Immunotherapy data heralds new era of lung cancer treatment

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A new era of lung cancer therapy is close to dawning, using drugs that can prevent tumour cells from evading the immune system, experts have said at the 4th European Lung Cancer Congress.

For decades, scientists and doctors thought immunotherapy –treatments that harness the immune system to fight a disease— was of marginal benefit in lung cancer, says Jean-Charles Soria, Institute Gustave Roussy in Paris, France.

However a new class of drugs known as "immunocheckpoint regulators" have shown huge potential, Soria says. New data on several of these drugs are presented at the conference.

Two of the most interesting immunocheckpoint molecules in this setting are known as PD-1 (programmed death) and PD-L1 (programmed death ligand-1). When these molecules interact in tumours, they prevent immune cells from attacking the cancer cells, allowing them to escape and multiply.

"Blocking PD1 and PDL1 can result in striking and durable responses, with global overall response rates of 20% to 25% as monotherapy in metastatic non-small-cell lung cancer," Soria says. "These impressive results have yet to be confirmed in other trials; nonetheless immune checkpoint inhibitors will most likely become part of daily practice for non-small-cell lung cancer in the near future."

"Immunotherapy has come of age and is here to stay."

At ELCC, Armida D'Incecco from Istituto Toscano Tumori in Livorno, Italy, and colleagues, suggest that combining immunotherapy drugs with other targeted therapies in lung cancer is likely to be beneficial.

D'Incecco's group studied the expression of PD-L1 and PD-1 in a group of 123 non-small-cell lung cancer patients. They also analysed the patients' cancers for mutations in two other molecules, one called EGFR —which is the target of existing drugs gefitinib and erlotinib, and another called KRAS.

Those tumours that expressed PD-L1 tended to also carry EGFR mutations, they found. And PD-1 expression in the tissue sample was associated with KRAS mutated status.

Among patients whose tumours carried EGFR mutations, and who were treated with targeted therapies, those whose tumours were also PD-L1 positive took longer to progress, and tended toward longer overall survival than PD-L1 negative patients.

These results suggest a strong correlation between PD-L1 expression and EGFR mutation and between PD-1 expression and KRAS mutations, supporting further investigation of anti-PD-L1 or anti-PD-1 agents in combination with targeted therapies.

Commenting, Jean-Charles Soria notes: "This study suggests that PDL1 expression is correlated with EGFR mutation. If this is true, then immunocheckpoint blockade combination with EGFR tyrosine kinase inhibitors is a major path towards improving outcome of patients who have EGFR-mutant non-small-cell lung cancer." Trials to explore this relationship are underway, he says.

In related presentations at ELCC:

- Abstract 127O: Aaron S. Mansfield and colleagues from the Mayo Clinic, Rochester, USA, found that 89 of 224 mesothelioma samples expressed PD-L1, and that survival was significantly worse for patients with PD-L1 expression (6 months median survival) compared to those without PD-L1 expression (14 months median survival). PD-L1 is expressed in a substantial proportion of malignant pleural mesotheliomas and is associated with poor survival. PD-L1 expression may have important implications for the management of patients with this disease.
- Abstract 102P: C.T. Harbison and colleagues from Princeton, USA, report that PD-L1 expression on NSCLC tumours may associate with other factors, including expression of immune genes, tumour progression markers, and driver mutations that may influence the likelihood of response to the human IgG4 PD-1 immune checkpoint inhibitor antibody nivolumab.
- Abstract 96PD: J.R. Brahmer and other US researchers report clinical activity, safety and subpopulation response analysis of nivolumab in 129 pre-treated NSCLC patients, with data updated to September 2013.

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