Circulating Tumor Cells and Evaluation of Targeted Therapy Effect in EGFR Mutation/ALK Translocation Metastatic Non-Small Cell Lung Cancer
Chunxia Su, Xuefei Li, Shengxiang Ren, Caicun Zhou
Shanghai Pulmonary Hospital, Shanghai/China

Background: Targeted therapies have considerably improved the prognosis of patients with non-small cell lung cancer (NSCLC). Although not precision enough, RECIST criteria was still the most often used response assessment method to reflecting the clinical benefits. We propose a non-invasive, folate receptor (FR)-based circulating tumor cell (CTC) detection approach to interpret treatment response of targeted therapy between baseline and follow-up CTC values in EGFR mutation/ALK translocation advanced NSCLC. Methods: One hundred and thirty eight patients were enrolled in our study. Peripheral blood was analyzed for CTCs enumeration on negative enrichment by immunomagnetic beads. Changes of CTCs levels were correlated with radiological response. Sequential analyses were conducted to monitor CTC signals during therapy and correlate radiological effects with treatment outcome. Results: CTCs were detected (≥8.7CTC) in 84.8% of patients. Pretreatment and pro-treatment blood samples from all 118 EGFR-mutant (19 deletion:56, L858R:57, G719x:3, L861Q:1, 19 deletion + L858R:1), 14 ALK translocation lung cancer patients and 6 EGFR wild type patients were collected. Of 89 eligible and evaluable patients, baseline CTC counts were not associated with response to treatment by RECIST (P=0.353). There is no difference between exon 19 deletion and L858R of baseline CTC values. (19 deletion:19.4 CTCs, L858R:20.9 CTCs, P=0.222) The change of CTCs values increased correlation with radiological response (P=0.042) after treatment of targeted therapy. There is no significant difference between exon 19 deletion and L858R of CTCs values pre and pro EGFR-TKI treatment. (3.32 vs. 12.1, P=0.783) Conclusion: This study confirms the predictive significance of CTCs in patients with EGFR mutation/ALK translocation NSCLC receiving targeted therapy. The change of CTCs value correlated significantly with radiological response. This strategy may enable non-invasive, specific biomarker assessment method for using CTC decreases as an early indication of response to targeted therapy and monitoring in patients undergoing targeted cancer therapies.

Keywords: Targeted therapy, CTC, Gene mutation, non-small cell lung cancer

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