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NEUROENDOCRINE TUMOURS

1308O Activity & safety of spartalizumab (PDR001) in patients (pts) with advanced neuroendocrine tumors (NET) of pancreatic (Pan), gastrointestinal (GI), or thoracic (T) origin, & gastroenteropancreatic neuroendocrine carcinoma (GEP NEC) who have progressed on prior treatment (Tx)

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Background: PDR001 is a high-affinity, humanized, anti-PD-1 IgG4 antibody that blocks PD-L1 & PD-L2 binding to PD-1. A phase 2, multi-center study assessed the efficacy & safety of PDR001 in pts with nonfunctional well- & poorly-differentiated (diff) neuroendocrine neoplasms.

Methods: Pts with advanced NET (GI, Pan, or T origin) who have progressed on prior Tx (including everolimus), & GEP NEC pts who have progressed on 1 line of chemoTx, were enrolled, regardless of PD-L1 expression. Primary endpoint was overall response rate (central; ORR). Secondary endpoints were duration of response, biomarker analyses & safety.

Results: Total 116 pts enrolled (33 panNET, 32 GI NET, 30 T NET, & 21 GEP NEC). Pts received PDR001 (400 mg, q4w) via 30 min IV infusion until disease progression/unacceptable toxicity. At data snapshot cut-off (Feb 09, 2018) with median follow-up of 7.6 mo in NET and 6 mo in GEP NEC, ORR was 7.4% in well-diff NET (pooled) & 4.8% in poorly-diff GEP NEC. Pts with T NET had higher ORR, while, clinical activity was marginal in other cohorts (Table). Most common grade 3/4 adverse events (>2.5%) regardless of causality were abdominal & back pain, anemia, dyspnea, & hypertension. PD-L1 expression was generally low; GEP NEC pts had a higher proportion of PD-L1 expression in immune cells >1% (43% vs T NET: 19%; panNET: 23%; GI NET: 10%). Biomarker results suggest a potential link between TIM-3 expression & lack of Tx response. Additional biomarker data will be presented.

Table: 1308O

	T*	P	GI	Overall NET (T+P+GI)	GEP NEC
Partial response, %	20.0	3.0	0	7.4	4.8
Stable disease, %	53.3	54.5	59.4	55.8	14.3
Unknown, %	10.0	3.0	6.3	6.3	14.3
Disease control rate, %	73.3	57.6	59.4	63.2	19.0

*All responses were observed in atypical carcinoid cohort.

Conclusions: These preliminary results suggest clinical activity of spartalizumab in pts with well-diff nonfunctional NET of T origin. Further studies are needed to explore the role of immunotherapy combinations, identifying predictive biomarkers for immunoncology (IO) response or strategies to increase response to IO in this pt population.

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