NSCLC, metastatic

THE EFFICACY OF FIRST-LINE CHEMOTHERAPY IS ASSOCIATED WITH KRAS MUTATION STATUS IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER: A META-ANALYSIS

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Aim: Non-small-cell lung cancer (NSCLC) patients harboring KRAS mutations were associated with worse prognosis and lower response to epidermal growth factor receptor (EGFR) targeted therapy including EGFR tyrosine kinase inhibitors (EGFR-TKIs) and anti-EGFR monoclonal antibodies than those with wild-type tumors. However, whether the underlying biological differences are associated with the efficacy of cytotoxic chemotherapy in advanced NSCLC patients remains controversial. Thus, we sought to perform a meta-analysis incorporating all available evidences to evaluate the clinical outcome according to the KRAS mutation status in patients with advanced NSCLC treated with front-line conventional chemotherapy.

Methods: We searched electronic databases for eligible literature. The primary outcomes were objective response rate (ORR), six-month and one-year progression-free survival (PFS) rate. The pooled odds ratio (OR) was calculated using random-effects model. Subgroup analyses stratified by literature type, mutation analysis method, therapeutic regimen, patient origin, EGFR mutation status in KRAS wild-type patients were proposed. All calculations were performed using REVIEW MANAGER version 5.0. Heterogeneity and publication bias were quantitatively evaluated.

Results: A total of 10 studies involving 1677 advanced NSCLC patients with known KRAS mutation status who had received first-line chemotherapy were included. KRAS mutants had lower ORR than wild-type patients (25.1% vs. 34.4%) significantly (OR 0.67, 95% CI 0.50-0.88, P = 0.004). Additionally, patients with KRAS mutation had numerically lower six-month (51.0% vs. 56.8%) and one-year (10.3% vs. 13.3%) PFS rate than wild-type patients, but there was no significant difference between the two groups (Six-month PFS: OR 0.75, 95% CI 0.54-1.04, P = 0.08; One-year PFS: OR 0.75, 95% CI 0.47-1.21, P = 0.25). Results of the subgroup analyses were almost concordant with the overall ones.

Conclusions: This comprehensive analysis revealed that advanced NSCLC patients with KRAS mutations had significantly lower ORR and potentially lower six-month/one-year PFS rates compared with wild-type patients after first-line chemotherapy. KRAS mutation status should be considered as an essential factor in studies regarding chemotherapy regimens or other non-targeted agents.

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