more SCLC and squamous cell carcinoma cases. Research Sponsor: U.S. National Institutes of Health.

**9025 Poster Session (Board #218), Fri, 8:00 AM-11:00 AM**

**Reliable detection of the presence of pulmonary carcinoma on whole-slide images by a deep learning model.** *First Author: Gouji Toyokawa, Department of Thoracic Surgery, Clinical Research Institute, National Hospital Organization, Kyushu Medical Center, Fukuoka, Japan*

**Background:** Lung cancer is one of the leading causes of cancer-related death worldwide, and its histopathological diagnosis is crucial for deciding on optimum treatment strategies. Recently, artificial intelligence (AI) models have been widely shown to be useful in various medical fields, particularly image and pathological diagnoses; however, AI models for the pathological diagnosis of pulmonary lesions that have been validated in large-scale test sets are yet to be seen. **Methods:** We trained a convolution neural network based on the Efficient Net B3 architecture to classify carcinoma from whole slide images (WSIs) using a training dataset of 3640 images. WSI diagnoses were available. We used a transfer learning approach, in which the starting weights were obtained from a pre-trained model on ImageNet. The model was then trained on our dataset using multiple instance learning, a semi-supervised learning approach. To classify a WSI, the model was applied in a sliding window fashion with an input tile size of 512x512 and a stride of 256. The maximum probability was then used as a WSI diagnosis. **Results:** We evaluated our model on a total of 2680 WSIs originating from five independent sources (two hospitals in Japan and three public datasets from around the world). The model achieved a Receiver Operator Curve Area Under the Curves (ROC AUCs) of 0.974, 0.974, 0.996, 0.988, and 0.981, respectively. **Conclusions:** We successfully established a reliable AI model for differentiating between lung carcinoma and non-neoplasm with a high ROC AUC on five independent test sets. If used in clinical practice, our model could help reduce the burden on pathologists and be useful for diagnosing pulmonary lesions in areas in which there are shortages of pathologists. Further prospective multicenter studies are warranted in order to validate the results obtained in the current study. Research Sponsor: None.

**9026 Poster Session (Board #219), Fri, 8:00 AM-11:00 AM**

**Role of T0 status in overall survival for unresectable stage III non-small cell lung cancer.** *First Author: Takefumi Komiya, Parkview Cancer Institute, Fort Wayne, IN*

**Background:** Occult (T0) primary non-small cell lung cancer (NSCLC) with mediastinal involvement is a known but rare clinical condition. Its prognosis has not been evaluated well in the literature. **Methods:** Using National Cancer Database (NCDB), cases diagnosed between 2004 and 2016 with unresectable clinical stage III NSCLC with N2 or N3 involvement were selected and assigned to T0 or T1-4 group according to AJCC staging version 6$^{th}$ or 7th. Clinical demographics including use of chemotherapy/immunotherapy in first course of treatment were collected. As validation, independent data using Surveillance, Epidemiology, and End Results Program (SEER) was analyzed accordingly. Survival analyses were conducted using Kaplan-Meier and log-rank tests. **Results:** A total of 458 and 84,263 cases met criteria for unresectable, N2/N3 stage III NSCLC with T0 and T1-4 status, respectively. T0 status was associated with younger age, recent diagnosis, adenocarcinoma histology, N3, and use of chemotherapy. Overall survival (OS) was improved in T0 over T1-4 group ($p < 0.0001$) with a five-year survival rate of 30.5% and 12.7%, respectively, with a validation with multivariate proportional hazard models. Propensity score matching analyses using all 458 patients in each group demonstrated a significant difference in OS ($p < 0.0001$). The difference was also significant in a subset of those who have undergone chemoradiation ($p < 0.0001$). Independent analysis using SEER data confirmed its superior survival of T0 over T1-4 with a five-year survival rate of 35.3% and 13.5%, respectively. **Conclusions:** Both NCDB and SEER analyses demonstrated better survival of T0 than T1-4 counterpart in the setting of unresectable stage III NSCLC, irrespective of chemotherapy status. This group may require a distinct assignment to new staging group after further investigation. Research Sponsor: None.

**9027 Poster Session (Board #220), Fri, 8:00 AM-11:00 AM**

**Base excision repair (BER) inhibitor TRC 102 (Methoxyamine) combined with pemetrexed (PEM)-based chemo-radiation (CRT) for locally advanced non-squamous non-small cell lung cancer (NS-NSCLC): Results of a phase I trial.** *First Author: Tithi Biswas, University Hospitals Seidman Cancer Center, Case Western Reserve University, Cleveland, OH*

**Background:** About 35% of all NSCLC presents with locally advanced disease and chemo-radiation results in 5-year OS of only ~31%. PEM-platinum combination is approved in stage IV NSCLC and has similar efficacy to platinum-etoposide in stage 3 NSCLC and a favorable toxicity profile (Proclaim trial). TRC102 is an oral small molecule inhibitor of BER. TRC102 potentiates the cytotoxicity of antimetabolites and alkylators and reverses chemotherapy resistance by rapidly and covalently binding to chemotherapy-induced abasic sites in DNA. TRC102 increased radio-sensitization by PEM of NSCLC cell lines and H1299 and A549 xenografts. **Methods:** Between 11/2015 and 5/2019, 15 patients were enrolled in a 3+ 3 design: 12 with stage III and 3 with oligometastatic stage IV NS-NSCLC. The primary objective was to determine dose-limiting toxicities (DLT's) and recommended Phase 2 dose (RP2D) of TRC102 in combination with PEM, cisplatin and radiotherapy. Secondary objectives were to assess toxicity, tumor response and PFS at 6 months. Based on pre-clinical data, PEM-TRC102 was given on day 1, and cisplatin/radiotherapy was initiated on day 3. This schedule was duplicated on day 21 and day 23 of the second cycle. After completion of radiotherapy, two additional cycles of PEM-cisplatin were given. Toxicities were assessed by NCI CTACAE version 4 and 5. **Results:** Median patient age was 69 years (45-79) and median follow up was 16.6 months (3.1-38.6). There were no DLTs or grade 5 toxicity. Hematologic and GI toxicities were the most common adverse events (Table) and radiation pneumonitis was not seen. The RP2D of TRC102 was 200 mg when given with cisplatin/radiotherapy and PEM. Of 15 evaluable patients, 3 had CR (20%) and 12 had PR (80%). The 2-year PFS rate was 49%. **Conclusions:** PEM-TRC102 combined with cisplatin/radiotherapy in non-squamous NSCLC was safe and well tolerated, and did not cause safety signals beyond those expected from CRT. Preliminary response data and PFS in this cohort was encouraging. A phase 2 trial, integrating post-CRT immunotherapy with this aggressive DNA-damaging regimen is warranted. Clinical trial information: NCT02535325. Research Sponsor: Lucille and Robert Gries Endowed Fund, the Vincent K. Smith Fund, and Early Phase Clinical Research Support (EPCRS) P30 Funding at the Case Comprehensive Cancer Center.

| | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Total (n = 15) |
|---|---|---|---|---|---|
| **Hematological toxicity** | | | | | |
| **Anemia** | 6 | 4 | 3 | | 13 |
| **Lymphopenia** | | 3 | 7 | 3 | 13 |
| **Decreased neutrophil count** | | | 6 | 1 | 7 |
| **Decreased Platelet count** | 10 | 2 | | | 12 |
| **GI toxicity** | | | | | |
| **Nausea** | 5 | 6 | | | 11 |
| **Vomiting** | 1 | 3 | | | 4 |
| **Dehydration** | | 3 | 2 | | 5 |
| **Esophagitis** | 1 | 7 | | | 8 |
| **Fatigue** | 1 | 3 | 1 | | 5 |
| **Anorexia** | 2 | 2 | 3 | | 7 |
| **Weight Loss** | | | 3 | | 3 |
| **Pulmonary Toxicity** | | | | | |
| **Pneumonitis** | | | | | 0 |
| **Cough** | 1 | 2 | | | 3 |
| **Skin toxicity** | | | | | |
| **Dermatitis** | 2 | 2 | | | 4 |

**9030 Poster Session (Board #223), Fri, 8:00 AM-11:00 AM**

**Detection of early-stage lung cancer by exhaled volatile organic compounds using a high-pressure photon ionization time-of-flight mass spectrometry.** *First Author: Mantang Qiu, Peking University People's Hospital, Beijing, China*

**Background:** Exhaled breath-based test is an attractive option for cancer detection due to its non-invasive nature. Exhaled volatile organic compounds (VOCs) are produced in various biochemical processes and might be sensitive tumor biomarkers. Here, we reported an exploratory study to investigate the performance of exhaled VOCs for detection of early-stage lung cancer using a high-resolution high-pressure photon ionization time-of-flight mass spectrometry (HPPI-TOFMS). **Methods:** Treatment-naïve patients with pulmonary nodules who received surgery at our department and without history of cancer were enrolled. Exhaled breath samples were collected before surgery and stored in Tedla bags. A $CO_2$ sensor was applicated during sample collection to ensure only "alveolar air" was collected. Exhaled samples were directly detected by HPPI-TOFMS, which has a resolution $> 3000$. Deep learning algorithm was used to build detection model based on HPPI-TOFMS data. **Results:** A total of 171 patients were included in this study, including 139 patients with lung cancer (114 of TNM stage I, 14 of stage II, 9 of stage III, and 2 of stage IV) and 32 patients with benign nodules. Mass spectrum peaks with $m/z <$ 500 detected by HPPI-TOFMS were retained and 32500 features were extracted from each exhaled breath samples. Based these extracted features, participants who were pathologically diagnosed as lung cancer could be discriminated from those with benign diseases with an accuracy of 96.19%, sensitivity of 96.43%, and specificity of 84.38%. Discrimination of lung cancer patients with lymph node metastasis (n = 12) from those without lymph node metastasis (n = 127) had an accuracy of 83.23%. **Conclusions:** Exhaled VOCs as detected by a high-resolution HPPI-TOFMS might be sensitive biomarkers for detection of early-stage lung cancer. Research Sponsor: None.

**9031 Poster Session (Board #224), Fri, 8:00 AM-11:00 AM**

**CT and PET radiomic features associated with major pathologic response to neoadjuvant immunotherapy in early-stage non-small cell lung cancer (NSCLC).** *First Author: Erica C. Nakajima, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD*

**Background:** An early biomarker of response to immunotherapy (IO) is needed urgently to identify the patients (pts) who will derive benefit. We reported the first clinical trial of neoadjuvant IO (nIO) in resectable non-small cell lung cancer (NSCLC) (NCT02259621). In this study, we investigated whether there was an association between MPR and radiomic features (RF) in [$^{18}$F]-fluorodeoxyglucose ([$^{18}$F]-FDG) PET and standard CT images obtained at baseline and after nIO in early stage NSCLC tumors. **Methods:** Prior to receiving neoadjuvant nivolumab or nivolumab/ipilimumab, patients with Stage I-IIIA NSCLC underwent two [$^{18}$F]-FDG PET-CTs and/or plain CTs: a baseline scan at enrollment (PRE), and after nIO (POST). After neoadjuvant treatment, tumors were resected and evaluated for MPR. Volumes of interest (VOIs) were drawn around primary tumors on the scans. Using our novel radiomic software, Imager-4D, VOIs were evaluated for 20 RFs assessing [$^{18}$F]-FDG standard uptake value (SUV) or Hounsfield unit (HU) heterogeneity and spatial distribution in PET and CT images respectively. The baseline, post-treatment, and percent change in RFs before and after nIO were compared between tumors with and without MPR. Wilcoxon test was used for the comparisons. **Results:** The PRE and POST scans of 24 pts were analyzed. All pts had PRE and POST CTs performed, and 17 pts had PRE and POST [$^{18}$F]-FDG PET-CT scans. 7 of 24 (29%) had MPR. In the CT scan analysis, HU-based RFs of voxel count, total volume, energy, entropy, homogeneity, contrast, and dissimilarity in POST CT scans each significantly association with MPR. In the PET scan analysis, SUV mean and voxel count RFs in the POST scans, and the percent change in the cluster shade RF between PRE and POST scans were significantly associated with MPR. **Conclusions:** Collectively, we identified a significant increase in heterogeneity in the POST CT images of NSCLC tumors that had MPR. This association may reflect increased T cell infiltration or tumor necrosis. In contrast, most [$^{18}$F]-FDG-based RFs did not distinguish MPR vs non-MPR tumors, although the sample size was limited. We will further investigate these HU-based RFs as non-invasive markers of response to IO in conjunction with pathologic markers of IO response and in a larger patient cohort. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

**9032 Poster Session (Board #225), Fri, 8:00 AM-11:00 AM**

**The association between immune-related adverse events and efficacy outcomes with consolidation pembrolizumab after chemoradiation in patients with stage III NSCLC: an analysis from HCRN LUN 14-179.** *First Author: Nikhil Shukla, Indiana University, Indianapolis, IN*

**Background:** Consolidation checkpoint inhibitor therapy (CPI) for up to 1 year following chemoradiation (CRT) is a current standard of care for pts with inoperable stage III NSCLC. However, some pts are not able to complete 1 year of CPI due to immune-related adverse events (irAES). In multiple retrospective studies, pts with stage IV NSCLC treated with CPI who experience irAEs generally receive fewer cycles of CPI without a significant detrimental effect on efficacy. The association between irAEs and outcomes with consolidation CPI after CRT has never been reported. Here we report the association between irAEs and efficacy outcomes from the HCRN LUN 14-179, a single-arm phase II trial of consolidation pembrolizumab following concurrent CRT in pts with unresectable stage III NSCLC. **Methods:** After completion of CRT eligible pts with stage III NSCLC without PD received pembrolizumab 200 mg IV q 3 wks for up to 1 yr. Demographics, disease characteristics, and number of cycles of pembrolizumab received were reported in pts who had any grade irAEs (except pneumonitis which included grade >2 only) [Group A] and those without irAEs (except grade 1 pneumonitis) [Group B]. Chi-square test (or Fisher's Exact test) were used for comparisons for categorical variables and Wilcoxon test for continuous variables. The Kaplan-Meier method was used to analyze time to metastatic disease (TMDD), PFS, and OS. A log-rank test was used to compare groups. **Results:** 92 eligible pts for efficacy analysis were enrolled from March 2015 to November 2016. 4 yr OS estimate for all pts is 46.2%. Any grade irAEs (except grade I pneumonitis) (n = 37 pts) included pneumonitis (18.5%), colitis (3.3%), increased creatinine (5.4%), elevated transaminases (3.3%), hyperthyroidism (7.6%), hypothyroidism (13.0%). Grade ≥ 2 irAEs (n = 32 pts) included pneumonitis (18.5%), hypothyroidism (10.8%), and colitis (3.3%). Group A/B: male (21/38), female (16/17), current or former smoker (35/52), stage IIIA (20/35), stage IIIB (17/20), non-squamous (21/30), squamous (16/25). Median number of pembrolizumab cycles received in Group A/B pts were 9 vs 15 (p = 0.0942) respectively. 4 yr efficacy endpoints in Groups A/B were TMDD 35.3% vs 41.3% (p = 0.83), PFS 27.8% vs 28.7% (p = 0.97), OS 43.5% vs 47.9% (p = 0.99), respectively. **Conclusions:** Despite receiving fewer cycles of consolidation pembrolizumab, pts who experienced any grade irAEs (excluding grade 1 pneumonitis) did not have significantly reduced efficacy outcomes. Clinical trial information: NCT02343952. Research Sponsor: Merck Sharp & Dohme Corp.

**9033 Poster Session (Board #226), Fri, 8:00 AM-11:00 AM**

**Outcomes of patients with stage III non-small cell lung cancer (NSCLC) that harbor a *STK11* mutation.** *First Author: Josiah An, University of Iowa Hospitals and Clinics, Iowa City, IA*

**Background:** *STK11* mutation ($STK11^m$) in patients with stage IV NSCLC is associated with inferior survival and poor response to immune check point inhibitors (ICI). The significance of $STK11^m$ in patients (pts) with stage III NSCLC treated with concurrent chemoradiation (CCRT) with and without consolidation ICI is unknown. **Methods:** Patient demographics, disease characteristics, treatment received and outcomes in pts with stage III NSCLC that harbor $STK11^m$ were retrospectively reviewed from 4 cancer centers. A cohort of pts with stage III NSCLC and wild type *STK11 (*$STK11^w$*)* from the University of Iowa served as a comparison group. SPSS version 25 was used for data analysis. **Results:** 75 pts with stage III NSCLC who had gene sequencing were included. 16/75 (21%) had $STK11^m$. The clinical characteristics for the 16 $STK11^m$ and 59 $STK11^w$ pts showed ($STK11^m$ vs. $STK11^w$): mean age: 58 vs. 64 yrs, non-squamous histology: 11/16 (69%) vs. 37/59 (63%), *KRAS* co-mutation: 6/16 (38%) vs. 11/59 (19%), *TP53* co-mutation: 9/16 (56%) vs. 15/59 (25%), PD-L1 ≥ 50%: 2/16 (13%) vs. 10/59 (17%), received CCRT 11/16 (69%) vs. 59/59 (100%) and consolidation ICI 6/16 (38%) vs. 17/59 (29%). Regarding the 6 $STK11^m$ pts who received ICI (4 pembrolizumab, 2 durvalumab), the median number of ICI infusions was 8 (range, 3-17) vs. 7 (range, 1-25) in the 17 pts with $STK11^w$ who received ICI (durvalumab). Progression free survival (PFS) for the $STK11^m$ vs. $STK11^w$ pts who received CCRT but not ICI was (4.2 vs. 34.3 months, respectively. P = 0.168), for the $STK11^m$ vs. $STK11^w$ pts who received CCRT and ICI was (11.3 vs. 17.5 months, respectively. P = 0.174), and for the $STK11^m$ vs. $STK11^w$ pts who received CCRT regardless of receiving ICI (11.3 vs. 32.9 months, respectively. P = 0.021). The median overall survival for $STK11^m$ pts (16 pts) was 25.5 months (95% CI, 13.7 to 37.2) while not yet reached for the $STK11^w$ group. **Conclusions:** In stage III NSCLC, $STK11^m$ was associated with inferior clinical outcomes. Larger studies are needed to identify the prognostic implications of $STK11^m$ in stage III NSCLC and whether ICI impacts survival for this subgroup. Research Sponsor: None.

