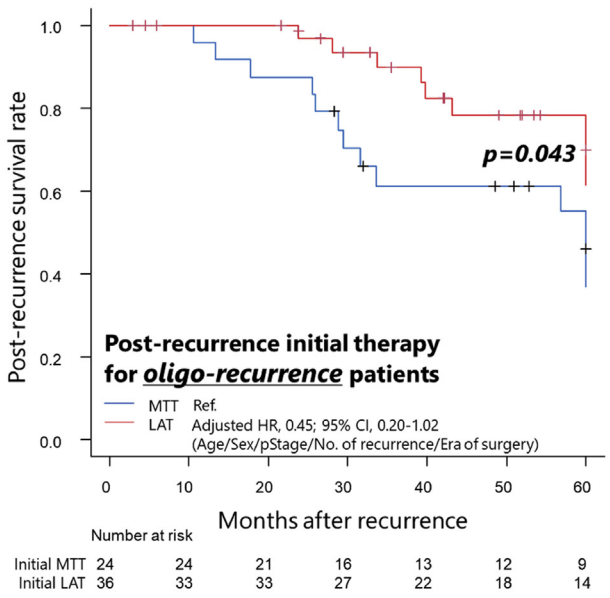

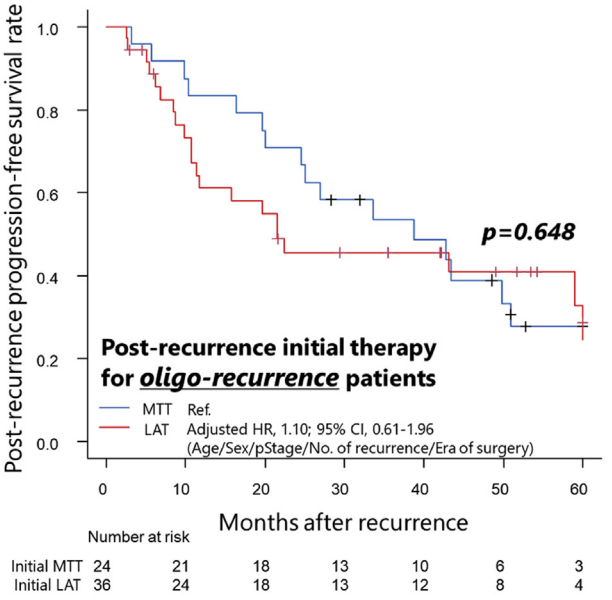

and 2017, we retrospectively evaluated 272 patients with post-operative recurrence. Oligo-recurrence was defined as 1-3 recurrent lesions. We investigated oligo-recurrence patients with driver mutations focusing on post-recurrence therapies and prognoses. **Results:** The median follow-up period was 52 months. In total, 155 (57%) patients had driver mutations, and as initial post-recurrence therapies, local ablative therapies and specific tyrosine-kinase inhibitors were administered to 37 and 100 patients, respectively. Of them, 70 (45%) met the criteria for oligo-recurrence, and as initial post-recurrence therapies, local ablative therapies and specific tyrosine-kinase inhibitors were administered to 36 and 24 patients, respectively. Compared with specific tyrosine-kinase inhibitors, local ablative therapies significantly improved post-recurrence survival (p=0.043) but not post-recurrence progression-free survival (p=0.648) in oligo-recurrence patients. In also the multivariable analyses adjusted for number of recurrence, the results were similar for both post-recurrence survival (local ablative therapies: hazard ratio, 0.45; 95% confidence interval, 0.20-1.02) and post-recurrence progression-free survival (local ablative therapies: hazard ratio, 1.10; 95% confidence interval, 0.61-1.96). Patients who received local ablative therapies, even if they were not the initial treatment, had superior post-recurrence survival than those treated with specific tyrosine-kinase inhibitors alone (p=0.027). **Conclusion:** Although specific tyrosine-kinase inhibitors have a profound therapeutic benefit in lung cancer patients with driver mutations, local ablative therapies should be considered the first treatment choice for patients with oligo-recurrent lung cancer. Furthermore, the combination of local ablative therapies and specific tyrosine-kinase inhibitors may be a promising treatment strategy.

