Greater patient selection may be needed for first line nivolumab to improve progression-free survival

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Greater patient selection may be needed for first line nivolumab to improve progression-free survival over chemotherapy in advanced lung cancer as the CheckMate 026 trial gave negative results in a broad group of patients expressing PD-L1 in their tumour cells. The findings were presented at the ESMO 2016 Congress in Copenhagen.

"Nivolumab represents a standard of care in the second-line treatment of advanced non-small cell lung cancer (NSCLC) as it improved overall survival compared to docetaxel in phase III trials in these patients," said lead author Dr Mark A. Socinski, Executive Medical Director, Florida Hospital Cancer Institute, US. "In the first line setting, nivolumab showed a promising response rate in a phase I trial in advanced NSCLC patients with 1% or greater PD-L1 expression in their tumour cells," he continued.

The phase III CheckMate 026 trial investigated the efficacy of first line treatment with nivolumab compared to platinum-based doublet chemotherapy in patients with advanced NSCLC and PD-L1 positive tumours (defined as present in 1% or more tumour cells). Patients with EGFR activating mutations and ALK translocations, which are sensitive to targeted therapy, were excluded. The primary endpoint was progression-free survival, assessed by an independent radiology review committee in patients with PD-L1 in 5% or more tumour cells. A total of 541 patients were randomised 1:1 to nivolumab or chemotherapy.

Patients who progressed on chemotherapy could crossover to nivolumab as second line treatment.

In the 423 patients with 5% or greater PD-L1 expression, progression-free survival was 4.2 months with nivolumab and 5.9 months with chemotherapy (hazard ratio [HR] 1.15, 95% confidence interval [CI] 0.91-1.45, p=0.25). Overall survival was 14.4 months for nivolumab versus 13.2 months for chemotherapy (HR 1.02, 95% CI 0.80-1.30). Among all treated patients, any and serious treatment-related adverse events were 71% and 18% with nivolumab, and 92% and 51% with chemotherapy, respectively.

"There were no new safety signals with nivolumab and it was less toxic than chemotherapy," said Socinski."There are a number of possible reasons for the disappointing progression-free survival results," he added. "Regarding overall survival, there was a high rate of crossover to immunotherapy on the chemotherapy arm. Overall survival in the chemotherapy arm was better than historical standards, which could be due to the fact that it had a greater proportion of women and Asian patients. We are conducting further analyses to evaluate these results." "Platinum-based chemotherapy is the standard first line treatment because it makes patients live longer and palliates symptoms," said Socinski. "If we are going to replace it with immunotherapy, we need to be confident that we are identifying the patients who will derive greater benefit."

Socinski concluded: "Combination immunotherapies may increase the proportion of patients who benefit in the first line. The phase III CheckMate 227 trial is investigating treatment with nivolumab plus ipilimumab in the first line setting relative to standard chemotherapy."

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: "Nivolumab did not improve progression-free survival over chemotherapy in this study. In my view the reason is because the trial included a broad range of patients with a low PD-L1 expression threshold of just 1% or greater. Standard first line treatment with platinum doublet chemotherapy gives a progression-free survival of six months and to beat that may require being more selective on who receives the drug."

He continued: "More research is needed about how to use the PD-L1 biomarker to select patients for treatment with nivolumab. In addition, phase I studies suggest that combination immunotherapy improves response rate and outcome, but at the expense of increased toxicity, compared to single agent immunotherapy in NSCLC. So, it will be important to investigate this strategy further."

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