New targeted therapy adds benefit to erlotinib in some patients with advanced lung cancer

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A subset of lung cancer patients seem to live longer and experience delays in disease progression when a new drug that targets a cancer-associated molecule called MET is added to treatment with erlotinib, the results of a double-blind Phase-II trial show.

Dr David Spigel, Director of lung cancer research for the Sarah Cannon Research Institute in Nashville, Tennessee reported the trial findings at the 35th Congress of the European Society for Medical Oncology (ESMO) in Milan, Italy.

The study included 128 patients with advanced non-small cell lung cancer who were randomly assigned to treatment with either erlotinib plus placebo, or erlotinib plus MetMAb, a monoclonal antibody that binds specifically to the MET receptor on cancer cells.

"MET is an important switch in cancer cells," Dr Spigel explained. "When turned on, it influences the growth of these cells. Importantly, MET activation has also been implicated in the resistance of lung cancers to EGFR inhibitors such as erlotinib. MetMAb helps target this switch and turn it off."

Dr Spigel and colleagues tested for mutations in the EGFR gene and for expression of MET in tumor samples from trial participants.

At the end of the trial, the researchers found that among the 51% of patients whose tumors expressed MET, those who received MetMAb plus erlotinib had better overall survival and longer progression-free survival than those who received erlotinib plus placebo.

In this subset of Met+ patients, adding MetMAb to erlotinib nearly halved the risk of disease progression or death during the study compared to those treated with erlotinib plus placebo.

"In those patients who were found to express the MET protein (the target of MetMAb), MetMAb appeared to improve the treatment benefit when added to erlotinib compared with erlotinib alone," Dr Spigel said.

Conversely, patients whose tumors did not express the MET protein appeared to do worse when treated with the MetMAb/erlotinib combination. "The reasons for this finding are unclear. It is possible that MetMAb may interfere with erlotinib's activity in these patients, but further study would be necessary to better understand this potential negative association," Dr Spigel said.

"The findings of this trial are important, and need to be validated in a larger randomized Phase-III trial in patients selected for MET expression," Dr Spigel said.

The results of this trial are important for three reasons, commented Professor Jean-Charles Soria from Institut Gustave Roussy, Paris, France.

"First, this is the second trial in lung cancer where targeting of MET in combination with erlotinib suggests a better outcome," Prof Soria said. "This confirms that MET is a relevant target in cancer."

"Also, the present Genentech-sponsored trial has identified a putative biomarker, namely MET immunohistochemical positivity, which appears to be easy to implement as immunohistochemistry testing is daily practice in pathology labs."

"Finally, in the present trial the biomarker-positive population not only derived a benefit in progression-free survival, but also an almost statistical overall

survival benefit, which is remarkable taking into account the small number of patients. One note of caution, however, is that these Phase-II results should be validated in a larger Phase-III trial."

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