A BLOOD BASED EGFR MUTATION ANALYSIS IN CIRCULATING PLASMA DNA FOR PREDICTION OF PRIMARY TUMOUR MUTATIONS IN LUNG CANCER

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Aim: Biopsy of the primary tumour for predictive testing is not always convenient nor possible and may incur both delays and complications. In a move towards blood based predictive testing for personalised medicine, we sought to determine the test performance of circulating tumour DNA (ctDNA) as a surrogate of underlying drug treatable EGFR primary tumour mutations.

Methods: EGFR mutation status (exons 19 and 21) in primary tumours was analysed using cobas®4800 (Roche) allele-specific PCR. ctDNA was extracted from matched plasma specimens using QIAamp DNA Blood Mini kit (QIAGEN). EGFR mutation detection in ctDNA was undertaken using custom-designed high-resolution melting (HRM) assay.

Results: From January 2012 to 2013 the peripheral blood of 98 patients who underwent surgery for lung cancer at The Royal Brompton Hospital were analysed for mutations in exons 19 and 21 of the EGFR gene. Five exon 19 deletions (5.1%) and 3 L858R mutations (3.1%) were identified in primary tumour tissues. In ctDNA, there were 16 exon 19 deletions (16.3%) and 2 L858R mutations (2.0%). After re-testing FFPE tissues using custom HRM assay, 8 previously undetected exon 19 deletions were identified. The final concordance between primary tumours and ctDNA was 92.8% for EGFR exon 19 deletions and 99.0% for L858R mutations. The sensitivity and specificity for blood based predictive EGFR testing was 84.6% (95% CI 59%-98%) and 97% (87%-100%) for exon 19 deletions and 67.7% (14%-99%) and 100% (97%-100%) for L858R mutation.

Conclusions: Blood based mutation testing is feasible. FFPE tumour biopsies cannot always be considered to be the “reference” as many EGFR mutations not initially detected in the tumour were detected in blood based ctDNA potentially increasing the treatable patient cohort by more than two-fold. This work was supported by the Peter and Mary Fu Foundation.

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