Abstract CT103: Clinical safety and efficacy of pembrolizumab (MK-3475) in patients with malignant pleural mesothelioma: Preliminary results from KEYNOTE-028


1. University of Pennsylvania, Philadelphia, PA;
2. The Royal Marsden/Nine Institute of Cancer Research, Sutton, United Kingdom;
3. Humanitas Research Hospital–Humanitas Cancer Center, Rozzano, Italy;
5. The Netherlands Cancer Institute, Amsterdam, Netherlands.

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Abstract

Background: The programmed death receptor 1 (PD–1) pathway is implicated in evasion of the antitumor immune response. Pembrolizumab is a potent, highly selective humanized monoclonal antibody against PD–1 designed to block interaction with its ligands, PD–L1 and PD–L2, thus removing inhibition of T-cell activation against cancer. PD–L1 is overexpressed in malignant pleural mesothelioma (MPM) and associated with poor prognosis. We assessed the safety and efficacy of pembrolizumab in patients with PD–L1–positive MPM.

Methods: KEYNOTE–028 (ClinicalTrials.gov, NCT02054806) is a nonrandomized, multicohort, phase Ib trial of pembrolizumab for PD–L1–positive advanced solid tumors. Key eligibility criteria for the MPM cohort were measurable disease, PD–L1 expression in ≥1% of cells in tumor nests or PD–L1–positive bands in stroma as determined by a prototype immunohistochemistry assay at a central laboratory, failure of standard therapy, Eastern Cooperative Oncology Group performance status (ECOG PS) 0–1, adequate organ function, and no autoimmune disease or interstitial lung disease. Pembrolizumab 10 mg/kg was given every 2 weeks for up to 2 years or until confirmed progression or unacceptable toxicity. Primary end points are safety, tolerability, and preliminary efficacy. Response was assessed per RECIST v1.1 by investigators every 8 weeks for the first 6 months and every 12 weeks thereafter.

Results: Of the 84 patients with MPM who were screened, 38 (45%) had PD–L1–positive tumors. Between March 2014 and December 2014, 25 patients with MPM were treated (68% men; median age, 65 years; 64% ECOG PS 1). 36% of patients had epithelioid histology. 88% of patients received ≥1 prior therapy (28% ≥2); 80% received a platinum and pemetrexed. Fifteen patients (60%) experienced a drug–related adverse event (DRAE); only 3 (12%) had grade ≥3 DRAEs. DRAEs
with incidence >25% were nausea (40%), fatigue (32%), and decreased appetite (28%). Four patients (16%) experienced immune–related AEs, but only 2 patients required dose interruption (1 because of ALT increased, 1 because of uveitis). There was no treatment–related mortality, and no patients discontinued because of DRAEs. Preliminary overall response rate (confirmed and unconfirmed) was 24% (n = 6); 13 patients (52%) had stable disease, resulting in a disease control rate of 76%. Four patients (16%) had progressive disease, and 2 patients had no assessment at the time of analysis. 16 patients (64%), including all responders, remain on treatment (duration 8+ to 24+ weeks).

Conclusion: Pembrolizumab is generally well tolerated and provides robust antitumor activity in patients with advanced PD-L1+ MPM. The 76% disease control rate in this previously treated MPM population is unprecedented and warrants further study.


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