New analysis helps guide use of erlotinib in advanced non-small cell lung cancer

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Patients with advanced non-small cell lung cancer should only receive treatment with the drug erlotinib before receiving standard chemotherapy if their tumor is known to harbor EGFR mutations, researchers report at the 3rd European Lung Cancer Conference in Geneva, Switzerland.

The results of biomarker analyses of a recently reported clinical trial confirm that patients with unknown or negative mutation status should be treated with the standard chemotherapy first, they say.

The TORCH trial was a randomized phase III trial conducted in Italy and Canada, which compared the efficacy of treatment with erlotinib, followed at progression of disease by cisplatin and gemcitabine, against the standard reverse sequence. Erlotinib is a drug that specifically targets the epidermal growth factor receptor (EGFR) tyrosine kinase.

The primary endpoint of the original TORCH study was overall survival and 900 patients were planned, however the study was stopped early as the first interim analysis showed that the erlotinib-first regimen was inferior to the standard approach.

In the new study, Dr Ming Tsao and colleagues conducted an exploratory analysis on the TORCH patient tumor samples that were available for analysis, looking for molecular biomarkers known to be potential predictors of benefit from EGFR inhibitors.

"Our results show a significant interaction in progression-free survival favoring treatment with erlotinib first in EGFR-mutated patients, and favouring first treatment with chemotherapy in EGFR wild type [non-mutated] patients," said Dr Tsao, from the Princess Margaret Hospital.

"However there was no significant interaction between treatment efficacy and overall survival. This shows that using erlotinib to treat patients with a mutated tumor is always effective, both in first and in second line; of course, it is much more convenient for these patients to receive it as first line, as shown also in other trials," Dr Tsao said.

Patients with EGFR mutations benefit from the erlotinib-first regimen because their tumors are very sensitive to the anti-tumor activity of the drug, he explained.

"The take-home message from this study is that in advanced non-small cell lung cancer patients, treatment with erlotinib first should only be applied to patients whose tumor is known to harbor EGFR mutation," said Dr Tsao. "Patients with unknown or negative mutation status should be treated with the standard chemotherapy first."

Commenting on the study which he was not involved in, Dr Tetsuya Mitsudomi from Aichi Cancer Center Hospital in Nagoya, Japan, member of the IASLC Board of Directors, said: "Many previous trials, for instance IPASS, NEJ002, WJTOG3405, OPTIMAL, EUROTAC, have already shown that EGFR mutation is the most reliable predictive marker for EGFR-TKI treatment. The current paper was able to confirm the importance of EGFR mutation testing when considering the use of erlotinib, especially in consideration of the far shorter progression-free survival obtained with erlotinib when the mutation was absent. Consequently, although it was thought that erlotinib is active even in lung cancer patients without EGFR mutation if compared with gefitinib, this study suggests that erlotinib should be avoided when treating patients

without EGFR mutation, at least in the first-line setting."

This biomarker analysis was preplanned but actually only 36% of the samples could be anlayzed for EGFR mutation. This relatively low tissue accrual rate is precedented by many clinical trials in which the mutation analysis was performed retrospectively. "Therefore, we also have to consider prospective determination of oncogene mutation when we want to raise this rate such as in NEJ, WJTOG, OPTIMAL and EUROTAC," Dr Mitsudomi added.

"In summary, the TORCH-BIO study adds improrant evidence to the research field of EGFR-TKI in lung cancer and emphazizes the importance of biomarker study for improvement of clinical outcome."

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