(HR 0.28, 95% CI 0.19 to 0.41, $P<0.0001$), which was consistent with the gain in PFS from the RCT AURA3 (10.1 months versus 4.4 months; HR 0.30, 95% CI 0.23 to 0.41, $P<0.001$), and a statistically significant improvement in OS (HR 0.41, 95% CI 0.27 to 0.62, $P<0.0001$). Median OS for osimertinib was not reached and was 14.1 months for PDC. **Conclusion:** The indirect comparison estimated a statistically significant improvement in PFS and OS with osimertinib compared with PDC. The PFS benefit was consistent with that of the confirmatory RCT. The combined evidence from RCT data and indirect comparisons described may bridge the potential gap and confounding in evidence for OS produced by subsequent treatments after first progression in the RCT. **Keywords:** adjusted indirect comparison, NSCLC, osimertinib

MA 12.09
EGFR T790M Co-Exist with Sensitive Mutation in the Same Cell Group in Lung Adenocarcinoma Patients

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Background: EGFR TKI therapy has improved lung adenocarcinoma patients' prognosis tremendously, but almost all of the patients inevitably develop acquired resistance, and EGFR T790M mutation is the major contributors. T790M restores the EGFR tyrosine kinase domain affinity to ATP, and therefore gefitinib is displaced from the binding pocket, and the 'driving' signal for proliferation is switched on again. Previous work has shown that after TKI therapy, lung adenocarcinoma patients kept the sensitive mutation and acquired resistance mutation simultaneously by sequencing methods or in vitro cell line experiments. Whether the two different type mutations are in the same cell group or in two different cell groups is unknown. None of them has observed what was happening in the tumor cells after TKI therapy. **Method:** RNA in situ hybridization methods was employed to examined EGFR T790M and L858R mutation in lung adenocarcinoma cancer tissues which was obtained before and after TKI therapy. EGFR expression was examined by immunohistochemistry. EGFR mutation were detected by ARMS PCR methods. **Result:** Twenty five patients were enrolled in this study which were divided into 3 groups. **Group 1**: 5 patients who had concurrent primary T790M and sensitive EGFR mutation. **Group 2**: 14 patients who acquired T790M mutation after receiving TKI therapy. Among them, 6 patients had biopsy tissues before and after TKI therapy. 8 patients only own tissues after TKI therapy. **Group 3**: 6 patients who had sensitive EGFR mutation and received TKI therapy, but re-biopsy tissues didn't had EGFR T790M. We found that the results of RNA ISH and ARMS PCR methods was identical in the majority of the examined tissues. Only one repeated biopsy tissue didn't identify EGFR T790M after TKI therapy by PCR in group 3, while the RNA ISH method detected T790M in this tissue which contain only 150 tumor cells. In the serial cut slides, we observed that T790M and L858R mutations were in the same cell group, not only in the primary resistance cases, but also in the acquired resistance cases. For the two cases which had tissues available after receiving third generation TKI therapy, we observed that T790M disappeared in the repeated biopsy specimen, leaving the sensitive mutation which existed from the beginning. **Conclusion:** In the primary and acquired resistance tissues, EGFR sensitive mutation and T790M co-exist in the same cell groups. EGFR sensitive mutation is a trunk and drive mutation, while T790M is a passenger mutation during the treatment process by TKI therapy. **Keywords:** EGFR, T790M, L858R

MA 12.10
Clinical Utility of Plasma EGFR T790M Mutation Detection in Advanced Non-Small Cell Lung Cancer Patients According to RECIST Criteria

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Background: Circulating tumor DNA (ctDNA) has emerged as a specific and sensitive blood based biomarker for detection of several mutations in non−small cell lung cancer (NSCLC). Other clinical applications for ctDNA include molecular assessment of patients at diagnosis and serial (real-time) monitoring of biomarker status or the development of resistance mutations. **Method:** Eighty patients with advanced NSCLC who either (Group 1) had a new diagnosis or (Group 2) had developed acquired resistance to an EGFR kinase inhibitor were analyzed with highly sensitive Biocept, Inc. TargetSelector™ Real Time PCR based plasma assays genotyping for the detection of EGFR mutations L858R, Del19 and T790M. In addition, group 1 was analyzed for KRAS, BRAF, ROS1 and ALK and circulating tumor cells (CTCs) before and after TKI treatment. **Result:** Our results showed concordance rates of EGFR, KRAS and ALK mutations for up to 90% between the tissue and blood samples in newly diagnosed patients (Group 1). Paired analysis of mutations status monitoring in this group (P= 0.016) showed that the pattern of mutant ctDNA and CTCs changed in response to systemic therapy in 83% of the cases (Partial response or disease progression; R2=0.808). Plasma ctDNA analysis of multiple mutations showed that 40% of patients had at least one more mutation besides the one detected in tissue biopsy; 28% of EGFR tissue positive patients also had a KRAS mutation. In addition, 75% of KRAS positive patients had a BRAF mutation. These results demonstrate that plasma ctDNA analysis may even detect mutations missed by standard tissue genotyping due to tissue heterogeneity. Plasma EGFR T790M mutation was analyzed in patients with clinical progression to TKI inhibitors. Considering the RECIST criteria, 58% of progressive disease, 10% of stable disease and 16% of partial response patients were positive for T790M. According to metastatic disease type (locoregional, oligometastatic, polimetastatic), the T790M mutation was found on 64.3% of polimetastatic patients, 30.8% of oligometastatic patients and 17.6% of loco-regional patients. **Conclusion:** TargetSelector™ ctDNA assay is capable of rapidly detecting EGFR, KRAS and ALK mutations and is highly concordant with mutations present in tumor tissue with the robustness needed for real world testing to identify patients who progress on first line TKI therapy as well as for real-time monitoring of patients' clinical status. Our findings highlight the importance of the RECIST criteria to define the progressive disease and determine the right moment to test for T790M mutation regardless the metastatic disease type. **Keywords:** ctDNA, NSCLC, TKI resistance

MA 12.11
The Alteration of T790M Prevalence Between 19 Deletions and L858R in NSCLC After EGFR-TKIs Therapy, a Meta-Analysis

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Background: Pre-treatment EGFR T790M mutation is more likely to coexist with L858R mutation than with exon 19 deletions (19del) in