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IMMUNOTHERAPY

Atezolizumab becomes POPLAR

Second-line and third-line systemic chemotherapy, with agents such as docetaxel, provides limited benefit for patients with advanced-stage non-small-cell lung cancer (NSCLC). Now, the results of POPLAR, a phase II trial conducted by Louis Fehrenbacher and collaborators, indicate that patients with NSCLC who have received prior treatment can benefit from anti-PD-L1 antibodies.

In this study, patients with progressive NSCLC after platinum-based therapy were randomly assigned to receive the anti-PD-L1 antibody atezolizumab ($n = 144$) or docetaxel ($n = 143$). Patients treated with atezolizumab had longer overall survival than those treated with docetaxel (12.6 months versus 9.7 months, $P = 0.04$), although the respective progression-free survival (PFS) was similar for both groups (2.7 months and 3 months). The prolonged overall survival in the absence of improved PFS suggests some patients can benefit from immunotherapy after disease progression because of the delayed antitumour effect of immunotherapy.

Baseline PD-L1 expression was measured to determine which patients derived more benefit from atezolizumab. The percentage of tumour cells expressing PD-L1 was defined as TC, and the percentage of tumour area covered by PD-L1-expressing tumour-infiltrating lymphocytes was defined as IC. The difference in overall survival was significant in patients with TC≥1% or IC≥1% ($P = 0.014$), as well as for those with TC≥5% or IC≥5% ($P = 0.005$). High levels of PD-L1 in both tumour cells and tumour-infiltrating lymphocytes were detected in less than 1% of patients, suggesting that different mechanisms regulate PD-L1 expression in NSCLC.

The results of this randomized clinical trial demonstrate that patients with progressive NSCLC after first-line chemotherapy can benefit from PD-L1 inhibition, especially those with tumours in which there is pre-existing immunity.

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ORIGINAL ARTICLE Fehrenbacher, L. *et al.* Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): a multicentre, open-label, phase 2 randomised controlled trial. *Lancet* http://dx.doi.org/10.1016/S0140-6736(16)00587-0 (2016)