PD01.08

Incidence and Predictors Associated with the Development of Peripheral Neuropathy in Non-Small Cell Lung Cancer Patients

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Background: Recommended chemotherapy for unresectable locally advanced or metastatic non-small cell lung cancer (NSCLC) includes platinum agents, taxanes and immunotherapy agents. However, these treatments have been associated with the development of peripheral neuropathy (PN). We present the incidence rates of PN and identify its predictors using a real-world data source. **Method:** In Optum's Humedica electronic health records database, we identified NSCLC patients diagnosed between 1/1/2008 and 12/31/2017, using a combination of ICD-9/ICD-10 diagnosis codes and structured data derived from physician notes. Patients with lung surgery or other primary cancers in the 12 months prior to diagnosis were excluded. Distinct lines of treatment (LOT) were established using business rules, and incidence rates of PN for each LOT were calculated. We identified predictors of PN development any time after treatment start by carrying out a stepwise Cox regression analysis using 27 covariates. **Results:** Of the identified 63,174 NSCLC patients, 26,061 had LOT 1, 9,938 had LOT 2, and 4,790 had LOT 3. Incidence rates for all patients, and those with and without a history of PN and diabetes for LOTs 1-3 and across all LOTs of a patient are shown in Table 1. Of the 27 covariates in the Cox regression, age≥65 (HR: 0.94; p=0.0083), male gender (HR: 1.12; p<0.0001), Asian race (HR: 0.72, p=0.0034), squamous cell histology (HR: 1.13; p<0.0001), a history of peripheral neuropathy (HR: 2.86; p <0.0001), and a history of diabetes (HR: 1.37; p <0.0001) were found to be significant predictors of developing PN.

Table 1

		LOT1 to last LOT[1] (n=26,061)	LOT 1[2] (n=26,061)	LOT 2[2] (n=9,938)	LOT 3[2] (n=4,790)
All patients	% (CI)	26.1% (25.5% - 26.6%)	19.8% (19.3% - 20.3%)	21.0% (20.2% - 21.8%)	22.3% (21.1% - 23.5%)
Patients with a history of PN and diabetes	% (CI)	55.3% (53.2% - 57.5%)	50.0% (47.8% - 52.2%)	44.6% (41.7% - 47.5%)	45.0% (41.1% - 48.9%)
Patients without a history of PN and diabetes	% (CI)	19.7% (19.1% - 20.3%)	13.8% (13.2% - 14.3%)	10.9% (10.1% - 11.8%)	10.3% (9.0% - 11.6%)

The period over which this has been assessed is:
1 Start of LOT1 to earlier of (365 days from end of last LOT or end of follow-up)
2 Start of LOT to start of next LOT, or if no next LOT, earlier of (365 days from end of LOT or end of follow-up)

Conclusion: Of all treated NSCLC patients, more than a quarter develop PN over the course of their treatments. Incidence rates increase with each LOT indicating an increased risk as patients continue treatment. Identifying covariates associated with PN allows identification of high-risk patients, which may contribute to lowering the risk of developing PN. **Keyword:** NSCLC, peripheral neuropathy, incidence, risk factors, treatment

PD01.09

Incidence and Predictors Associated with the Development of Pneumonitis in Non-Small Cell Lung Cancer Patients

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Background: Pneumonitis (Pn) is a known side effect of non-small cell lung cancer treatments that include chemotherapy, radiation, immunotherapy and targeted therapies. The development of Pn may require cessation of therapy. We present the incidence rates of Pn and identify its predictors, by line of treatment, using a real-world data source. **Method:** In Optum's Humedica electronic health records database, we identified NSCLC patients diagnosed between 1/1/2008 and 12/31/2017, using a combination of ICD-9/ICD-10 diagnosis codes and structured data derived from physician notes. Patients with lung surgery or other primary cancers in the 12 months prior to diagnosis were excluded. Distinct lines of treatment (LOT) were established using business rules, and incidence rates of Pn for each LOT were calculated. We identified predictors of Pn development any time after treatment start by carrying out a stepwise Cox regression analysis using 27 covariates. **Results:** Of the 63,174 NSCLC patients that were identified, 26,061 had LOT1, 9,938 had LOT2, and 4,790 had LOT3. Incidence rates for all patients, and those with and without a history of Pn for LOTs 1-3 and across all LOTs of a patient are shown in Table 1. Of the 27 covariates in the Cox regression, male gender (HR: 1.19; p<0.0001), squamous cell histology (HR: 1.38; p<0.0001), comorbid patients (Charlson Comorbidity Index >0) (HR: 1.08; p=0.008), a history of pneumonitis (HR: 2.39; p<0.0001), and a history of diabetes (HR: 1.09; p=0.007) were found to be significant predictors of developing Pn.