**9034 Poster Session (Board #227), Fri, 8:00 AM-11:00 AM**

**Evaluation of the incidence of pneumonitis in United States veterans with non-small cell lung cancer receiving durvalumab following chemoradiation.** *First Author: Theodore Seth Thomas, Washington University, St Louis, MO*

**Background:** Locally advanced, unresectable non-small cell lung cancer is commonly treated with concurrent chemoradiation therapy (CRT). Durvalumab is a PD-L1 immune checkpoint inhibitor (ICI) administered following completion of CRT. Pneumonitis is a known toxicity of ICI therapy. In the landmark PACIFIC study the incidence of pneumonitis in patients receiving durvalumab was 33.9% (any grade) and 3.4% (grade 3/4) compared to placebo 24.8% and 2.6% (*Antonia et al, NEJM 2017)*. The incidence of pneumonitis is thought to be higher in real-world populations. This study evaluated the incidence of pneumonitis in a cohort of U.S. Veterans. **Methods:** Durvalumab recipients were identified using VA Informatics and Computing Infrastructure databases. Using pharmacy records we confirmed durvalumab and corticosteroid prescriptions. Clinical information was obtained via the electronic medical record. The primary outcome was the development of pneumonitis. We defined asymptomatic pneumonitis as the presence of new radiographic findings consistent with pneumonitis without documented clinical symptoms. We recorded pneumonitis grade as reflected in clinical documentation. If not specifically graded, we used Common Terminology Criteria for Adverse Events (CTCAE v4.0) to assess severity. Logistic regression analysis evaluated associations between pneumonitis and age, comorbidities, radiation dose and stage. Cox proportional hazards analysis evaluated associations between pneumonitis and risk of death. **Results:** A total of 123 veterans received durvalumab through 3/31/2019 (with follow up through 11/15/2019). Asymptomatic radiographic infiltrates occurred in 49 (39.8%) patients. There were 26 cases of clinically important pneumonitis Grade 2: 9(7.3%), Grade 3: 14 (11.4%), Grade 4: 2(1.6%), and grade 5: 1 (.08%). Acute hypersensitivity reactions occurred in five (4.1%) patients. Reported reasons for discontinuation of durvalumab included: disease progression [38 (31%)], toxicity [30 (24.3%)], and patient death [1 (1.6%)]. There was no association between age, time from radiation end to durvalumab initiation, radiation dose, smoking history, chemotherapy used or disease stage on development of pneumonitis. Cox analysis did not demonstrate an association between pneumonitis and risk of death. **Conclusions:** Clinically significant pneumonitis was more frequent in this cohort than reported in prior clinic trial populations. Further studies to identify pneumonitis risk factors are needed. Research Sponsor: None.

**9035 Poster Session (Board #228), Fri, 8:00 AM-11:00 AM**

**I-SABR phase II randomized study of nivolumab immunotherapy and stereotactic ablative radiotherapy in early stage NSCLC: Interim analysis adverse effects.** *First Author: Joe Y. Chang, The University of Texas MD Anderson Cancer Center, Houston, TX*

**Background:** Stereotactic Ablative Radiotherapy (SABR) provides > 95% local control and has become standard care of medically inoperable stage I NSCLC. However, cumulatively about 40% of patients develop recurrence in the regional lymph nodes, distant organs, or secondary lung cancer. Combined immunotherapy and SABR (I-SABR) may reduce these recurrences by stimulating stronger cancer specific immune response. **Methods:** This is an ongoing phase II randomized study (SABR vs. I-SABR) to evaluate the efficacy and toxicity of I-SABR in medically inoperable, early stage (T1-T3: < 7 cm, including multi-primary tumors), isolated recurrence NSCLC without lymph node or distant metastasis. The primary objective is event-free survival (any recurrence and/or death). Secondary objectives include rates of ≥Grade 2 toxicity. 4-D CT image guided SABR (50 Gy in 4 fractions or 70 Gy in 10 fractions) was delivered to all patients. Patients randomized to I-SABR received additional concurrent Nivolumab (240 mg, every two weeks for total of 7 doses or 480 mg every four weeks for total of 4 doses). 140 patients are anticipated to enroll. We report here interim analysis of toxicity. **Results:** 92 patients (median age: 72, range: 57 to 90) were enrolled and randomized (47 to SABR; 45 to I-SABR). With median follow up of 14.5 months (range 2 to 28 months), there were no treatment-related grade 4/5 adverse events. For the I-SABR arm, there was one case of possible related grade 3 dyspnea, skin rash and 2 cases of probable grade 3 fatigue. There were possible/probable treatment related 2 cases of grade 2 pneumonitis, fatigue, pruritus and 1 case of grade 2 hyperthyroidism and arthralgia. No patients discontinued treatment due to adverse effects. For the SABR arm, there were possible treatment related 1 case of grade 2 fatigue and pneumonitis. All symptoms resolved with or without treatment. **Conclusions:** Combined Nivolumab immunotherapy and SABR (I-SABR) appear to be well-tolerated in this fragile patient population with no grade 4/5 toxicity. All toxicities were tolerable and resolved. The major barrier for patient enrollment and/or randomization is patient's perception of potential toxicities and additional clinic visits. Continued enrollment and additional follow up are needed to validate these findings. Clinical trial information: NCT03110978. Research Sponsor: BMS.

**9036 Poster Session (Board #229), Fri, 8:00 AM-11:00 AM**

**Efficacy of DNA versus RNA NGS-based Methods in MET Exon 14 skipping mutation detection.** *First Author: Magdalena Jurkiewicz, Columbia University Medical Center, New York, NY*

**Background:** Exon 14 skipping mutations in the mesenchymal-epithelial transition (*MET*) gene are reported in 2-5% of lung adenocarcinomas and are mutually exclusive of other driver mutations. Small-molecule *MET* tyrosine kinase inhibitors, capmatinib and tepotinib, showed durable responses in previously treated and treatment-naïve patients harboring *MET*-exon-14 skipping mutations. Studies suggest that for detection of *MET*-ex14 mutations, DNA-based assays alone may be sub-optimal when compared to RNA-based NGS assays. We compared the performance of DNA and RNA-based assays for detection of MET-ex14 variants. **Methods:** We examined NGS-based profiling data of lung adenocarcinomas (or when this diagnosis could not be excluded) to identify MET-ex14 mutations missed by DNA but identified by RNA analysis. The carcinomas were profiled by a DNA-based NGS panel that targets MET exons 2, 14, 16, 18 and 19. Cases without driver mutations were reflexed to an NGS-based RNA fusion panel (Archer's Anchored Multiplex PCR). **Results:** Over a 21-month period, MET-ex14 skipping events were detected in 16/644 (2.5%) lung carcinomas by DNA profiling. RNA analysis on driver-negative cases identified 9 additional MET-ex14 mutations. All 16 MET-ex14 DNA variants occurred at or around the intron 14 splice donor site, as the assay did not include the intron 13 splice acceptor site. Clinical characteristics of the *MET* positive cohort include a male to female ratio of 0.8:1.0, an average age of 76.5 years and 52% non-smoker status. All tumors were adenocarcinomas (including one with a $<$ 10% spindle/pleomorphic component) with the exception of 3 adenosquamous carcinomas and 1 squamous cell carcinoma. **Conclusions:** DNA based NGS-panels can potentially miss MET-ex14 skipping events in lung carcinomas, when the primers do not target both 3′ splice site of intron 13, and the 5′ splice site of intron 14. A reflex work flow interrogating RNA fusions can potentially capture such events. The clinical and molecular characterization of the variants detected only by RNA NGS assays warrants further exploration. Research Sponsor: None.

**9037 Poster Session (Board #230), Fri, 8:00 AM-11:00 AM**

**Artificial intelligence based on deep learning for differential diagnosis between benign and malignant pulmonary nodules: A real-world, multicenter, diagnostic study.** *First Author: Tao Xu, Department of Respiratory and Critical Care Medicine, the Affiliated Hospital of Qingdao University, Qingdao, China*

**Background:** Lung cancer is the most common cancer worldwide. Artificial intelligence (AI) platform using deep learning algorithms have made a remarkable progress in improving diagnostic accuracy of lung cancer. But AI diagnostic performance in identifying benign and malignant pulmonary nodules still needs improvement. We aimed to validate a Pulmonary Nodules Artificial Intelligence Diagnostic System (PNAIDS) by analyzing computed tomography (CT) imaging data. **Methods:** This real-world, multicentre, diagnostic study was done in five different tier hospitals in China. The CT images of patients, who were aged over 18 years and never had previous anti-cancer treatments, were retrieved from participating hospitals. 534 eligible patients with 5-30mm diameter pulmonary nodules identified by CT were planning to confirm with histopathological diagnosis. The performance of PNAIDS was also compared with respiratory specialists and radiologists with expert or competent degrees of expertise as well as Mayo Clinic's model by area under the curve (AUC) and evaluated differences by calculating the 95% CIs using the Z-test method. 11 selected participants were tested circulating genetically abnormal cells (CACs) before surgery with doctors suggested. **Results:** 611 lung CT images from 534 individuals were used to test PNAIDS. The diagnostic accuracy, valued by AUC, in identifying benign and malignant pulmonary nodules was 0.765 (95%CI [0.729 - 0.798]). The diagnostic sensitivity of PNAIDS is 0.630(0.579 – 0.679), specificity is 0.753 (0.693 – 0.807). PNAIDS achieved diagnostic accuracy similar to that of the expert respiratory specialists (AUC difference: 0.0036 [-0.0426 - 0.0497]; p = 0.8801) and superior when compared with Mayo Clinic's model (0.120 [0.0649 - 0.176], p $<$ 0·0001), expert radiologists (0.0620 [0.0124 - 0.112], p = 0.0142) and competent radiologists (0.0751 [0.0248 - 0.125], p = 0.0034). 11 selected participants were suggested negative in AI results but positive in respiratory specialists' result. 8 of them were malignant in histopathological diagnosis with tested more than 3 CACs in their blood. **Conclusions:** PNAIDS achieved high diagnostic accuracy in differential diagnoses between benign and malignant pulmonary nodules, with diagnostic accuracy similar to that of expert respiratory specialists and was superior to that of Mayo Clinic's model and radiologists. CACs may be able to assist CT-based AI in improving their effectiveness but it still need more data to be proved. Clinical trial information: ChiCTR1900026233. Research Sponsor: None.

**9038 Poster Session (Board #231), Fri, 8:00 AM-11:00 AM**

**Clinical impact of targetable gene alterations on therapeutic outcomes in stage II/III locally advanced non-small cell lung cancer patients.** *First Author: Yoshitaka Zenke, National Cancer Center Hospital East, Kashiwa, Japan*

**Background:** The clinical significance of genetic alterations in stage II/III non-small cell lung cancer (NSCLC) patients has not yet been clarified. We have prospectively analyzed NSCLC patients for cancer-related gene alterations and have followed up clinical course of the patients, establishing a large-scale clinico-genomic database in our nationwide genome screening project (LC-SCRUM-Japan). **Methods:** Submitted tumor samples were subjected to a targeted next-generation sequencing (NGS) system, Oncomine™ Comprehensive Assay. Therapeutic and prognostic data were collected and updated every year. **Results:** Since March 2015 to May 2019, 5166 non-squamous NSCLC patients from 263 institutions had been enrolled in the LC-SCRUM-Japan, and 754 of them were diagnosed as stage II/III. The median age of the 754 patients was 67 years (range, 21-92), and 503 (67%) were male, 595 (79%) smokers and 631 (84%) stage III. Of 640 available samples, 258 (40%) had targetable gene alterations, comprising 106 KRAS mut, 42 EGFR mut, 29 BRAF mut, 20 MET ex14skip/amp, 16 ALK fus, 12 ROS1 fus, 11 ERBB2 ex20ins, 8 RET fus, 7 EGFR ex20ins, 5 AKT1 mut, 1 NRG1 fus, 1 FGFR2/3 fus. In patients who received surgery (n = 159), 3-year disease-free survival rate was worse in patients with targetable gene alterations than in those without (40% vs 58% months; p = 0.03). In patients who received cytotoxic chemo-radiotherapy (n = 148), the response rate was similar in patients with targetable gene alterations and those without (70% vs. 77%); however, 3-year progression-free survival rate tended to be shorter in patients with targetable gene alterations than in those without (19% vs 35%; p = 0.08). **Conclusions:** In stage II/III NSCLC, the total frequency of targetable gene alterations was similar to that previously evaluated in our stage IV cohort (45%), and the current standard therapies showed early progression in the targetable gene-altered patients. A novel effective multimodality treatment in combination with targeted therapies is needed for this population. Research Sponsor: Japan Agency for Medical Research and Development.

**9039 Poster Session (Board #232), Fri, 8:00 AM-11:00 AM**

**Real-world survey of pneumonitis/radiation pneumonitis among patients with locally advanced non-small cell lung cancer treated with chemoradiotherapy after durvalumab approval: A multicenter retrospective cohort study (HOPE-005/CRIMSON).** *First Author: Go Saito, Department of Respirology, Graduate School of Medicine, Chiba University, Chiba, Japan*

**Background:** Durvalumab was approved as a consolidation therapy after chemoradiotherapy (CRT) for locally advanced non-small cell lung cancer (NSCLC) and established as the standard of care. However, since the approval of durvalumab, little has been reported on the frequency, severity, or clinical course of pneumonitis/radiation pneumonitis throughout the course of CRT. **Methods:** We conducted a 17-center, retrospective cohort study of consecutive patients with locally advanced NSCLC who received concurrent chemoradiotherapy (CCRT) with platinum-based chemotherapy between May 2018 and May 2019. **Results:** A total of 275 patients were included; their median age was 69.9 (range, 40.3-87.5), mean $V_{20}$ was 19.4% (range, 1.4-37.9), and mean "mean lung dose" was 10.9 Gy (range, 1.5-31.3). Of these, 204 patients received durvalumab consolidation therapy (74.2%). Median follow-up time from the initiation of CCRT was 8.4 months (range, 1.5-15.7). During follow-up, 225 patients (81.8%) developed any-grade pneumonitis/radiation pneumonitis. Of these, more than half (134 of 225) were asymptomatic (grade 1), 18 (6.5%) were ≥grade 3, and 4 patients (1.5%) had fatal pneumonitis/radiation pneumonitis. By the time of initial assessment of response to CCRT, 64 (23.3%) patients had developed radiation pneumonitis. Logistic regression revealed that only $V_{20}$ ≥25 % was an independent risk factor of symptomatic (≥grade 2) pneumonitis/radiation pneumonitis (OR: 2.74, 95% CI: 1.35-5.53, p = 0.0045). Of the 275 patients, 67 were treated with corticosteroids for pneumonitis/radiation pneumonitis (24.7%), and 14 (5.1%) needed home oxygen therapy after the treatment of pneumonitis/radiation pneumonitis. Among patients treated with corticosteroids, 21 patients received durvalumab rechallenge. Of the 21 patients, 6 (29%) showed pneumonitis/radiation pneumonitis relapse, of which 3 (14%) resulted in suspension of durvalumab rechallenge, but none were fatal. **Conclusions:** Although over four-fifths of the patients treated with CCRT after the approval of durvalumab developed pneumonitis/radiation pneumonitis, more than half of them were asymptomatic, and ≥grade 3 events accounted for 6.5%. Sometimes patients needed corticosteroid therapy, which was in many occasions effective, and some also underwent durvalumab rechallenge. $V_{20}$ was an independent risk factor of symptomatic pneumonitis/radiation pneumonitis. Research Sponsor: None.

**9040 Poster Session (Board #233), Fri, 8:00 AM-11:00 AM**

**Prognostic role of mid-treatment PET/CT and plasma cytokines in patients undergoing chemoradiation for locally advanced non-small cell lung cancer (LA-NSCLC).** *First Author: Jing Zeng, University of Washington, Seattle, WA*

**Background:** Patients with unresectable LA-NSCLC are treated with concurrent chemoradiation (CRT) and consolidation immunotherapy with survival that range from months to years or even decades. Early predictive biomarkers have potential to identify patients who are unlikely to benefit from continuing standard of care therapy and require a change in management. We investigated biomarkers that are widely available (PET/CT scan and plasma cytokine levels) to develop early predictors (mid-CRT) of survival in a phase II clinical trial of chemoradiation for LA-NSCLC. **Methods:** 37 Patients with AJCC v7 stage IIB-IIIB NSCLC were prospectively enrolled on the FLARE-RT trial (NCT02773238) from 2016-9. All patients underwent chemoradiation; 18 also received adjuvant durvalumab. PET/CT exams were performed at week 3 of CRT and response status was pre-defined by published metrics. 21 patients consented to peripheral blood collection at baseline and week 3, and plasma levels of 43 common inflammatory cytokines were measured. Bootstrapping over 100 iterations of the least absolute shrinkage and selection operator (LASSO) was performed to reduce feature dimensionality and guard against false discoveries. Cox regression of selected cytokine levels and PET response status, as well as time-dependent receiver-operating characteristic (ROC) analysis, were evaluated for associations to overall survival (OS). **Results:** Median follow-up was 18 months with 1-year OS 81% and PFS 52%. Mid-CRT PET response (as determined by pre-defined metrics) was strongly associated with OS (HR 5.6 [1.4-22.0], p = 0.015) after adjusting for radiation target volume, with 1-yr OS 94% for responders vs. 68% for non-responders (p = 0.017). Plasma TNF$\alpha$ level was also prognostic for OS (HR 1.9 [1.1-3.5], p = 0.030). TNF$\alpha$ retained significance for OS (HR 2.3 [1.2-4.6], p = 0.016) after adjusting for PET response. Bivariate mid-CRT PET response and TNF$\alpha$ generated a parsimonious model to predict OS (AUC = 0.85, 18-month horizon). **Conclusions:** Risk stratification for long-term survival after chemoradiation in patients with LA-NSCLC may be achievable based on mid-chemoradiation assessment of widely available biomarkers (PET imaging and plasma TNF$\alpha$ level). Combined functional imaging and peripheral blood biomarkers will be validated in a larger sample of our trial cohort, along with other independent patient populations. Clinical trial information: NCT02773238. Research Sponsor: U.S. National Institutes of Health.

**9041 Poster Session (Board #234), Fri, 8:00 AM-11:00 AM**

**Peripheral blood T-cell receptor immune repertoire characterization of resectable stage IIIA non-small cell lung cancer patients receiving neoadjuvant chemo-immunotherapy treatment from NADIM study.** *First Author: Alberto Cruz Bermudez, Instituto Investigacion Sanitaria Puerta de Hierro-Segovia de Arana, Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain*

**Background:** Characterization of the peripheral blood T-cell receptor (TCR) repertoire has become a novel approach to predict the clinical benefit to anti-PD1/PDL1 therapy. However, there is lack of knowledge about the clinical relevance of TCR repertoire in terms of pathological response and clinical outcomes (PFS and OS) in chemo-immunotherapy. To answer this question we have analysed samples from the NADIM study (NCT03081689), in which resectable stage IIIA NSCLC patients were treated with neoadjuvant chemo-immunotherapy with Nivolumab. **Methods:** Using ION Torrent-based next-generation sequencing we have analysed TCR repertoire of peripheral blood from 30 patients receiving chemo-immunotherapy. Using 25ng of total RNA from PBMCs, clonal convergence, evenness and diversity were calculated at diagnosis (pre-treatment) and after 3 cycles of Nivolumab plus carboplatin (post-treatment). Regarding pathological responses, patients were classified in 3 groups: complete response (pCR) (0% viable tumour at the resection specimen), mayor response (pMR) ( $<$ 10% viable tumour) and incomplete response (pIR) ( $>$ 10% of viable tumour). At data analysis, PFS and OS median follow-up times were longer than 20 months. **Results:** No statistically significant differences in TCR repertoire in terms of evenness (p = 0,373), diversity (p = 0,691) or convergence (p = 0,054) between pre- and post-neoadjuvant treatment were observed. Similarly, no significant differences were observed in these metrics between pathological response groups. However, a detailed analysis of the clones showed that the percentage of frequent clones (greater than 0.1%) that increase after neoadjuvant therapy does show differences between the different pathological response groups (pIR vs pMR), being elevated in patients who presented responses greater than 90% (p = 0.0385). Regarding the clinical benefit, having this parameter higher than the median (43,90% in this cohort) is associated with a higher PFS (p = 0.0490) and OS (p = 0.078) using KM Log-rank test. **Conclusions:** Evenness, Diversity and Convergence derived from immune repertoire analysis do not appear to be clinically useful in the context of neoadjuvant chemo-immunotherapy in lung cancer. However, the detailed analysis of the clones seems promising. The increase of the most frequent clones after treatment seems to be associated to different clinical variables such as pathological response and PFS in these patients. Clinical trial information: NCT03081689. Research Sponsor: BRISTOL MYERS SQUIBB.

