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Immune Checkpoint Inhibitors in Progressive Neuroendocrine Tumors

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BACKGROUND: Management of progressive metastatic neuroendocrine tumors (NETs) is challenging due to limited treatment options. Recently, use of immune checkpoint inhibitors has exploded onto the field of oncology, however, unfortunately, many of the rare tumors are untouched by this immune-oncology revolution. Most of the known immune checkpoints are a set of cellular receptors or ligands, which once activated, blunt T cell response against cancer cells. Oberg et al. reported the potential benefit of interferon (INF-alfa) in NETs. Ryschich et al. were first to demonstrate the presence of CD3+T cells in pancreatic NETs. A retrospective study from Korea reported PD-L1 expression in metastatic gastroenteropancreatic NETs. 7 out of their 32 patient tumor tissue were found to be positive for PD-L1.

Similarly, Lang et al. reported PD-L1 expression in 13 out of their 45 GI NETS. We present four NET patients who had progressed through all FDA-approved agents and were at brink of hospice (Table 1).

Currently, no clinical data exists on efficacy of immune checkpoint inhibitors in NETs.

METHODS: Retrospective record based descriptive study of NET patients treated with immune checkpoint inhibitors at Markey Cancer Center.

RESULTS: One of our pancreatic NET patient showed significant improvement in quality of life and radiological stable disease for 14 months. Unfortunately, patient has finally progressed in May 2017 with new breast nodules which are histo-pathologically confirmed to be NET. Our remaining three patients continue to show radiological stable disease (8 mo, 6 mo and 4 mo). All four patients have tolerated the treatment well with improvement in quality of life. Table 1.

CONCLUSION: Our case series suggests clinical activity of immune checkpoint inhibitors in NETs. Our findings should be validated in prospective clinical trials.

Table 1:
Summary of immune checkpoint inhibitor experience in neuroendocrine tumors.

Diagnosis	Prior Treatments	Duration of Treatment	Outcome
43 y/o, Stage IV, G-II, nonfunctional pNET	somatostatin analog, sunitinib, capecitabine and temozolamide, everolimus and fosbretabulin	14 months on pembrolizumab	Progression in May 2017 after 14 month of radiological and clinically stable disease on pembrolizumab.
71 y/o, Stage IV,G-I, gastrin producing,pNET	somatostatin analog, everolimus, capecitabine and temozolomide, fosbretabulin	8 months on nivolumab	Stable disease per imaging
48 y/o, Stage IV, G-II, nonfunctional, Bronchial NET	Everolimus, capecitabine and temozolamide, sunitinib	6 months on pembrolizumab	Stable disease per imaging
49 y/o, Stage IV, G-II, Nonfunctional, NET of unknown primary	somatostatin analogs, everolimus, capecitabine and temozolamide	4 months on nivolumab	Stable disease per imaging;KPS increased from 70% to 90%