Cetuximab plus chemotherapy in patients with advanced non-small-cell lung cancer (FLEX): an open-label randomised phase III trial.

BACKGROUND: Use of cetuximab, a monoclonal antibody targeting the epidermal growth factor receptor (EGFR), has the potential to increase survival in patients with advanced non-small-cell lung cancer. We therefore compared chemotherapy plus cetuximab with chemotherapy alone in patients with advanced EGFR-positive non-small-cell lung cancer. METHODS: In a multinational, multicentre, open-label, phase III trial, chemotherapy-naive patients (≥18 years) with advanced EGFR-expressing histologically or cytologically proven stage IIIB or stage IV non-small-cell lung cancer were randomly assigned in a 1:1 ratio to chemotherapy plus cetuximab or just chemotherapy. Chemotherapy was cisplatin 80 mg/m² intravenous infusion on day 1, and vinorelbine 25 mg/m² intravenous infusion on days 1 and 8 of every 3-week cycle) for up to six cycles. Cetuximab—at a starting dose of 400 mg/m² intravenous infusion over 2 h on day 1, and from day 8 onwards at 250 mg/m² over 1 h per week—was continued after the end of chemotherapy until disease progression or unacceptable toxicity had occurred. The primary endpoint was overall survival. Analysis was by intention to treat. This study is registered with ClinicalTrials.gov,
number NCT00148798. FINDINGS: Between October, 2004, and January, 2006, 1125 patients were randomly assigned to chemotherapy plus cetuximab (n=557) or chemotherapy alone (n=568). Patients given chemotherapy plus cetuximab survived longer than those in the chemotherapy-alone group (median 11.3 months vs 10.1 months; hazard ratio for death 0.871 [95% CI 0.762-0.996]; p=0.044). The main cetuximab-related adverse event was acne-like rash (57 [10%] of 548, grade 3).

INTERPRETATION: Addition of cetuximab to platinum-based chemotherapy represents a new treatment option for patients with advanced non-small-cell lung cancer. FUNDING: Merck KGaA.