**9042 Poster Session (Board #235), Fri, 8:00 AM-11:00 AM**

**Clinical characteristics, genomic features, and recurrence risk of early-stage MET exon 14 mutant non-small cell lung cancer (NSCLC).** *First Author: Gonzalo Recondo, Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute, Boston, MA*

**Background:** *MET* exon 14 alterations occur in ~3% of patients (pts) with NSCLC. Although clinical and genomic features of *MET* exon 14 mutant (mut) NSCLC are better characterized in the metastatic setting, less is known about early-stage disease for this molecular subtype. **Methods:** Clinicopathologic and genomic data were collected from patients (pts) with resected stage I-III *MET* exon 14 mutant NSCLC at the Dana-Farber Cancer Institute (DFCI) and the Memorial Sloan Kettering Cancer Center (MSKCC). We estimated the disease-free survival (DFS) and overall survival (OS) of patients from the date of surgical resection. The prevalence of *MET* exon 14 mutations in stage I-III NSCLC was assessed using OncoPanel NGS v3.0 at DFCI. **Results:** The prevalence of *MET* exon 14 alterations in resected tumors of pts with stage I-III NSCLC at DFCI using Oncopanel v3 was 2.8% (17/613) overall: 2.9% (16/542) in non-squamous and 1.4% (1/71) in squamous histology. We identified 131 pts with resected stage I-III (I = 73, II = 28, III = 30) *MET* exon 14 mut NSCLC at DFCI (Oncopanel v1-v3) and MSKCC (MSK-IMPACT), with a median age of 71 years (yrs) (range: 43-88). There were no significant differences in sex, smoking status, or type of *MET* alteration across stages. In stage I resected tumors there was a higher proportion of adenocarcinoma histology compared to stages II and III (p = 0.009). The median harmonized TMB (mTMB) was similar across stages (p = 0.43). Common genomic co-alterations included *MET* amplification (amp) (5.3%), *CDK4/6* amp (19.1%), *MDM2* amp (35.1%), *TP53* mut (17.6%) and *CDKN2A/B* loss (9.2%). The median DFS in stage I, II, and III NSCLC was 8.3 yrs (95% CI: 3.1-8.3), 2.6 yrs (95% CI: 1.0-2.6), and 2.1 yrs (95% CI: 0.7-2.7), respectively (p = 0.017). The median OS in stage I, II, and III NSCLC was 9.2 yrs (95% CI: 8.5 -10.5), not reached (NR) (95% CI: NR-NR), and 4.1 yrs (95% CI: 3.6-4.1), respectively (p = 0.052). Concurrent *MET* amp was independently associated with worse DFS (HR: 4.9, 95% CI: 1.8-13.1; p = 0.002) in multivariate analysis. **Conclusions:** *MET* exon 14 mutations are present in 2.8% of resected stage I-III NSCLCs. Given the prevalence of this molecular alteration in early-stage NSCLC, clinical trials exploring the role of adjuvant and neoadjuvant MET targeted therapies in this population may be warranted. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

**9043 Poster Session (Board #236), Fri, 8:00 AM-11:00 AM**

**Contemporary management and associated outcomes of 3,151 patients with stage III non-small cell lung cancer (NSCLC) in a real-world setting: Results of KINDLE, a multicountry observational study.** *First Author: Abdul Rahman Jazieh, Oncology Department, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia*

**Background:** Stage III NSCLC is a heterogeneous disease requiring a multimodality approach. We conducted a global study to characterise the patients (pts), treatment patterns and their associated outcomes for this disease in a real-world setting in the pre-IO era. **Methods:** KINDLE is a retrospective, multicountry, multi-centre study capturing data on patient and disease characteristics, treatments and outcomes. The study included pts with stage III NSCLC diagnosed between January 1$^{st}$, 2013 and December 31$^{st}$, 2017 and with at least 9 months of documented follow-up. Descriptive statistics were used to describe patient demographics, disease characteristics and treatment modalities. Inferential statistics was used to correlate various clinical and treatment variables with progression free survival (PFS) and overall survival (OS). **Results:** 3151 patients were enrolled at 125 centres in three geographical regions; 1046 pts in Middle East and North Africa, 1874 pts in Asia and 231 pts in Latin America. Median age was 63 years (range 21-92); 76.5% were male; 69.2% with a smoking history; 55.9% were staged as IIIA (AJCC 7$^{th}$ ed.); 53.7% had adenocarcinoma and 36.6% squamous cell, and 31.7% were known to have an EGFR mutation. 21.4% of patients underwent curative surgical resection. First line therapy included more than 25 different regimens, the most common being concurrent chemo-radiotherapy (cCRT) in 29.4%, chemotherapy (CT) alone in 17%, sequential chemo-radiotherapy (sCRT) in 10.4%, and radiotherapy (RT) alone in 8.5%. Median PFS for the whole cohort was 12.5 mos (95% CI; 12.06 – 13.14) and median OS 34.9 mos (95% CI; 32.00 – 38.01). Stage IIIA patients who were eligible for and underwent surgery + CT, had longer OS than patients who did not undergo surgery, receiving other treatments. Non-surgical approaches included CT, RT, and CRT. In stage IIIB, OS was significantly improved for cCRT vs. CT alone (p = 0.0015) or RT alone (p = $<$ 0.0001) or sCRT (p = 0.0216). Improved survival was observed with sCRT compared with RT alone and chemotherapy vs RT alone. **Conclusions:** KINDLE, a large multicountry observational study, reveals the diversity of treatment practices that exist in stage III NSCLC and provides insights on the outcomes in a real-world setting. The unmet medical need remains high and approaches are required to optimize patient outcomes including implementation of guidelines, physician education and improved access to innovative medicines and quality care. Research Sponsor: AstraZeneca.

**9044 Poster Session (Board #237), Fri, 8:00 AM-11:00 AM**

**A retrospective evaluation of PD-L1 expression on primary non-small cell lung cancer (NSCLC) samples and associated involved hilar or mediastinal lymph nodes (N1 or N2) (REPLICA).** *First Author: Eleni Karapanagiotou, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom*

**Background:** Little is known about the PD-L1 expression in early stage NSCLC as well as the possible heterogeneity of PD-L1 expression in different sites. This study provides information on both PD-L1 expression in stage II and III NSCLC and the relationship between PD-L1 expression in the primary site (lung) and metastatic lymph nodes (LNs) N1 and/or N2. **Methods:** Samples (primary tumor and N1/N2) from 500 patients who underwent lung resection and lymphadenectomy for NSCLC without prior treatments were collected and analyzed for PD-L1 expression using the 22C3 pharmdx Agilent assay. The tumor proportion score (TPS) is documented for each sample according to the following categories: PD-L1: < 1%, 1-49%, ≥ 50%. PD-L1 stained slides were reviewed by two pathologists independently; for discrepant cases the two pathologists reviewed the stains jointly and the consensus score used for the data analysis. Agreement between the two pathologists was assessed by overall agreement and kappa statistic. The association between PD-L1 expression in the primary tumor and lymph node was assessed by cross-tabulation. **Results:** A total of 456 tumors and involved LNs were included in the analysis. Pathologist one assessed 435 primary tumor and LN pairs and pathologist 2 assessed 453 tumor and LNs pairs. The overall agreement between pathologists on PD-L1 expression in primary tumor samples was 77%; K = 0.59 (95% CI 0.57 – 0.63) and in LNs 83%; k = 0.62 (95% CI 0.56 – 0.70). Primary tumors showed PD-L1 < 1% in 235/422 (55,6%), PD-L1 1-49% in 146/422 (34,6%) and PD-L1 > = 50% in 41/422 (9.8%). 77% (327/422) showed no heterogeneity in PD-L1 expression between the primary tumor and involved LNs. In tumors with PD-L1 < 1% expression, 94% of the LNs showed PD-L1 < 1% expression and less than 1% showed PD-L1 > = 50%, 6% of the LNs showed PD-L1 1-49%. When the primary tumor was PD-L1 > = 50% nearly half (46%) of the involved LNs showed the same degree of PD-L1 positivity and 10% of them showed PD-L1 < 1%; 44% of the LNs showed PD-L1 1-49%. When the primary tumor showed 1-49% PD-L1 staining, 60% of the LNs showed the same staining pattern, 36% showed PD-L1 < 1% and only 4% showed PD-L1 > = 50% expression. **Conclusions:** In stage II and III NSCLC, half of the primary tumors show negative PD-L1 expression. Discrepant PD-L1 expression between primary tumors and LN metastases was seen in 23% of the cases, and when present, PD-L1 expression in LN tumors tended to be lower than that in primary tumors. Research Sponsor: MERCK.

**9045 Poster Session (Board #238), Fri, 8:00 AM-11:00 AM**

**AFT-16: Phase II trial of atezolizumab before and after definitive chemoradiation (CRT) for unresectable stage III non-small cell lung cancer (NSCLC).** *First Author: Helen J. Ross, Mayo Clinic, Phoenix, AZ*

**Background:** A minority of the > 40,000 patients (pts) diagnosed with stage III NSCLC annually in the US are cured by CRT, more recently followed by adjuvant immune checkpoint inhibitors (ICI). PD-L1 blockade with CRT may attenuate tumor-related immunosuppression via depletion of regulatory T cells and clonal expansion of effector T cells. Further, CRT may expose otherwise hidden antigens that present additional targets to the reconstituting immune system. Adjuvant ICI has improved survival. Whether ICI before CRT will further improve outcomes is unknown. **Methods:** This Alliance Foundation Trials (AFT) study evaluated safety and efficacy of atezolizumab before and after CRT. 4 cycles of atezolizumab 1200 mg IV q 21 days with restaging after cycles 2 and 4 were followed by carboplatin and paclitaxel (C/P) weekly with 60 Gy radiation and C/P consolidation followed by atezolizumab for 1 year of therapy. Primary endpoint is disease control rate (DCR) (complete response + partial response (PR) + stable disease (SD)) at 12 weeks (wks). Secondary endpoints include overall response rate, progression-free survival, overall survival, safety and quality of life assessed by EORTC QLQ-30. Correlatives include PD-L1 and tumor mutation burden as predictive biomarkers. Tumor tissue was obtained at study entry; plasma and immune cells were isolated at multiple timepoints. **Results:** 64 pts with stage III NSCLC, performance status (PS) 0-1, no active autoimmune disease or significant organ dysfunction enrolled at 13 Alliance sites from 11/2017 to 7/2019. 62 pts received ≥ 1 dose of atezolizumab and are included in the primary analysis; median age 63.9 years (38.1-86.5), 51.6% female, 77.4% white, 61.3% former smokers, 56.5% PS 0. DCR at 12 wks was 77.4% (80% confidence interval 69.2-84.3%) (30.7% PR, 46.8% SD). 54 pts reported adverse events (AEs) during induction, mostly grade (gr) 1. There were 13 serious AEs, most unrelated to study treatment; 1 gr 3 anaphylactic reaction, 1 gr 3 colitis, and 1 gr 4 Guillain-Barre syndrome were attributable to atezolizumab. Baseline PD-L1 status was available for 49 pts. DCR was 82.4% for pts with PD-L1 negative and 90.9% for pts with PD-L1 positive tumors. **Conclusions:** Atezolizumab prior to and following CRT for stage III unresectable NSCLC was well tolerated with an encouraging 12-wk DCR. Analysis of secondary endpoints is ongoing. Further study of induction ICI therapy is warranted in patients with unresectable stage III NSCLC. Support: AFT, Genentech; Clinical trial information: NCT03102242. Research Sponsor: Alliance Foundation Trials, Pharmaceutical/Biotech Company.

**9046 Poster Session (Board #239), Fri, 8:00 AM-11:00 AM**

**A mid-chemoradiation dynamic risk model integrating tumor features and ctDNA analysis for lung cancer outcome prediction.** *First Author: Everett J Moding, Stanford University, Stanford, CA*

**Background:** Circulating tumor DNA (ctDNA) molecular residual disease after curative intent therapy predicts disease progression in localized lung cancer. We hypothesized that integrating pre-CRT features and ctDNA levels during chemoradiation therapy (CRT) can predict patient outcomes earlier to enable response-adapted therapy. **Methods:** We identified pre-CRT features prognostic of disease progression after CRT for Stage II-III non-small cell lung cancer (NSCLC) in a historical "pre-CRT" training cohort of 109 patients. In addition, we applied CAPP-Seq ctDNA analysis pre-CRT and a median of 21 days into CRT (mid-CRT) to a "ctDNA" training cohort of 42 patients treated at MD Anderson and an independent validation cohort of 21 patients treated at Stanford. Prognostic pre-CRT features and mid-CRT ctDNA concentration were integrated using a Bayesian proportional hazards approach to generate a Continuous Individualized Risk Index (Kurtz et al. Cell 2019) for NSCLC (CIRI-NSCLC) to predict freedom from progression (FFP). **Results:** Adenocarcinoma histology (HR 2.6, P = 0.0005) and *KEAP1* mutation (HR 2.7, P = 0.002) but not stage (P = 0.16), age (P = 0.60), or gender (P = 0.98) were significantly associated with FFP in the pre-CRT training cohort. Mid-CRT ctDNA concentration as a continuous variable was significantly associated with FFP in the ctDNA training cohort (HR 1.6, P = 0.04), and applying an optimal threshold identified in the training cohort (3.2 hGE/ml) significantly stratified FFP in the independent ctDNA validation cohort (HR 4.8, P = 0.02). CIRI-NSCLC enabled individualized real-time updating of the probability of FFP as model features became available over the course of CRT. CIRI-NSCLC outperformed individual model features in the independent validation cohort when compared by C-statistic (CIRI-NSCLC: 0.85; mid-CRT ctDNA: 0.76; histology: 0.66; *KEAP1*: 0.60). Across the whole cohort, patients with a greater than 66% risk of progression predicted by CIRI-NSCLC (n = 10) had an FFP of 10.0% at 12 months while patients with a less than 33% risk of progression predicted by CIRI-NSCLC (n = 22) had an FFP of 79.7% at 12 months (HR 15.0, P < 0.001). **Conclusions:** Our results suggest that CIRI-NSCLC can identify patients at very high and low risk of progression. Prospective evaluation will be necessary to test the potential utility of adapting treatment based on CIRI-NSCLC. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

**9047 Poster Session (Board #240), Fri, 8:00 AM-11:00 AM**

**Real-world treatment patterns and clinical outcomes in *EGFR*-mutant unresectable locally advanced NSCLC (LA-NSCLC): A retrospective multicenter study of 367 patients.** *First Author: Nan Bi, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital & Shenzhen Hospital, Beijing, China*

**Background:** The chemoradiation therapy (CRT) is the standard care for unresectable LA-NSCLC. The addition of EGFR-TKIs in first-line treatment of *EGFR*-mutant subpopulation is debatable. **Methods:** We retrospectively collected data for patients with unresectable stage III NSCLC harboring *EGFR* mutations from nine major academic cancer institutions in China from Jan 2012 to December 2018. Patients with *ALK* rearrangements were excluded. Patients were categorized into three subgroups according to the primary treatment: 1) RT+TKI: Combined RT and EGFR-TKI with/out chemotherapy ; 2) no TKI: CRT alone; 3) upfront TKI: EGFR-TKI followed by RT at local-regional progression. PFS and OS were calculated from the date of diagnosis. Log-rank test was used to assess for differences and Cox proportional hazards model was used to adjust for covariates. **Results:** A total of 367 patients met selection criteria were included in the study. Patients receiving TKI were older (≥60 years: 54.7% TKI *v* 36.4% and RT+TKI 33.3% CRT; P = 0.001), and more patients receiving CRT had uncommon *EGFR* mutations ( 10.3% CRT *v* 2.3% RT+TKI and 4.0% TKI; P = 0.020). Other baseline characteristics were well balanced among groups. With a median follow-up of 40.8 months, the median PFS and OS were 16.6 and 55.4 months for the entire cohort. The median PFS and OS for the three subgroups were shown in the table. On multivariable analysis, after adjusting for age, KPS status, smoking status, stage, and type of *EGFR* mutations, TKI+RT was independently associated with improved PFS (HR, 0.57; 95% CI, 0.41 to 0.78 ) and OS (HR, 0.61; 95% CI, 0.39 to 0.97) relative to upfront TKI ; TKI+RT was also associated with improved PFS (HR, 0.38; 95% CI, 0.27 to 0.54 ) relative to CRT, but not OS (HR, 0.66; 95% CI, 0.40 to 1.11). **Conclusions:** The use of upfront EGFR-TKI with deferred RT at progression was associated with inferior OS in patients with *EGFR*-mutant unresectable LA-NSCLC. First-line use of radiotherapy and EGFR-TKI was associated with the longest PFS and OS, which requires further prospective, randomized evaluation. Research Sponsor: National Natural Science Foundation of China (grants 81572971 ) .

| Endpoints | RT+TKI (N = 88) Median (95% CI) | CRT alone (N = 78) Median (95% CI) | Upfront TKI (N = 201) Median (95% CI) | P-value |
|---|---|---|---|---|
| PFS | 21.6 (13.8 to 29.4) | 12.6 (10.8 to 14.2) | 16.5 (14.1 to 18.9) | < 0.001 |
| OS | 67.4 (57.5 to 77.3) | 54.2 (40.0 to 68.3) | 46.5 (34.5 to 58.6) | 0.055 |

**9048 Poster Session (Board #241), Fri, 8:00 AM-11:00 AM**

**Non-pneumonitis immune-mediated adverse events (imAEs) with durvalumab in patients with unresectable stage III NSCLC (PACIFIC).** *First Author: Jarushka Naidoo, Department of Oncology, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD*

**Background:** The phase 3 PACIFIC trial established durvalumab (durva) after chemoradiotherapy (CRT) as SoC for pts with unresectable stage III NSCLC. We report exploratory analyses to characterize non-pneumonitis (np) imAEs that occurred with durva in PACIFIC. **Methods:** PACIFIC was a double blind trial of pts without disease progression after platinum-based concurrent CRT (≥2 cycles). Pts were randomized 2:1 to receive durva 10 mg/kg or placebo (pbo) IV q2w for ≤12 months, stratified by age, sex and smoking history. We characterized the time to onset, duration, and management/outcomes of np imAEs and their association with (1) baseline pt/disease factors and (2) AEs (excluding all-cause pneumonitis). **Results:** Of 709 treated pts, 19% and 11% experienced imAEs and np imAEs of any grade, respectively; proportionally more had np imAEs with durva (71/475; 15%) vs pbo (5/234; 2%). Thyroid disorders (54/475; 11%), rash/dermatitis (9/475; 2%), and diarrhea/colitis (5/475; 1%) were the most common np imAEs with durva; rash/dermatitis had the shortest time to onset (Table). Among durva treated pts with np imAEs, 11% had grade 3/4 np imAEs, 41% had np imAEs that resolved, and none had fatal np imAEs; interventions included endocrine replacement therapy (73%), systemic corticosteroids (34%), high dose corticosteroids (16%), and discontinuation (10%). There were no apparent differences in baseline factors between pts with or without np imAEs. Durva had a broadly manageable safety profile irrespective of the occurrence of np imAEs. However, a higher proportion of durva treated pts with vs without np imAEs experienced all-cause, grade 3/4 events (41% vs 29%); none were fatal (excl. pneumonitis). **Conclusions:** Np imAEs occurred infrequently in PACIFIC, but were more common with durva vs pbo; thyroid disorders and rash/dermatitis were the most common np imAEs. Of durva treated pts with np imAEs, 11% experienced np imAEs of grade 3/4. Overall, np imAEs were broadly manageable and did not lead to high rates of discontinuation, and no association with baseline factors was seen, suggesting this should not deter use of durva in eligible pts. Clinical trial information: NCT02125461. Research Sponsor: AstraZeneca.

