Antitumor activity and safety of pembrolizumab in patients with PD-L1-positive nasopharyngeal carcinoma: Interim results from a phase 1b study

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Background: Engagement of the programmed death 1 (PD-1) receptor by its ligands, PD-L1 and PD-L2, normally down-regulates T-cell effector activity. Many tumors express PD-L1 and may employ this pathway to evade antitumor immunity. Nasopharyngeal carcinoma (NPC) exhibits high expression of PD-1, and expression of PD-1/PD-L1 in these tumors correlated with poor outcome. Pembrolizumab is a potent, highly selective humanized monoclonal antibody against PD-1 designed to block interaction with PD-L1 and PD-L2 and thereby enhance antitumor immune response.

We present results on the safety and antitumor activity of pembrolizumab in patients (pts) with PD-L1-positive (PD-L1+) advanced solid tumors. Key eligibility criteria for the NPC cohort included advanced (unresectable and/or metastatic) solid tumor, a failure of prior therapy, PD-L1 expression in >1% of cells in tumor nests or PD-L1+ bands in stroma as determined by a proteotypic immunohistochemical assay at a central laboratory, and ECOG performance status 0–1. Pembrolizumab 10mg/kg was given every 2 weeks for up to 2 years or until confirmed progression or unacceptable toxicity. Primary end points were safety, tolerance, 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: 27 pts were enrolled. Median (range) age was 52.0 (18−68) years; 63% were Asian. 92.5% received prior therapies for recurrent/metastatic disease (33.3% received >5 therapies). One pt experienced a complete response, 6 pts experienced partial responses and 14 had stable disease. The best overall (confirmed and unconfirmed) response rate was 25.9% (95% CI, 11.1−46.3). Most common adverse events (AEs) (>20%) were fatigue (33.3%), pruritus (29.6%), nausea (25.9%), and pyrexia (25.9%). Drug-related AEs occurred in 70.4% of pts; most common (>10%) were pruritus (25.9%), fatigue (11.1%), rash (11.1%), mucositis (11.1%), fever (11.1%), and hyperglycemia (11.1%); grade ≥3 AEs occurred in 6/27 (22.2%) pts. Currently 8 pts remain on pembrolizumab treatment.

Conclusion: This is the first demonstration of clinical activity of PD-1 blockade in patients with recurrent/metastatic NPC. Pembrolizumab was well tolerated and had significant antitumor activity as assessed by confirmed and unconfirmed response rate (25.9%) in pts with NPC. This preliminary result for clinical efficacy will be further investigated.

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