Background: Circulating tumor DNA (ctDNA) sampling has emerged as a non-invasive approach to characterizing genomic alterations in blood of patients (pts) with metastatic, non-small cell lung cancer (mNSCLC). ctDNA or 'liquid biopsy' may be used to guide treatment and prognosis. **Method:** This was a prospective pilot study of pts with histologically confirmed mNSCLC. Pts were enrolled prior to initiating a new line of therapy. Tumor and ctDNA specimens were collected prior to treatment and radiology scans were performed at standard intervals; ctDNA collections continued until progression. ctDNA was assessed by Inivata (InvisionFirst) using amplicon-based targeted next generation sequencing with 36-gene panel to detect single nucleotide variants, short insertions/deletions, copy number variations and structural variants. ctDNA features were calculated for each pt and included number of genomic alterations (numGA), number of mutations (numMUT), number of amplifications/fusions (numAMPFUS), sum mutant allele frequency (sumMAF), and maximum mutant allele frequency (maxMAF). Univariate and multivariable Cox proportional hazards models were used to identify ctDNA features associated with progression-free survival (PFS). ctDNA from baseline (T0) to the blood collection closest to progression or censor date (T1) was used to assess change in sumMAF and maxMAF. All models included ctDNA features as continuous variables. **Result:** 27 pts were evaluable. 85.19% were white; 37.04% were male. 85.19% were adenocarcinoma histology; remaining were squamous. 45.83% received prior systemic therapy. Average number of lines of prior therapy was 1.81. 44.44% had prior radiation therapy. 81.48% of pts had at least one genomic alteration detected in ctDNA at baseline. The median numGA, numMUT, and numAMPFUS, maxMAF, sumMAF was 2.00, 2.00, 0.00, 1.61, and 2.34 respectively. TP53, KRAS, and EGFR were the most frequently identified genomic alterations (59.26%, 25.93%, and 22.22%, respectively). EGFR alterations were the most commonly identified genomic alteration in ctDNA. 86.00% of EGFR alterations were actionable. Univariate Cox regression analysis identified numAMPFUS (HR=3.12, p=0.01), sumMAF (HR=1.02, p=0.02), and maxMAF (HR=1.05, p=0.00) to be significantly associated with PFS. Only maxMAF was retained in the final multivariable Cox model. Each percentage point increase in maxMAF from T0 to T1 resulted in a 4% decrease in the risk of progression/death (HR=0.96, p=0.08). **Conclusion:** In this pilot study, pts with higher levels of baseline maxMAF detected in ctDNA were associated with increased risk of progression/death. Following initiation of treatment, results suggest increased change in maxMAF may be associated with a decreased risk of progression/death. **Keywords:** Non-Small Cell Lung Cancer, ctDNA, Survival

P2.01-63
Radiosurgery Followed by Tumor Treating Fields (TTFields) for Brain Metastases (1-10) from NSCLC in the Phase 3 METIS Trial

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Background: Tumor Treating Fields (TTFields) are non-invasive, loco-regional, anti-mitotic treatment modality comprising alternating electric fields. TTFields have demonstrated efficacy in preclinical non-small cell lung cancer (NSCLC) models. TTFields treatment to the brain was safe and extended overall survival in newly-diagnosed glioblastoma. The METIS study [NCT02831959] investigates the efficacy and safety of TTFields in NSCLC patients with brain metastases. **Method:** NSCLC patients (N=270) with 1-10 brain metastases are randomized 1:1 to stereotactic radio surgery (SRS) followed by continuous TTFields ((150 kHz, >18 hours/day) within 7 days of SRS or supportive care. The TTFields portable device delivers TTFields to the brain using 4 transducer arrays, while patients receive the best standard-of-care for their systemic disease. Patients are followed every two months until second intracranial progression. Key inclusion criteria: KPS ≥70, new diagnosis of 1 inoperable or 2−10 supra- and/or infratentorial brain metastases from NSCLC amenable to SRS; KPS ≥70; and optimal therapy for extracranial disease. Prior WBRT or surgical resection of metastases, a single resectable lesion or recurrent brain metastases were exclusionary. Primary endpoint was time to 1st intracranial progression. Secondary endpoints included time to neurocognitive failure (HVLT, COWAT and TMT), overall survival, radiological response rate (RANO-BM and RECIST V1.1); quality-of-life; adverse events; time to first/second intracranial progression for patients with 1−4 and 5−10 brain metastases; bi-monthly intracranial progression rate from 2−12 months; and time to second intracranial and distant progression. The sample size (N=270) was calculated using a log-rank test (Lakatos 1988 and 2002) with 80% power at a two sided alpha of 0.05 to detect a hazard ratio of 0.57. In August 2018, an independent Data Monitoring Committee (DMC) performed a review of the METIS trial data collected to that point. The DMC concluded that no unexpected safety issues have emerged on the study, and recommended to continue the METIS study as planned. **Result:** "Section not applicable" **Conclusion:** "Section not applicable" **Keywords:** TTFields for brain metastases from NSCLC, Radiosurgery plus Tumor Treating Fields (TTFields)

