Editorial

Biomarkers in the era of individualized medicine

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TNM staging has been a gold standard in the evaluation and treatment strategy for lung cancer. Preoperative anatomical discrimination of the exact range of tumor spreading is a key determinant for surgical resectability. In addition, postoperative pathologic evaluation of microscopic occult metastatic foci predicts the long-term prognosis. Classical prognostication based on the anatomical tumor extent has remained valid for decades despite the ongoing search for new prognostic markers. Many biomarkers have been suggested and validated, however, no single biomarker is as effective as TNM staging. These biomarkers represent the biological behavior of lung cancer cells; however, a sole biomarker without implication on treatment outcome has not been successful.

The basic architecture of the TNM system is closely related to the application of local treatment as well as anatomical progression of cancer. Because prognosis of lung cancer was mainly determined by curative local treatment rather than systemic therapy, prognostic stratification was established based on the anatomical extent of disease. Recently, there has been significant advancement in systemic therapy for lung cancer, e.g., targeted therapy and immune checkpoint inhibitors. Among these, epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR TKI) is the most well-known and has a long history in targeted therapy of lung cancer. Many types of EGFR mutation profiles have been clarified; moreover, EGFR mutation status is related to the responsiveness to EGFR TKI, indicating that the EGFR mutation profile can predict the treatment outcomes as well as the biological behavior of cancer cells. Therefore, EGFR mutation status is already established as a biomarker for advanced metastatic lung cancer. However, the role of EGFR mutation in patients with resectable lung cancer remains unclear.

EGFR mutation rate is related to stages of the disease and is relatively common in early-stage lung cancer (1). However, the role of EGFR mutation as a prognostic factor in resectable lung cancer is controversial. A study has indicated that EGFR mutation is a good prognostic factor in patients with early lung cancer (2); however, another study has shown that it is a poor prognostic factor in patients with advanced lung cancer (3). In one study that included a wide range of surgical stages, EGFR mutation was not a prognostic factor, but just a factor harboring other favorable prognostic factors for example, early stage, female sex and never smoker (4). Therefore, the role of EGFR mutation as a prognostic biomarker in surgically resectable lung cancer remains to be determined.

Isaka and colleagues reported the prognostic role of EGFR mutational status in N1-N2 pulmonary adenocarcinoma (5); of the 202 patients with N1-N2 adenocarcinoma included in their study, 100 patients had EGFR mutation. Whereas, the presence of EGFR mutation was not a prognostic factor for the overall and disease-free survival, the type of mutational status was a significant prognostic factor and exon 19 deletion showed better prognosis than exon 21-point mutation (L858R). Thus, the EGFR mutation status should be evaluated for the prediction of prognosis.

Since the study included a relatively small number of patients and the distribution of pathologic stage was uneven

across the different mutation types, a large cohort study is required to validate the findings. In addition, other hidden bias might have influenced the long-term survival after surgical resection. However, the study is valuable since EGFR mutations types were actively incorporated, which can be utilized for developing the second-line treatment strategy following failure of surgical resection. Several studies have shown that EGFR mutation and EGFR TKI responsiveness are important prognostic factors for patients with recurrence after surgical resection (6,7).

It is unclear whether the presence of effective second-line treatment should be considered before and after surgical resection or whether such information is helpful to the patients. Routine evaluation of the EGFR mutation profile may be unnecessary for patients without recurrence. However, multidisciplinary decision-making has become increasingly popular in cancer treatment. Sharing common prognostic markers with medical oncologists may enhance inter-department communication and deepen our understanding of systemic treatment. Developing biomarkers that can accurately represent the biological behavior of cancer and predict treatment outcomes is an ongoing research focus in the field of lung cancer and will be a crucial step for the establishment of individualized medicine.

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Footnote

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