Neoadjuvant immunotherapy prior to surgery is safe and feasible in early lung cancer

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Neoadjuvant immunotherapy with the PD-1 inhibitor nivolumab is safe and feasible prior to surgery for early lung cancer, researchers reported at the ESMO 2016 Congress in Copenhagen.

"Until now nivolumab and the other anti-PD-1 and anti-PD-L1 drug studies have only been reported in metastatic or advanced lung cancer," said lead author Dr Patrick Forde, Assistant Professor of Oncology, Sidney Kimmel Comprehensive Cancer Centre, Johns Hopkins, Baltimore, US. "This was the first study of neoadjuvant PD-1 blockade in early stage lung cancer."

The primary objective of the study was to see whether it was safe and feasible to administer neoadjuvant nivolumab to patients with early stage non-small-cell lung cancer (NSCLC) prior to resection of the tumour. Treatment was considered feasible if it did not delay surgery.

Exploratory aims included extensive correlative analyses of the pretreatment biopsy and post-treatment resected tumour including PD-L1 staining, multiplex immunohistochemistry and T cell receptor sequencing. An additional exploratory analysis looked at the degree of pathological regression. This was analysed by a lung cancer pathologist using a method previously reported for use in measuring response to neoadjuvant chemotherapy in NSCLC. Major pathological regression (90% or more) was defined as a resected specimen with less than 10%

remaining viable tumour cells.

The study included 20 patients who had a tumour biopsy taken. They then received two doses of nivolumab at four and two weeks prior to surgical resection of the tumour.

The results in the first 16 patients were presented today. The investigators found that there were no significant safety concerns and no delays to surgery with nivolumab.

Six of 15 patients (40%) had major pathological regression of their tumour following nivolumab. All of those tumours had dense infiltration of immune cells and either a complete pathologic response or isolated remaining tumour cells. An additional five patients had some regression of their tumour noted and evidence of immune infiltration. Multiplex IHC demonstrated infiltration of cytotoxic T cells into the tumours and also detection of new T cell clones in the tumour that did not appear to be present in the pre-treatment biopsy.

Forde said: "We found that neoadjuvant administration of nivolumab is safe and feasible in stage I-IIIA NSCLC and also a preliminary signal that anti-PD-1 immunotherapy may have activity in early stage lung cancer. Following these initial results we are expanding the study.

One cohort will receive a third dose of nivolumab preoperatively and the other will receive the combination of nivolumab and ipilimumab preoperatively. This expanded study will continue to be conducted in collaboration with investigators at Johns Hopkins University and Memorial Sloan-Kettering Cancer Centre. Others, such as the Lung Cancer Mutation Consortium in the United States, are also conducting larger studies of neoadjuvant immune checkpoint inhibition in NSCLC."

Commenting on the study, Professor Pieter Postmus, chair of Thoracic

Oncology at the University of Liverpool, UK, said: "There is a potential for bias when comparing a small biopsy, which might not represent the whole tumour, with the resected tumour. This is not a validated way to measure response to a treatment. It describes a biological effect but whether that has any clinical impact on survival is unproven."

"Although we do not know for the time being if a major pathological response is correlated with improved survival, this method could first be validated in a cohort of patients with advanced disease by comparing the percentages of viable tumour cells in tumour biopsies taken before and four to eight weeks after immunotherapy," continued Postmus. "If in this way regression - as defined in the preoperative study - correlates with survival in patients with advanced cancer, it is likely to hold true in less advanced or resectable patients. Long-term survival data will be the ultimate test for these neoadjuvant immunotherapy strategies."

Provided by European Society for Medical Oncology

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