**Somatic EGFR mutations and efficacy of tyrosine kinase inhibitors in NSCLC.**

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**Source**

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**Abstract**

Early clinical studies of tyrosine kinase inhibitors (TKIs) that target the EGFR in patients with advanced non-small-cell lung cancer (NSCLC) showed that some patients experienced rapid, durable, complete or partial responses. These data were the basis for attempts to identify specific subgroups of patients who would further benefit from these agents. The discovery of somatic mutations in EGFR that correlated with sensitivity to TKIs identified a plausible explanation for these observations. Clinical and pathological factors such as female sex, never having smoked, Asian origin and adenocarcinoma histology correlate with the presence of EGFR mutations and objective responses to TKIs in patients with NSCLC. Recent studies in metastatic colorectal cancer highlighted that somatic mutations in KRAS represent a negative predictor of response to anti-EGFR monoclonal antibodies; KRAS mutations also represent an important mechanism of resistance to TKIs in NSCLC. Many large clinical studies are currently investigating the predictive and prognostic value of EGFR mutational status and other candidate biomarkers. We summarize the literature and present an overview of the field of anti-EGFR therapy in NSCLC, focusing on the influence of somatic EGFR mutations on selection of patients for TKI therapy and the influence of EGFR pathway regulation.