The Study of TTF-1 Expression and Mutation Specific-antibody for Detection of EGFR Gene Mutation in Non-small Cell Lung Cancer

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The Thai Cancer, 2016, 31.58.005

**Background:** Specific somatic mutations of the epidermal growth factor receptor (EGFR) associate with increasing response to EGFR tyrosine kinase inhibitors (TKIs) treatment in non-small cell lung cancer (NSCLC). Assessment of EGFR mutation status by gene-based assay remains expensive and is not routinely reimbursed in Thailand. The objective of this study is to test a simple immunohistochemical (IHC) method using EGFR mutation-specific antibodies for detection of EGFR status and to study the correlation of routine IHC staining of TTF-1 expression and EGFR mutation status.

**Method:** Seventy-six NSCLC patients whose EGFR status had been tested from January 2010 to July 2014 were enrolled in this study. We performed IHC analyses using 2 EGFR mutation-specific antibodies to E746-A750 del in exon 19 and the other to L858R in exon 21 for all samples. IHC staining were score as 0 (no, or faint staining intensity in <10% tumor cells), 1+ (faint intensity and >10% tumor cells), 2+ (moderate intensity and 10% tumor cells) and 3+ (strong intensity and 10% tumor cells). We also evaluated TTF-1 expression by IHC staining.

**Results:** The reference DNA sequencing showed exon 21 L858R EGFR mutations in 17 (22.4%) patients, exon 19 deletions in 12 (15.8%) patients, G719X mutation in 1 (1.3%) patients, exon 20 insertion in 1 (1.3%) patients, multiple sites mutation in 1 (1.3%) patients and no mutation detected in 44 (57.9%) patients. With the DNA sequencing results were set as the reference standard, the prevalence of mutation detected by IHC-based analyses was 25.8% (8/31), 44.4% (8/18), 100% (7/7) and 66.7% (8/12) respectively, for samples with scores 0, 1+, 2+ and 3+. At IHC cut point value 2+, sensitivity and specificity for antibodies L858R were 52.9% wand 98.3 respectively. Likewise for antibodies E746-A750, cut point value 2+ showed sensitivity and specificity as 50.0% and 95.3% E746-A750 respectively. There was high correlation of EGFR mutation in TTF1 expression patients (96.8%, 31 of 32). The negative predictive value of TTF1 expression for EGFR expression was 90.0%.

**Conclusion:** A simple IHC-based analysis using EGFR mutation-specific antibodies in this study have a good correlation with gene-based for EGFR mutation analysis. The addition of TTF-1 testing will provide a better selection of patient for EGFR molecular testing. These simple IHC tests could be useful where molecular-based assay is not readily accessible.