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A Pilot Study of Pembrolizumab and Embolization or 90Y Radioembolization for Patients with Metastatic Well-Differentiated Neuroendocrine Tumors

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BACKGROUND

Well-differentiated neuroendocrine tumors (WD-NET) have a relatively low tumor mutation burden and do not commonly express the programmed death ligand 1 (PD-L1), characteristics which may limit the anti-tumor activity of PD-L1 inhibitors in this disease. Response rate to single agent immune checkpoint inhibitors (ICI) for patients with G1-3 NET is <15%. The intensity of anti-tumor immune response may be enhanced by addition of liver-directed therapy (LDT), such as embolization or ^{90}Y radioembolization targeting one or several liver lesions. This pilot study aimed to evaluate whether combining pembrolizumab with LDT results in abscopal effects for patients with WD-NET.

METHODS

In a prospective pilot study, adult patients with WHO grade 1-3 (Ki-67 index <30%) metastatic NET of any primary site received concurrent pembrolizumab 200mg every 3 weeks up to 35 doses and a single session of either liver transarterial embolization (TAE) with spherical polyvinyl alcohol particles (PVA) or transarterial radioembolization (TARE) with Yttrium-90 glass microspheres. Embolotherapy was performed for the purpose of tumor antigen exposure to the immune system and targeted no more than one liver segment. Patients with liver lesions <5cm were treated with TAE, while patients with lesions >5cm were treated with TARE. Treatment was terminated in the event of disease progression, performance status deterioration, and/or intolerable toxicity. Primary endpoint was overall response rate (ORR) at disease site(s) not targeted by embolotherapy (abscopal response). Secondary endpoints were PFS and safety.

RESULTS

A total of six patients (4 women, median age 59 years) with grade 2 (Ki-67 index 5-17%, 5 patients) or grade 3 (Ki-67 index 23%, 1 patient) WD-NET from ovary, small bowel, thymus, rectum, lung, and pancreas primary sites were included. Enrollment to TAE and TARE groups was halted after 3 out of 8 planned patients were recruited into each group due to slow accrual. No abscopal responses were observed. PFS was 6 and 10 months for patients in TAE group, and 1, 2, and 5 months in TARE group. Grade 3 pneumonitis occurred in one patient 17 days following TAE and required hospital admission and corticosteroids. Another patient was admitted to the hospital for grade 3 nausea, vomiting, and fatigue five days following TARE.

CONCLUSIONS

Combination therapy with pembrolizumab and TAE or TARE did not lead to abscopal responses in a small group of patients with metastatic WD-NET.

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