P2.01-64
Systemic Inflammatory Markers as a Predictors of Response to Crizotinib in Patients with ALK-Positive Non-Small-Cell Lung Cancer

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Background: The significance of the presence of a systemic inflammatory response (SIR) in predicting survival has been demonstrated in patients with cancer. Moreover, neutrophil-to-lymphocyte ratio (NLR), lymphocyteratio (NLR), lymphocyte-to-monocyte ratio (LMR) and platelet-to-lymphocyte ratio (PLR) have been also investigated in patients with both early and advanced non-small-cell lung cancer (NSCLC). However, determination of SIR predicting outcomes of patients who are likely to response to crizotinib in ALK-positive NSCLC patients has not been clearly demonstrated. The aim of this study was to investigate the prognostic and predictive value of NLR, LMR and PLR in patients with ALK-positive NSCLC treated with crizotinib. **Method:** Eighty-two patients with ALK-positive NSCLC who were treated with crizotinib were retrospectively analyzed. The cutoff values for NLR, LMR and PLR were defined by the receiver operating characteristic (ROC) curve analysis. Univariate and multivariate analyses were used to evaluate the prognostic significance of NLR, LMR and PLR. Logistic regression analysis was also performed to determine predictive indicators of response to crizotinib. **Result:** Among 82 patients, 35 (42.7%) were male and 47 (57.3%) were female, with a median age of 52.5 years (range; 20−77 years). Crizotinib treatment was administered as a first-line in 26.8% of patients, second-line in 56.1%, third-line in 12.2% and forth-line and later in 4.9%. The objective response rate was 77.2% (CR+PR) and stable disease was obtained in 7.6% of patients. According to the ROC curve, the recommended cutoff values of NLR, LMR and PLR were 3.14, 2.31 and 185,5 respectively. The median follow-up time was 19.3 months. ECOG performance status (PS)

(p=0.014) and response to crizotinib (p=0.001) for progression-free survival (PFS) and ECOG PS (p<0.001), response to crizotinib (p<0.001), NLR (p=0.029) and LMR (p=0.028) for overall survival (OS) were found to be prognostic factors by univariate analysis. On the other hand, multivariate analysis showed that only ECOG PS and response to crizotinib were independent prognostic indicators for both PFS and OS. A logistic regression analysis indicated that NLR and LMR was found to be an independent factor for predicting response to crizotinib (p=0.007, OR:0.10 and p=0.044, OR: 0.20, respectively). **Conclusion:** Our findings showed that NLR and LMR are readily feasible and simple and also inexpensive biomarkers predicting response of crizotinib for patients with ALK-positive advanced NSCLC.

P2.01-65
Temporal Changes of Radiation-Induced Lung Injury Following Proton Therapy for Non-Small Cell Lung Cancer (NSCLC)

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Background: Proton therapy (PT) is increasingly being used in locally advanced non-small cell lung cancer (NSCLC), but is there currently a limited understanding of its radiation-induced lung injury pattern that can cofound radiologic interpretation. Here we characterize imaging of radiation-induced lung injury on CT (computed tomography) and FDG-PET (^{18}F-deoxy-glucose-positon emission tomography) following PT. **Method:** After institutional IRB approval, longitudinal imaging from adult NSCLC patients undergoing PT over a 5-year period at our institution were retrospectively analyzed by two thoracic radiologists. Tumor size and FDG standard uptake value max (SUV_{max}) were recorded. In addition, early (<12 months after PT) and late (>12 months) radiation-induced lung injuries were quantified (0-3 Likert score), including consolidation, ground glass, interlobular septal thickening, bronchiectasis and pleural effusion, on all serial imaging.

