Somatic EGFR mutation and gene copy gain as predictive biomarkers for response to tyrosine kinase inhibitors in non-small cell lung cancer.

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Source

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Abstract

PURPOSE:

The aim of this systematic review and meta-analysis was to characterize common EGFR molecular aberrations as potential predictive biomarkers for response to monotherapy with tyrosine kinase inhibitors (TKI) in non-small cell lung cancer (NSCLC).

EXPERIMENTAL DESIGN:

We systematically identified articles investigating EGFR status [somatic mutational and gene copy aberrations (copy number)] in patients with NSCLC treated with TKIs. Eligible studies had to report complete and partial response rates stratified by EGFR status. We used random effects models for bivariable meta-analysis of sensitivity and specificity; positive and negative likelihood ratios (+LR and -LR, respectively) were also calculated and were considered as secondary end points.

RESULTS:

Among 222 retrieved articles, 59 were considered eligible for the somatic EGFR mutation meta-analysis (1,020 mutations among 3,101 patients) and 21 were considered eligible for the EGFR gene copy number meta-analysis (542 gene gain among 1,539 patients). EGFR mutations were predictive of response to single-agent TKIs [sensitivity, 0.78; 95% confidence interval (95% CI), 0.74-0.82; specificity, 0.86; 95% CI, 0.82-0.89; +LR, 5.6; -LR, 0.25]. EGFR gene gain was also associated with response to TKIs, albeit with lower sensitivity and specificity. In subgroup analysis, the only recognized trend was for a higher predictive value in Whites compared with East Asians for both mutation and gene copy number.

CONCLUSION:

This analysis provides empirical evidence that EGFR mutations are sensitive and specific predictors of response to single-agent epidermal growth factor receptor TKIs in advanced NSCLC. The diagnostic performance of mutations seems better than that of EGFR gene gain.