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Phase II Study of Pembrolizumab and Lenvatinib in Advanced Well-Differentiated Neuroendocrine Tumors

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BACKGROUND

Immune checkpoint inhibitors have not been shown to be active in well-differentiated NETs, with response rates <5%. Lenvatinib is a multitargeted TKI which targets VEGF and FGF receptors and has been reported to be effective in pancreatic and gastrointestinal NETs (40% and 18.5% ORR, respectively). The combination of antiangiogenic and checkpoint inhibitor therapies can be synergistic in other cancers. We therefore evaluated the combination of lenvatinib and pembrolizumab in well-differentiated GI and thoracic NETs.

METHODS

A prospective, phase II trial evaluated patients with advanced GI/thoracic NETs (pancreatic NETs were excluded due to high response rate of lenvatinib monotherapy in this patient population), with evidence of progression within 8 months of study entry and at least two prior lines of systemic therapy. Patients received lenvatinib 20mg daily and pembrolizumab 200mg IV every three weeks until unacceptable toxicity or progression of disease. Primary endpoint was objective response rate, and an interim analysis was planned once 20 patients were enrolled. 4 ORRs were required to continue enrollment.

RESULTS

20 patients were enrolled on protocol from April 2021 – January 2022 (9 small intestine, 5 lung, 2 thymic, 2 unknown primary, 1 cecal, 1 presacral primaries). Two patients reached an OR with PR (10%) (atypical lung and small intestinal primaries). Median PFS was 10 months (95% CI 5.9 – 14.1 months). 12 (60%) patients experienced probably- or definitely- associated grade 3 AEs (10 hypertension). 14 patients (70%) required dose reductions or discontinued one of the medications. Two patients discontinued treatment prior to radiographic assessment.

CONCLUSIONS

The combination of pembrolizumab and lenvatinib did not show sufficient response in patients with NETs to warrant continued enrollment on trial.

ABSTRACT ID 21453