lungs specific antigens (TTF1 and Napsin) besides EMA, P40, CK7, Synaptophysin, Chromogranin A, CD56, Calretinin, PD-L1, ALK (D5F3) by immunocytochemistry (ICC). EGFR fusions, ALK, RET and ROS1 fusions were evaluated from plasma by NGS. Results: C-ETACs (EPCAM and CK positive) could be obtained from 458 samples out of 498 (92.0%). Among the 95 samples that were characterized by staining for organ specific antigens, 100% samples were positive for Napsin whilst 67.0% samples were TTF1 positive. Classification of lung cancer subtypes of adenocarcinoma, adenosquamous carcinoma, squamous cell carcinoma and neuroendocrine tumors was possible in 94 out of 95 samples (98.9%). ctDNA was obtained from 332 samples. EGFR mutations were detected in 110 (33.1%) samples, which had concordance with tissue EGFR status in 89% of 124 EGFR positive samples. ALK fusion was detected in 2 (0.6%) samples which had concordance of 100% with tissue ALK status. None of the tissue evaluated carried RET or ROS1 fusion and none were detected in any plasma sample.

Conclusion: Our results show that ICC based characterization of C-ETACs can provide necessary diagnostic information non-invasively to substitute conventional procedures dependent on tissue extraction. Additionally, ctDNA based detection of molecular characteristics completes most clinical decision-making requirements in lung cancer.

PD01.13
Stereotactic Modulating Radiation Therapy (SMRT) For Oligo-Metastatic Non-Small Cell Lung Cancer

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Background: Patients with oligometastatic non-small cell lung cancer (PD1>50%) are now treated with a PD1 inhibitor as single agent therapy. Patients with (PD1<50%) are now treated with platinum doublet chemotherapy concurrent with a PD1 inhibitor. Stereotactic body radiotherapy (SBRT) has improved outcomes in oligometastatic non-small cell lung cancer with two recent randomized clinical trials showing improvement in progression free survival and overall survival. As a result, immunotherapy combined with SBRT or chemo-immuno-SBRT is emerging as a new standard of care for select patients with oligometastatic non-small cell lung cancer. High doses of stereotactic ablative radiotherapy (SABR) are safe and effective and are commonly used to treat lung cancer. At moderate doses, radiation can increase interferon expression resulting in an increase in Th1 T-Helper cell differentiation with a resulting increase in CD8+ anti-tumor cytotoxic T-Lymphocytes (CTL). We propose the term stereotactic modulating radiation therapy (SMRT) to describe the moderate doses of SBRT. We hypothesize that moderate dose SMRT therapy will improve outcomes in oligometastatic lung cancer compared to higher dose SABR therapy. We have initiated a phase II clinical trial to test SABR and SMRT radiotherapy in combination with immunotherapy or chemo-immunotherapy.

Method: Oligometastatic NSCLCs (<5 sites of disease) are treated with three cycles of systemic therapy. Tumors with PDL1>50% receive immunotherapy. Patients with PDL1<50% receive platinum doublet chemotherapy with immunotherapy. After three cycles patients are evaluated for response and randomized to SMRT or SABR. SMRT cohort 6-8Gy x 3-5 = 24-30Gy; SABR cohort 10-24G x 1-5 = 24-60Gy. Patients with tumor >5cm or residual adenopathy after cycle 3 receive hypofractionated radiation (2.5Gy x 20 = 50Gy) concurrent with cycle 4 and then randomize to SMRT or SABR. All patients receive maintenance therapy. Results: The primary end point is toxicity of immunotherapy or chemo-immunotherapy with SMRT or SABR by CTCAE v 4.03. Secondary endpoints are response rate by RECIST v 1.1 and iRECIST, patient reported quality of life, DFS, and OS. Exploratory endpoints investigate the immune response and cytokine levels in tumor microenvironment and peripheral blood prior to systemic therapy, after cycle 3, and after SBRT.

Conclusion: The widespread adoption of immunotherapy and chemo-immunotherapy makes it crucial to understand the interaction between radiation therapy and PD1 inhibitors. This study investigates high dose stereotactic ablative radiotherapy (SABR) compared to moderate dose stereotactic modulating radiotherapy (SMRT) in an effort to identify patients most likely to benefit from this combination. Keywords: Oligometastatic Non-Small Cell Lung Cancer, Chemo-immunotherapy, Stereotactic Body Radiotherapy SABR, Immunotherapy

PD01.14
Targeting the Chemoradiation Resistance of Lung Cancers with KRAS/TP53 Co-Mutations

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Background: Oligometastatic non-small cell lung cancer (NSCLC) is a biologically heterogeneous disease with distinct genetic alterations affecting tumor chemoradiation resistance. We hypothesized that KRAS and TP53 mutations may be involved in the development of chemoradiation resistance in NSCLC. We aimed to identify the prevalence of KRAS and TP53 mutations in a series of oligometastatic NSCLC patients treated with chemoradiation therapy and to correlate these findings with clinical outcomes.

Method: We performed whole-exome sequencing on tumor samples from 50 patients with oligometastatic NSCLC undergoing chemoradiation therapy. KRAS and TP53 mutations were identified and correlated with clinical outcomes, including progression-free survival and overall survival.

Results: Among the 50 patients, KRAS mutations were present in 30% and TP53 mutations in 20% of the samples. Patients with KRAS mutations had significantly lower progression-free survival compared to those without KRAS mutations (median 6 months vs. 12 months, p=0.03). Similarly, patients with TP53 mutations had lower progression-free survival compared to those without TP53 mutations (median 6 months vs. 12 months, p=0.04).

Conclusion: Our study demonstrates the involvement of KRAS and TP53 mutations in the chemoradiation resistance of oligometastatic NSCLC. These findings may have implications for the development of targeted therapies to overcome chemoradiation resistance in this patient population.