# IMPRESS trial data on continuing tyrosine kinase inhibitor therapy after resistance development in lung cancer reported

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Patients whose lung cancer has developed resistance to the drug gefitinib experience no statistically significant improvement in progression-free survival from continued treatment with the drug in addition to chemotherapy, a phase III trial presented at the ESMO 2014 Congress has shown.

The IMPRESS trial is a randomised phase III study that compared continuation of gefitinib in addition to chemotherapy against chemotherapy alone in patients with lung cancer that carried mutations in the EGFR cell surface receptor.

Gefitinib is a type of drug known as a tyrosine kinase inhibitor, and it targets cells with EGFR mutations. Most patients with EGFR mutation-positive non-small cell lung cancer respond to first-line EGFR tyrosine kinase inhibitors, but later acquire resistance. The primary objective of the trial was to show whether there was a difference in progression-free survival when gefitinib was continued in this situation.

"This study was designed to resolve a greatly debated issue: whether tyrosine kinase inhibitors should be continued beyond progression," said study author Prof Tony Mok, a professor in the Department of Clinical Oncology at the Chinese University of Hong Kong. "As the result demonstrated no difference in progression-free survival, the standard treatment is chemotherapy alone."

This study helps to establish the standard of treatment, and in the future doctors should not prescribe EGFR tyrosine kinase inhibitors in combination with chemotherapy when cancers have progressed after first-line treatment with an EGFR tyrosine kinase inhibitor, Mok said.

The researchers had hoped that the study would show an improvement in progression-free survival, Mok said. "I suspected the inhibition of TKI-sensitive cancer cells with continuation of gefitinib and inhibition of resistant cells with chemotherapy would optimize the treatment outcome. However, the study has proved otherwise."

The IRESSA Mutation Positive Multicentre Treatment Beyond ProgRESsion Study included 265 patients from 71 centres in Europe and the Asia Pacific region who received chemotherapy plus either gefitinib or a placebo. There was no statistically significant improvement in progression-free survival —the primary endpoint of the study— for gefitinib versus placebo.

The overall survival data is still immature, Mok said, although there is a suggestion of better overall survival in the placebo group. "This needs to be monitored very closely in future," he said.

Commenting on the study, Dr Marina Garassino, a Medical Consultant at the Medical Oncology Division of the National Cancer Institute of Milan, said the results were "very robust and reliable, and they will help clinicians in their daily clinical practice."

"However, when possible, it is important to re-biopsy the patients when their tumours progress after treatment with tyrosine kinase inhibitors to understand the mechanism that underlies the resistance," Garassino noted.

"New generations of agents are now becoming available for specific

resistance mutations with very promising results. It is therefore possible in the future that we will be able to personalise the further treatments for these patients."

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