Significant survival gains with atezolizumab vs docetaxel for non-small-cell lung cancer

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The first phase III study of PD-L1 inhibitor atezolizumab in previously-treated non-small-cell lung cancer has seen significant improvements in survival compared to standard chemotherapy, researchers reported today at the ESMO 2016 Congress in Copenhagen.

PD-L1 inhibitors are of a class of cancer immunotherapies called checkpoint inhibitors, and work by inhibiting one of the mechanisms of resistance developed by cancer cells in order to evade the immune system.

"The goal of this treatment is to allow the immune system to control and possibly eliminate cancer calls, so atezolizumab might be useful in a very large setting of different cancers," said investigator Dr. Fabrice Barlesi, head of Multidisciplinary Oncology and Therapeutic Innovations Deparment at Aix-Marseille University and the Assistance Publique Hôpitaux de Marseille, France.

The OAK study enrolled 1225 patients with previously treated non-small-cell lung cancer and, after stratifying them according to PD-L1 status, number of prior chemotherapy regimens and histology, randomised them to intravenous atezolizumab (1200mg every 3 weeks) or docetaxel (75 mg/m2 every 3 weeks).

In the preliminary analysis of data from 850 patients, researchers saw a 27% improvement in overall survival in the patients receiving azetolizumab compared to those treated with docetaxel (p=0.0003),

regardless of their PD-L1 expression levels and including patients with PD-L1 expression of less than 1%.

When patients were stratified according to their level of PD-L1 expression, the overall survival was 59% greater among patients in the highest tertile of PD-L1 expression who were treated with azetolizumab, compared to the same group treated with docetaxel (P

However even in patients with no PD-L1 expression, there was still a significant 25% improvement in overall survival with atezolizumab compared to those treated with docetaxel. The improvements in overall survival were similar in patients with squamous and non-squamous histology.

"This is the first phase III study of atezolizumab, a PD-L1 inhibitor, and it confirms the efficacy seen in the POPLAR phase II study, along with the results of PD-1 inhibitors" said Barlesi.

"Azetizolumab offers a new second-line therapeutic strategy for patients with non-small-cell lung cancer, regardless of the PD-L1 status of the tumor."

Commenting on the study, Professor Martin Reck, from the Department of Thoracic Oncology at

Lung Clinic Grosshansdorf, Germany, said: "This is a very important piece of information on the role of PD-L1/PD-1 antibodies in treatment of non-small-cell lung cancer, and confirms the overall survival benefits shown in the POPLAR and CHECKMATE trials."

"Interestingly, the study also showed an improvement in overall survival, even in patients with no PD-L1 expression, which means we have a problem with using PD-L1 negativity as an exclusion factor for

treatment," Reck explained.

"My suggestion would be that PD-L1 is perhaps one imperfect surrogate marker to describe the activity; it's a good enrichment factor but we need additional markers for the characterization of patients who might not benefit from this treatment or who might really benefit."

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