**Timing of np imAEs in durva treated pts (≥5 pts with events)**

| Np imAE category (any grade) | Time to onset from 1st dose, median (range), days [n]* | Duration, median (range), days [n]† |
|---|---|---|
| Thyroid disorders | 85.0 (14–378) [54] | 63.5 (15–224) [20] |
| Rash/Dermatitis | 37.0 (6–111) [9] | 117.0 (18–738) [6] |
| Diarrhea/Colitis | 61.0 (2–254) [5] | 74.0 (12–151) [5] |

*Based on the 1st event reported for each pt. †Excludes ongoing events.

**9049 Poster Session (Board #242), Fri, 8:00 AM-11:00 AM**

**The impact of residual metabolic primary tumor volume after completion of thoracic irradiation in patients with inoperable stage III NSCLC.** *First Author: Olarn Roengvoraphoj, Department of Radiotherapy and Radiation Oncology, University Hospital, LMU Munich, Munich, Germany*

**Background:** The metabolic tumor volume (MTV) is a functional and volumetric PET/CT parameter that has been investigated in recent years with respect to its predictive and prognostic value in different tumor entities. In this study, we investigated the role of residual MTV after completion of thoracic irradiation in inoperable stage III non-small cell lung cancer (NSCLC). **Methods:** We analyzed retrospective and prospective data of 56 patients with inoperable stage III NSCLC treated with chemoradiotherapy (CRT) and chemoradioimmunotherapy (CRT-IO). All patients received an 18F-FDG-PET/CT 3 to max. 6 months after completion of thoracic irradiation. The measurement of the residual MTV of the primary tumor was performed by calculating the SUVmean of the liver + 2SD as threshold. The patients were divided into the following groups: residual-MTV < 1ml; residual-MTV 1-25ml and residual-MTV > 26ml. Survival, local recurrence, and distant metastasis rates were calculated using the Kaplan-Meier method from the last day of thoracic irradiation. **Results:** The median follow-up was 45 months (range 16-74) in the CRT group and 16 months in the CRT-IO group (range13-19). Twenty-two (39%) patients had a residual MTV < 1ml (1st group), 19 (34%) a residual MTV between 1-25ml (2nd group) and 15 (27%) a residual MTV > 25ml (3rd group) after completion of thoracic irradiation. Median overall survival was 61, 20 and 12 months (p = 0.006) in the 1st, 2nd and 3rd groups, respectively. 12-month survival was 86%, 50% and 33% after CRT vs. 88%, 71% and 50% after CRT-IO in the 1st, 2nd and 3rd groups, respectively. The median time to in-field recurrence in the 1st, 2nd and 3rd groups was 51, 20 and 15 months (p = 0.011). The prognostic value of the residual MTV on OS was confirmed exclusively in the CRT patient cohort (p = 0.04), but not in the CRT-IO patient cohort (p = 0.174). Residual MTV demonstrated no influence on the local recurrence rate in the CRT-IO patient cohort, but only in patients treated with CRT (p = 0.007). **Conclusions:** Patients with inoperable stage III NSCLC in whom the residual MTV was < 1ml after completion of thoracic irradiation showed significantly better survival than patients with a residual MTV of 1-25ml and MTV > 25ml. The subgroup analysis confirmed the prognostic value of residual MTV only in patients who received chemoradiotherapy without consolidation immunotherapy. Research Sponsor: None.

**9050 Poster Session (Board #243), Fri, 8:00 AM-11:00 AM**

**Neoadjuvant endobronchial delivery of gene mediated cytotoxic immunotherapy (GMCI) for non-small cell lung cancer (NSCLC): Safety and immunologic activity.** *First Author: Laura K. Aguilar, Candel Therapeutics, Needham, MA*

**Background:** GMCI is a tumor-specific immuno-oncology approach implemented through local delivery of *aglatimagene besadenovec*(AdV-tk) followed by anti-herpetic prodrug. This leads to immunogenic tumor cell death, antigen presenting cell activation, and T cell stimulation resulting in $CD8^+$ T cell dependent protection, as demonstrated in preclinical models and clinical trials in other tumor types. This is the first study to assess endobronchial delivery of AdV-tk for NSCLC. **Methods:** This Phase I dose escalation trial enrolled patients with suspected NSCLC who were candidates for surgery. A single AdV-tk injection was performed by endobronchial ultrasound (n = 11) or mediastinoscopy (n = 1) during the diagnostic staging procedure 3 weeks prior to surgery. Three dose levels were evaluated: $2.5x\ 10^{11}$, $5x10^{11}$, and $1x10^{12}$ vector particles (vp) in a 3+3 design. Valacyclovir was administered for 14 days, starting the day after AdV-tk injection. To assess the local and systemic effects of GMCI, immune biomarkers were evaluated in blood and tumor samples before and after GMCI. **Results:** From 2017-2019, 12 patients (9 men, 3 women, median age 65 [range 55-80]) received GMCI followed by surgery. Average tumor size was 5.1 cm (largest diameter) and final pathologic stage was I (n = 4), II (n = 3), and III (n = 5). Treatment-related adverse events were CTC grade 1 fever (n = 1), flu-like symptoms (n = 1) and nausea/vomiting/diarrhea (n = 1). The only > grade 2 lab abnormality was transient grade 3 lymphopenia (n = 2). A measurable reduction in tumor size was observed in one patient. The average amount of tumor necrosis was 29.4%. Significant infiltration of $CD8^+$T cells (5.2-fold compared to baseline, p = 0.001) was found in tumor 19-22 days after AdV-tk injection. Within the $CD8^+$tumor infiltrating lymphocytes, there was increased expression of CD38 (2.5-fold, p = 0.002), Ki67 (4.8-fold, p = 0.02), PD1 (1.9-fold, p = 0.002), CD39 (2.9-fold, p = 0.04) and CTLA-4 (4.8-fold, p < 0.001), without significant detected differences in Tim3 or TIGIT. Simultaneously, peripheral blood $CD8^+$ cells displayed significant increases in CD38 (3.4-fold, p = 0.006), HLA-DR (4.2-fold, p = 0.002), and Ki67 (5.8-fold, p = 0.017). **Conclusions:** Intratumoral injection of AdV-tk into lung tumors was safe and feasible. Further, AdV-tk effectively induced peripheral blood and intra-tumoral CD8 T cell activation. Consequent upregulation of inhibitory receptors suggests a potential benefit for combination therapies. Clinical trial information: NCT03131037. Research Sponsor: Advantagene.

**9051 Poster Session (Board #244), Fri, 8:00 AM-11:00 AM**

**Neoadjuvant nivolumab (N) plus cisplatin (C)/pemetrexed (P) or cisplatin /gemcitabine (G) in resectable NSCLC.** *First Author: Ralph Zinner, University of Kentucky, Department of Medical Oncology, Lexington, KY*

**Background:** Patients (pts) with resectable stage IB (≥4cm)-IIIA non-small-cell lung cancer (NSCLC) derive modest overall survival benefit with neoadjuvant or postoperative adjuvant chemotherapy. Neoadjuvant therapy can speed the discovery of promising regimens by using pathologic response as a surrogate for OS. Major pathologic response (MPR), defined as < 10% viable tumor, was strongly associated with improved OS. PD-(L)1 checkpoint inhibitors in combination with chemotherapy are standard of care in advanced NSCLC. We hypothesize that the addition of N to neoadjuvant CP or CG will increase the MPR rate compared to historical controls. **Methods:** This is an investigator-initiated trial for pts with newly diagnosed AJCC 8th stage IB (≥4cm)-IIIA squamous or non-squamous EGFR/ALK WT NSCLC with a plan to have surgery. Pts receive 3 courses of N 360mg IV q 3w added to C 75mg/m2 IV q 3w plus P 500 $mg/m^2$ IV q 3wks or G 1250$mg/m^2$ IV d1, d8 with surgery 3 wks after the last dose. The primary objective is MPR. To estimate pathologic response, the resected pathology specimens are cut >1 section/cm. Using the Aperio Digital scanning system©, slides were imaged, and then annotated by at least 2 pathologists for viable tumor vs. treatment effect with respective areas then automatically calculated and percentage of viable tumor calculated. Our primary endpoint will be reached if 10/34 (29%) planned pts have at least an MPR. **Results:** From 6/2018-8/2019, 13 pts were enrolled all of whom had surgery. Median age was 69 (49-80), 38% women, 31% nonsquamous, 54% stage IIIA, and 77% PD-L1 positive (≥1%, SP263). Pre-surgical grade 3 toxicity occurred in 2/13 pts, one of whom was changed to carboplatin for courses 2 and 3. Grade 3 toxicities were neutropenia (2/13), anemia (1/13), and renal (1/13). One pt. developed hypothyroidism 4 mos after surgery. One pt died 6 weeks after surgery from complications unrelated to study drugs. Our primary endpoint was met; 11/13 (85%), had at least an MPR with 6/13 (46%) and 5/13 (38%) having an MPR and pCR respectively. Radiologic response rate was 46% (PR 5, CR 1). Pts with either PD-L1+ or PD-L1- had MPRs. With a median follow-up of 10 months there are no recurrences. **Conclusions:** The combination of nivolumab added to platinum doublets was well tolerated. The primary endpoint of MPR in at least 10/34 pts was surpassed with MPR or pCR in 11/13 pts post-surgery. MPR was seen independent of PD-L1 score. Exploratory outcomes assessing markers of immune bias in tumor tissue and plasma are in process. Clinical trial information: NCT03366766. Research Sponsor: Bristol-Myers Squibb.

**9052 Poster Session (Board #245), Fri, 8:00 AM-11:00 AM**

**Efficacy and safety of nivolumab for malignant mesothelioma in the real world.** *First Author: Koji Mikami, Division of Respiratory Medicine, Department of Internal Medicine Department of Thoracic Oncology Hyogo College of Medicine, Nishinomiya, Hyogo, Japan*

**Background:** Until recently, the standard treatment for advanced malignant pleural mesothelioma (MPM) was only cisplatin plus pemetrexed. Nivolumab, an anti-programmed death-1 monoclonal antibody, shows efficacy against pretreated MPM and has been approved in Japan, but the data regarding the efficacy and safety of nivolumab in MPM are limited to those from a small number of patients of the MERIT study. Therefore, it is important to accumulate real-world data on the efficacy and safety of nivolumab for MPM. **Methods:** We retrospectively analyzed all patients with MPM who received nivolumab at Hyogo College of Medicine Hospital from August 2018 to December 2018. **Results:** A total of 77 patients (61 males and 16 females) were included. There were 62, 10, and 5 patients with performance statuses of 0–1, 2, and 3, respectively. There were 63, 8, and 6 patients with epithelioid, sarcomatoid, and bi-phasic histologies, respectively. Nivolumab was administered as second-, third-, and ≥fourth-line treatment to 48, 15, and 11 patients, respectively. In 66 patients who were examined for efficacy, the response rate (RR) was 24.2% and the disease control rate (DCR) was 63.6%. By the histology type, the RR and DCR were 15.1% and 62.3% for the epithelioid type, 62.5% and 87.5% for the sarcomatoid type, and 20.0% and 40.0% for the bi-phasic type, respectively. The median progression-free survival (mPFS) was 4.1 months and the median overall survival (mOS) was 13.3 months. Analyzing the efficacy based on the neutrophil-to-lymphocyte ratio (NLR) in the peripheral blood, the RRswere 14.7% in the NLR≥3.5 group and 25.8% in the NLR $<$ 3.5 group. The mPFS and mOS in the NLR≥3.5 group were 3.1 months and 11.4 months, respectively,whereas those in the NLR $<$ 3.5 group were 5.6 months and not reached, respectively. There were no significant differences in the RR, PFS, and OS between the groups, but a trend of better RRs and longer survivals wasobserved in the NLR $<$ 3.5 group than in the NLR≥3.5 group. Regarding adverse events, fatigue (grades 1 − 2) was observed in 8, hypothyroidism (grade 1–2) in 11, renal dysfunction (grade 1–3) in 6, loss of appetite (grade 1–2) in 2, pneumonitis (grade 3) in 1, rash (grade 1) in 2, and hypopituitarism (grade 3) in 1 patient(s). **Conclusions:** This retrospective study revealed the effectiveness and safety of nivolumab for MPM in the real-world setting.Nivolumab can be used as a standard second-line treatment for MPM. Furthermore, it has been suggested that the NLR may be a predictive marker of the effect of nivolumab for MPM, as pointed out in other carcinomas. Research Sponsor: None.

**9053 Poster Session (Board #246), Fri, 8:00 AM-11:00 AM**

**A gentle therapy: Weekly epirubicin, as second-line treatment in elderly patients with malignant pleural mesothelioma (MPM).** *First Author: Roberto Bollina, ASST Rhodense, Rho - Milan, Italy*

**Background:** MPM is a rapidly progressive tumor with a poor prognosis. Treatment options are limited for patients (pts) with PMP who experience disease progression after first-line pemetrexed-based chemotherapy (CT). This retrospective study wants to evaluate, in the age of immunotherapy, whether a gentle CT can be used as second line of treatment in elderly pts, above all maintaining quality of life (safety and tolerability ) and improving progession free survival (PFS ). Currently second-line CT is increasingly use, because many elderly pts are fit at the progression of the disease. No standard second/further line CT exist for MPM after failure of first-line pemetrexed based CT. The purpose of the study is to evaluate the clinical activity of weekly epirubicin as second-line CT in elderly with MPM. **Methods:** From July 2015 to March 2019, in Medical Oncology Dept. of ASST Rhodense 98 pts were elegible for analysis. Pts had histologically confermed unresectable MPM. Histology was epithelioid in 86 pts, sarcomatoid in 7 and biphasic in 5 pts. A Carboplatin(AUC4)-pemetrexed doublet was administered in 70 pts and 28 received gemcitabine as single agent how first line. A quality of life questionnaire was administered to each pt and geriatric comprehensive assessment (GCA) was performed. Epirubicin ( E ) was always administered with a schedule at 20 mg/msq day 1,8,15 every 28 until disease progression or intolerance. The primary endpoint was PFS, and secondary endpoints were the overall response rate (ORR) and QofL an overall survival (OS). **Results:** Of the 98 elegible pts, 71 was males, and 27 was female . Median age: 78 (range 72-86) PS: 0/1/2 was respectively in 32%, 60% and 8% of pts. A median of 5 cycles of E (range 2 -16) was delivered; 3% of pts required dose modification. PFS was of 7 months (range 3-16) . ORR was as follow: 0 CR, 18 PR (17%), 44 SD (44%) and PD occurred in 36 pts (39%). OS was 11 months (range 5-22). No life threatening event occurred. No grade 3-4 toxicities were observed . Liver toxicity grade 1-2in 10 pts (10%), thrombocytopenia grade 1 in 9 pts (9%), neutropenia grade 1-2 in 40 pts (40%), fatigue grade 2 in 33pts (32%), nausea grade 1 in 20 pts (20%). The analitical and stratified data will be exposed. **Conclusions:** Also in the era of immunotherapy, a simple treatment, E in weekly schedule has demonstrated to be a gentle therapy with a possibility to treat in second line, pre-treated elderly pts with MPM in progression after first line therapy, with an acceptable profile . Now this schedule could be considered as a safe and standard secon-line CT in elderly pts. Research Sponsor: None.

**9054 Poster Session (Board #247), Fri, 8:00 AM-11:00 AM**

**Phase II study of olaparib in malignant mesothelioma (MM) to correlate efficacy with germline and somatic mutations in DNA repair genes.** *First Author: Raffit Hassan, Thoracic and GI Malignancies Branch, National Cancer Institute, NIH, Bethesda, MD*

**Background:** BRCA1 associated protein 1 (*BAP1*), a nuclear deubiquitinase involved in DNA double-strand break repair is frequently mutated in MM. Because poly(ADP-ribose) polymerase inhibitors (PARPIs) induce synthetic lethality in *BRCA1/2* mutant cancers, we sought to evaluate efficacy of olaparib in patients with MM and correlate it with pathogenic germline and somatic mutations in DNA repair genes. **Methods:** Phase II single-center study (NCT03531840) enrolled patients with advanced pleural or peritoneal mesothelioma who had progressed on prior therapies, age $>$18 years, ECOG performance status $<$1, adequate organ and bone marrow function. Olaparib 300mg was given twice daily orally in 3 week cycles until disease progression or toxicity. Efficacy was assessed by CT scan every 6 weeks using RECIST criteria. Whole exome sequencing (WES) was performed on blood and tumor samples to identify pathogenic germline and somatic mutations in DNA repair genes. Primary objective was to determine response rate based on germline or somatic mutation status of DNA repair genes. **Results:** Between July 2018 to May 2019, 23 patients were enrolled, 15 pleural and 8 peritoneal MM [14 male; median age 63 (range 41-75 years); median number of prior treatments 3 (range 1-5)]. Median olaparib cycles received was 4 (2-21). WES to identify pathogenic mutations in the germline and tumor was performed in 23 and 17 patients respectively. Four patients had germline *BAP1*, 1 germline *MRE11A*, and 5 had somatic *BAP1* mutations. Of 22 evaluable patients, 1(4%) had partial response (PR), 17 (77%) had stable disease at 6 weeks and 4 (18%) had progressive disease. Patient with PR had a germline mutation in *MRE11A*. Median progression free survival (PFS) and overall survival (OS) for all patients was 3.4 months (95% CI: 2.7 – 4.8 months) and 8.1 months (95% CI: 4.5 months – not estimable) respectively. Median PFS of germline *BAP1* mutant patients (n = 4) was 2.3 months (95% CI: 1.3 – 3.6 months) compared to 4.1 months (95% CI: 2.7 – 5.5 months) for *BAP1*wild type patients (n = 18;P = 0.026). Median OS was 4.6 months (95% CI: 3.1 – 4.9 months) for patients with germline *BAP1* mutation versus not reached for those without germline *BAP1* mutation (P = 0.0058). The most common side effects of olaparib were anemia (16%), lymphopenia (24%), nausea (14%), and increased creatinine (9%). **Conclusions:** Olaparib has limited anti-tumor activity in previously treated MM patients including those with germline or somatic *BAP1* mutations. Presence of germline *BAP1* mutations was associated with decreased PFS and OS. Clinical trial information: NCT03531840. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

