zeste homolog 2 (EZH2) histone-lysine methyltransferase in mediating a chemoresistant phenotype through silencing of the SLFN11 gene product, a factor implicated in DNA damage repair deficiency. Furthermore, transient gene expression changes in survival cell fractions following chemotherapy have been demonstrated to contribute to disease relapse and can potentially be targeted. Given the exceptional initial response rates SCLC has to cisplatin and etoposide, we endeavored to define molecular changes that occur in surviving cell fractions following initial chemotherapy challenge to refine our understanding of SCLC relapse biology and identify candidate factors. We initially identified optimal dosing schemes across a panel of SCLC cell lines and quantified cell number and proliferation, establishing seven to ten days as a time window for maximal cytoreduction following chemotherapy in vitro. We then performed transcriptional profiling via RNA-sequencing on cell lines treated with either single-agent cisplatin or combination cisplatin + etoposide across a 24-day time course and utilized principal component analysis to identify genes whose expression exhibits transient expression patterns across the time course. Using gene set enrichment analysis, we confirmed fidelity of our dataset by identification of expected transient downregulated genes involved in ribosomal biogenesis and concordantly upregulated genes involved in xenobiotic response and DNA damage. Consistently, between both single-agent cisplatin and combination treatment time courses, we identified a significant transient upregulation of a suite of transcription factors. Importantly, we observed a 10- to 30-fold upregulation of these factors compared to baseline that is transient and peaks at timepoints with lowest absolute viable cell number. Current work is focused on determining the sufficiency and necessity of these factors in the progression of SCLC following initial chemotherapy.

B08
Impact of Concurrent STK11 Loss and c-MYC Amplification in Metastatic Non-Small Cell Lung Cancer (NSCLC)

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Introduction: Despite significant therapeutic advances, clinical outcome remains poor in most patients (pts) with NSCLC, due at least in part to their genotype. STK11 is a master kinase that controls cellular metabolism, while c-MYC is an oncogene altered in many cancers promoting proliferation. Preclinical data (PMID:24793789) suggest that c-MYC amplification in the setting of STK11 loss can lead to unchecked growth of cancer cells. We anecdotally observed rapid progression, primary treatment refractoriness, and dramatic clinical decline in several pts with metastatic NSCLC (mNSCLC) with concurrent STK11 loss and c-MYC amplification. Hence, we investigated the incidence and the prognostic impact of these biomarkers in mNSCLC.

Methods: This study was performed through the Precision Medicine Exchange Consortium (PMEC), a consortium of 10 US academic medical centers that share clinically annotated genomic data under a central IRB-approved protocol. The PMEC database (PMEC-DB) was queried for NSCLC pts with either STK11 loss ( cohort A), c-MYC amplification ( cohort B), or both ( cohort C). Comprehensive genomic profiling (CGP) was performed on tumor tissue utilizing the Foundation One 315 gene assay. Demographic and disease characteristics were analyzed. Survival curves were estimated using the Kaplan-Meier method. Results: Among the 1,952 pts with NSCLC in the PMEC-DB, 396 pts met the inclusion criteria with 246 (62%), 103 (26%), and 47 (11.8%) pts in cohorts (p = 0.12). KRAS mutations were detected more frequently in cohort C (58 % vs. 18% vs 38%; p<0.0001). Clinical outcome data were available in 99 (25%) pts and were distributed among cohorts A, B, and C, in similar proportion to the overall study set with 60, 24, and 15 pts, respectively. Cohort C was associated with a nonadenocarcinoma histology compared to cohorts A and B (53.3%, 16.7%, and 33.3%, respectively, p = 0.011). Non-adenocarcinoma subtypes in Cohort C were NSCLC NOS 33.3%, squamous 6.7%, and large cell neuroendocrine 13.3%. There was no difference in median overall survival (mOS) between cohorts A, B, and C (10 months, 17 months, and 11 months respectively, p = 0.68).
Conclusion: Concurrent STK11 loss and c-MYC amplification in NSCLC is uncommon, but had no impact on survival in a limited patient set. This study underscores the importance of large-scale, clinically annotated genomic data sharing initiatives in systematically exploring the clinical relevance of rare genomic alterations.