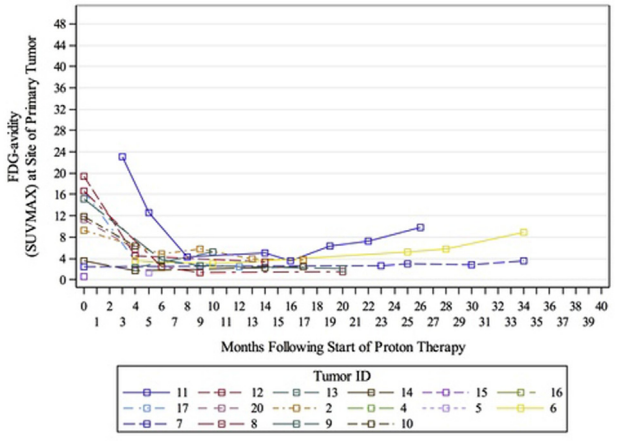

Figure: Temporal changes in FDG avidity in NSCLC following proton therapy. FDG (SUVmax) on PET/CT NSCLC treated with proton therapy exhibits a steady decrease glucose avidity over the first year following therapy.

Result: 19 consecutive locally advanced NSCLC patients (mean age 69.3 yrs) had PT during the study period and had serial images available for review. The mean imaging follow-up period from PT start was 30 months. Five patients developed local failure. In the remaining 14 patients, tumor size and FDG avidity steadily decreased over time (mean SUVmax = 10.8 at baseline and 2.5 at 12 months). Ground glass and interlobular septal thickening presented as early changes, increasing through months 6-12 and 9-12 respectively but generally resolved by 24 months. 68% of patients developed a pleural effusion (< 2 years), increasing in severity over the 1st 18 months. Consolidation consistently increased in severity throughout the observation period (max >48 months) Among 11 tumors, 8 achieved maximum severity in late changes of band-like or mass-like consolidation within 24 months and then typically plateaued. Late development of a pleural effusion, mass-like fibrosis, increased tumor caliber and increased FDG avidity were associated with local tumor recurrence. **Conclusion:** Radiation-induced lung injury follows a predictable temporal pattern on CT. Knowledge of expected timeline of the imaging findings may prevent unnecessary imaging and/or biopsies. We are currently analyzing a larger cohort of 100 NSCLC patients to compare post radiation changes in local recurrence and local control. **Keywords:** proton therapy, Non-Small Cell Lung Cancer, computed tomorgraphy

P2.01-66
Genomic Landscapes of DNA Copy Number Alterations in Primary Lung Cancers and Matched Brain Metastases

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Background: Lung cancer (LC) is the leading cause of cancer mortality worldwide. The majority of LC patients will develop distant metastases at some point during their disease, and brain is among the most common sites of relapse. However, little is known about the mutational landscape of brain metastases (BM) and their potential inter-tumor heterogeneity. Better knowledge on this subject may pave the way to new therapeutic strategies. Here, we map the DNA copy number alterations (CNAs) by sequencing a cohort of primary LC samples and matched BM. **Method:** The study group included 57 patients (21 females and 36 males, median age 61±8 years; 35 adenocarcinomas, 18 squamous-cell carcinomas, 2 large-cell carcinomas, 1 adenosquamous carcinoma and 1 small-cell lung cancer). From all patients pair-matched tissue samples from primary tumor and corresponding BM were collected, fixed in formalin and embedded in paraffin. All patients were therapy-naïve at the time of primary tumor collection. Genomic DNA was extracted using the QIAamp DNA FFPE Tissue Kit (Qiagen, Germany), followed by NGS library preparation using the NEBNext Ultra II DNA kit (NEB, USA). Samples were sequenced shallowly (average depth 26 Mreads) on the NextSeq 500 system (Illumina, USA). The R package QDNAseq was used to call and visualize DNA copy number levels. The