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# Predictive and Prognostic Impact of Epidermal Growth Factor Receptor Mutation in Non-Small-Cell Lung Cancer Patients Treated With Gefitinib

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Sae-Won Han , Tae-You Kim <sup>\*</sup>, Pil Gyu Hwang , Soohyun Jeong , Jeongmi Kim , In Sil Choi , Do-Youn Oh , Jee Hyun Kim , Dong-Wan Kim , Doo Hyun Chung , Seock-Ah Im , Young Tae Kim , Jong Seok Lee , Dae Seog Heo , Yung-Jue Bang , and Noe Kyeong Kim

From the Department of Internal Medicine, Department of Pathology, and Department of Thoracic and Cardiovascular Surgery, Seoul National University Hospital; Department of Internal Medicine, Seoul Municipal Boramae Hospital; Department of Internal Medicine, Seoul National University Bundang Hospital; Cancer Research Institute, Seoul National University College of Medicine; Petagen Inc, Seoul, Korea.

\* To whom correspondence should be addressed. E-mail: [kimty@snu.ac.kr](mailto:kimty@snu.ac.kr)

*Purpose:* This study was undertaken to investigate the effects of epidermal growth factor receptor (EGFR) mutation and its downstream signaling on response and survival in non-small-cell lung cancer (NSCLC) patients treated with gefitinib.

*Patients and Methods:* For 90 consecutive NSCLC patients who had received gefitinib, EGFR mutation was analyzed by DNA sequencing of exons 18, 19, 21, and 23 in the EGFR tyrosine kinase domain. Expressions of phosphorylated (p) -Akt and p-Erk were determined via immunohistochemistry. Response rate, time to progression (TTP), and overall survival were compared between each group according to EGFR mutation, as well as p-Akt and p-Erk expression.

*Results:* Seventeen patients (18.9%; 95% CI, 10.8 to 27.0) harbored EGFR mutations. These mutations include deletions in exon 19 in seven patients, L858R in six patients, G719A in three patients, and a novel A859T in one patient. Response rate in patients with EGFR mutation was 64.7% (11 of 17 patients; 95% CI, 42.0 to 87.4), in contrast to 13.7% (10 of 73 patients; 95% CI, 5.8 to 21.6) in patients without mutation ( $P < .001$ ). Moreover, these 17 patients with EGFR mutation had significantly prolonged TTP (21.7 v 1.8 months;  $P < .001$ ) and overall survival (30.5 v 6.6 months;  $P < .001$ ) compared with the remaining 73 patients without mutation. Although no

significant correlation was detected between EGFR mutation and expressions of p-Akt or p-Erk, p-Akt overexpression was associated with prolonged TTP in patients with EGFR mutation.

*Conclusion:* Our data further support the importance of EGFR mutation with regard to gefitinib sensitivity. In addition to its predictive role, EGFR mutation confers significant survival benefits on NSCLC patients treated with gefitinib.

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