Afatinib a better choice for EGFR-mutated lung cancer in first-line treatment

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Patients with EGFR-activating mutations in advanced lung cancer seem to benefit more from afatinib than gefitinib as first-line treatment, researchers report at the first ESMO Asia 2015 Congress in Singapore.

In the global, randomised, open-label Phase IIb LUX-Lung 7 (LL7) trial, the irreversible ErbB family blocker afatinib significantly improved efficacy versus gefitinib across a range of clinically relevant endpoints, such as progression-free survival, time-to-treatment failure and objective response rate. "Based on these results I would consider afatinib as the EGFR tyrosine kinase inhibitor (TKI) of choice for the first-line treatment for patients with EGFR mutation-positive non-small-cell lung cancer (NSCLC)," lead author, Professor Keunchil Park, head of the Division of Hematology/Oncology at Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, said.

NSCLC is the most common type of lung cancer: activating epidermal growth factor receptor (EGFR) gene mutations are more frequently observed in non-smokers and women, and occur in 50% of Asians and only 10% of non-Asians. The targeted agents afatinib and gefitinib block key pathways involved in tumour growth and spread. They have both been approved for the treatment of naive patients, based on the results of Phase III trials, confirming their superiority compared to chemotherapy. Unlike the first-generation EGFR inhibitor gefitinib, the irreversible ErbB family blocker afatinib is suggested to be active in prolonging tumour response and delaying disease progression.

In the first head-to-head LUX-Lung 7 trial, afatinib candidates to be a better choice for EGFR-mutation positive NSCLC naive patients who had received no prior treatment. "First-line afatinib treatment significantly reduced the risk of lung cancer progression by 27% versus gefitinib," Park said. "Interestingly, the improvement in progression-free survival became more pronounced over time with a significantly higher proportion of patients alive and progression-free at 18 months (27% vs 15%; p=0.018) and 24 months (18% vs 8%; p=0.018), showing a greater long-term benefit of using the irreversible ErbB family blocker afatinib."

Out of the 319 patients who were randomised to afatinib or gefitinib, a significantly higher proportion responded to the first than the second (70.0% versus 56.0%; p=0.008) with a median duration of response of 10.1 months (95% CI, 7.82-11.10) and 8.4 months (95% CI, 7.36-10.94), respectively. Regarding the tolerability profile, Park said: "Overall, the frequency of severe adverse events was similar in both arms with slightly different toxicity profiles. The adverse events observed with both treatments were predictable and manageable, leading to an equally low rate of treatment discontinuation in both arms (6.3%)."

ESMO spokesperson Dr. Martin Reck, Chief oncology physician at the Department of Thoracic Oncology, Hospital Grosshansdorf, Germany, who was not involved in the study, cautions that the individual patient and his or her comorbidities will still guide the selection of EGFR inhibitor. "Following these trial results, afatinib will be one of the most attractive EGFR tyrosine kinase inhibitors. However, tolerability also plays a determining role in the selection and dosing of a tyrosine kinase inhibitor. The tolerability profiles between gefitinib and afatinib are different and the selection of the therapy will still be based on the individual clinical decision," he said.

The primary analysis of overall survival data is planned in 2016 and will

provide further responses.

Commenting on future research directions for naive patients with non-small-cell lung cancer, Reck says: "One of the most important improvements that we have achieved in first-line treatment of NSCLC has been the implementation of molecular diagnosis. If a treatable molecular alteration like an EGFR mutation or an ALK translocation can be diagnosed, treatment with a targeted agent like an EGFR-TKI or an ALK-TKI would represent the most efficacious treatment. In all other patients platinum-based chemotherapy is still the standard. Current trials are evaluating whether immune checkpoint inhibitors will be superior to chemotherapy in patients with PDL-1 expressing tumours and whether monotherapy or combinations will replace chemotherapy in selected patients in the future."

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