**9055 Poster Session (Board #248), Fri, 8:00 AM-11:00 AM**

**Phase I study of TRC102 in combination with cisplatin and pemetrexed in patients with advanced solid tumors/Phase II study of TRC102 with pemetrexed in patients with mesothelioma refractory to pemetrexed and cisplatin or carboplatin.** *First Author: Marianna Koczywas, Department of Medical Oncology and Therapeutics Research, City of Hope, Duarte, CA*

**Background:** Treatment options remain limited in malignant pleural mesothelioma refractory to pemetrexed +/- platinum. TRC102 (methoxyamine hydrochloride) is a novel biochemical inhibitor of the BER pathway. Available data support the hypothesis that TRC102 bound DNA is a substrate for topoisomerase II, which cleaves TRC102-bound DNA sites to produce strand breaks in cancer cells that cause cellular apoptosis and enhance the cytotoxic effects of chemotherapy. **Methods:** This was a parallel cohort trial of a Phase I of TRC102 in combination with cisplatin (CDDP) and pemetrexed in patients with advanced solid tumors (Arm A) and a Phase II of TRC102 with pemetrexed in patients with mesothelioma refractory to platinum and pemetrexed (Arm B). **Results:** In Arm A dose escalation, 16 pts (11M/5F) were treated; 9 evaluable through 3 TRC102 dose levels (50, 75, and 100 mg/day, PO), with CDDP 60 mg/m$^2$ and pemetrexed 500 mg/m$^2$ (levels 1- 3); and 5 evaluable at TRC102 100 mg/day PO, CDDP 75 mg/m$^2$, pemetrexed 500 mg/m$^2$ (level 4). Cycles were every 21 days. There were no DLT's, establishing level 4 as the RP2D. The only grade 4 treatment-related AE was thrombocytopenia on cycle 22 (level 2). Cycle 1 grade 3 AEs were 1 hypophosphatemia (level 1) and 1 leukopenia (level 2). There were 3 PRs (all parotid salivary gland tumors). Median PFS (95%CI) = 7.1% (1.4 – 15.5) mos. Arm B was designed as the first stage of a two stage Gehan design trial of patients with mesothelioma who had progressed on or recurred within 6 months of pemetrexed + platinum frontline treatment. 14 pts were treated with TRC102 50 mg/day D1-4 and pemetrexed 500 mg/m$^2$ every 21 days. There were 2 PRs (both in epithelioid cancer of which 1 was confirmed), meeting the pre-specified criteria for continued interest ( $>$ 0/14). mPFS (95% CI) was 4.3 (1.4 - 6.8) mos. 8 pts had stable disease for at least 1 cycle (4 stable at cycles 6, 9, 10 and 12). There were 1 grade 4 neutropenia and 5 grade 3 AE's (1 each – anemia, neutropenia, leukopenia, fatigue, hyponatremia). **Conclusions:** TRC102 in combination with CDDP and pemetrexed exhibited antitumor activity, particularly in salivary gland tumors, and a tolerable safety profile at the doses tested. The combination of TRC102 and pemetrexed demonstrated activity in malignant mesothelioma that progressed on prior pemetrexed. Additional studies are warranted to confirm preliminary signals of activity. Clinical trial information: NCT02535312. Research Sponsor: U.S. National Institutes of Health.

**9056 Poster Session (Board #249), Fri, 8:00 AM-11:00 AM**

**Genomic landscape and immune phenotype of malignant pleural mesothelioma.** *First Author: Meera Patel, Wayne State University/Karmanos Cancer Institute, Detroit, MI*

**Background:** Malignant pleural mesothelioma (MPM) is a relatively uncommon malignancy with poor prognosis and no major therapeutic breakthroughs over the past decade. Better understanding of the genomic landscape and distribution of immune biomarkers in this disease has the potential to enable development of novel therapies. **Methods:** We analyzed molecular profiles of 222 MPM tumors using next-generation sequencing of 592 genes utilizing Caris Life Sciences platform. Genes were grouped into pathways: DNA damage repair (DDR) (*ATM, BRCA2, BRIP1, BAP1, CHEK2, ERCC2, FANCA/D2/E/L, MLH1, MSH6, MUTYH, NBN, PMS2, RAD50/51B, WRN*), cell cycle regulation including *TP53* (*RB1,CCNE1, CDKN2A, CCND1, CCND3, CDKN1B*), chromatin remodeling (CR) (*ARID2, ASXL1, DNMT3A, EP300, EZH2, KDM6A, KMT2C, KMT2D, NSD3, PBRM1, SMARCB1/A4, SETD2*), RAS/MAPK (*KRAS, MAP2K1, NF1, NF2*), and PI3K/AKT (*AKT, PIK3CA, PIK3R1/R2, PTEN, RICTOR, TSC1, TSC2, ZNF703*). Tumor mutational burden (TMB), PD-L1 expression (SP142 IHC, tumor staining), and MSI/MMR were analyzed. Seventy-two cases also had whole transcriptome sequencing data. Differences in alterations were compared for age, gender, and pathways. **Results:** Median age of patients (pts) was 72 yr (range, 37-90), 73% were male. Gene pathway alterations were seen in 81% of cases. DDR, specifically homologous recombination (HR), was the most commonly mutated pathway (36.9%), followed by RAS (25.2%) and CR (18.9%). Genes mutated in ≥5% of cases included *BAP1* (26.3%), *NF2* (23.5%), *TP53* (15.5%), *SETD2* (10.2%). PD-L1 was high (≥50% tumor cells positive) in 11.4% (n = 24), intermediate (1-49%) in 31.4% (n = 66), and negative ( < 1%) in 57.1% (n = 120) pts. TMB was high (≥10 mutations/Mb) in 9.6% of tumors (n = 20). None of the tumors were dMMR/MSI-H. HR gene *BAP1* and CR gene *SETD2* mutations trended to be more prevalent in pts ≥70 yo (p = 0.02). CR trended to be more commonly mutated in females (p = 0.02). No other significant differences were found in specific gene/pathway alterations, PD-L1 expression, or TMB in the context of age and gender. Distribution of PD-L1 expression was not different among various pathways. No highly recurrent, targetable fusion isoforms were seen among the 85 identified (mean 1.1 fusions/tumor), which have not yet been characterized for pathogenicity. **Conclusions:** The majority of MPM tumors harbor alteration in one of the key cellular pathways. HR pathway mutations are the most common. The majority of tumors were PD-L1 negative and carry low TMB indicating low immunogenicity. No age and gender specific differences exist except for *BAP1* and *SETD2* mutations. Research Sponsor: None.

**9057 Poster Session (Board #250), Fri, 8:00 AM-11:00 AM**

**MiST1: A phase IIa trial of rucaparib in patients harbouring BAP1/BRCA1 deficient relapsed malignant mesothelioma.** *First Author: Dean Anthony Fennell, University Hospitals of Leicester, Leicester, United Kingdom*

**Background:** Malignant Mesothelioma (MM) remains an incurable cancer lacking effective treatments in the relapsed setting. Personalised therapy is still in its infancy. Homologous recombination (HR) deficiency associated with BRCA1 mutation has been shown to predict sensitivity to inhibition of poly-ADP ribose. In MM, BRCA1 associated protein 1 carboxy-terminal hydrolase (BAP1) is frequently mutated. It regulates both HR, and BRCA1 expression which is lost in 38% of mesotheliomas. Mesothelioma Stratified Therapy 1 (MiST1) was designed to test the hypothesis that BAP1/BRCA1 negative mesotheliomas would exhibit defective HR and exhibit sensitivity to PARP inhibition. **Methods:** MiST1 was a single centre, open label single arm phase IIa design with prospective molecular stratification; cytoplasmic/negative *BAP1* or *BRCA1* deficient MM was deemed eligible. Treatment was 600mg BD rucaparib (R) PO daily every 28 days for 6 cycles or until disease progression, unacceptable toxicity, withdrawal or death. Primary outcome was disease control rate at 12 weeks (DCR12w); secondary outcomes safety and toxicity profile, objective response rate (ORR) and DCR at 24 weeks (DCR24w). The null hypothesis states the true DCR12w is less than or equal to 25% and was tested against a one-sided alternative hypothesis that the DCR12w will be equal to or greater than 50%. **Results:** Between February 2019 and June 2019, 26 patients (pts) were eligible and consented to MiST1, median age 65.5 years, 85% are male and 15% female. Of these pts 15% had an ECOG performance status (PS) of 0 and 85% had an ECOG PS of 1. Molecular eligibility was 89% for BAP1 alone, 50% BRCA1 alone, and 39% BAP1+BRCA1. Primary tumour site was thoracic (96%) and subtype epithelioid (81%). DCR12w was 57.7% (95% CI, 36.9 - 76.7), DCR24w was 23.1% (95% CI, 9.0 – 43.7) and ORR was 11.5% (95%CI, 2.5 – 30.2). R was well tolerated with 9% (15/166) grade (G) 3/4 toxicities seen in 10 pts (38%), with no G5 toxicities. The most common adverse events were nausea occurring in 18 pts (69%), fatigue in 14 pts (54%), and decreased appetite in 10 pts (38%). Six cycles of R was received by 8 pts (30.8%). Dose reductions occurred in 9 pts (n = 8; 1 dose and n = 1; 2 doses). Dose delays occurred in 14 pts. **Conclusions:** MiST1 using the PARP inhibitor R met its primary endpoint of disease control rate at 12 weeks, showing promising efficacy with manageable toxicity. HR deficiency mutation signature enrichment is being investigated to refine the identification of responders to PARP inhibition. PARP inhibition warrants further investigation in MM. Clinical trial information: NCT03654833. Research Sponsor: British Lung Foundation, Pharmaceutical/Biotech Company.

**9058 Poster Session (Board #251), Fri, 8:00 AM-11:00 AM**

**Safety and efficacy of tazemetostat, an enhancer of zeste-homolog 2 inhibitor, in patients with relapsed or refractory malignant mesothelioma.** *First Author: Marjorie Glass Zauderer, Memorial Sloan Kettering Cancer Center, New York, NY*

**Background:** Breast cancer gene 1 (BRCA1)-associated protein 1 (BAP1), a nuclear deubiquitinase, is commonly inactivated in malignant mesothelioma. Preclinical data showed that BAP1 inactivation sensitizes mesothelial cells to inhibition of enhancer of zeste-homolog 2 (EZH2), a methyltransferase implicated as an oncogenic driver in this tumor. This study evaluated the safety and efficacy of tazemetostat (TAZ), a potent and selective EZH2 inhibitor, in relapsed/refractory (R/R) malignant mesothelioma with BAP1-inactivation. **Methods:** EZH-203 (NCT02860286) was a 2-part, open-label, phase 2 study that assessed the pharmacokinetics (PK), safety, and efficacy of TAZ in pts with R/R malignant mesothelioma. In part 1, pts received TAZ 800 mg QD on day 1 (D1) and 800 mg BID, beginning day 2 of cycle 1 (C1). In part 2, pts received 800 mg of TAZ BID on D1 of C1. A two-stage Green-Dahlberg design was used for part 2. Primary endpoints were PK profiling of TAZ in all pts (part 1), and disease control rate (DCR) at week 12 in pts with BAP1-deficient R/R malignant mesothelioma (part 2). Secondary endpoints included safety, overall response rate (ORR), progression-free survival, overall survival, and duration of response (DOR). **Results:** The study enrolled 74 pts with R/R malignant mesothelioma, 70 pts (95%) were centrally confirmed to be BAP1-deficient. Median prior lines of therapy were 2 (range, 1-9). Observed clinical data in the presence of CYP3A4 inhibitors and inducers suggest a low DDI potential of TAZ. The 12 week DCR was 47% (n = 35). The ORR per RECIST version 1.1 was 3% [complete response: 0%; partial response (PR): 3% (n = 2)]. Of the 2 patients with PR, 1 had a DOR of 21 weeks and the other is ongoing (15.3 weeks at data cut off). 47 pts (64%) and 21 pts (28%) had stable disease (SD) and progressive disease, respectively. Overall, 91% pts discontinued, either due to disease progression (n = 65), death (n = 5), or treatment discontinuation (n = 1). Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in ≤5% of patients, most commonly anemia (5%) and dyspnea (4%). No pts discontinued due to TEAEs. There were no treatment related deaths. **Conclusions:** Based on disease control rate and stable disease, TAZ showed antitumor activity in pts with BAP1-deficient R/R malignant mesothelioma. TAZ monotherapy was generally well-tolerated. The current data support further clinical evaluation of TAZ in these pts. Furthermore, this trial presents an optimal paradigm for drug development in molecularly-enriched cohorts in mesothelioma. Clinical trial information: NCT02860286. Research Sponsor: Epizyme, Inc.

**9059 Poster Session (Board #252), Fri, 8:00 AM-11:00 AM**

**Peritoneal mesotheliomas characterized by less cell-cycle alterations and more *TRAF7* alterations than malignant pleural mesotheliomas.** *First Author: Michael Offin, Memorial Sloan Kettering Cancer Center, New York, NY*

**Background:** While peritoneal mesotheliomas (PM) are clinically distinct from malignant pleural mesotheliomas (MPM) it is unknown if genetic alterations reflect these differences. Here we report the molecular alterations and clinicopathologic characteristics of a prospectively collected PM cohort as compared to MPM. **Methods:** Patients with PM (n = 59) and targeted next generation sequencing (NGS; MSK-IMPACT) from January 2014 to January 2019 were assessed and followed through February 2020. Germline variants were analyzed in consented patients. NGS was compared to patients with MPM (n = 194) assessed in the same time interval. **Results:** Median age at diagnosis was 61 (range: 20-77), 56% were women (n = 33), and 92% had epithelioid histology (n = 54). 66% had ascites (n = 39) and 24% developed extra-abdominal metastases (n = 14; including lung, pleura, and mediastinum). 68% (n = 40) underwent surgical debulking and 80% (n = 47) had infusional therapy (median lines: 3) including platinum/pemetrexed (n = 38), EPIC (n = 22), HIPEC (n = 15), and immunotherapy (n = 16). The median overall survival (OS) from diagnosis was 5.4 years (median follow up 3.5 years). The median tumor mutation burden (TMB) was 1.8 mut/Mb (range: 0-14.9) in PM vs 2.0 mut/Mb (range: 0-31.5) in MPM (p = 0.049). More patients with PM had *TRAF7* alterations than in MPM (5/59 vs 3/194; p = 0.02) while fewer had *CDKN2A*/*CDKN2B* (4 vs 55; p = 0.0004). All patients with TRAF7 altered PM had well-differentiated papillary epithelioid histology. There was no difference in the prevalence of other common alterations such as *BAP1* (32 vs 98; p = 0.66), *NF2* (12 vs 55, p = 0.24), *SETD2* (11 vs 24; p = 0.28), and *TP53* (9 vs 28; p = 0.84) in PM vs MPM respectively. Patients with *BAP1*-altered PM had shorter OS (4.6 vs 9.8 years; HR 2.6, 95% CI 1.1-6.4; p = 0.04) while *TRAF7*-altered PM had improved OS (not reached vs 4.8 years; HR 0.3, 95% CI 0.1-0.9; p = 0.04) compared to wild type. 13% (4/30) of patients with PM had pathogenic variants on germline NGS (*POT1* I78T, *MUTYH* R109Y, *BAP1* E402*, *APC* I1037K). **Conclusions:** NGS confirms the distinct biology of PM compared to MPM. Specifically, the former shows fewer cell cycle (*CDKN2*) alterations compared to MPM. In contrast to MPM, *BAP1* alteration was associated with shorter survival. As previously described, we found enrichment of *TRAF7* in well differentiated papillary epithelioid PM associated with improved survival but notably some *TRAF7* alterations were identified in poorly differentiated MPM. Consistent with other reports, the prevalence of germline alterations was 13%. Research Sponsor: National Cancer Institute of the National Institutes of Health (T32 CA009207, P30 CA008748).

**9060 Poster Session (Board #253), Fri, 8:00 AM-11:00 AM**

**Role of immunotherapy in stage IV large cell neuroendocrine carcinoma of the lung.** *First Author: Takefumi Komiya, Parkview Cancer Institute, Fort Wayne, IN*

**Background:** Despite approvals of immune checkpoint inhibitors in both small cell and non-small cell lung cancers, role of immunotherapy in large cell neuroendocrine carcinoma (LCNEC) in lung is undefined. **Methods:** Using National Cancer Database (NCDB), Stage IV LCNEC cases diagnosed in 2014-2016 with at least 30-day follow up were analyzed. Clinical demographics included age (20-69 vs. 70+), sex (male vs. female), race (whites vs. others), insurance (uninsured vs. others), institution (academic vs. others), Charlson-Deyo score (0-1 vs. 2-3), brain metastasis (Yes vs. No), liver metastasis (Yes vs. No). Information regarding cancer treatment was limited to first course of therapy, including surgery for primary lesion (Yes vs. No), radiation (Yes vs. No), chemotherapy (Yes vs. No), and immunotherapy (Yes vs. No). Survival analysis was performed using Kaplan-Meier curves and Log-rank tests. Cox proportional hazard model was used for multivariate analyses. A two-sided p-value $< 0.05$ was considered as significant. **Results:** Among 661 eligible cases, 37 patients were treated with immunotherapy. No significant association between use of immunotherapy and clinical demographics was observed except for use of chemotherapy ($p = 0.0008$). Chemotherapy was administered in 34 (92%) and 406 (65%) of cases in immunotherapy and non-immunotherapy groups, respectively. Use of immunotherapy was associated with improved overall survival (Log-rank $p = 0.0168$). Landmark analysis in the immunotherapy group showed 12 and 18-month survival of 34.0% and 29.1%, respectively, as compared with 24.1% and 15.0% in the non-immunotherapy group Multivariate analysis demonstrated that female sex, presence of liver metastases, surgery, use of chemotherapy and immunotherapy (HR = 0.64, $p = 0.0164$) had significantly improved survival. Propensity score matching in overall survival showed a nonsignificant trend ($p = 0.0733$) in favor of immunotherapy group. **Conclusions:** This retrospective study using one of the largest cancer databases suggests that use of immunotherapy may improve survival of LCNEC patients. Prospective studies are warranted for further validation. Research Sponsor: None.

**9061 Poster Session (Board #254), Fri, 8:00 AM-11:00 AM**

**Carboplatin versus cisplatin for the treatment of extensive-stage small cell lung cancer (SCLC): A National VA Database analysis.** *First Author: Ibrahim Azar, Karmanos Cancer Institute, Detroit, MI*

**Background:** Current standard of care first line treatment for extensive stage SCLC includes combination of platinum-etoposide doublet with an immune checkpoint inhibitor. Carboplatin is preferred over cisplatin in the extensive stage disease because of its favorable toxicity profile. Data comparing the efficacy of carboplatin with cisplatin in the metastatic setting are limited. **Methods:** Data from the National VA Cancer Cube database were compiled. Only pathologically confirmed cases of extensive stage SCLC that received platinum-based multiagent chemotherapy were included. Interval-censored Weibull and Cox proportional hazard regression models were used to estimate median overall survival (OS) and hazard ratio (HR), respectively. Two survival curves were compared by a Wald test. **Results:** Overall, 2600 SCLC cases were studied: 1968 received carboplatin-based therapy (Carbo-SCLC) while 632 received cisplatin-based therapy (Cis-SCLC). Median OS of Carbo-SCLC and Cis-SCLC was 0.71 years (95% CI 0.68-0.75) versus 0.70 years (95% CI 0.64-0.76), respectively (HR = 0.99; 95% CI 0.90-1.10; $p = 0.90$). Median OS of patients with ECOG-PS of 0, 1, 2 and 3 was similar for Carbo-SCLC and Cis-SCLC. HR of death for Carbo-SCLC compared to Cis-SCLC stratified by performance status were: ECOG-PS 0: 1.04 (95% CI 0.78-1.38; $p = 0.80$); ECOG-PS 1: 0.87 (95% CI 0.71-1.06; $p = 0.17$); ECOG-PS 2: 0.92 (95% CI 0.69-1.24; $p = 0.6$); ECOG- PS 3: 1.13 (95% CI 0.66-1.92; $p = 0.66$). Multivariable regression analysis accounting for age and ECOG-PS shows a HR of 0.92 (95% CI 0.80-1.05; $p = 0.24$). **Conclusions:** Cisplatin-based chemotherapy was not associated with a survival advantage over carboplatin-based chemotherapy in extensive-stage SCLC., including in patients with robust performance status and young patients. The findings from this large dataset along with the favorable toxicity profile of carboplatin support its use as the platinum agent of choice in extensive stage SCLC. Research Sponsor: None.

