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バイオマーカーで何が変わるのか**
—EGFR 遺伝子変異と EGFR チロシンキナーゼ阻害剤—

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—EGFR Gene Mutation and EGFR Tyrosine Kinase Inhibitors—

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Summary

Gefitinib and erlotinib are epidermal growth factor receptor (EGFR)-specific tyrosine kinase inhibitors (TKIs). Lung cancer with activating mutation of the EGFR gene exhibits a dramatic response to EGFR-TKI. About 90% of EGFR mutations are either deletion mutation of exon 19 or leucine to arginine missense mutation at codon 858 of exon 21. Once the EGFR gene is mutated, tumor cells become highly dependent on (addicted to) the EGFR pathway. At the same time, the affinity of EGFR for EGFR-TKI exceeds that for ATP. For these two reasons, lung cancer with EGFR mutation is in general very sensitive to EGFR-TKI. Recent clinical trials have repeatedly shown that the response rate of lung cancer with EGFR mutation is usually in the range of 70～80% and median progression-free survival is ~10 months when EGFR TKI is given. With conventional chemotherapy, median PFS is ~6 months. However, probably due to crossing-over of treatment, no significant difference of overall survival between these two treatments was evident in the trials. Almost all patients whose tumor initially responded to EGFR-TKI eventually developed acquired resistance. Mechanisms of acquired resistance include secondary T790M mutation of the EGFR gene and MET gene amplification. Strategies to circumvent this resistance are currently under development.

Key words

Tyrosine kinase inhibitor, Biomarker, Acquired resistance, Personalized medicine