evaluation, patients 75 years or older comprised almost a quarter of all patients with EGFR-mutant advanced NSCLC. Afatinib and chemotherapy were not used at all in this population. Gefitinib was used most commonly, with similar toxicities and health utilities between older and younger patients. Osimertinib and erlotinib were used too infrequently in this study for conclusive age comparisons. **Keywords:** older adults, quality of life, Epidermal growth factor receptor

P1.01-43
Next-Generation Sequencing in the Exploration of Genetic Heterogeneity for Lung Adenocarcinoma Patients with EGFR Activating Mutations

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Background: Increasing evidence leads to a ratiocination that genetic heterogeneity of the lung adenocarcinoma patients with sensitive EGFR mutations may impact clinical responses and outcomes to EGFR-TKIs. **Method:** We performed targeted NGS with a gene panel covering 416 cancer-related genes to profile genetic characteristics of 69 lung adenocarcinoma patients with activating EGFR mutations and assessed the contribution of targeted NGS to exploration of genetic heterogeneity of such cohort. **Result:** We detected total 200 actionable genetic alterations (mean 2.9 variations per patient, range: 1-7 variations) in tumor DNA and 140 actionable genetic alterations (mean 2.0 variations per patient, range: 0-5 variations) in matched plasma ctDNA, respectively. The concurrent genes with the highest mutation rate were *TP53* (observed in 72.5% patients), other uncommon *EGFR* mutations (observed in 21.7% patients), *EGFR* amplification (observed in 20.3% patients), *RB1* (observed in 10.1% patients), *PIK3CA* (observed in 7.2% patients), and *MYC* (observed in 5.8% patients). NGS provides EGFR mutation detection in plasma with a test sensitivity of 88.2% and specificity of 100.0%. Novel mutations potentially related to primary drug resistance were identified including: *CDC73*, *SMAD4*, and *CTNNB1* missense mutations; *RB1*, *ARID1A*, *ARID2*, *DNMT3A*, *STK11*, and *ATR* frameshift indel; *CDKN2B-PATA31D1*, *NFKBIA-OR11H12* fusion gene; PRKCI, CCNE1, MCL1, ARAF copy number gain; RB1 loss. The pathways analysis showed that unique pathways in the primary resistant cohort included: 1) immune related pathways: Toll-like receptor signaling pathway, T cell receptor signaling pathway; 2) epithelial-mesenchymal transition (EMT) related pathways: TGF-beta signaling pathway; 3) downstream pathway of EGFR: PIK3CA/AKT/mTOR signaling pathway; 4) cell function related pathways: Mismatch repair pathway, AMPK signaling pathway, TNF signaling pathway, Notch signaling pathway, and Transcriptional misregulation in cancer. **Conclusion:** In conclusion, we note the complexity and heterogeneity of activating *EGFR*-mutant lung adenocarcinoma that may confer primary resistance to EGFR TKI using NGS platform. This study highlights the advantage of the NGS than traditional methods on testing *EGFR* mutations, enabling further refinement in sub-classification for the improved personalization of lung cancer treatment. **Keywords:** primary resistant mechanism, activating EGFR mutation, Genetic heterogeneity

P1.01-44
Outcome of Uncommon EGFR Mutation Positive Newly Diagnosed Advanced NSCLC Patients: A Single-Centre Retrospective Analysis

