

LUNG CANCER

MET-negative patients—eclipsing benefits

Although the EGFR inhibitor erlotinib has improved survival in patients with non-small-cell lung cancer (NSCLC), resistance eventually develops. Data from preclinical models support at least additive effects when anti-MET and anti-EGFR therapies are combined. Thus, David Spiegel and coauthors conducted a global, randomized, placebo-controlled phase II study in

patients with recurrent NSCLC to compare erlotinib and onartuzumab with erlotinib and placebo. “As erlotinib is approved in the refractory setting in unselected patients with NSCLC, the goal of this trial was to learn if the addition of a novel MET antibody could improve upon efficacy”, explains Spiegel.

No difference in progression-free survival was found in the intention-to-treat population. However, when MET-positive patients were assessed, a significant reduction in the risk of disease progression was noted compared with patients who were MET-negative. In MET-positive patients, the combination resulted in an overall survival improvement three times greater than in the placebo arm. Crucially, the exact opposite effect was observed in patients with MET-negative tumours. Patients assigned to onartuzumab had significantly shorter overall survival compared with patients receiving placebo (median 8.1 months versus 15.3 months).

Most adverse events were comparable between the arms, although peripheral oedema was increased in patients treated with onartuzumab.

The addition of onartuzumab in MET-positive patients resulted in a similar median survival as that observed in MET-negative patients receiving erlotinib alone, indicating that the combination in MET-positive patients abrogated the negative prognostic effect seen in MET-negative patients. A phase III trial in MET-positive patients with this combination is ongoing. This study underscores the importance of optimal patient selection according to biomarker status for the appropriate allocation of targeted therapies.

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Original article Spiegel, D. R. *et al.* Randomized phase II trial of onartuzumab in combination with erlotinib in patients with advanced non-small-cell lung cancer. *J. Clin. Oncol.* doi:10.1200/JCO.2012.47.4189

