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PD-1 Blockade in Advanced Adrenocortical Carcinoma

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BACKGROUND: Adrenocortical carcinomas (ACC) are rare and aggressive malignancies with limited treatment options.

METHODS: Patients with advanced ACC were enrolled in a phase II study to evaluate the clinical activity of pembrolizumab 200 mg every 3 weeks, without restriction on prior therapy. The primary endpoint was objective response rate. Efficacy was correlated with tumor programmed death-ligand 1 (PD-L1) expression, microsatellite-high and/or mismatch repair deficient (MSI-H/MMR-D) status, and somatic and germline genomic correlates.

RESULTS: We enrolled 39 patients with advanced ACC and herein report after a median follow-up of 17.8 months (range, 5.4 to 34.7). The objective response rate to pembrolizumab was 23% (9 patients; 95% confidence interval [CI], 11 to 39) and the disease control rate was 52% (16 patients; 95% CI, 33 to 69). The median duration of response was not reached (lower 95% CI 4.1 months). Two of 6 patients with MSI-H/MMR-D tumors responded. The other 7 patients with objective responses had microsatellite stable (MSS) tumors. The median progression-free survival was 2.1 months (95% CI, 2.0 to 10.7) and median overall survival was 24.9 months (95% CI, 4.2 to not reached). Thirteen percent (N = 5) of patients had treatment-related grade 3/4 adverse events. Tumor PD-L1 expression and MSI-H/MMR-D status were not associated with objective response.

CONCLUSION: MSI-H/MMR-D tumors, for which pembrolizumab is a standard therapy, are more common in ACC than has been recognized. In advanced ACC that is MSS, pembrolizumab provided clinically meaningful and durable antitumor activity with a manageable safety profile. (ClinicalTrials.gov number, NCT02673333)