**9062 Poster Session (Board #255), Fri, 8:00 AM-11:00 AM**

**Correlation of decreased expression of PD-L1 on circulating tumor cells and clinical benefit in SCLC Patients treated with RRx-001, a CD47 down-regulator, in a phase II trial.** *First Author: Corey Carter, EpicentRx, Torrey Pines, CA*

**Background:** In a Phase 2 trial called QUADRUPLE THREAT (QT) (NCT02489903), where 2nd line+ small cell lung cancer (SCLC) patients were treated with RRx-001 and a platinum doublet, the programmed death-ligand 1 (PD-L1) status of circulating tumor cells (CTCs) in 14 patient samples was evaluated. **Methods:** 26 consented patients received weekly RRx-001 4 mg followed by a reintroduced platinum doublet; epithelial cell adhesion molecule (EPCAM+) CTCs from 10 ml of blood on two consecutive timepoints cycle 1 day 1 and cycle 3 day 8 (cycle duration = 1 week) were detected by EpCAM-based immunomagnetic capture and flow cytometric analysis. CTCs were further characterized for protein expression of PD-L1. Tumor response was classified as partial or complete response based on the response evaluation criteria in solid tumors (RECISTv1.1) measured every 6 weeks. **Results:** The analyzed clinical data set comprised 14 RECIST-evaluable patients. 50% were females (7/14) and the median age (years) at baseline was 64.5 (Min = 48.5, Max = 84.2, SD = 10.3). The logistic model McFadden goodness of fit score (0 to 100) is 0.477, which is a strong correlation value. The logistic model analyzing the association of CTC PD-L1 expression at two timepoints and response had an approximate 92.8% accuracy in its prediction of clinical benefit (SD/PR/CR). Accuracy is defined in the standard way as 1- (False positive rate + False negative rate). The estimated ROC displayed in Figure 1 suggests a ROC AUC of 0.93 (95% CI: 0.78, 0.99), an excellent measure of performance. **Conclusions:** Reduction of PD-L1 expression was correlated with good clinical outcome after RRx-001 + platinum doublet treatment. PD-L1 expression reduction in favor of RRx-001 RECIST clinical benefit was clinically significant as compared to non-responders with progressive disease (PD). In the ongoing SCLC Phase 3 study called REPLATINUM (NCT03699956), analyses are planned to correlate response and survival with expression of CD47 and PD-L1 on CTCs. Clinical trial information: NCT02489903. Research Sponsor: EpicentRx.

**9063 Poster Session (Board #256), Fri, 8:00 AM-11:00 AM**

**Effect of anlotinib in advanced small cell lung cancer (SCLC) patients relapsed within three months after second-line treatment: A subgroup analysis from a randomized, double-blind phase II trial (ALTER 1202).** *First Author: Jianhua Shi, Linyi Cancer Hospital, Linyi, China*

**Background:** Anlotinib had significantly improved progress-free survival (PFS) and overall survival (OS) of advanced small cell lung cancer (SCLC) patients received at least two lines chemotherapy in the ALTER 1202 trial. Here, we reported the effect of anlotinib in advance SCLC patients relapsed within 3 months after second-line treatment. **Methods:** The ALTER 1202 was a randomized, double-blind phase 2 trial including patients with advanced SCLC that received at least two previous lines of chemotherapy. Eligible patients were randomized in a 2:1 ratio to receive either anlotinib or placebo until tumor progression or unacceptable toxicity. The subgroup analysis assessed the effect of anlotinib in patients relapsed within 3 months after second-line treatment. The primary outcome was PFS. The secondary outcomes were OS, objective response rate (ORR), disease control rate (DCR) and safety. This trial was registered with ClinicalTrials.gov, number NCT03059797. **Results:** In the ALTER1202 trial, 67 patients in anlotinib group and 34 patients in placebo group relapsed within 3 months after second-line treatment. Among them, the median PFS was 3.98 months (95% confidence interval [CI], 2.79 to 4.24) with anlotinib versus 0.72 months (95% CI, 0.69 to 0.82) with placebo (hazard ratio [HR], 0.14; 95% CI, 0.08 to 0.26; $P < 0.0001$). Meanwhile, anlotinib significantly prolonged OS compared with placebo (7.29 months [95% CI, 6.51 to 10.51] versus 4.37 months [95% CI, 2.33 to 6.47]; HR, 0.42 [95% CI, 0.23 to 0.74]; $P = 0.0059$) in patients relapsed within 3 months after second-line treatment. ORR was 4.48% (3 PR) for anlotinib and 2.94% (1 PR) for placebo ($P = 0.708$). DCR was 73.13% for anlotinib and 11.76% for placebo ($P < 0.0001$). The most common adverse events were hypertension (38.81%), anorexia (28.36%), fatigue (22.39%) and Elevation of alanine aminotransferase (17.91%). **Conclusions:** Anlotinib improved PFS and OS in advanced SCLC patients relapsed within 3 months after second-line treatment and was well tolerated. Research Sponsor: None.

**9064 Poster Session (Board #257), Fri, 8:00 AM-11:00 AM**

**Phase II study of gedatolisib for small-cell lung cancer (SCLC) patients (pts) with genetic alterations in PI3K/AKT/mTOR pathway based on a large-scale nationwide genomic screening network in Japan (EAGLE-PAT/LC-SCRUM-Japan).** *First Author: Hibiki Udagawa, National Cancer Center Hospital East, Kashiwa, Japan*

**Background:** Development of targeted therapy for SCLC based on a large-scale genomic screening is an innovative challenge. Gedatolisib is a highly potent dual inhibitor of PI3K/mTOR and is expected to have an effect for tumors with PI3K/AKT/mTOR pathway alterations. SCLC harboring this pathway alterations is rare. Thus, we conducted a phase II study based on a nationwide genomic screening network in Japan (LC-SCRUM-Japan) to develop novel targeted therapies. **Methods:** SCLC pts with targetable genetic alterations were screened at 154 institutions in Japan. A multicenter, single-arm phase II study was conducted to evaluate the efficacy and safety of gedatolisib in advanced SCLC pts with genetic alterations in the PI3K/AKT/mTOR pathway. The primary endpoint was objective response rate (ORR). The planned sample size was 19 (threshold and expected ORR of 20% and 50%, one-sided alpha of 5%, and power of 80%). **Results:** 930 SCLC pts were screened from July 2015 to January 2020. Targetable genetic alterations were identified in 148 pts (16%), including 53 PI3K/AKT/mTOR (6%), 81 MYC family (9%), 10 EGFR (1%) and 15 KRAS (2%). A total of 12 pts with genetic alterations in the PI3K/AKT/mTOR pathway (5 PIK3CA, 6 PTEN, and 1 AKT1 mutation) were enrolled in the phase II study. The median age was 67 years (range 58-79), 7 pts were male and 5 pts received 2 or more prior chemotherapy (range 1-4). The ORR was 0% and disease control rate was 25%. The median progression-free survival (PFS) was 0.9 months (95% CI, 0.4 to 3.0). The median overall survival was 5.8 months (95% CI, 1.1 to NR). Treatment-related G3 adverse events (hypertension, hypoalbuminemia, oral mucositis, ALT increased and creatinine increased) were observed in 4 pts. One patient with PTEN I8fs mutation had a long duration of stable disease (PFS; 6.7 months). **Conclusions:** This Large-scale nationwide genomic screening network was effective to identify rare targetable genetic alterations and had a potential role to develop targeted therapies in SCLC. This phase II study didn't show promising clinical benefit of gedatolisib for advanced SCLC pts with genetic alterations in the PI3K/AKT/mTOR pathway. The safety profile of gedatolisib was similar to that reported previously. Clinical trial information: UMIN000020585. Research Sponsor: Japan Agency for Medical Research and Development.

**9065 Poster Session (Board #258), Fri, 8:00 AM-11:00 AM**

**Preliminary efficacy data of platinum-pretreated small cell lung cancer (SCLC) cohort of NCI 9881 study: A phase II study of cediranib in combination with olaparib in advanced solid tumors.** *First Author: Joseph W. Kim, Yale Cancer Center, Yale School of Medicine, New Haven, CT*

**Background:** Cediranib, a pan-vascular endothelial growth factor receptor tyrosine kinase inhibitor, suppresses expression of *BRCA1, BRCA2*, and *RAD51* and increases sensitivity of tumors to poly-(ADP-ribose) polymerase (PARP) inhibitors *in vitro*. Olaparib, a PARP inhibitor, demonstrated clinical efficacy in patients with advanced solid tumors carrying a germline *BRCA* mutation. We therefore tested the anti-tumor activity of cediranib and olaparib combination in patients (pts) with advanced solid tumors. Here, we report the data from the SCLC cohort. **Methods:** This multi-institutional, two-stage, phase 2 study enrolled pts with metastatic SCLC previously treated with a minimum of one prior line of platinum-based chemotherapy in advanced setting. Patients were treated with cediranib 30mg po daily plus olaparib 200mg po BID until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR) by RECIST v1.1. Baseline tumor biopsies were obtained for biomarker analyses. **Results:** Baseline characteristics of the 25 pts enrolled are summarized below. The overall ORR rate was 28% (95% CI: 0.104,0.456). Median duration of response was 3.8 months (mos). Six of 8 pts had an objective response lasting longer than 3 mos up to 10.3 months. Disease control rate (# of pts with CR, PR or SD / # evaluable pts) was 88% (95% CI: 0.75,1.01). Median progression free survival was 4.1 mos (95% CI: 2.3, 6.2). Median OS was 5.5 mos (95% CI: 3.4, NA). Grade 3/4 adverse events (G3/4 AEs), irrespective of attribution, occurred in 14 of 25 (56%). G3/4 AEs occurring in $>$ 10% of pts were hypertension (21%), fatigue (17%) and weight loss (13%). **Conclusions:** The cediranib/olaparib combination resulted in promising clinical activity with ORR of 28% in biomarker-unselected pts with platinum-pretreated SCLC. The regimen required prompt initiation of antihypertensives, but AEs were overall manageable. Analyses of mutation status in homologous recombination DNA repair genes are going and will be correlated with clinical activity. Clinical trial information: NCT02498613. Research Sponsor: U.S. National Institutes of Health.

| Median (range) | SCLC (n = 25) |
|---|---|
| Age | 67, (46-79) |
| # of prior therapies | 2 (1-5) |
| Platinum-sensitive disease ( > 90 days interval to start subsequent therapy) | 80% |
| Prior immunotherapy (IO) | 52% |
| Interval from the last dose IO to start of study drugs, in days | 97, (31-651) |

**9066 Poster Session (Board #259), Fri, 8:00 AM-11:00 AM**

**The efficacy and safety profile of anlotinib with etoposide plus cisplatin/carboplatin in treatment-naive extensive-stage small cell lung cancer(SCLC) patients: Results from a phase II single-arm trial.** *First Author: Pengbo Deng, Department of Respiratory Medicine, Xiangya Hospital, Central South University, Changsha, China*

**Background:** Combination of etoposide and cisplatin/carboplatin is the most commonly used initial chemoptherapy regiment in extensive-stage small cell lung cancer. A meta-analysis released that, there is no significant difference was observed in Objective response rate(ORR), progression-free survival (PFS), or overall survival(OS) in patients(pts) receiving cisplatin-base versus carboplatin-based regimens. We performed a single-arm phase II trial to determine if maintain of single-agent anlotinib, an oral VEGFR, FGFR, PDGFR and c-Kit tyrosine kinase inhibitor, after 4-6 cycles of anlotinib + etoposide + cisplatin/carboplatin would improve PFS and ORR. **Methods:** SCLC pts (18~70 yrs, extensive-stage SCLC, no prior systematic chemo/ICI therapy) received anlotinib( 12mg QD from day 1 to 14 of a 21-day cycle) +etoposide( 100mg/m$^2$, d1~3 of 21-day cycle)+ cisplatin( 75-80mg/m$^2$,Q3W)/ carboplatin( AUC = 5~6,Q3W) for 4~6 cycles, and anlotinib maintenance. The dual-primary endpoint were PFS and ORR. **Results:** Between Oct.2018 to Dec.2019, 27 pts enrolled and included in the efficacy and safety analysis: age: median 62 (range:44-71); male 93%; cisplatin/ carboplatin/ both 11%/78%/11%; 37%(10/27) of pts required chemotherapy dose modification only, and the other 30% (8/27) of pts required anlotinib+ chemotherapy dose modification.The median PFS was 9.61 months ( 95%CI:7.80-11.42). ORR was 77.78% (21/27), disease control rate (DCR) was 96.30% (26/27).Toxicities≥grade 3 included: neutropenia 22%, leukopenia 11%, hand-foot syndrome 15%, nausea 4%, mucositis 4%, edema 4%, anorexia 4%, xerostomia 4% and fatigue 4%; there were no grade 5 toxicities. **Conclusions:** Combined treatment with anlotinib plus etoposide and cisplatin/carboplatin for treatment-naive extensive-stage SCLC was well tolerated with promising PFS and ORR to date but showed no new risk for AEs. Based on these encouraging results, phase III trial of anlotinib plus etoposide and cisplatin/carboplatin for treatment-naive SCLC has been warranted. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

**9067 Poster Session (Board #260), Fri, 8:00 AM-11:00 AM**

**Early ctDNA response assessment for prediction of platinum sensitivity in small cell lung cancer.** *First Author: Yonina R. Murciano-Goroff, Memorial Sloan Kettering Cancer Center, New York, NY*

**Background:** Small cell lung cancer (SCLC) is an aggressive disease, characterized by inevitable chemotherapy resistance and rapid progression. We hypothesized that circulating tumor DNA (ctDNA) analysis can rapidly identify sensitivity to platinum-based therapy. **Methods:** Patients with SCLC at Memorial Sloan Kettering Cancer Center underwent serial plasma collections, including prior to the start of treatment and prior to Cycle 2 Day 1 of therapy (C2D1). Tumor mutations were identified from pre-treatment biopsies by MSK-IMPACT and/or pre-treatment plasma by CAncer Personalized Profiling by deep Sequencing (CAPP-Seq). Median variant allele fraction (VAF) of all mutations was monitored on subsequent blood draws using CAPP-Seq. Progression free survival (PFS) was measured from the time of first pre-treatment blood draw. **Results:** Plasma was collected from 19 patients treated with carboplatin and etoposide, including three who received concurrent atezolizumab. Seven were female, and mean age was 64.5 years. ctDNA was detected in 17 patients (89%), including in the two patients in our series with limited stage disease. The most common mutations were in *TP53* and *RB1* in 14 and 6 patients, respectively. Fourteen patients had available plasma at C2D1. At baseline prior to treatment, median VAF did not differ significantly between radiologic responders and non-responders (9.4% versus 30.3%, p = 0.35). After one cycle of chemotherapy, the VAF percent decrease was significantly more in responders versus non-responders (-96.9% versus -10.3%, p $<$ 0.001). Median VAF was therefore significantly lower by C2D1 in patients who responded compared to non-responders (0.51% versus 27.2%, p = 0.02). Those who ultimately responded to therapy all had a $>$ 2 fold decrease in VAF by C2D1. With a median follow-up of 180 days, PFS was significantly longer in patients with $>$ 2 fold decrease in VAF by C2D1 (6.4 versus 1.9 months, log rank p $<$ 0.001). **Conclusions:** A 2-fold decrease in plasma VAF by C2D1 predicted platinum-sensitivity in SCLC and was associated with longer PFS. ctDNA may permit early assessment of benefit and expedite alternative treatment options for those without significant decrease in median VAF after one cycle of therapy. Research Sponsor: U.S. National Institutes of Health, Philanthropy from patients.

**9068 Poster Session (Board #261), Fri, 8:00 AM-11:00 AM**

**First-line durvalumab plus platinum-etoposide in extensive-stage (ES)-SCLC (CASPIAN): Impact of brain metastases on treatment patterns and outcomes.** *First Author: Yuanbin Chen, Cancer & Hematology Centers of Western Michigan, Grand Rapids, MI*

**Background:** In the Phase 3, randomized, open-label CASPIAN study, first-line durvalumab (D) added to etoposide plus either cisplatin or carboplatin (EP) significantly improved OS vs EP alone (HR 0.73 [95% CI 0.59–0.91]; p = 0.0047) in pts with ES-SCLC at the planned interim analysis. Here we describe treatment patterns and outcomes for pts according to brain metastases. **Methods:** Treatment-naïve pts (WHO PS 0/1) with ES-SCLC received 4 cycles of D 1500 mg + EP q3w followed by maintenance D 1500 mg q4w until disease progression (PD) or up to 6 cycles of EP q3w and optional prophylactic cranial irradiation (PCI; investigator's discretion). Pts with either asymptomatic or treated and stable brain metastases were eligible. Brain imaging was suggested for pts with suspected brain metastases, but was not mandated at screening or during treatment. The primary endpoint was OS. Analysis of OS and PFS in pt subgroups with and without brain metastases was prespecified. Other analyses in these subgroups were post hoc. Data cutoff: Mar 11, 2019. **Results:** At baseline, 28 (10.4%) of 268 pts in the D + EP arm and 27 (10.0%) of 269 pts in the EP arm had known brain metastases; of these, only 3 pts (~11% of those with baseline brain metastases) in each arm received radiotherapy (RT) to the brain prior to study entry. D + EP consistently improved OS vs EP in pts with or without known brain metastases at baseline (HR 0.69 [95% CI 0.35–1.31] and 0.74 [0.59–0.93], respectively); PFS was also consistently improved with D + EP regardless of the presence or not of baseline brain metastases (HR 0.73 [0.42–1.29] and 0.78 [0.64–0.95]). Among pts without known brain metastases at baseline, similar proportions developed new brain metastases at first PD in the D + EP (20/240; 8.3%) and EP arms (23/242; 9.5%), despite 19 (7.9%) pts in the EP arm having received PCI. Overall, 48 of 268 (17.9%) and 49 of 269 (18.2%) pts in the D + EP and EP arms received RT to the brain subsequent to study treatment; rates remained similar across the D + EP and EP arms regardless of baseline brain metastases (11 of 28 [39.3%] and 11 of 27 [40.7%] pts with known baseline brain metastases, compared to 37 of 240 [15.4%] and 38 of 242 [15.7%] pts without known baseline brain metastases). **Conclusions:** In CASPIAN, OS and PFS outcomes were improved with D + EP vs EP regardless of baseline brain metastases, consistent with the ITT analyses. Rates of new brain metastases at first PD were similar between arms, although PCI was permitted only in the control arm. Rates of subsequent RT to the brain were also similar in both arms. Clinical trial information: NCT03043872. Research Sponsor: AstraZeneca.