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Background: The significance of uncommon EGFR mutations in newly diagnosed advanced NSCLC patients is incompletely known. We aimed to analyze the demographic profile, outcome and treatment attributes of these patients. **Method:** We retrospectively surveyed 5738 advanced NSCLC patients who underwent EGFR testing in our centre from 2013 to 2017 by in-house primer probes on real time PCR platform. Descriptive data was accumulated from electronic medical records. Survival plot was calculated from Kaplan Meir and compared between groups using Log Rank test. **Result:** Out of 1260 EGFR mutation positive patients, 83 (6.58%) had uncommon mutations in isolation or in various combinations. Uncommon mutations were more frequent in men than in women (59% vs.41%), in never smokers than in smokers (65.1 % vs. 20.5%) and in adenocarcinomas than non -adenocarcinomas (96.4% vs. 3.6%). Overall Exon18G719X, Exon20insertion, Exon20T790M, Exon20S768I , Exon21(L858R/L861Q) were present in 9.6%, 19.3%, 12%, 3.6% and 3 .6% patients respectively . Dual mutation positivity was found in 50.6% patients. One patient (out of 83) had triple mutations: Exon18G719X, Exon20S768I and Exon21L858R. On classifying patients as per TKI sensitivity, it was found that TKI sensitive single and dual mutations were found in 15.7 % and 4.8% respectively .TKI insensitive single mutations were found in 31.3% and a combination of TKI sensitive and insensitive mutations was found in 48.2 % patients. The median duration of follow up was 13 months. Five patients were lost to follow up. Overall 50.6% patients received oral TKI and 34.9% received chemotherapy as first line therapy. Response to first line therapy could be assessed in 54 patients, out of whom 28 had partial response, 14 had stable disease and 12 had progression. Median progression free survival (PFS) on first line therapy was 8.3 months (CI 5.3-12.9). Median overall survival of patients who received TKI during the course of their disease was 20.2months (CI 11.4 -28.9). Median overall survival of the entire cohort was 15.8 months (CI 10.1-21.5). Among all uncommon mutations, patients with dual mutations did better, with a median overall survival time of 22.6 months (CI 8.2-37.0, P=0.005) . It was observed that TKI Sensitive/ TKI Insensitive Dual mutations had a superior overall survival of 28.2 months (CI 15.2-41.2,P=0.042) as compared to TKI Sensitive (single or dual) and TKI Insensitive single uncommon EGFR mutations. **Conclusion:** Uncommon EGFR mutations constitute a distinct heterogeneous group, hence it is imperative to understand each subgroup more to define optimal treatment. **Keywords:** advanced NSCLC, Uncommon EGFR

P1.01-45
Crizotinib Efficacy in ALK-Positive Advanced Stage Non-Small Cell Lung Cancer Patients: A Real-World Experience from Turkey

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Background: ALK mutation is observed in 4% of patients diagnosed with NSCLC. The present study aimed to evaluate the efficacy of crizotinib, an ALK inhibitor, and clinical characteristics of ALK-positive NSCLC patients. **Method:** In this multicenter, retrospective study, data of ALK-positive advanced stage NSCLC patients who received crizotinib were retrieved from hospital records. **Result:** Data of 353 ALK-positive metastatic NSCLC patients receiving crizotinib in any treatment line were analyzed. The mean age of the patients was 53.2±12.6 years [median, 53 years (21-85 years)] and 193 (54.7%) patients were male. Age at diagnosis was significantly higher in males than in females (54.8±11.8 years and 51.3±13.2 years, respectively; p=0.044). The rate of patients who never smoked was 50.1%. The most common histological subtype was adenocarcinoma (96%). The frequency of brain metastasis at the time of diagnosis was 23.4%. The most common initial symptoms were cough (56%) and dyspnea (53%). Initial ECOG score was 0 or 1 in 80% of the patients. Crizotinib had been used in 37% of the patients in the 1st-line treatment, in 45% of the patients in the 2nd-line treatment, and in 18% of the patients in the ≥3rd-line treatment. ORR was 69.4% and DCR was 83.6% (Table 1). ORR and DCR in the patients received crizotinib were 70.2% and 84.7% in the 1st-line treatment, respectively and were 74.1% and 87.4% in the 2nd-line treatment, respectively. The frequency of brain metastasis was 40.2% at 12 months. Of these patients, the median PFS and OS were 11.3 and 28.0 months, respectively. The most common side effects were fatigue, visual disturbances, nausea, abdominal discomfort, and pretibial edema. **Conclusion:** Clinical characteristics of ALK-positive patients and crizotinib efficacy are consistent with studies. Response rates and survival outcomes are similar regardless of treatment lines. Crizotinib is safely used in these patients. **Keywords:** NSCLC, ALK inhibitor, crizotinib

