Patients With PD on Brigatinib (n=107)	n	1-Year OS Post-PD,[a] % (95% CI)	Unadjusted HR (95% CI)	Adjusted HR[b] (95% CI)
Continued brigatinib	84	66(53—99)	0.32(0.17—0.62)	0.53(0.26—1.08)
At 90 mg qd (arm A without escalation)	23	62(38—99)	0.49(0.22—1.11)	0.61(0.25—1.46)
At 180 mg qd	61	68 (51—99)	0.26(0.13—0.54)	0.48(0.21—1.06)
Arm A with escalation	23	70(44—99)	0.29(0.12—0.72)	0.51(0.19—1.33)
Arm B	38	66(44—99)	0.25(0.11—0.57)	0.45(0.18—1.16)
Did not continue brigatinib	23	31(13—100)	Reference	Reference

[a]Kaplan-Meier estimate from time of first PD [b]Adjusted for duration of prior crizotinib exposure, number of prior treatment regimens (1, 2, or ≥3), time to investigator-assessed PD, PD due to new lesions only (yes/no), and ECOG performance status at PD (0, 1, or ≥2)

P1.01-006
Effect of EML-Alk Fusion Variant and Fusion Abundance on the Efficacy of Crizotinib in Non-Small Cell Lung Cancer

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Background: EML4-ALK fusion gene is a molecular subtype of non-small cell lung cancer (NSCLC), which is carcinogenic both in vitro and in vivo. Most of the EML4-ALK-positive NSCLC patients have effectively sensitivity with an ALK tyrosine kinase inhibitor (TKI), such as crizotinib. However, the treatment outcomes and duration of response are heterogeneous. EML4-ALK has several variants. The effects of ALK fusion variants on the efficacy of crizotinib is still unclear, although many scientists are committed to this work. In addition, we also unknown the effects of ALK variants allele fraction (AF) on the efficacy of crizotinib. **Method:** Among 54 patients with advanced NSCLC were treated with crizotinib as the first-line or further-line ALK-TKI between 2013 and 2017, eventually, we identified 48 patients whose the tumor samples were detected by IHC(38), FISH(2), NGS(5),PCR(1) and ARMS(2). Through retrospective analysis, we assumed the efficacy of crizotinib on the basis of the PFS according to the ALK variants and its allele fraction. **Result:** Among the 29 ALK-positive patients, the most common ALK variants was variant 1 in 13 patients (44.9%), followed by variant 3 in 7 patients (24.1%), variants 2 in 2 patients (6.9%), other variants in 7 patients (24.1%). We divided all variants into two subgroups: V1/3 and V2/others. We found 35.4% of the samples test results between the next generation sequencing (NGS) and hospital immunohistochemical were not concordance. Further analysis found that patients who did not match that PFS were shorter (p=0.036). By the NGS, we observed from the figure that the variant 2/others group, the median PFS had a longer trend than V1/3 group, although not statistically significant (p>0.05). The level of AF was no correlated with PFS (P=0.346). **Conclusion:** The above results show that next-generation sequencing (NGS) can identify ALK variants and AF, therefore, NGS can be used as a supplement to a detection method. The type of EML4-ALK fusion variants may has a certain correlation with PFS in patients who oral crizotinib treatment. Since the sample size of this study is small, we have not yielded accurate results and found only these phenomena. We believe that in the near future, most NSCLC patients can be detected by NGS detection of gene mutations, especially EML4-ALK fusion gene, and according the different of the fusion gene variant type which can be estimated the efficacy of the ALK-TKIs, to provide the basis of individualized treatment options for NSCLC patients. **Keywords:** Effect, EML-Alk fusion variant, fusion abundance, efficacy of Crizotinib, NSCLC

P1.01-007
ALK Testing Trends and Patterns Among Community Practices in the United States

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Background: The CAP/IASLC/AMP molecular testing guidelines recommend ALK testing on patients with lung adenocarcinoma, regardless of clinical characteristics. FISH is the recommended assay to detect ALK rearrangement, however other assays, such as NGS and IHC, are available. There have been limited published data to assess adherence to ALK testing guidelines using large real-world data sources. The objective of this study was to assess real-world ALK testing patterns among community practices in the United States. **Method:** The Flatiron database provides real-world clinical data collected from EHRs used by US cancer care providers. The Flatiron network comprises ~15% of US cancer patients and is geographically and demographically diverse. Patients with ≥2 visits within the Flatiron Network after Jan 1, 2011, ≥18 years of age, and an stage IIIB/IV NSCLC diagnosis from 2011 through 2017 Q1 were included in this analysis. Logistic regression was used to identify patient characteristics associated with receiving ALK testing. **Result:** Of 29,903 patients identified from community-based clinics (mean age: 71.6, 52.2% male), ALK testing rates have steadily increased over time from 32.2% in 2011 to 61.0% in 2016 for all NSCLC patients, and 41.0% in 2011 to 74.0% in non-squamous patients. Patients that are younger, no history of smoking, women and living in the West region were more likely to be tested for ALK. Patients with Medicaid insurance, recurrent disease and squamous histology were less likely to be tested. The most common first assay to test for ALK was FISH (70%) followed by NGS (8%), PCR (4%) and IHC (1%). The median time from specimen receipt by lab to test result ranged from 6 days (FISH) to 11 days (NGS). Patients who had NGS testing were more likely to initiate chemotherapy prior to test result (34% of patients tested with NGS) than FISH (20%). 1235 patients had at least one FISH and another ALK test, with the percent agreement between FISH and other assays (NGS, PCR, IHC) ranging from 92% to 97%. **Conclusion:** Several patient characteristics predicted ALK testing indicating that some subgroups of patients may be under tested, according to guidelines. Consistent with guidelines, FISH was the most common assay and turnaround times from lab receipt to test result was under 2 weeks. There was a high agreement between FISH and NGS, indicating the potentially clinical utility of NGS, however NGS had also the longest turnaround time and the highest proportion of patients initiating treatment prior to test results. **Keywords:** ALK, biomarker testing

