Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010) a randomised controlled trial

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Abstract

Background Despite recent advances in the treatment of advanced non-small-cell lung cancer, there remains a need for effective treatments for progressive disease. We assessed the efficacy of pembrolizumab for patients with previously treated, PD-L1-positive, advanced non-small-cell lung cancer. Methods We did this randomised, open-label, phase 2/3 study at 202 academic medical centres in 24 countries. Patients with previously treated non-small-cell lung cancer with PD-L1 expression on at least 1% of tumour cells were randomly assigned (1:1:1) in blocks of six per stratum with an interactive voice-response system to receive pembrolizumab 2 mg/kg, pembrolizumab 10 mg/kg, or docetaxel 75 mg/m2 every 3 weeks. The primary endpoints were overall survival and progression-free survival both in the total population and in patients with PD-L1 expression on at least 50% of tumour cells. We used a threshold for significance of p<0·00825 (one-sided) for the analysis of overall survival and a threshold of p<0·001 for progression-free survival. This trial is registered at ClinicalTrials.gov, number NCT01905657. Findings Between Aug 28, 2013, and Feb 27, 2015, we enrolled 1034 patients: 345 allocated to pembrolizumab 2 mg/kg, 346 allocated to pembrolizumab 10 mg/kg, and 343 allocated to docetaxel. By Sept 30, 2015, 521 patients had died. In the total population, median overall survival was 10·4 months with pembrolizumab 2 mg/kg, 12·7 months with pembrolizumab 10 mg/kg, and 8·5 months with docetaxel. Overall survival was significantly longer for pembrolizumab 2 mg/kg versus docetaxel (hazard ratio [HR] 0·71, 95% CI 0·58–0·88; p=0·0008) and for pembrolizumab 10 mg/kg versus docetaxel (0·61, 0·49–0·75; p<0·0001). Median progression-free survival was 3·9 months with pembrolizumab 2 mg/kg, 4·0 months with pembrolizumab 10 mg/kg, and 4·0 months with docetaxel, with no significant difference for pembrolizumab 2 mg/kg versus docetaxel (0·88, 0·74–1·05; p=0·07) or for pembrolizumab 10 mg/kg versus docetaxel (HR 0·79, 95% CI 0·66–0·94; p=0·004). Among patients with at least 50% of tumour cells expressing PD-L1, overall survival was significantly longer with pembrolizumab 2 mg/kg than with docetaxel (median 14·9 months vs 8·2 months; HR 0·54, 95% CI 0·38–0·77; p=0·0002) and with pembrolizumab 10 mg/kg than with docetaxel (17·3 months vs 8·2 months; 0·50, 0·36–0·70; p<0·0001). Likewise, for this patient population, progression-free survival was significantly longer with pembrolizumab 2 mg/kg than with docetaxel (median 5·0 months vs 4·1 months; HR 0·59, 95% CI 0·44–0·78; p=0·0001) and with pembrolizumab 10 mg/kg than with docetaxel (5·2 months vs 4·1 months; 0·59, 0·45–0·78; p<0·0001). Grade 3–5 treatment-related adverse events were less common with pembrolizumab than with docetaxel (43 [13%] of 339 patients given 2 mg/kg, 55 [16%] of 343 given 10 mg/kg, and 109 [35%] of 309 given docetaxel). Interpretation Pembrolizumab prolongs overall survival and has a favourable benefit-to-risk profile in patients with previously treated, PD-L1-positive, advanced non-small-cell lung cancer. These data establish pembrolizumab as a new treatment option for this population and validate the use of PD-L1 selection. Funding Merck & Co..