Epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) have improved the prognosis of patients with non-small cell lung cancers (NSCLCs). Genetic testing by next-generation sequencing (NGS) has been used in multiple companion diagnoses or cancer genome profiling. This advance in genetic testing yielded new insights into the treatment of patients with NSCLC with mutations resistant to EGFR-TKIs. Recent studies have also reported the efficacy of EGFR-TKIs in the perioperative period.

In this issue, we will briefly summarize new findings on adjuvant and neoadjuvant EGFR-TKIs and treatment for resistance to EGFR-TKIs. Subsequently, we will introduce seven papers on these topics.

A randomized controlled trial of osimertinib as adjuvant therapy (ADAURA study) showed that disease-free survival (DFS) in the osimertinib arm was significantly prolonged in patients with stage IB to IIIA EGFR mutation-positive NSCLC (1,2). Currently, a NeoADAURA study (ClinicalTrials.gov Identifier: NCT04351555, JapicCTI-205325) using osimertinib as neoadjuvant therapy: a case report. J Thorac Dis 2020;12:1582-7.

In many patients with EGFR-mutated advanced NSCLC, EGFR-TKIs as first-line therapy resulted in the acquisition of resistance within 1 year. In 50–60% of resistant cases, there was a T790M mutation in the exon 20 region of the EGFR gene (3). In a phase III AURA3 study comparing osimertinib with platinum-based chemotherapy in T790M mutation-positive NSCLC patients, osimertinib significantly prolonged progression-free survival (PFS) (median PFS; 10.1 vs. 4.4 months, hazard rate =0.30) (4). Furthermore, in a phase III FLAURA study comparing osimertinib with gefitinib or erlotinib as a first-line treatment for locally advanced EGFR mutation-positive NSCLC, PFS, and overall survival (OS) with osimertinib were significantly prolonged, and its toxicity was significantly reduced (5). Osimertinib was also effective.
in cases of brain metastasis (6). Therefore, osimertinib is a promising option for the first-line treatment of EGFR mutation-positive NSCLC.

Even in patients treated with osimertinib for T790M mutation-positive NSCLC, resistance to osimertinib was reported to develop within 10 months (4). This acquired resistance includes C797S mutation, the activation of alternative pathways or downstream targets and histological transformation (3). In the future, the mechanism of resistance to osimertinib as a first-line treatment should be actively re-examined to elucidate it.

Du et al. reported a case in which NSCLC patients with EGFR mutations were safely treated with gefitinib before left lower lobectomy and mediastinal lymphadenectomy. Dai et al. reported a case in which patients suffered from severe postsurgical infection after lung lobectomy and recovered by multiple debridement and drainage procedures. Wang et al. introduced a novel surgical method for accurately localizing and resecting pulmonary nodules by injecting indocyanine green (ICG) under the guidance of an electromagnetic navigation bronchoscope. Zang et al. discussed the efficacy of salvage surgery after EGFR-TKI resistance. Jia et al. introduced first-line treatment selection by using organoids of an EGFR-mutated and TP53-mutated stage Ia1 patient with early metastatic recurrence after radical surgery and follow-up. Zheng et al. discussed therapeutic strategies for acquired resistance after gefitinib treatment. Song et al. reported a case of the rare osimertinib-resistant L718Q mutation. Although further studies are needed, we hope that these reports will help readers in their daily practice.

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