P1.01-008
Real-World Patient Characteristics, Testing and Treatment Patterns of ALK+ NSCLC

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Background: Based on clinical trials, ALK+ patients have been described as typically younger and never/former smokers, however patients enrolled in clinical trials may be different than those in the real-world. While the ALK positivity rate has been described as about 4% among all NSCLC patients, limited information is available on the positivity rates in patient subgroups. The objective of this study is to describe the real-world ALK positivity rates, patient characteristics and treatment patterns in ALK+ NSCLC patients. **Method:** The Flatiron database provides real-world clinical data collected from EHRs used by US cancer care providers. The Flatiron network comprises ~15% of US cancer patients and is geographically and demographically diverse. Patients with ≥2 visits within the Flatiron Network after Jan 1, 2011, ≥18 years of age, ≥1 ALK+ test result and an stage IIIB/IV NSCLC diagnosis from 2011 through 2017 Q1 were included in this analysis. Logistic regression was used to examine the association of ALK positivity and initiation of ALK inhibitor therapy based on patient characteristics. Survival model adjusting for censoring was used to estimate the time to ALK inhibitor order. **Result:** 599 out of 15,551 ALK tested patients were identified to have an ALK positive test result, for a positivity rate of 3.9%. The ALK positivity

rate varied by age (<65: 6.3% vs. ≥65: 2.9%), smoking status (no history of smoking: 11.6% vs. history of smoking: 2.3%), and histology (non-squamous: 4.0% vs. squamous: 1.8%). Factors associated with ALK positivity included younger age, academic practice, male, non-squamous histology, and no history of smoking. 78% of patients with ALK+ disease had evidence of an order for an ALK inhibitor after NSCLC diagnosis. The median time from test result to ALK inhibitor order was 24 days, with 42% of patients without an order for an ALK inhibitor within 90 days. Among patients with an order for an ALK inhibitor, 23% received chemotherapy prior to their ALK test result and 20% received chemotherapy after their test result but before the first order of ALK inhibitor. Patients diagnosed after 2014 and patients who received chemotherapy prior to the ALK test result were more likely to have an order for an ALK inhibitor. **Conclusion:** The ALK positivity rate and patient characteristics in this real-world NSCLC population are consistent with clinical trials, with some subgroups having higher positivity rates. ALK inhibitors were the most frequently ordered treatment, however many patients had a delayed time to ordering the ALK inhibitor. **Keywords:** treatment patterns, ALK, biomarker testing

P1.01-009
Clinically Primary and Secondary Resistance to ALK Inhibitors in ALK-Positive Advanced Non-Small-Cell Lung Cancer

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Background: Crizotinib is a standard of care in anaplastic lymphoma kinase(ALK)-positive advanced non-small-cell lung cancers (NSCLC).Undoubtedly, the resistance to crizotinib is a current bottleneck. Hence, it is necessary to explore the resistance mechanisms to ALK inhibitors. **Method:** From October 2010 to May 2017,225 ALK-positive NSCLC patients treated with crizotinib were reviewed at the Guangdong General Hospital in China. The status of *ALK* rearrangement was assessed by Lysis ALK Break Apart fluorescence in situ hybridization, reverse transcription polymerase chain reaction ,or Ventana ALK immunohistochemistry. Next generation sequencing(NGS) was used to test the tissue or plasma from patients with resistance to crizotinib. Primary resistance to crizotinib occurred when Progression-free survival was less than 3 months for the patients treated with crizotinib. **Result:** Among enrolled patients, 72.4%(163/225) gained secondary resistance, and 8.9%(20/225) had primary resistance. Molecular mechanisms of clinically primary resistance were shown in Fig a. The variants of ALK fusion were different between primary and secondary resistance patients. There were more variants of ALK fusion appeared in the group with primary resistance except E6-A20 and E13-A20.Among secondary resistant patients , non-EML4 partners fusion, such as DMD-ALK fusion,YWHAQ&TAF1B-ALK fusion, GALNT14-ALK fusion and SLC19A3-CCL20-ALK fusion were found, which responded to crizotinib treatment. Acquired ALK L1196M/G1269A mutations were found in both primary and secondary resistant patients, and while ALK I1171T mutation was only found in secondary resistant patients. Wnt signaling pathway was activated significantly after the treatment of crizotinib according to Kyoto Encyclopedia of Genes and Genomes(KEGG) and GeneOntology(GO) analyzes. Moreover, AMER1 aberrance was inclined to appear in the primary resistance patients, which was significant different between the two groups in KEGG and GO analyzes. **Conclusion:** ALK mutations could exist in both primary and secondary resistance to crizotinib in ALK-rearranged NSCLC. Response to crizotinib was also observed in ALK-rearranged NSCLC patients with non-EML4 partners. NGS may facilitate precision treatment for both primary and secondary resistant patients though they have a few differences in molecular mechanisms of resistance. **Keywords:** Resistance to ALK inhibitors