B09
The CANOPY Program: Three Phase 3 Studies Evaluating Canakinumab in Patients with Non-Small Cell Lung Cancer (NSCLC)

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Background: Canakinumab (CANA) is a selective IL-1β inhibitor that aims to target tumor-promoting inflammation to reduce immune suppression. In the CANTOS study, CANA treatment was associated with reduced lung cancer incidence and mortality in patients (pts) with stable post-myocardial infarction who had elevated high-sensitivity C-reactive protein levels, thus providing a rationale to investigate its potential therapeutic role in lung cancer. Methods: CANOPY-A, CANOPY-1, and CANOPY-2 are phase III, multicenter, randomized, double-blind, placebo-controlled studies. In CANOPY-A, pts (~1,500) with stages IIA–IIIA and IIIB (T>5 cm N2), any histology, completely resected (R0) NSCLC, who received cisplatin-based chemotherapy (CTX), will be enrolled and randomized 1:1 to receive either CANA (200 mg Q3W SC) or placebo (Q3W SC) for 18 cycles. As of Oct 8, 2019, there are 278 study locations per clinicaltrials.gov. The primary endpoint will be disease-free survival. Key secondary endpoint will be overall survival (OS). CANOPY-1 and CANOPY-2 will each consist of part 1 (open-label, safety run-in) and part 2 (randomized, placebo-controlled; efficacy and safety evaluation). Eligible pts should have ECOG PS ≤1 and no EGFR sensitizing mutations and/or ALK rearrangements. In CANOPY-1, pts with previously untreated stage IIIB/IIIA and IIIB (T>5 cm N2) NSCLC and known PD-L1 status (part 2 only) will be enrolled. Part 1 will consist of 3 cohorts of ~9 pts each (based on different platinum-CTX) to confirm the recommended phase 3 regimen (RP3R) for CANA. Pts will be treated with full doses of CTX plus pembrolizumab plus CANA. Enrollment and safety observation period for part 1 is complete. In part 2, pts (~600) will be randomized (1:1) to receive CANA (200 mg Q3W SC) or placebo + pembrolizumab + platinum-doublet CTX for 4 cycles, followed by maintenance until progressive disease. As of Oct 15, there are 129 study locations per clinicaltrials.gov. In CANOPY-2, pts with stage IIIB–IV NSCLC, who received prior PD-(L)1 inhibitor therapy and platinum-based CTX, and no PD-(L)1 selection, will be enrolled. Part 1 will enroll ~9 pts to confirm the RP3R of CANA. Pts will be treated with full doses of CANA 200 mg SC + docetaxel 75 mg/m2 i.v. on day 1 of each 21-day cycle. Enrollment to part 1 of the study is complete. In part 2, pts (~226) will be enrolled and randomized 1:1 to receive CANA (200 mg Q3W SC) or placebo + docetaxel. As of Oct 23, there are 85 study locations per clinicaltrials.gov. In part 1 (both studies), the primary endpoint is the incidence of dose limiting toxicities in the first 42 days of treatment. In part 2, the primary endpoints are progression-free survival (PFS) and OS in CANOPY-1, and OS in CANOPY-2. Common secondary endpoints (both studies) include overall response rate, disease control rate, time to response, duration of response, PFS (CANOPY-2), pharmacokinetics, safety, patient-reported outcomes, and immunogenicity. All three studies (CANYAP-A, CANOPY-1, and CANOPY-2) are currently recruiting.

B10
Prevalence of EGFR Mutation Among Vietnamese Non-Small Cell Lung Cancer: A Preliminary Study

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Aims: To investigate the distribution of epidermal growth factor receptor (EGFR) mutations, and explore any relationships with characteristics of non-small cell lung cancer (NSCLC) patients. Materials and Methods: EGFR mutations were assessed by Scorpions and ARMS technologies (therascreen® EGFR RQ PCR Kit - Qiagen) in randomized sample block of 200 NSCLC patients from Vietnam National Cancer Hospital. Relationships between EGFR mutation and patient characteristics were analyzed by R statistical software. Results: The EGFR mutation rate was 41% (83/200); 19-del and L858R mutations occurred predominantly, accounting for 55.4% and 27.2%, respectively, in mutated cases. Moreover, 3.5% patients were found to carry double mutations. EGFR mutations occurred more frequently in women (75%) than in men (27.1%) (P<0.001). Mean ages of patient with mutation and without mutation were 56.51 (±8.86) and 58.83 years (±9.05), respectively (p=0.073). Gender distribution was significantly different between the 2 groups of mutation and no mutation (p<0.001). In EGFR mutation group, 98.8% of them possessed the Vietnamese health insurance and 9.6% of them which their first diagnosis had no relation with lung carcinoma. Conclusions: The EGFR mutation rate was 41% in NSCLCs in Vietnam, so that about 40% of patients might benefit from targeted therapies. Further studies are required to have a comprehensive understanding about the other clinical characteristics and EGFR mutation in Vietnamese patients.

B11
Accurate Detection of MET exon 14 Skipping Mutations in Non-Small Cell Lung Cancer (NSCLC) with Comprehensive Genomic Sequencing: Results from the GEOMETRY Mono-1 Study

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Background: MET exon 14 skipping mutations (METex14) occur in 3–4% of patients (pts) with NSCLC. Accurate detection of the genomic variants that result in METex14 in MET-driven tumors could facilitate timely intervention with selective MET inhibitors (METI) and improve...