

IMMUNOTHERAPY

Benefit with anti-PD-L1

In the past few years, antibodies targeting PD-1, such as pembrolizumab and nivolumab, have improved the treatment of patients with non-small-cell lung cancer (NSCLC). OAK is the first phase III trial in lung cancer of an agent targeting the ligand PD-L1. The results of this trial, reported by Achim Rittmeyer, David Gandara and coauthors, reveal that the monoclonal anti-PD-L1 antibody atezolizumab is a valid therapeutic option for patients with NSCLC.

OAK builds on the favourable results of the phase II POPLAR trial. In the OAK trial, patients with progressive squamous or non-squamous stage IIIB or IV NSCLC who had received 1–2 previous cytotoxic chemotherapy regimens (with at least one being platinum-based) were randomly assigned to receive either atezolizumab ($n=609$) or docetaxel ($n=578$). At a median follow-up duration of 21 months,

median overall survival was 13.8 months with atezolizumab, compared with 9.6 months with docetaxel ($P=0.0003$). Subgroup analysis showed an improvement in overall survival regardless of PD-L1 expression levels. Progression-free survival (PFS) was similar between both groups (2.8 months versus 4 months). Gandara explains: “results from OAK and other trials with anti-PD-L1 or anti-PD-1 agents have shown that end points such as PFS or objective response rate (ORR) might not adequately capture the potential survival benefit of this drug class, mainly owing to their unique mechanism of action.” Lower rates of grade 3/4 treatment-related adverse events were observed with atezolizumab than docetaxel (37% versus 54%).

On his future plans, Gandara states: “we are exploring the non-classical response patterns observed with these agents, which



might help explain the discordance between PFS/ORR and overall survival. To this end, we plan to do a long-term follow-up of patients enrolled in the OAK trial to evaluate the potential benefits associated with continuing atezolizumab treatment beyond progression, and until a loss of clinical benefit is observed.”

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ORIGINAL ARTICLE Rittmeyer, A. *et al.* Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. *Lancet* [http://dx.doi.org/10.1016/S0140-6736\(16\)32517-X](http://dx.doi.org/10.1016/S0140-6736(16)32517-X) (2016)

FURTHER READING 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* **387**, 1837–1846 (2016)