Keywords: oligo-recurrence, driver mutation, local ablative therapy

P53.05
Inhibition of Tumor Cell Intrinsic Complement Regulatory Proteins Leads to Decreased Tumor Growth in a Mouse Model of NSCLC

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Introduction: The complement system is part of the innate immune system that interfaces with adaptive immunity. Complement activation triggers a series of proteolytic cascades that converge on C3, leading to the formation of the membrane attack complex (MAC) that causes cell lysis of target cells. Within the complement system, there are multiple regulatory proteins that act to inhibit or decrease complement activation; these proteins include Factor H (fH), CD55, and CD59. Complement activation can mediate tumor progression through production of anaphylatoxins (C3a/C5a) that act to block anti-tumor immunity. However, complement activation can also inhibit tumor growth through the formation of the MAC complex leading to cancer cell killing. Previous studies by our lab showed that complement inhibition, either with use of a global genetic $C3^{-/-}$ mouse or with pharmacologic agents targeting the C3a and C5a receptors, inhibited tumor growth and metastasis by acting as immunomodulators in a tumor cell-extrinsic manner. Here we hypothesize that tumor cell-intrinsic upregulation of complement regulatory proteins, such as fH and CD55, leads to increased tumor growth by inhibiting formation of the MAC complex and thereby preventing tumor cell lysis and death. **Methods:** We used an orthotopic syngeneic mouse model where murine cancer cells are implanted into the left lungs of syngeneic mice. These studies used CMT167 and LLC cells, which have KRas mutations, and EA1 and EA2 cells, which express the fusion kinase Eml4-Alk. Using RNAseq, we compared the transcriptome of cancer cells recovered from tumors to the transcriptome of their respective cell lines grown *in vitro*. To study the role of complement regulatory proteins in tumor cells, we silenced fH in murine cell lines using both shRNA constructs as well as a CRISPR knockout. These cells were implanted into the lungs of mice and tumor volume was measured after 2-3 weeks. Knockdown was validated by qPCR. We treated mice with a novel tumor-targeting fH antibody and monitored tumor growth by CT imaging. **Results:** RNAseq analysis indicates an increase in complement regulatory proteins *in vivo* versus *in vitro* in our cell lines, specifically fH in EA1, LLC, and CMT167 cells and CD55 in CMT167 cells. We observed a decreased volume of fH knockdown tumors compared to control tumors in EA1 cells orthotopically injected into the left lung of WT C57Bl/6 mice. CMT167 fH knockdown cells did not show a difference in tumor growth. However, CMT167 CD55 knockdown cells formed smaller tumors *in vivo* compared to the control tumors. Furthermore, the use of a tumor cell-targeting fH antibody led to decreased tumor growth in EA1 tumors compared to control. **Conclusion:** Taken together, our data indicate that tumor cell-intrinsic complement regulatory proteins play a role in

tumor progression. Inhibition of these proteins leads to decreased tumor growth in a mouse model of NSCLC indicating that targeting these pathways has a therapeutic potential to treat NSCLC patients. **Keywords:** complement, Factor H, NSCLC

P53.06
A Multi-Phase Quality Initiative to Improve Processes of Care for Non-small Cell Lung Cancer (NSCLC) in US Community Cancer Centers

