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Avelumab in Unresectable/ Metastatic, Progressive, Grade 2-3 Neuroendocrine Neoplasms (NEN): Combined Results from NET-001 and NET-002 Trials

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BACKGROUND: Higher grade NENs continue to be a treatment dilemma, with the best treatment in any situation still unknown. Although immunotherapy has revolutionized the treatment of many cancers, its role in NENs remains unclear.

METHODS: NET-001 and NET-002 are a pair of phase II studies investigating avelumab, a PD-L1 blockade agent. (NCT03278405, NCT03278379) Patients with WHO G2-3 NENs from a gastroenteropancreatic (GEP) or lung primary, 0-2 prior lines of therapy (excluding SSAs), were treated with avelumab 10mg/kg intravenously every 2 weeks for 26 cycles. NET001 investigated G3 poorly differentiated NECs whereas NET002 investigated G2-3 well differentiated NET. The primary endpoint in both trials was overall response rate (ORR) by RECIST v1.1; secondary endpoints included progression-free survival, overall survival, disease control rate at 6 months and toxicity.

RESULTS: Twenty-seven patients were enrolled (21 GEP, 6 lung; 10 in NET-001, 17 in NET-002). The median age was 64 (range 37-80), 30% had ECOG PS 1-2, and 78% received ≤ 1 prior therapy. The median Ki-67 index was 35% (range 10-100). In the efficacy population (n=24), 12 patients had died at time of data lock. The median time on treatment was 85 days (7 cycles). No objective responses were observed. Stable disease was achieved in 33% of patients, and the disease control rate at 6 mo was 21%.

The median PFS was 3.3 months (range 1.2-24.6), and median OS was 14.2 months. In the safety population (n=25), treatment-related adverse events (all grades) occurred in 58% of patients. Three patients had treatment-related grade 3-4 AEs leading to treatment discontinuation (hepatitis – 2, infusion-related reaction - 1).

CONCLUSION: Single-agent PD-L1 blockade with Avelumab showed limited antitumor activity in patients with G2-3 NENs. Correlative studies are underway. Further studies are needed to explore the role of dual immunotherapy and other combinations in this population with few treatment alternatives.

ABSTRACT ID: 164