Oral Session

O1-147  EXPRESSION OF NOTCH-1 IN EGFR-TKI ACQUIRED RESISTANT LUNG ADENOCARCINOMA

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Background: Notch pathway may well play a part in determining the sensitivity to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI). However to date, no study has investigated the association between Notch-1 expression and acquired resistance using lung cancer specimens. The objective of this study is to assess the correlation between Notch-1 expression and specific markers of epithelial-mesenchymal markers in EGFR-TKI required resistant lung adenocarcinoma.

Materials and methods: Malignant pleural effusion (MPE) was extracted from the pleural cavity of lung cancer patients pre- and post- Gefitinib treatment. Patients with lung adenocarcinoma harboring EGFR exon 19 deletion or exon 21 L858R mutations without T790M mutation or MET amplification were included. mRNA expressions of Notch-1, E-cadherin, Vimentin and Snail were determined using qPCR.

Results: From September 2010 to December 2011, 58 tumor samples were assessed for eligibility. 26 samples were excluded. Totally 32 samples from 23 lung adenocarcinoma patients were eligible, including 17 samples before Gefitinib treatment and 15 samples after acquisition of Gefitinib treatment. Among them, there were 9 paired MPE samples of Gefitinib primary sensitive and acquired resistance. The median duration of Gefitinib of treatment was 6.1 months. Median age of these patients was 56 y (36–68); 14 males and 9 females, of whom 13 were exon 19 deletion mutations, 10 were exon 21 L858R mutations. In clinical samples, a trend of increased Notch-1 with down-regulation of epithelial marker and up-regulation of mesenchymal markers was shown in Gefitinib-acquired resistant lung cancer.

Conclusions: These results indicate that Gefitinib-acquired resistance in lung cancer undergoing EMT occurs through activation of Notch-1 signaling. Notch-1 inhibition appears to be a novel strategy for overcoming EGFR TKI sensitivity to lung cancer.