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Introduction: Accurate staging, biomarker identification, and high-fidelity processes of care are critical for evidence-based treatment of NSCLC. To this end, the Association of Community Cancer Centers (ACCC) conducted a national, multi-phase effort to identify and provide guidance on key issues related to optimal care for patients with stage III/IV NSCLC. **Methods:** The quality improvement (QI) initiative, guided by an expert steering committee, included 5 phases: 1: Site Selection; 2: Topic Identification, Quality Measure Development & Education; 3: Data Collection & Analysis; 4: Implementation of Educational Intervention; 5: Analyze & Repeat. After site selection, baseline data were collected to assess key areas (demographics and clinical features, biomarker testing, process of care) across all sites using standardized data collection instruments. Baseline data were reviewed with each project team and a QI topic was selected via planning tele-conferences. An onsite (or virtual) full-day workshop was conducted with multidisciplinary cancer team members, including invited expert faculty, to define goals and develop site-specific QI projects. The main objects were to implement process-level improvements and develop quantitative benchmarks. Follow-up data collection (quantitative, qualitative, and process-level) was specific to each project and site (some were modified due to COVID-19) and all sites provided follow-up data on biomarker testing. Statistical analyses included summary statistics, frequency tables, and chi-square tests. **Results:** In pre-implementation (baseline) data collected at the six sites from 2018-2019, median patient ages were 65-72 years; 50% Stage III and 50% Stage IV. The race distribution of patients and proportions insured under Medicare, Medicaid, or commercial varied substantially across sites. Biomarker testing also varied in 2018-2019, with clinicians having requested testing for 48-94% of Stage IV patients (with four sites >80%). When biomarkers were evaluated, EGFR and ALK were included in 70-100% of tests, BRAF and ROS1 in 14-87% of tests, and NTRK testing was rare. PDL1 was evaluated in 40-97% of patients. Important process-level improvements were achieved with the QI projects in 2020. Two sites focused on immune-related adverse events (irAEs), conducting a clinician survey to assess gaps in knowledge and care around identification and management of irAEs and developing a patient questionnaire to identify early signs of irAEs. A site focused on clinical trial enrollment and education and established a referral partnership with an NCI-designed cancer center. Two sites focused on biomarker testing, making progress towards standardization. Interventions included creation of a process map for ordering, optimizing workflow by standardizing key elements and template order-sets, increasing liquid biopsy use, and implementing pathology-driven reflex testing at diagnosis. Three sites improved testing rates of Stage IV patients from baseline to follow-up (48% to 81%; 67% to 100%; 80% to 100%). When biomarkers were tested in 2020, the use of panel testing was 87% overall (>70% for every site). Liquid biopsy was used regularly at three sites, testing 23%, 25%, and 40% of patients. **Conclusion:** This initiative aided six cancer programs in improving processes of care for patients with stage III/IV NSCLC. Despite some COVID-19 disruption, participating sites remained committed to implementing changes around biomarker testing, well-coordinated care delivery, and symptom management. **Keywords:** biomarker testing, immune-related adverse events, Quality of Care

P53.07
Clinical and Genomic Insights Into of Chinese Lung Cancer Patients with HER2 Amplification

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Introduction: HER2 alterations was one of subsets of patients with specific genetic alterations of NSCLC patients. Despite that HER2 alterations in NSCLC have been studied for years, there is still no consensus about subgroup definitions, especially for HER2 amplification. In this study, we analyzed the genomic and clinical characteristics of HER2-amplified Chinese lung cancer patients, in order to find the appropriate treatment modalities for these patients. **Methods:** We reviewed 7643 Chinese lung cancer patients with paired tumor-normal samples sequenced by a 1021 gene panel. Tumor mutational burden (TMB) was defined as the number of somatic non-synonymous mutations per megabase of the panel region. **Results:** 2.8% patients (214/7643) had HER2 amplification, and 95 of them carried only HER2 amplification. The copy number ranged from 3 to 265, and median was 10. Based on the median, the patients were divided into higher and lower groups. RTK-RAS and PI3K signal pathway were common in these patients. TP53 was the most common concomitant mutation in both higher group (80%) and lower group (80%) patients. The lower group showed higher proportion patients with genetic mutation in RTK-RAS pathway than higher group (84.6% vs 58.2%, p=0.00626). The main reason was that lower group had higher proportion NF1 gene mutation (25% vs 0). Then, TMB was compared in two groups, and lower group showed higher TMB than higher group (16 vs 11, p=0.0069). 15 of 95 patients had the data of survival in multiple-lines, including 4 of treated with immunotherapy, 4 of treated with afatinib, and 11 of treated with chemotherapy. The progression free survival(PFS) of two groups was no difference (4 vs 4, p=0.27). However, the patients treated with immunotherapy showed longer PFS than patients treated with chemotherapy (5.5 vs 2, p=0.0078). Patients treated with afatinib also had longer PFS than those treated with chemotherapy, although there was no significant difference (4 vs 2, p=0.079). **Conclusion:** In conclusion, the patients with lower copy numbers of HER2 had more mutation in RTK-RAS pathway that may be a potential target to combination treatment for this patients. Meanwhile, our study showed immunotherapy and target therapy were better than chemotherapy for patients with HER2 amplification. **Keywords:** HER2 amplification, TMB, NSCLC

P53.08
Concomitant Fibrates and Immunotherapy in Non-Small Cell Lung Cancer Patients in the Veterans Health Administration

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