

Pembrolizumab With Front-line Chemotherapy Boosts Overall Survival in Patients with Metastatic Non-Small Cell Lung Cancer

Pembrolizumab with front-line chemotherapy boosts overall survival and progression-free survival in patients with metastatic nonsquamous non-small cell lung cancer.

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April 19, 2018 – In patients with advanced metastatic non-small cell lung cancer (NSCLC), the addition of pembrolizumab to front-line chemotherapy significantly prolonged overall as well as progression-free survival, a randomized, double-blind study showed.

Leena Gandhi MD, PhD, with the NYU Perlmutter Cancer Center in New York, reported the findings of a global phase III study in the April 16, 2018 issue of *The New England Journal of Medicine*.

Pembrolizumab is a highly selective monoclonal antibody that blocks programmed death (PD-1) receptor on immune cells and promotes antitumor activity. It is an approved second-line therapy for patients with advanced NSCLC. However, due to the rapid disease progression in advanced NSCLC and the associated clinical deterioration, more than 50% of these patients do not receive immunotherapy.

In this placebo-controlled study, the investigators assessed the potential of a front-line combination therapy using pembrolizumab, pemetrexed and a platinum-based drug to prolong survival in patients with advanced metastatic NSCLC without sensitizing *EGFR* or *ALK* mutations.

A total of 616 patients (≥ 18 years) were randomly assigned in a 2:1 ratio to receive an intravenous dose of pembrolizumab (200 mg; n=410) or saline placebo (n=206). All patients received a mix of pemetrexed (500 mg/square meter) and one of the platinum-based drugs, cisplatin (75 mg/sq meter) or carboplatin (5 mg/mL/min), intravenously. Randomization was stratified based on the choice of platinum-based drug, tumor PD-L1 (Programmed Death Ligand-1) expression and smoking history.

The 2 primary end points of the study were overall survival and progression-free survival. Safety, response rate and duration of response served as secondary end points.

The pembrolizumab combination group fared significantly better in both primary end points across all stratified groups. At 12 months, the overall survival in the pembrolizumab group was 69.2% compared with 49.4% in the placebo group (hazard ratio [HR] for death, 0.49; 95% CI, 0.38-0.64; $P < 0.001$).

The median progression-free survival was 8.8 months and 4.9 months in the pembrolizumab group and placebo group, respectively (HR for progression or death, 0.52; 95% CI, 0.43 - 0.64; $P < 0.001$). Similar response was observed for all secondary endpoints.

In the pembrolizumab group, higher incidence of acute kidney injury (5.2%) was reported compared with the placebo group (0.5%). The investigators stated that in several earlier studies, renal adverse effects have also been associated with pemetrexed and platinum-based drugs.

Dr Leena Gandhi and colleagues concluded, “An important question for further study is whether the addition of pembrolizumab to pemetrexed and a platinum-based drug has greater efficacy than pembrolizumab monotherapy in these patients.”

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Gandhi L, Rodríguez-Abreu D, Gadgeel S, et. al., Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. *N Engl J Med*. 2018; [Epub ahead of print]