Table 1. Response rates of the patients

		Treatment line			
	Overall N (%)	1 N (%)	2 N (%)	3 N (%)	Other N (%)
Complete response	28 (7.9)	9 (7.3)	14 (8.9)	4 (9.8)	1 (5.6)
Partial response	217 (61.5)	78 (62.9)	103 (65.2)	25 (61.0)	10 (55.6)
Stable disease	50 (14.2)	18 (14.5)	21 (13.3)	7 (17.1)	4 (22.2)
Progressive disease	67 (13.3)	19 (15.3)	20 (12.7)	5 (12.2)	3 (16.7)
Undefined	11 (3.1)				
ORR	245 (69.4)	87 (70.2)	117 (74.1)	29 (70.8)	11 (61.2)
DCR	295 (83.6)	105 (84.7)	138 (87.4)	36 (87.1)	7 (83.4)
Undefined	11 (3.1)				

P1.01-46
Circulating Tumor DNA Analysis for Predicting Response to Osimertinib and Disease Progression in EGFR-Mutant Non-Small-Cell Lung Cancer

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Background: Circulating tumor DNA (ctDNA) has emerged as a promising non-invasive modality to detect biomarkers associated with a broad array of malignancies, including lung cancer. We aimed to assess whether ctDNA could be used to predict response to EGFR-tyrosine kinase inhibitor (EGFR-TKI) therapy and disease progression. **Method:** Plasma samples were serially collected at every clinic visit from patients with metastatic EGFR-mutant non-small-cell lung cancer (NSCLC) enrolled in a clinical trial of osimertinib treatment, local ablative therapy (LAT) upon progression, followed by osimertinib re-challenge (NCT02759835). Patients with no prior EGFR-TKI treatment or patients with T790M-positive NSCLC after EGFR-TKI treatment receive osimertinib. Upon progression, patients with ≤5 progressing sites undergo LAT and resume osimertinib. ctDNA was detected using droplet-digital PCR *EGFR* mutation detection assays. The changes in ctDNA mutant allele levels were correlated with response to treatment and tumor progression. To identify additional genetic changes that may be related to osimertinib resistance, an enhanced Tagged-Amplicon Sequencing NGS assay (InVisionSeq™) was utilized which covers SNVs, InDels and amplifications in 36 genes commonly mutated and therapeutically actionable in NSCLC. **Result:** 353 samples from 17 patients were analyzed. At baseline, EGFR mutations were detected in 15 (88%) patients. One patient with overall low metastatic tumor burden and another patient with most tumor burden in the brain did not have detectable ctDNA at baseline. For patients treated with osimertinib before first progression, 12 (86%) achieved a partial response (PR) and 2 (14%) had stable disease (SD) as their best response. ctDNA decreased after initiation of osimertinib in these patients with 7 (50%) patients having no detectable ctDNA within 28 days. In those with ongoing PR (n=5) and prolonged stable disease (n=1), ctDNA remains undetectable (n=5) or low (n=1). Among 7 patients who had first progression, 5 (71%) patients had an increase in corresponding mutant *EGFR* allele in ctDNA 2-4 months before radiographic progression. While exploration of osimertinib resistance mechanisms by InVisionSeq™ is ongoing, early results demonstrate that allele frequencies of mutations in genes, including *EGFR*, *PIK3CA*, and *TP53* closely reflected response and resistance to osimertinib. *MET* and *EGFR* amplification, as well as emergence of *EGFR* C797S mutant were identified as key resistance mechanisms by ctDNA analysis. Full details on all patients will be presented at the meeting. **Conclusion:** Quantitative assessment of plasma ctDNA is a relatively non-invasive tool to monitor the therapeutic response to treatment with EGFR-TKI and for early detection of resistance mechanisms for clinical decision making. **Keywords:** EGFR-mutant NSCLC, osimertinib, Circulating Tumor DNA