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Background: To investigate the clinical applicability of the high throughput screening (HTS) using patient-derived tumor cells (PDC) which were established from patients with non-small cell lung cancer undergoing surgery.

Methods: PDCs were isolated and cultured from surgical specimen from NSCLC at Samsung Medical Center. We performed the HTS for 24 drugs (23 targeted agents and 1 positive control drug) with a micropillar/microwell chip platform using PDCs. Scanned images of the live cells were obtained using an optical fluorescence. With 6 dosages per drug in 7 replicates, the dose response curves and corresponding IC_{50} values were calculated from the scanned images.

Results: From October 2015 to February 2016, 15 samples from patients with non-small cell lung cancer were collected. PDCs were successfully established in 12 (80%) patients, and nine of 12 cases were successfully cultured in 3-d suitable for 23-drug HTS platform. Three PDCs demonstrated a sensitivity to Neratinib (HER-2/EGFR inhibitor). These PDCs are currently being profiled to elucidate the underlying molecular mechanisms for neratinib sensitivity.

Conclusion: Differential chemosensitivity were observed which suggests that this HTS platform based on 3D culture with micropillar/microwell chips and PDC model could potentially provide a preclinical tool for predicting the efficacy of targeted agents in lung cancer.

Keywords: 3D culture, preclinical model, Patient-derived cell, High-throughput screening (HTS)

P2.06-044
Frequency of Mutations and Related Factors in Lung Adenocarcinoma Cases in Turkey

Topic: LAB, Other

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Background: Epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK) and c-ros oncogene 1 receptor tyrosine kinase (ROS1) gene mutations in lung adenocarcinoma (LA) cases give an opportunity to use some of targeted therapy agents. The aim of this study is to obtain EGFR, ALK and ROS1 gene mutation frequencies in Turkey and to examine the factors affecting these frequencies.

Methods: EGFR, ALK, ROS1 mutation analyses were examined in a total of 971 LA cases; 745 men (76.7%), and 226 women (23.3%) diagnosed in 12 hospitals from different districts of Turkey were enrolled in the study. The demographic characteristics, smoking status, asbestos exposure history, radiological findings associated with asbestos exposure (AE) were investigated with relation to the frequencies of EGFR, ALK and ROS1 gene mutations. In the univariate analysis of the study data chi-square and t-tests were used. To determine the independent factors associated with gene mutations, multivariate logistic regression model was created with

the variables that give p <0.10 level of significance in univariate analysis.

Results: The mean age of 971 patients was 60.8±9.8 years (range: 23-91). Smoking rate was 92.6% in men, 42.5% in women (p<0.001). The number of patients with AE history was 279 (28.7%) and the number of patients with radiologic findings associated with AE was 114 (11.7%). The frequencies of EGFR, ALK and ROS1 mutations were 15.9% (152/956), 3.3% (26/768) and 1.6% (6/379), respectively. Female patients were more likely to have EGFR mutations compared with male patients (37.8% versus 9.3%; p<0,001). Never-smokers had higher incidence of EGFR mutations than smokers (39.6% versus 10.3%; p<0.001). The patients with radiological findings of AE had a 24.6% rate of EGFR mutations compared with a 14.7% rate of patients with no radiological findings (p=0.007). ALK rearrengement was detected in patients with younger age, having history of AE or radiological findings associated with AE (11.1%; p<0.001, 5.9%; p=0.014, 6.7%; p=0.044, respectively). No associated factor was found with ROS1 fusion frequency.

Conclusion: To have a relationship between radiographic findings associated with AE or AE history and EGFR and ALK mutation frequencies is an original finding. The obtained results will be useful in the discussion of standards of treatment with the new agents and pathogenesis. **This study was carried out through the project named as "Network cooperation for the management of environmental and occupational exposure to mineral fibers induced pulmonary pathologies" which was supported by General Directorate of Health Researches, Republic of Turkey, Ministry of Health.*

Keywords: EGFR, ALK, lung adenocarcinoma, ros1

P2.06-045
Initiative for Early Lung Cancer Research on Treatment (IELCART)

Topic: LAB, Other

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Background: Randomized controlled trial evidence to guide treatment of early stage lung cancer has been challenging for a variety of reasons. There is now increasing recognition of the power of large databases collected in the context of clinical care to provide important information and there are new statistical techniques for analysis to address unrecognized confounders. We have initiated a new multicenter, international collaborative network for this purpose.

Methods: Based on an extensive literature review, scientific articles, and a series of focus sessions with a panel of expert surgeons, as well a panel of former patients, a series of critical questions regarding treatment of early lung cancer has been developed. Data forms of relevant data from both physicians and patients pre- and post-surgery to account for potential confounders have been developed, tested, and are being entered into a web-based data collection system that also includes relevant imaging data. Sites are being registered into this new network

Results: The four primary questions we found needing additional evidence that would be of most concern in regard to treatment of early lung cancer were the following

- Under what circumstances should limited resection be performed?
- How large should resection margins be when performing limited resection?
- When should a watchful waiting approach be considered?
- When should radiotherapy be considered an option for primary treatment

The entire Mount Sinai Health System network which includes 5 hospitals has started enrollment. Treatment is according to usual care but documented in the IELCART registry. Four additional health systems are in the process of joining which requires completing the enrollment application and obtaining IRB approval to submit data to the IELCART registry. Since starting in March 2015, we have enrolled over 30 participants. Actual time required by the surgeon to complete the surgical data prior to surgery is a few minutes. Time to the patient and coordinator to complete the data forms prior to surgery requires between 30 and 60 minutes.

Conclusion: We anticipate that approximately 10 health care systems will ultimately enroll in the IELCART. Within 2 years, we anticipate starting to have statistically meaningful results in answering the relevant questions. Beyond these, the IELCART registry by continuing to collect data as part of routine clinical practice will provide an important resource to answer future questions in a timely manner as they arise, including performing studies in the neo-adjuvant setting and companion diagnostics.

Keywords: stage I, radiotherapy assessment, Surgery