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Real-world experience of first-line afatinib in patients with *EGFR*-mutant advanced NSCLC: a multicenter observational study

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Abstract

Background: This study aimed to evaluate the efficacy, side-effects and resistance mechanisms of first-line afatinib in a real-world setting.

Methods: This is a multicenter observational study of first-line afatinib in Malaysian patients with epidermal growth factor receptor (*EGFR*)-mutant advanced non-small cell lung cancer (NSCLC). Patients' demographic, clinical and treatment data, as well as resistance mechanisms to afatinib were retrospectively captured. The statistical methods included Chi-squared test and independent t-test for variables, Kaplan-Meier curve and log-rank test for survival, and Cox regression model for multivariate analysis.

Results: Eighty-five patients on first-line afatinib from 1st October 2014 to 30th April 2018 were eligible for the study. *EGFR* mutations detected in tumors included *exon 19* deletion in 80.0%, *exon 21 L858R* point mutation in 12.9%, and rare or complex *EGFR* mutations in 7.1% of patients. Among these patients, 18.8% had Eastern Cooperative Oncology Group performance status of 2–4, 29.4% had symptomatic brain metastases and 17.6% had abnormal organ function.
Afatinib 40 mg or 30 mg once daily were the most common starting and maintenance doses. Only one-tenth of patients experienced severe side-effects with none having grade 4 toxicities. The objective response rate was 76.5% while the disease control rate was 95.3%. At the time of analysis, 56 (65.9%) patients had progression of disease (PD) with a median progression-free survival (mPFS) of 14.2 months (95% CI, 11.85–16.55 months). Only 12.5% of the progressed patients developed new symptomatic brain metastases. The overall survival (OS) data was not mature. Thirty-three (38.8%) patients had died with a median OS of 28.9 months (95% CI, 19.82–37.99 months). The median follow-up period for the survivors was 20.0 months (95% CI, 17.49–22.51 months).
Of patients with PD while on afatinib, 55.3% were investigated for resistance mechanisms with *exon 20 T790 M* mutation detected in 42.0% of them.

Conclusions: Afatinib is an effective first-line treatment for patients with *EGFR*-mutant advanced NSCLC with a good response rate and long survival, even in patients with unfavorable clinical characteristics. The side-effects of afatinib were manageable and *T790 M* mutation was the most common resistance mechanism causing treatment failure.

Keywords: Afatinib, Dose adjustment, *Epidermal growth factor receptor* (*EGFR*), Real-world, Tyrosine kinase inhibitor

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