PUD-07

SECONDARY T790M MUTATION CONFERRING SHORTER PROGRESSION-FREE SURVIVAL OF NON-SMALL-CELL LUNG CANCER PATIENTS WITH TUMOR RESPONSIVE TO GEFITINIB

J-Y Shih[1], C-H Gow[1], Y-L Chang[2], P-C Yang[1]
Department of [1]Internal Medicine, [2]Pathology,
National Taiwan University Hospital, Taipei, Taiwan

BACKGROUND/AIMS: The epidermal growth factor receptor (EGFR) mutations are strongly predictive of gefitinib efficacy in non-small-cell lung cancer. Secondary T790M mutation is one of the causes of gefitinib resistance.

METHODS: We analyzed the sequences of exons 18-21 of EGFR from tissue before gefitinib treatment and after disease progression from 14 patients with partial response to gefitinib. We also followed 5 patients with gefitinib-sensitive mutation had stable disease as the maximal response to get tissue after disease progressed.

RESULTS: In the sensitive group, all were non-smoker, and only 1 was male. Gefitinib was the first line of treatment in 8 patients, the second in 1, the third in 2 and the fourth in 1. Median follow-up from the start of gefitinib was 17.3 months. In the pre-gefitinib tissue, L858R mutation was found in 6 patients, small deletion of exon 19 in 5 patients, and wild type EGFR in 3 patients. After disease progression, all the original mutations were found in the corresponding tissues. Secondary T790M mutation was detected in 5 patients with L858R, one patient with deletion in exon 19 and none in patients with wild type EGFR. Patients without T790M mutation had better progression-free survival than those with T790M mutation (median 9.2 months and 6.0 months respectively, p=0.03). There was no difference in overall survival between patients with and without secondary T790M mutation. No secondary T790M was found in 5 patients of stable disease group.

DISCUSSION/CONCLUSIONS: Secondary T790M mutation occurs in gefitinib sensitive patients, but not in patients of stable disease. Patients with T790M mutation had shorter progression-free survival.

Keywords: EGFR, Gefitinib, Lung cancer