**9069 Poster Session (Board #262), Fri, 8:00 AM-11:00 AM**

**RESILIENT part I, an open-label, safety run-in of liposomal irinotecan in adults with small cell lung cancer (SCLC) who have progressed with platinum-based first-line (1L) therapy: Subgroup analyses by platinum sensitivity.** *First Author: David R. Spigel, Sarah Cannon Research Institute, Nashville, TN*

**Background:** Most patients with extensive SCLC develop drug resistance to platinum-based 1L therapy or discontinue for other reasons, and second-line (2L) therapies are limited. RESILIENT (NCT03088813) is a two-part phase 2/3 study assessing the safety, tolerability and efficacy of 2L liposomal irinotecan monotherapy in adults with SCLC who progressed with platinum-based 1L therapy. Preliminary data from RESILIENT part 1 (cut-off May 8 2019; ≥ 12 weeks follow-up) showed that liposomal irinotecan 70 mg/m$^2$ free base every 2 weeks was generally well tolerated and had encouraging antitumor activity (Paz-Ares *et al*. WCLC 2019 OA03.03). Objective response rate (ORR; secondary endpoint) was 44% (11/25). Here we report efficacy analyses in *post hoc* subgroups by platinum sensitivity. **Methods:** RESILIENT part 1 was an open-label, single-arm study comprising dose-finding and dose-expansion phases. Eligible patients were aged ≥ 18 y, with an ECOG performance status score of 0/1 and adequate organ function; a single line of prior immunotherapy was allowed. Participants received liposomal irinotecan 70 mg/m$^2$ or 85 mg/m$^2$ free base every 2 weeks, with tumor assessments every 6 weeks (RECIST v1.1). Analyses were undertaken for the dose-finding phase recommended dose (RD) in subgroups of platinum-resistant/sensitive patients (with/without progression within 90 days from completion of 1L therapy). **Results:** During dose finding, 5 patients received liposomal irinotecan 85 mg/m$^2$ (deemed not tolerable; dose-limiting toxicity) and 12 received 70 mg/m$^2$ (deemed tolerable; RD for dose-expansion phase in which 13 more patients were included). Analyses included all 25 patients receiving the RD (mean exposure, 13.95 weeks [median 14.86; SD 7.222]). In the platinum-sensitive subgroup (33.3% men; median age 62.0 y) ORR was 53.3% (8/15) and 12-week disease control rate (DCR12wks) was 60% (9/15); in the platinum-resistant subgroup (50% men, median age 58.0 y) both ORR and DCR12wks were 30% (3/10). Overall and progression-free survival (secondary endpoints) are not yet mature. **Conclusions:** ORR and DCR12wks were numerically higher in platinum-sensitive than in platinum-resistant patients with SCLC who had progressed with platinum-based 1L therapy before receiving 2L liposomal irinotecan 70 mg/m$^2$ in this phase 2 study. RESILIENT part 2, an ongoing, phase 3, randomized controlled trial vs topotecan, will provide further data. Clinical trial information: NCT03088813. Research Sponsor: Ipsen.

**9071 Poster Session (Board #264), Fri, 8:00 AM-11:00 AM**

**The impact of adjuvant therapy for non-metastatic thymic carcinoma: An analysis of the surveillance, epidemiology, and end results (SEER) database.** *First Author: Richard Lee O'Neal, University of Kentucky, Markey Cancer Center, Greenville, KY*

**Background:** Thymic Carcinoma is a rare malignancy with an aggressive clinical course. While the importance of surgery in the non-metastatic setting has been well defined, the optimal role of radiation and/or systemic therapy in this setting remains controversial. This study utilized the Surveillance, Epidemiology, and End Results (SEER) database to investigate the impact of adjuvant therapy on overall survival in patients with thymic carcinoma. **Methods:** We identified adults in the SEER database with thymic carcinoma diagnosed between 1989 to 2015 for analysis. As the primary treatment for non-metastatic thymic carcinoma is surgery, we excluded patients who did not have surgery as a component of their treatment Patients were categorized into Masaoka-Koga stage groups (I-IIa, IIb, III, and IV). Kaplan-Meier estimates of 10-year OS and multivariate Cox proportional hazards regression analyses were performed. **Results:** 515 patients met the inclusion criteria, of which 125 were stage I-IIa, 46 were stage IIb, 191 were stage III, and 143 were stage IV. A multivariate analysis was performed, adjusting for age, sex, race, and tumor size. When compared to surgery, no statistical improvement in survival was seen with adjuvant radiation or chemotherapy in stage I-IIa or IIb thymic carcinoma. In stage III disease, standard of care surgery was compared with adjuvant radiation (hazard ratio 0.69 (95% confidence interval 0.29 – 1.63], p = 0.39), adjuvant chemotherapy (hazard ratio [HR] 0.84 [95% confidence interval 0.28 – 2.53], p = 0.76), and adjuvant chemo-radiotherapy (HR 0.40 [0.18 – 0.93], p = 0.03). On Kaplan-Meier analysis, triple therapy (surgery + chemo-radiotherapy) was also associated with a marked improvement in 10-year overall survival at 55.3%, compared to 39.8%, 23.9%, and 20.8% (adjuvant radiation, adjuvant chemotherapy, and surgery alone, respectively). **Conclusions:** This study finds that in stage III thymic carcinoma, surgery followed by chemo-radiotherapy is associated with improved overall survival compared to single or dual-modality treatments. Because of the rarity of this disease, there are no large randomized studies evaluating the most appropriate treatment modalities, therefore this data may assist with clinical decision making in non-metastatic thymic carcinoma. Research Sponsor: None.

**9072 Poster Session (Board #265), Fri, 8:00 AM-11:00 AM**

**Treatment strategies for thymic carcinoma in a real-life setting: Insights from the rythmic network.** *First Author: Nicolas Girard, Institut Curie, Institut du Thorax Curie-Montsouris, Paris, France*

**Background:** Thymic carcinomas are an aggressive and difficult to treat subset of thymic epithelial tumors (TETs) that represent a heterogeneous group of rare intrathoracic malignancies. Most of the current knowledge and guidelines tumors rely on surgically-oriented databases focusing on early-stage disease, and small prospective, single-arm trials conducted in metastatic thymic carcinomas, mostly in a refractory, late-line setting. "Réseau tumeurs THYMiques et Cancer" (RYTHMIC) is the nationwide network for TETs in France. The management of any patient has to be systematically discussed on a real-time basis at a national multidisciplinary tumor board; a database is hosted by the French Thoracic Cancer Intergroup (IFCT). **Methods:** We took advantage of the RYTHMIC prospective database to describe baseline characteristics, analyze treatment strategies, and provide landmark outcomes in a cohort of consecutive patients with thymic carcinoma. The inclusion period was January 2012 to April 2017. **Results:** A total of 213 patients were analyzed. Overall, 60 (28%) patients were considered as surgical candidates upfront, 91 (43%) received primary chemotherapy, and 62 (29%) received exclusive chemotherapy. Median OS was 49.2 months (IC95%: 34.8-63.6); OS was significantly longer in patients with a lower stage at diagnosis ($p < 0.001$), who were operated on upfront, as opposed to patients who received primary or exclusive chemotherapy ($p < 0.001$). Surgery, conducted upfront or after primary chemotherapy, was significantly associated with more prolonged OS ($p < 0.001$); complete resection and postoperative radiotherapy were also predictors of better outcome (p = 0.018 and p = 0.081, respectively). Exclusive chemotherapy was delivered to 62 patients with advanced disease, who all received platinum-based regimen as first-line treatment; PAC regimen was delivered to 66% of patients. Best objective response to first-line chemotherapy was partial response in 33 (53%) patients. Median PFS was 8.0 months (IC95%: 5.0-11.1). Median OS was 32.9 months (IC95%: 20.6-45.1). Response to first-line chemotherapy and squamous histology were the only significant predictors of OS (p = 0.002 and p = 0.040, respectively). **Conclusions:** Our cohort is the first to analyze in depth outcomes and treatment strategies in a prospective cohort of consecutive patients with thymic carcinoma. While we confirm the major prognostic impact of surgery, our data highlight the need for optimized multidisciplinary management and innovative therapies as the survival of patients remains limited. Research Sponsor: None.

**9073 Poster Session (Board #266), Fri, 8:00 AM-11:00 AM**

**Prevalence of autoimmune diseases in thymic epithelial tumors (TET) insights from RYTHMIC.** *First Author: Jose Carlos Benitez, Gustave Roussy, Villejuif, Paris, YT, France*

**Background:** TET are associated with autoimmune disorders (AID) in up to 30% of patients (pts). However, there have been wide variations in the reported prevalence of AID in TET pts in small single-center series. RYTHMIC (Réseau tumeurs THYMiques et Cancer) is a French network mandated to systematically discuss every case of TET. We aimed to describe the prevalence of AID in a large French population. **Methods:** RYTHMIC database, hosted by IFCT (Intergroupe Francophone de Cancérologie Thoracique), prospectively includes all consecutive pts with a diagnosis of TET discussed in French national or regional tumor boards. We analyzed epidemiologic, clinical and pathological characteristics of pts with TET's related AID. **Results:** From January 2012 to December 2019, 2909 pts were included in the database. The mean age at diagnosis of TET was 54 and 52% were male. In the overall population, Masaoka Koga stages were well balanced with 12.6% (n = 187) stage I, 8.8% (n = 131) stage IIa, 8.4% (n = 124) stage IIb, 11.1% (n = 164) stage III and 8.5% (n = 125) stage IV. There were 364 (12.5%) events of AID in 302 pts. 62 pts (17%) had more than 1 AID. Among the events, 236 were myasthenia gravis (MG) (64.8%), 19 Hypogammaglobulinemia syndrome (5.2%), 15 pure red cell aplasia (4.1%), 18 thyroiditis (4.9%) and 16 systemic erythematous lupus (4.4%). Diagnosis of AID was mostly done at tumor diagnosis (n = 239, 65.7%) but some patient had AID diagnosed before diagnosis (n = 67, 18.4%) or during follow up (n = 32, 8.8%). Among pts presenting AID, B2 was the most common subtype (n = 133, 36.5%). The incidence of AID per subtype was as follow: A (n = 10/81, 12.3%), AB (n = 48/225, 21.3%), B1 (n = 35/130, 26.9%), B2 (n = 133/295, 45.0%), B3 (n = 46/113, 40.7%), thymic carcinoma (n = 16/275, 5.8%). **Conclusions:** The prevalence of AID in pts with TET was 12.5%, $>$ 40% in B2 and B3 subtypes. Diagnosis of AID can be delayed compared to the diagnosis of TET. Immunotherapy indication should be carefully assessed in pts with TET other than thymic carcinoma. Research Sponsor: None.

**9074 Poster Session (Board #267), Fri, 8:00 AM-11:00 AM**

**Low-dose oral etoposide is an active option for patients with heavily pretreated thymic epithelial tumors.** *First Author: Margaret Ottaviano, Department of Clinical Medicine and Surgery, University Federico II of Naples, Naples, Italy*

**Background:** Platinum based regimens are used in the first line setting for advanced Thymic Epithelial Tumors (TETs). Angiogenesis plays an important role in TETs: VEGF is overexpressed in TETs, and associated with aggressiveness and advanced stage. Etoposide inhibits angiogenesis *in vitro* and *in vivo* by decreasing VEGF production and microvessel density. The aim of this study is to assess the activity of metronomic oral etoposide, with identification of circulating predictive and pharmacodynamics biomarkers. **Methods:** Patients with advanced platinum pretreated TET referred from 2014 to 2019 at Rare Tumors Reference Center of Naples, were prospectively enrolled in this study. Oral etoposide 50 mg daily for 3 weeks on and 1 week off every 28 days, has been delivered until progression of disease, complete response or unacceptable toxicity. Response rate (RR), progression free survival (PFS), toxicity and ratio between time to etoposide progression (TTPe) and time to previous best treatment progression (TTPp) were evaluated. Serum samples were prospectively obtained from ten patients with simultaneously radiological assessment. cfDNA quantification was assessed using Qubit Fluorometric Quantitation. **Results:** 21 patients were enrolled: median age 59 years range (41 - 88); 70% male, 60% T (4 B1, 3 B2, 4 B3, 1 B1-B2); 40% had TC. A median of 5 (range 1-9) prior therapy regimens had been administered. Median follow-up since etoposide was 5 years (range 0.5-5). Obtaining an overall response rate of 85%, 3 patients achieved complete response and 15 partial response. Median PFS was 16 months [95%CI 3-60] with respectively a median PFS of 12 for T (95%CI 3-38) and 19 for TC (95%CI 6-60). No grade 3-4 related events occurred, G1-2 myelotoxicity has been registered in 20% of patients. Therapy is still ongoing for 15 patients and all are still alive. Median TTPe was 16 months, TTPp was 9 months and TTPe / TTPp ratio equal to 1.7. The median cfDNA of 8 responder patients, before starting therapy, was 2.2 ng/$\mu$l (0.178-5.24), dropping dramatically at radiological response to 0.5 ng/$\mu$l (0.323-2.56). 2 out of 3 non-responder patients had a median baseline value of 2.49 ng/$\mu$l, increasing to 4.6 ng/$\mu$l at progression. Variation of circulating VEGF correlates with radiological response. **Conclusions:** Taking into account that other antiangiogenic drugs, showing some activity in second and further lines treatment, are very expensive and associated with several side effects, we suggest that low dose oral etoposide might become the preferred treatment option in heavily pretreated TETs. Research Sponsor: CRCTR (Reference Rare Tumors Center of Campania Region).

**TPS9075 Poster Session (Board #268), Fri, 8:00 AM-11:00 AM**

**CANOPY-A: A phase III, multicenter, randomized, double-blind, placebo-controlled trial evaluating canakinumab as adjuvant therapy in patients (pts) with completely resected non-small cell lung cancer (NSCLC).** *First Author: Edward B. Garon, David Geffen School of Medicine, University of California/TRIO-US Network, Los Angeles, CA*

**Background:** In the CANTOS study, canakinumab (selective IL-1β inhibitor) treatment was associated with reduced incidence and mortality from NSCLC in pts with stable post-myocardial infarction with elevated high-sensitivity C-reactive protein (hs-CRP) levels. In CANOPY-A study, we investigate the therapeutic role of canakinumab in NSCLC. **Methods:** The CANOPY-A study (NCT03447769) is evaluating the efficacy and safety of canakinumab as adjuvant therapy in adult pts with completely resected NSCLC. Pts with AJCC/UICC v.8 stages II–IIIA and IIIB (T $>$ 5 cm, N2), any histology, completely resected (R0) NSCLC who completed adjuvant cisplatin-based chemotherapy ($\geq$2 cycles) and radiotherapy (if applicable) are eligible. Pts must not have had prior neoadjuvant chemotherapy or radiotherapy. Pts (~1500) are randomized 1:1 to receive canakinumab (200 mg Q3W, SC) or placebo (Q3W, SC) for 18 cycles or until disease recurrence as determined by investigator, unacceptable toxicity, treatment discontinuation at the discretion of the investigator or patient, start of a new antineoplastic therapy, death, or loss to follow-up. Randomization is stratified by AJCC/UICC v.8 stage (IIA vs IIB vs IIIA vs IIIB with T $>$ 5 cm, N2 disease), tumor histology (squamous vs non-squamous), and region (western Europe and North America vs eastern Asia vs rest of the world). Primary objective: disease-free survival (DFS) per local investigator assessment. Secondary objectives: overall survival (OS), lung cancer specific survival, safety, pharmacokinetics, immunogenicity, and patient reported outcomes. Adult pts with stage IIA–IIIA, IIIB (N2 disease only) NSCLC who are candidates for complete resection surgery (and therefore prospective candidates for the main study) will be asked to participate in a biomarker sub-study to understand how resection may impact biomarkers involved in the IL-1β inflammatory pathway and mutations present in blood. In the sub-study, the levels of hs-CRP, other cytokines, and additional biomarkers in blood will be assessed at pre- and post-surgery (endpoint: summary statistics of hs-CRP and other pharmacodynamics [PD] biomarkers). For pts who will enroll in the main study, possible associations between pre- and post-surgery biomarker levels with canakinumab efficacy will be assessed (endpoint: DFS and OS by hs-CRP and other PD biomarkers). The CANOPY-A study is currently enrolling. As of Jan 13, 2020, there are 307 study locations. Clinical trial information: NCT03447769. Research Sponsor: Novartis.

**TPS9076 Poster Session (Board #269), Fri, 8:00 AM-11:00 AM**

**Checkmate 77T: A phase III trial of neoadjuvant nivolumab (NIVO) plus chemotherapy (chemo) followed by adjuvant nivo in resectable early-stage NSCLC.** *First Author: Tina Cascone, The University of Texas MD Anderson Cancer Center, Houston, TX*

**Background:** Although surgery for early NSCLC is potentially curative, 5-year overall survival (OS) rates for patients with stage IIA–IIIB disease are historically $<$ 50%, representing a population of high unmet need. Conventional neoadjuvant or adjuvant chemo provides only a 5% absolute improvement in OS at 5 years. A rational approach to improve survival in these patients is to eradicate micrometastatic disease and potentially induce anti-tumor immunity to minimize the risk of relapse with peri-operative regimens including NIVO, a fully human anti–programmed death receptor-1 antibody. Early phase trials indicate that NIVO-based regimens have the potential to deepen pathological responses and extend survival in this setting (Reuss JE et al. Poster presentation at ASCO 2019. Abstract 8524; Cascone T et al. Oral presentation at ASCO 2019. Abstract 8504; Provencio M et al. Oral presentation at WCLC 2019. Abstract OA13.05). Data from the phase 2 single-arm NADIM trial (NCT03081689) demonstrated the highly encouraging major pathological response (MPR) rate of 83% with neoadjuvant NIVO plus chemo followed by adjuvant NIVO in patients with resectable stage IIIA NSCLC (Provencio M et al. Oral presentation at WCLC 2019. Abstract OA13.05). These results require validation in a large randomized controlled study. CheckMate 77T (NCT04025879) is a phase 3, randomized, double-blind trial evaluating neoadjuvant NIVO plus chemo followed by adjuvant NIVO in resectable early stage NSCLC. **Methods:** Approximately 452 patients aged $\geq$ 18 years with resectable stage IIA–IIIB (T3N2 only) NSCLC, ECOG performance status 0–1, and available lung tumor tissue will be enrolled at 113 sites in North America, South America, Europe, Asia, and Australia. Patients with *EGFR/ALK* mutations, brain metastasis, prior systemic anti-cancer treatment or radiotherapy, and autoimmune disease are excluded. Patients will be randomized to receive neoadjuvant NIVO plus carboplatin- or cisplatin-based doublet chemo followed by surgery and adjuvant NIVO, or neoadjuvant placebo plus carboplatin- or cisplatin-based doublet chemo followed by surgery and adjuvant placebo. The primary endpoint is event-free survival, assessed by blinded independent central review. Secondary endpoints include OS, pathological complete response and MPR assessed by blind independent pathological review, safety and tolerability. The start date was September 2019. The estimated primary completion date is May 2023. Clinical trial information: NCT04025879. Research Sponsor: Bristol-Myers Squibb.

