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Pembrolizumab (P) Monotherapy in Patients with Previously Treated Metastatic High Grade Neuroendocrine Neoplasms (HG-NENs)

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BACKGROUND: There is currently no standard therapy for metastatic HG-NENs after progression on platinum based therapy and available chemotherapy is of limited benefit. Given the promising activity of checkpoint inhibitors in small cell lung cancer, we initiated a phase II trial of P (PD-1 inhibitor) in pts with previously treated metastatic HG-NENs

METHODS: A prospective, open-label, phase 2 trial, for which pts with metastatic, histologically confirmed HG-NENs (Ki67 > 20%), excluding lung/thymus origin, were eligible after prior platinum based therapy. Other eligibility criteria included ECOG PS 0–1, adequate hematological, hepatic, and renal function. Pt selection was not based on PD-L1 expression but archival tissue was mandated for correlative testing of immunophenotype. P was administered at a dose of 200 mg every 3 weeks intravenously and radiographic evaluation was conducted every 9 weeks. The primary endpoint was overall response rate (ORR).

RESULTS: Between 11/ 2016 and 1/ 2018, 21 pts (11 males/ 10 females) were enrolled from two institutions and received at least one dose of P, thus completing accrual. Nine grade 3 toxicities were observed (42%) with 6 (28%) at least possibly related to P (elevated liver enzymes, hypercalcemia and hyperkalemia). Other common grade 1-2 toxicities observed include fatigue

(28%), diarrhea (19%) and nausea/vomiting (33%). ORR was 4.7% and disease control rate was 19%. Median PFS and OS were 9.1 weeks (95% CI (6.71,13.14) and 15.4 weeks 95% CI (13, not reached) respectively. Correlative studies are underway and will be presented at the meeting.

CONCLUSION: P showed limited activity as a single agent in HG-NENs in this study. Correlative testing to guide biological basis of response and evaluate the one exceptional responder ongoing. Future studies combining immunotherapeutic agent with a cytotoxic drug may be of interest in this aggressive tumor type. Clinical trial information: NCT02939651