Table 1

		Across all LOTs[1] (n=26,061)	LOT1[2] (n=26,061)	LOT2[2] (n=9,938)	LOT3[2] (n=4,790)
All patients	% (CI)	21.6% (21.1% - 22.1%)	15.3% (14.8% - 15.7%)	15.5% (14.8% - 16.2%)	14.6% (13.6% - 15.6%)
Patients with a history of pneumonitis	% (CI)	40.0% (38.2% - 41.9%)	34.1% (32.3% - 35.9%)	31.4% (29.5% - 33.5%)	28.7% (26.3% - 31.2%)
Patients without a history of pneumonitis	% (CI)	19.5% (19.0% - 20.0%)	13.1% (12.7% - 13.6%)	11.2% (10.6% - 12.0%)	9.3% (8.3% - 10.3%)

The period over which this has been assessed is:
1 Start of LOT1 to earlier of (365 days from end of last LOT or end of follow-up)
2 Start of LOT to start of next LOT, or if no next LOT, earlier of (365 days from end of LOT or end of follow-up)

Conclusion: Of all treated NSCLC patients, more than 20% develop Pn over the course of their treatments, and ~15% in any one LOT. Prior history of pneumonitis significantly increases the risk of developing the disease during treatment. Physicians may appropriately tailor treatments and care of patients affected by the identified predictors of Pn. **Keyword:** NSCLC, pneumonitis, incidence, risk factors, treatment

PD01.10

Diagnostic Non-Invasive Biopsy Can Substitute Conventional Tissue Dependent Procedures in Suspected Cases of Lung Cancer

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Background: Obtaining tissue from lung lesions for histopathological analysis is conventionally the only method of definitive diagnosis of lung cancer. However, there are considerable risks associated with invasive procedures including Pneumothorax, Haemothorax, Empyema, Pulmonary Embolism besides bleeding and pain. Additionally, the tissue is oftentimes necrotic and may not cover tumor heterogeneity. Liquid biopsies for detection of ctDNA are now approved for considering treatments with Tyrosine Kinase Inhibitors (TKI) but wholesome, substitutive non-invasive biopsy for diagnosis is presently unavailable. We present here a breakthrough, non-invasive biopsy based on a Circulating Tumor Associated Cell (C-TAC) Assay that enables efficient immunofluorescent interrogation coupled with molecular characterization in a single blood draw. **Method:** We obtained 15 ml of venous blood draw from 498 known patients of lung cancer, [327 (65.7 %) male, 171 (34.3 %) female]. C-TACs were enriched by paradoxical cytotoxic processing and characterised for cancer (EPCAM, PanCK) and

lung specific antigens (TTF1 and Napsin) besides EMA, P40, CK7, Synaptophysin, Chromogranin A, CD56, Calretinin, PD-L1, ALK (D5F3) by immunocytochemistry (ICC). EGFR mutations, ALK, RET and ROS1 fusions were evaluated from plasma by NGS. **Results:** C-TACs (EPCAM and CK positive) could be obtained from 458 samples out of 498 (92.0 %). Among the 95 samples that were characterised 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-TACs 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.

PD01.11
Artificial Intelligence Can Detect Lung Cancer From High Resolution Microscopic Images of Conditioned Peripheral Blood

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Background: Lung cancer is a leading cause of death worldwide with about 2.1 million new cases and 1.8 million deaths expected during 2019. Screening for lung cancer however remains challenging. Low Dose Computed Tomography (LDCT) the approved screening test has low specificity and carries the risk of radiation. A non-invasive, specific and sensitive screening test is an urgent unmet public health imperative. Considering that pulmonary embolism is a significant risk in lung cancer, we hypothesized that detection of circulating emboli in peripheral blood using deep learning microscopy would be a credible approach to detect lung cancer. **Method:** We processed peripheral blood from 3977 asymptomatic individuals who underwent routine scans and multiple CA marker evaluation (1475 males [37 %], 2502 females [63%]), 89 patients of lung cancer (61 males [69 %] and 28 females [31%]) of whom 37 had detectable disease, 49 were on therapy and 3 had no radiological evidence of disease. Mono-nucleated cells obtained after centrifugation of blood samples were processed with CellWizard^{TM}, a paradoxically cytotoxic cell media. Apoptosis resistant cells in the milieu are unaffected while cells with responsive cell death mechanism are killed. The process leaves behind Circulating Tumor Cells and Circulating Ensembles of Tumor Associated Cells (C-ETACs). High resolution images of the media wells holding the samples were then obtained on the 5th day. A deep machine learning algorithm was deployed with a training set of images from 44 samples each of asymptomatic individuals with category 1 and known cases of lung cancer respectively. **Results:** Among the 37 cases of lung cancer, the AI algorithm detected C-ETACs in 31 cases (84% sensitivity); 40 out of 49 (82%) patients with ongoing treatment could be detected. Patients with no evaluable disease were not classified as positive. Out of 3977 asymptomatic individuals, 2278 individuals were negative for all scans and CA markers; from whom 82 individuals (4%) were predicted by AI to be positive for lung cancer. AI evaluation of conditioned peripheral blood had sensitivity of 84% in detecting lung cancers, specificity of 96% in predicting patients negative for lung cancer with overall accuracy of 96%. The 82 individuals detected by AI as being positive for malignancy may have cancer other than that of the lung and are being monitored prospectively. **Conclusion:** High resolution microscopic images of conditioned peripheral blood coupled with an artificial intelligence algorithm is a cost-effective, non-invasive method to screen asymptomatic individuals for lung cancer without the risk of radiation.

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 NSCLCa (< 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 or 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 SBRT, Immunotherapy

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

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