**TPS9077** **Poster Session (Board #270), Fri, 8:00 AM-11:00 AM**

**ALCHEMIST: Adjuvant targeted therapy or immunotherapy for high-risk resected NSCLC.** *First Author: Jacob Sands, Lahey Hospital and Medical Center, Boston, MA*

**Background:** ALCHEMIST (Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trial) is a clinical trial platform of the National Cancer Institute that offers biomarker analysis for high-risk resected non-small cell lung cancer (NSCLC) to support randomized trials of novel adjuvant therapies within the National Clinical Trials Network (NCTN). EA5142, a trial of adjuvant nivolumab for patients (pts) without EGFR / ALK alterations, has completed enrollment. Given the survival benefit seen with 1st-line chemo-immunotherapy (chemo-IO) for advanced NSCLC without EGFR / ALK alterations, there was compelling rationale for the launch of a trial offering concurrent immunotherapy with adjuvant chemo. Here we report updated enrollment to ALCHEMIST as of Jan 14, 2020. **Methods:** ALCHEMIST includes a screening trial (A151216, 5362 registered) that enrolls pts with completely resected clinical stage IB ($\geq$4 cm)–IIIA (per AJCC 7) NSCLC. Tissue and blood are collected, biomarker testing includes EGFR sequencing, ALK FISH and PD-L1 IHC. 733 active sites are enrolling across the NCTN. Pts with EGFR mutations may enroll to adjuvant erlotinib vs observation (A081105, 352 randomized); those with ALK fusions may enroll to adjuvant crizotinib vs observation (E4512, 99 randomized). A trial offering adjuvant nivolumab vs observation regardless of PD-L1 status (EA5142, 935 randomized) recently completed enrollment. To support ongoing investigation of adjuvant immunotherapy, ALCHEMIST is adding A081801 (opens spring 2020). Pts will be randomized to one of 3 arms: chemo-IO with pembrolizumab during and after chemo vs sequential chemo followed by pembrolizumab vs chemo alone. Pts with pathological N2 nodes are eligible and can undergo postoperative radiotherapy after completing chemo. Pts are eligible if enrolled to A151216, negative for EGFR and ALK alterations, and with PD-L1 testing completed (required for stratification). Local testing for EGFR, ALK and PD-L1 will be accepted for enrollment; central testing will not delay randomization. Pts may not have received any therapy except surgery for the lung cancer and must be age $>$18, Eastern Cooperative Oncology Group performance status 0-1, have no active autoimmune disease requiring systemic treatment within 2 years, must not be pregnant or nursing, have no active second malignancy within 3 years and meet standard organ function values. By building off the ongoing ALCHEMIST platform, we hope to facilitate rapid enrollment to A081801 across participating NCTN sites. Clinical trial information: NCT02194738. Research Sponsor: U.S. National Institutes of Health.

**TPS9078** **Poster Session (Board #271), Fri, 8:00 AM-11:00 AM**

**Trial in progress: Neoadjuvant immune checkpoint blockade in resectable malignant pleural mesothelioma.** *First Author: Joshua E. Reuss, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD*

**Background:** While the role of surgery in limited-stage (stage I-III) malignant pleural mesothelioma (MPM) is controversial, many centers have adopted an aggressive tri-modality approach incorporating (neo)adjuvant chemotherapy, surgical resection and radiotherapy. Despite this, most patients relapse and die from their disease. Immune checkpoint blockade (ICB) has shown promise in advanced MPM, but the mechanisms of response and resistance remain elusive. Improving the mechanistic understanding of ICB in MPM while concurrently optimizing the treatment strategy for limited-stage MPM are two urgent unmet needs. This multicenter multi-arm phase I/II study seeks to evaluate the safety and feasibility of neoadjuvant ICB in resectable MPM, incorporating novel genomic and immunologic analyses to deliver mechanistic insight into the biology of ICB in MPM. **Methods:** Patients with surgically resectable stage I-III treatment-naïve epithelioid or biphasic MPM receive neoadjuvant treatment with nivolumab every 2 weeks for 3 doses with or without 1 dose of ipilimumab (arm A: nivolumab monotherapy; arm B: nivolumab + ipilimumab). After macroscopic complete resection, patients receive optional investigator-choice adjuvant chemotherapy +/- radiation. Following this, patients will receive up to 1 year of adjuvant nivolumab. Feasibility and safety are co-primary endpoints of this study with feasibility defined by a delay in surgery of $\leq$24 days from the preplanned surgical date and safety defined by adverse events according to CTCAE v5.0. Bayesian-designed stopping rules have been implemented for feasibility and safety. Secondary endpoints include assessment of pathologic response and radiographic response using RECIST 1.1 for MPM. Correlative analyses will be performed on tissue specimens obtained pre- and post-ICB, as well as blood obtained pre, during, and post-ICB. Key correlates include multiplex immunofluorescence and longitudinal ctDNA assessment. Whole exome sequencing, T-cell receptor sequencing, and the MANAFEST functional neoantigen assay will be utilized to identify neoantigen-specific T-cell clonotypes and track these clonotypes temporally (during/post ICB) and spatially (across immune compartments). Single-cell RNA sequencing will be used to characterize the functionality of expanded T-cell clonotypes. Accrual to arm B will commence following complete accrual to arm A with a planned total enrollment of 30 patients. This study is open with 1 patient enrolled at the time of submission. Clinical trial information: NCT03918252. Research Sponsor: Bristol Meyers Squibb.

**TPS9079** **Poster Session (Board #272), Fri, 8:00 AM-11:00 AM**

**A phase III randomized trial of pleurectomy/decortication plus chemotherapy with or without adjuvant hemithoracic intensity-modulated pleural radiation therapy (IMPRINT) for malignant pleural mesothelioma (MPM) (NRG LU-006).** *First Author: Andreas Rimner, Memorial Sloan Kettering Cancer Center, New York, NY*

**Background:** Pleurectomy/Decortication (P/D) with neoadjuvant or adjuvant chemotherapy has become a common lung-sparing surgical approach for MPM. Adjuvant hemithoracic IMPRINT was developed at Memorial Sloan Kettering Cancer Center and safe in a multi-institutional phase II study, with promising survival outcomes. The National Cancer Institute (NCI) sponsored this phase III randomized cooperative group trial to test the efficacy of this lung-sparing trimodality approach for resectable MPM. **Methods:** Patients with newly diagnosed MPM amenable to P/D are enrolled and undergo P/D followed by adjuvant platinum/pemetrexed (preferred) or neoadjuvant chemotherapy followed by P/D. Patients are stratified by histologic subtype, resection status (R0/1 vs. R2), and center patient volume ($\leq$10 vs. $>$ 10 P/Ds per year). Within 8 weeks after completion of the second modality patients are randomized 1:1 to undergo hemithoracic IMPRINT vs. no further therapy. All IMPRINT contours and treatment plans will be centrally reviewed. A contouring atlas and treatment planning constraints for target structures and organs at risk including acceptable and unacceptable variations and deviations were developed. Photon and proton therapy are permitted. The primary endpoint of the study is overall survival. Secondary endpoints include local failure-free, distant-metastases-free and progression-free survival, treatment-related toxicities (CTCAE v5.0) and change in quality-of-life (EORTC QLQ-C30 mean score changes at 9 months post randomization). The target accrual is 150 patients. This study was activated on January 29, 2020. Over 20 institutions have already committed to opening the study which is open to all National Clinical Trials Network (NCTN) sites. Treatment planning guidelines and helpful hints for photon and proton therapy will be presented. Conclusions: NRG LU-006 (clinicaltrials.gov: NCT04158141) is open to accrual. This is the first NRG Oncology randomized phase III trial on MPM and evaluates the use of IMPRINT following lung-sparing P/D and chemotherapy. This project was supported by grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Oncology SDMC), U24CA180803 (IROC) from the National Cancer Institute (NCI). Clinical trial information: NCT04158141. Research Sponsor: U.S. National Institutes of Health.

**TPS9080** **Poster Session (Board #273), Fri, 8:00 AM-11:00 AM**

**Phase I study of AMG 757, a half-life extended bispecific T-cell engager (HLE BiTE immune therapy) targeting DLL3, in patients with small cell lung cancer (SCLC).** *First Author: Taofeek Kunle Owonikoko, Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, GA*

**Background:** SCLC is an aggressive neuroendocrine tumor with poor prognosis and few treatment options. Delta-like ligand 3 (DLL3) is an inhibitory Notch ligand that is highly expressed on the surface of most SCLC tumors but minimally expressed in normal tissues. As such, DLL3 may be a promising therapeutic target. AMG 757 is an HLE BiTE immune therapy designed to redirect cytotoxic T cells to cancer cells by binding to DLL3 on cancer cells and CD3 on T cells, resulting in T cell activation and expansion and T cell-dependent killing of tumor cells. In addition to its direct antitumor effect, BiTE immune therapy can inflame the tumor microenvironment. Combining AMG 757 with a PD-1 pathway inhibitor may lead to increased antitumor activity by enabling sustained T cell-dependent killing of tumor cells. **Methods:** NCT03319940 is an open-label, ascending, multiple-dose, phase 1 study evaluating AMG 757 as monotherapy; the protocol was recently amended to also evaluate AMG 757 in combination with pembrolizumab. The study will include a dose exploration (monotherapy and combination) followed by a dose expansion (monotherapy). Key eligibility criteria: adult patients with relapsed/refractory SCLC whose disease progressed or recurred after at least 1 platinum-based chemotherapy regimen, ECOG performance status 0–2, at least 2 measurable lesions per modified RECIST 1.1, no untreated or symptomatic brain metastases, and adequate organ function. Primary objectives are to evaluate safety/tolerability and determine the maximum tolerated dose or recommended phase 2 dose of AMG 757 as monotherapy and in combination with pembrolizumab. Secondary objectives are to characterize pharmacokinetics and evaluate preliminary antitumor activity; exploratory objectives are to assess immunogenicity and changes in biomarkers in blood and tumor tissue. In the dose exploration phase, dose escalation/de-escalation decisions will be guided by a Bayesian logistic regression model; backfill enrollment at dose levels deemed safe and tolerable will be allowed. The study is open and recruiting patients. Clinical trial information: NCT03319940. Research Sponsor: Amgen Inc.

**TPS9081** **Poster Session (Board #274), Fri, 8:00 AM-11:00 AM**

**RESILIENT part II: an open-label, randomized, phase III study of liposomal irinotecan injection in patients with small-cell lung cancer who have progressed with platinum-based first-line therapy.** *First Author: Luis G. Paz-Ares, Hospital Universitario 12 de Octubre, Madrid, Spain*

**Background:** Although small cell lung cancer (SCLC) is often sensitive to established first-line therapies, many patients relapse and develop drug resistance, and second-line therapies are limited. RESILIENT (NCT03088813) is a two-part phase 2/3 study assessing the safety, tolerability, and efficacy of liposomal irinotecan monotherapy in patients with SCLC who progressed with platinum-based first-line therapy. Preliminary data from the dose-ranging part of the study (part 1) showed that liposomal irinotecan 70 mg/m$^2$ administered every 2 weeks was well tolerated and had promising antitumor activity (Paz-Ares *et al.* ASCO 2019; poster 318). Here, we present the design of the second, larger part of the study, which will evaluate the efficacy and safety of liposomal irinotecan versus topotecan in the same patient population. **Methods:** Part 2 of RESILIENT is a phase 3, open-label study with a planned sample size of 450. Patients are randomly allocated 1:1 to intravenous liposomal irinotecan or intravenous topotecan. Liposomal irinotecan is administered every 2 weeks at 70 mg/m$^2$ (free-base equivalent) and topotecan is administered for 5 consecutive days every 3 weeks at 1.5 mg/m$^2$. As of January 2020, 80 patients have been enrolled in part 2 of the trial. Tumor assessments are performed using the Response Evaluation Criteria in Solid Tumors version 1.1 and the Response Assessment in Neuro-oncology criteria for CNS lesions; symptom improvement is measured using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30. Safety assessments include monitoring for adverse events. The primary endpoint is overall survival (OS) and secondary endpoints are progression-free survival (PFS), objective response rate, and proportion of patients reporting symptom improvement. Patients will continue study treatment until disease progression, unacceptable toxicity or study withdrawal and will then be followed for survival until death or study end (when all patients have died, withdrawn consent or are lost to follow-up). Clinical trial information: NCT03088813. Research Sponsor: Ipsen.

**TPS9082** **Poster Session (Board #275), Fri, 8:00 AM-11:00 AM**

**NRG Oncology/Alliance LU005: A phase II/III randomized clinical trial of chemoradiation versus chemoradiation plus atezolizumab in limited stage small cell lung cancer.** *First Author: Helen J. Ross, Mayo Clinic Arizona, Phoenix, AZ*

**Background:** Limited stage small cell lung cancer (LS-SCLC) is treated with standard of care platinum/etoposide (EP) and thoracic radiation therapy (TRT) with curative intent, however the majority of patients are not cured and median overall survival is approximately 30 months. Addition of atezolizumab to chemotherapy in extensive stage SCLC has improved progression free and overall survival in a non-curative setting leading to hope that addition of an immune checkpoint inhibitor to standard chemoradiotherapy could benefit LS-SCLC patients. LU005 is a randomized phase II/III trial of standard concurrent chemoradiation with or without atezolizumab for patients with LS-SCLC. **Methods:** Patients are randomly assigned in a 1:1 ratio to standard EP chemotherapy with concurrent TRT (45 Gy BID or 66 Gy QD) with or without atezolizumab beginning concurrently with TRT, and continued every 3 weeks for up to 12 months. Eligible patients have LS-SCLC, PS 0-2, adequate organ function, no concerning comorbidities (including no active autoimmune disease) and are eligible for TRT. Patients are randomized prior to their second cycle of EP and thoracic radiation begins with the second overall cycle of chemotherapy (first cycle of study therapy) in both treatment arms. Prophylactic cranial radiation (PCI) is recommended for patients who respond to treatment. The phase II/III primary endpoints are progression free (PFS) and overall survival (OS) respectively. Secondary endpoints include objective response rates, local and distant disease control, and quality of life/patient reported outcomes assessment. Translational science component includes blood and tissue based immune related assays. This study activated in May 2019. 50 of 506 planned patients have been accrued as of 2/1/2020. Supported by grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Oncology SDMC), U23CA180803 (IROC) from the National Cancer Institute (NCI) and Genentech. *Authors Ross and Higgins are co-first authors and contributed equally to this work. Clinical trial information: NCT03811002. Research Sponsor: U.S. National Institutes of Health.

**TPS9083** **Poster Session (Board #276), Fri, 8:00 AM-11:00 AM**

**A phase III trial-in-progress called REPLATINUM that compares RRx-001 + a platinum doublet to a platinum doublet in third-line or beyond small cell lung cancer.** *First Author: Daniel Morgensztern, Washington University School of Medicine in St. Louis, St. Louis, MO*

**Background:** Despite several recent checkpoint inhibitor approvals extensive stage small cell lung cancer (SCLC) is associated with a poor prognosis and remains an area of high unmet need. RRx-001 is a first-in-class, minimally toxic small molecule immunotherapeutic that inhibits c-Myc, downregulates the antiphagocytic checkpoint, CD47, repolarizes tumor associated macrophages (TAM) from protumor M2 to antitumor M1 and resensitizes to previously active first line therapies. On the basis of favorable results from a Phase 2 trial called QUADRUPLE THREAT (NCT02489903) in combination with a platinum doublet in later line SCLC, a Phase 3 trial called REPLATINUM was started in 3$^{rd}$ line or beyond SCLC in Q4 2019. Enrollment is ongoing. **Methods:** This US-based, open-label, randomized, phase 3 study (NCT03777657) compares RRx-001 4mg + a platinum doublet (carboplatin or cisplatin + etoposide) versus a platinum doublet for pts with 3$^{rd}$ line or beyond SCLC that have previously received a checkpoint inhibitor. Approximately 120 pts from 25 centers will be randomized 1:1 to receive RRx-001 4 mg in combination with a platinum doublet vs. a platinum doublet. The platinum doublet will be administered on both arms for up to 4 cycles; on the RRx-001 arm only patients with stable disease or better are eligible to continue on RRx-001 4 mg + carboplatin AUC 2-4 maintenance therapy. If radiologic progression occurs on the control arm prior to the 4$^{th}$ cycle, patients are eligible to crossover to the RRx-001 treatment arm. PFS is the primary endpoint. Secondary endpoints include OS and ORR. Exploratory endpoints include c-Myc, CD-47 and PD-L1 on circulating tumor cells and SIRP-alpha expression on circulating monocytes. Clinical trial information: NCT03777657. Research Sponsor: EpicentRx.

**TPS9084** **Poster Session (Board #277), Fri, 8:00 AM-11:00 AM**

**A phase Ib/II study of niraparib plus temozolomide plus atezolizumab versus atezolizumab as maintenance therapy in extensive-stage small cell lung cancer (TRIO-US L-06).** *First Author: Amy Lauren Cummings, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA*

**Background:** Maintenance therapy is a promising therapeutic approach for extensive-stage small cell lung cancer (ES-SCLC), especially in light of IMpower 133 (Horn NEJM 2018). SCLC models of poly (ADP-ribose) polymerase (PARP) protein 1 and 2 inhibition suggested synergy with temozolomide (TMZ) (Wainberg AACR 2016). Combining PARP inhibition and TMZ with atezolizumab after first-line therapy for ES-SCLC may improve disease control. **Methods:** This is a phase 1b/2, randomized, open-label study of TMZ plus niraparib, a PARP inhibitor, with atezolizumab versus atezolizumab as maintenance therapy in adult patients with ES-SCLC after completion of platinum-based first-line chemotherapy. The primary outcome for phase 1b is the RP2D of TMZ in combination with niraparib, and for phase 2, progression-free survival (PFS). Secondary endpoints include safety, objective response rate, and overall survival. Exploratory endpoints include adverse events and patient-reported outcomes, including health-related quality of life. Phase 1b participants are required to have an advanced and incurable solid malignancy. Part one of phase 1b includes an accelerated lead-in of 12 participants treated in cohorts of 6 with an initial dose level of niraparib 200 mg po daily in 28-day cycles and low-dose TMZ 40 mg po daily on days 1-5 of each cycle. Part two includes a safety lead-in of 6 patients receiving standard-of-care atezolizumab, to which R2PD niraparib and TMZ will be added. For phase 2, participants are required to have ES-SCLC with a complete response or partial response per RECIST 1.1 following 4 to 6 cycles of platinum-based chemotherapy and ability to proceed to randomization within 7 weeks after day 1 of the last cycle of prior chemotherapy. Prophylactic WBRT is allowed prior to study. 52 participants will be stratified by a history of brain metastases and randomized 1:1 to atezolizumab with or without RP2D niraparib plus TMZ. There will be no crossover between arms. To date, cohort 1 had two DLTs. Enrollment to dose level -1 and an intermediate dose have been completed without a DLT. The atezolizumab safety lead-in begins enrollment in March 2020. Clinical trial information: NCT03830918. Research Sponsor: TESARO/GSK.