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Introduction: Based on our preclinical findings that the HGF/MET activation was a potential mechanism of acquired resistance to alectinib, we conducted a phase II trial of the ALK/MET inhibitor crizotinib, in patients with EML4-ALK-positive non-small-cell lung cancer (NSCLC) refractory to alectinib. **Methods:** Patients with ALK-rearranged tumors who had developed disease progression during alectinib treatment received single agent crizotinib monotherapy. The primary endpoint was set as objective response rate; assuming that 50% in eligible patients indicate potential usefulness, whereas 15% would be the lower limit of interest. The estimated accrual number is 9 patients based on Simon's minimax design with one-sided α of 0.05 and ß of 0.20. The secondary endpoints included progression-free survival, overall survival, and adverse events. **Results:** From Jun 2016 to Aug 2018, a total of 9 patients were registered. All patients had the prior alectinib use as the last treatment prior to the registration of this trial; all achieved partial response (PR) in the prior alectinib therapy with the median treatment duration of 6.7 months. Crizotinib was administered with the median treatment interval of 50 days ranging from 20 to 433 days. Treatment was interrupted in 3 patients (33%) with the median duration of 14 days. The overall response rate was 33.3% (3 of 9; 90% confidence interval: 9.8—65.5 and 95% confidence interval [CI]: 7.5-70.1), which failed to meet the predefined criteria. Two (22%) patients had brain metastases at baseline, both of whom achieved PR. With the median follow-up time of 21.2 months, median progression-free survival time was 2.2 months. The progression-free survival time in each patient was not predicted by the treatment duration of prior alectinib therapy. One-year-overall survival rate and median survival time were 66.7% and 24.1 months, respectively. As for safety, the most common was AST/ALT elevation (44%) and appetite loss (33%). Of them, one patient developed transient grade 4 AST/ALT elevation that led to the treatment discontinuation. Others events were consistent with the known safety profiles of the investigational agent without any treatment-related deaths. All nine experienced recurrences mostly in the preexisting disease sites. Five (56%) received post-progression ALK-TKIs. **Conclusion:** In our series, crizotinib monotherapy after progression on the first ALK-TKI alectinib therapy produced a certain efficacy with known adverse events. **Keywords:** Crizotinib, Alectinib, ALK-TKI

P84.03
GLASS: Global Lorlatinib for *ALK*(+) and *ROS1*(+) Retrospective Study: Real World Data of 123 NSCLC Patients

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Introduction: Lorlatinib is a third-generation tyrosine-kinases inhibitor (TKI) targeting *ALK*/*ROS1* fusions. The FDA has approved lorlatinib for TKI-pretreated *ALK*(+) NSCLC, while its approval for ROS1(+) is still pending. Here we present the largest real-world data of NSCLC patients harboring *ALK/ROS1* rearrangements treated with lorlatinib. **Methods:** This is an international, multicenter, retrospective study, which aimed to describe the efficacy and safety of lorlatinib in previously treated *ALK/ROS1(+)* NSCLC. All patients were treated through an early access program, when no other targeted therapy was available.123 patients were enrolled retrospectively (data cut-off 1/1/2019). Outcome and response were defined by each investigator upon RECIST 1.1 criteria. **Results:** From March 2015 to January 2019, 106 *ALK*(+) and 17 *ROS1*(+) patients were recruited from 8 different countries. The ALK(+) cohort included 50% males, 73% never-smokers and 68% with brain metastases. Extracranial (EC) and intracranial (IC) response rates (RR) were 60% and 62%, with disease control rates (DCR) of 91% and 88% respectively. Mean duration of therapy (DoT) was 23.9±1.6 months and median overall survival (mOS) was 89.1±19.6 months. ROS1 cohort enrolled 53% males, 65% never-smokers and 65% had brain metastases. EC and IC RR were 62% and 67% with DCR of 92% and 78% respectively. Median DoT was 18.1±2.5 months and mOS of 90.3±24.4 months. OS and DoT in both cohorts were not significantly correlated with line of therapy nor other parameters. The most common adverse events of any grade were peripheral edema (48%), hyperlipidemia (47%), weight gain (25%) and fatigue (30%). CNS adverse events such as cognitive effect of grade 1-2 were reported in 18% of patients. **Conclusion:** Lorlatinib shows outstanding extracranial and intracranial efficacy in *ALK* or *ROS1(+)* NSCLC. The observed mOS of 89±19 months in *ALK*(+) NSCLC supports previous reports, while mOS from of 90±24 months is unprecedented for ROS1(+) NSCLC. **Keywords:** ROS1(+), ALK(+), lorlatinib

P84.04
HIP1-ALK Positive Non-Small-Cell Lung Cancer: Clinicopathological Characteristics and Prognosis

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