CONFEREECE ABSTRACT

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A comparison study of droplet digital PCR and qPCR for EGFR T790M detection in plasma of NSCLC patients

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Abstract: Background: Specific mutations in epidermal growth factor receptor (EGFR) are predictive for response to EGFR tyrosine kinase inhibitors (TKIs) in non-small cell lung cancer (NSCLC) patients. However, most patients acquire resistance to the first generation-TKIs and in about half of these patients the resistance is driven by EGFR T790M mutation. Recently, third generation-TKIs are shown to be effective in patients harbouring this mutation. Although re-biopsy of tumour tissue is regarded as a gold standard in recurrent and NSCLC patients, the procedure can be challenging and hazardous, and tumour heterogeneity between primary and metastatic sites can be a limiting factor for accurate mutational analysis. In recent years, liquid biopsy for the detection of circulating tumour DNA (ctDNA) has been used for EGFR mutation analysis using qualitative PCR assays. Since the detection rate of qPCR for T790M is only 30%-50%, droplet digital PCR (ddPCR) has emerged as a more reliable assay for the detection of T790M in ctDNA. In the present study, we compared the performance of ddPCR and qPCR in plasma of patients with NSCLC.

Methods: Plasma were collected from NSCLC patients diagnosed in the Subang Jaya Medical Centre. Extracted ctDNA were analysed for three common EGFR mutations (exon 19 deletions, L858R, T790M) using both Droplet Digital PCR (ddPCR\(^\text{TM}\), BioRad) and qPCR (PANAMutyper\(^\text{TM}\) R EGFR). Results: In our study, a preliminary assessment using both platforms was performed with 25 EGFR positive plasma samples. Of these, 11 samples had tumour tissues previously tested for EGFR mutations with qPCR (PNAclamp EGFR test kit). We retrospectively applied ddPCR and qPCR assays to detect exon 19 deletions, L858R and T790M in all the plasma samples. EGFR mutation analysis based on tumour biopsy samples were used as the reference standard. Overall, our results showed about 70% concordance between these two assays. Digital PCR appeared to have a greater sensitivity for T790M mutation (40%) compared to qPCR (28%). Conclusion: Droplet digital PCR may have good application prospects in monitoring patients with EGFR T790M mutation in selecting patients for third generation EGFR-TKI treatment.

Keywords: non-small cell lung cancer; Droplet digital PCR; mutation


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