A result of prospective biomarker trial on excision repair cross complementing group 1 (ERCC1) in advanced non-small-cell lung cancer: ERCC1 trial

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Chemotherapies with platinum doublet have an important role in managing lung cancers in spite of progress on epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) or anaplastic lymphoma kinase (ALK)-inhibitor. However, we cannot customize current cytotoxic chemotherapies to heighten an effect of treatment and prevent adverse drug reactions because there are no available biomarkers in practice. Development of biomarkers to predict a survival benefit for platinum-based chemotherapy is of importance in treatment for patients with lung cancer. Excision repair cross complementing group 1 (ERCC1) is one of the most promising biomarker (1), which proteins play an essential role in nucleotide excision repair (2).

In retrospective studies, increased ERCC1 expression may be related with platinum resistance and survival in patients with non-small cell lung cancer (NSCLC) (3). In this study, Lee *et al.* performed the trial, which was a phase III randomized trial including 85 UK hospitals, to estimate a survival benefit of ERCC1. To their knowledge, this is the first prospective phase III randomized trial.

The aim was to determine whether non-platinum therapy was superior to platinum therapy for patients with ERCC1-positive, but non-inferior for patients with ERCC1-negative tumors in chemotherapy-naive patients with NSCLC, age with 18 or more than, histologic confirmation, stage IIIb or IV, performance status 0 or 1, and stable brain metastases (if present). For immunohistochemical stainings, 8F1 was used as anti-ERCC1 antibody, and centralized ERCC1 testing was performed. Moreover, anti-XPF clone 3F2/3, which is specific for the XPF-ERCC1 protein complex, was added to this trial. Their study revealed that patients with non-platinum chemotherapy had significantly poor prognoses than patients with platinum chemotherapy in advanced squamous cell carcinomas, however ERCC1 expression using the 8F1/XPF antibodies could not predict overall survival and progression-free survival for patients with squamous cell carcinoma or non-squamous cell carcinoma (1).

Previously, many researchers tried to evaluate the effectiveness of ERCC1 as biomarkers using various approaches such as immunohistochemical staining (3,4) or mRNA expression (5), and almost studies revealed that the expression of ERCC1 could predict a survival benefit for platinum-based chemotherapy. Moreover, usefulness of ERCC1 was reported in other organs such as ovarian cancer or gastric cancer (6,7). However, results of recent studies are controversial, because results of some studies fail to predict a benefit for platinum-based chemotherapy and those are inconsistent with previous studies.

Although the study of Lee *et al.* was designed to include 1,272 patients at the beginning, it was stopped because the Independent Data Monitoring Committee indicated that patients with platinum-based chemotherapy had significantly better overall survival and progression-free survival than patients with non-platinum-based chemotherapy did in patients with squamous cell carcinoma, reanalysis of International Adjuvant Lung

Cancer Trial (IALT) revealed that the 8F1-ERCC1 antibody was not predictive and the observed ERCC1 trial data of Lee *et al.* were consistent with findings of reanalysis of IALT (1,2). When we evaluate this study, we should consider that this study had several difficult factors such as the technique of the ERCC1 assessment, or case number (2).

On ERCC1 expression studies to predict a benefit for platinum-based chemotherapy, it is hard to detect the reason why results of recent studies are inconsistent with those of previous studies. Some indicated that it might be because of quality of ERCC1 antibodies (8). ERCC1 has four isoform with 201 to 204, and only one isoform [202] is functional (8). Future studies focusing on ERCC1 isoform [202] may be able to detect factors which are associated with platinum resistance and can predict a survival benefit for platinum-based chemotherapy. However, ERCC1, using current commercial antibodies, should not be used in therapeutic decision making of platinum-based chemotherapy for patients with lung cancer.

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Footnote

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References

1. Lee SM, Falzon M, Blackhall F, et al. Randomized Prospective Biomarker Trial of ERCC1 for Comparing Platinum and Nonplatinum Therapy in Advanced Non-Small-Cell Lung Cancer: ERCC1 Trial (ET). J Clin Oncol 2017;35:402-11.
2. Friboulet L, Olaussen KA, Pignon JP, et al. ERCC1 isoform expression and DNA repair in non-small-cell lung cancer. N Engl J Med 2013;368:1101-10.
3. Olaussen KA, Dunant A, Fouret P, et al. DNA repair by ERCC1 in non–small-cell lung cancer and cisplatin-based adjuvant chemotherapy. N Engl J Med 2006;355:983-91.
4. Ota S, Ishii G, Goto K, et al. Immunohistochemical expression of BCRP and ERCC1 in biopsy specimen predicts survival in advanced non-small-cell lung cancer treated with cisplatin-based chemotherapy. Lung Cancer 2009;64:98-104.
5. Cobo M, Isla D, Massuti B, et al. Customizing cisplatin based on quantitative excision repair cross-complementing 1 mRNA expression: a phase III trial in non-small-cell lung cancer. J Clin Oncol 2007;25:2747-54.
6. Dabholkar M, Vionnet J, Bostick-Bruton F, et al. Messenger RNA levels of XPAC and ERCC1 in ovarian cancer tissue correlate with response to platinum-based chemotherapy. J Clin Invest 1994;94:703-8.
7. Metzger R, Leichman CG, Danenberg KD, et al. ERCC1 mRNA levels complement thymidylate synthase mRNA levels in predicting response and survival for gastric cancer patients receiving combination cisplatin and fluorouracil chemotherapy. J Clin Oncol 1998;16:309-16.
8. Postel-Vinay S, Soria JC. ERCC1 as Predictor of Platinum Benefit in Non-Small-Cell Lung Cancer. J Clin Oncol 2017;35:384-6.

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