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Pembrolizumab new option in one-line treatment of adv lung cancer and high PD-L1 expression

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Pembrolizumab is set to become a new option for first line treatment of patients with advanced lung cancer and high PD-L1 expression, according to the results of the phase III KEYNOTE-024 trial presented at the ESMO 2016 Congress in Copenhagen and published in the *New England Journal of Medicine*.

"Pembrolizumab is a PD-1 antibody approved for second line treatment of patients with advanced non-small-cell lung cancer (NSCLC) and PD-L1 expression in their tumour cells," said lead author Professor Martin Reck, chief oncology physician, Department of Thoracic Oncology, Lung Clinic Grosshansdorf, Germany. "KEYNOTE-024 is the first phase III trial of pembrolizumab as first line treatment in patients with high PD-L1 expression, who represent 27-30% of those with advanced NSCLC."

KEYNOTE-024 investigated the efficacy of pembrolizumab compared to standard of care with platinum-based chemotherapy in untreated patients with advanced NSCLC and high PD-L1 expression (defined as expression in at least 50% of tumour cells). Patients with EGFR activating mutations and ALK translocations were excluded from recruitment. "There is a substantial need to find better options than chemotherapy for these patients," said Reck.

The trial included 305 patients from 16 countries who were randomised

1:1 to pembrolizumab or chemotherapy. Patients in the chemotherapy arm who progressed were eligible to crossover to pembrolizumab as second line treatment - this occurred in 44% of these patients.

The investigators found that pembrolizumab significantly improved the primary endpoint of progression-free survival by approximately four months compared to chemotherapy (10.3 months versus 6.0 months, hazard ratio [HR] 0.50). The secondary endpoint of overall survival was also significantly prolonged, and 80% of patients on pembrolizumab were alive at six months compared to 72% on chemotherapy (HR=0.60).

"The significant improvement in overall survival with pembrolizumab was remarkable given that more than 40% of patients crossed over from the control arm to pembrolizumab after progression of the disease," said Reck.

Pembrolizumab was associated with a higher overall response rate compared to chemotherapy (45% versus 28%), a longer duration of response, and lower incidences of all and serious (3/4) adverse events.

"This data will completely change the management of patients with advanced NSCLC," said Reck. "All endpoints of efficacy and tolerability favoured treatment with pembrolizumab, suggesting it should become one standard of care for first line treatment of patients with advanced NSCLC and high PD-L1 expression. This is primarily an opportunity for patients without oncogenic alterations.

More information is needed for those with alterations."

He concluded: "This is a landmark trial for the 30% of patients with advanced NSCLC who are high expressers of PD-L1. The new treatment algorithm should include upfront testing for PD-L1 expression to identify patients who will benefit from first line treatment with

pembrolizumab."

Commenting on the results, Professor Johan Vansteenkiste, Professor of Medicine, Catholic University Leuven, and Chief Oncology Physician, Unit of Respiratory Oncology, University Hospital KU Leuven, Belgium, said: "This study may change current practice for the treatment of patients with advanced NSCLC. It is the first time a therapy has improved progression-free survival over the current standard first line treatment with platinum-based doublet chemotherapy."

"The reason KEYNOTE-024 met its primary endpoint, in contrast with other studies, is probably because the trial only included patients who had PD-L1 expression of at least 50% and were therefore optimal candidates for treatment with pembrolizumab," he added.

"A study is needed to confirm these findings in patients with high PD-L1 expression," continued Vansteenkiste. "Additional research should be done to find out whether patients with lower levels of PD-L1 expression also benefit more from pembrolizumab than chemotherapy."

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