

# C-25

## A Pilot Study of Pembrolizumab and Peptide Receptor Radionuclide Therapy for Patients with Metastatic Well-Differentiated Neuroendocrine Tumors

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### BACKGROUND

Expected progression free survival (PFS) for patients with grade 3 well-differentiated neuroendocrine tumors (WD NET) treated with peptide receptor radionuclide therapy (PRRT) is approximately 9 months, and objective response rate (ORR) is 35%. Response rate to single agent immune checkpoint inhibitors (ICI) for patients with G1-3 NET is <15%. Delivery of targeted radiation using PRRT may potentiate the anti-tumor immune response. The purpose of this study is to evaluate safety and efficacy of the combination of PRRT and PDL-1 inhibitor pembrolizumab in high risk NET.

### METHODS

In a single arm prospective pilot study, adult patients with WHO grade 2 or 3 (Ki-67 index > 10%) metastatic NET of any primary site received concurrent pembrolizumab 200mg every 3 weeks up to 35 doses and up to 4 doses of <sup>177</sup>Lu-DOTATATE PRRT (200mCi) at 8 week intervals. Treatment was terminated in the event of disease progression, performance status deterioration, and/or intolerable toxicity. Primary endpoint was best observed objective response rate (ORR) by RECIST v.1.1. Secondary endpoints were PFS and safety.

### RESULTS

A total of 26 patients (15 men, median age 60 years) with grade 2 (Ki-67 index 10-20%, 6 patients) or grade 3 (Ki-67 index 21-70%, 20 patients) WD NET (15 pancreas, 6 small bowel, 3 lung, 2 other primary sites) were included. As of June 25, 2023, 13 patients have been on study for more than 24 weeks, of whom four have demonstrated PR, with all patients having shrinkage of their disease (mean 27% decrease in RECIST measurable lesions). Of the 13 patients who have been on study less than 24 weeks, three have discontinued due to progression, and 10 patients remain on trial. Grade 3 adverse events included cytopenias related to PRRT in four patients and diabetes mellitus attributable to pembrolizumab in one patient. Updated safety, PFS, and ORR analyses will be reported.

### CONCLUSIONS

Preliminary results indicate that combination treatment with <sup>177</sup>Lu-DOTATATE PRRT and pembrolizumab is well tolerated and leads to durable disease control in a subset of patients.

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