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Toxicity Update on the First Real World Experience of Peptide Receptor Radionuclide Therapy (PRRT) in Neuroendocrine Tumors (NET) Since US FDA Approval

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BACKGROUND: Real-world toxicity data on 177Lu-DOTATATE in the US is lacking. We recently reported the first real-world experience of PRRT in NET (Konda et al, E-Abstract ASCO 2019). Here, we present updated toxicity data in these patients.

METHODS: We reviewed medical records of patients who began PRRT between 03/14/18-10/01/18 at the Ohio State University. 177Lu-DOTATATE was administered at 200mCi over 20-30min every 8 weeks for 4 doses. Arginine-lysine 25gm/25gm in 1L saline and intravenous palonosetron 0.25mg were infused over 4hrs, starting 30min pre-treatment. Clinical evaluation occurred 2 weeks before and after each PRRT dose, and radiographic assessment using contrast CT/ MRI was performed following 2 and 4 doses. Patients who received ≥1 PRRT doses were considered evaluable for adverse events (AEs).

Results: 52 patients were evaluable for toxicity. All patients had metastatic disease. Primary site was GI (65%), pancreas (12%), lung (8%), unknown (8%), GI and pancreas (4%), ampulla (2%), and 1 patient (2%) had paraganglioma. 31% of patients had grade 1 (G1), 54% G2, 6% G3 (Ki-67: 25%, 29%, and 40%), and 10% unknown grade of tumor. 8% of patients were systemic therapy

naïve, 31% received ≥2 prior systemic therapies (not including a somatostatin analogs), and 38% had ≥1 prior liver-directed therapy. Most TRAEs were grade 1/2 including fatigue, nausea/vomiting, abdominal pain, transaminase elevation, and cytopenias. 9/52 (17%) had Grade 3/4 TRAEs that led to treatment discontinuation (Table 1). Attribution of AEs for patients #1-8 in Table 1 was possibly related to PRRT and likely/possibly related to disease; and for patient #9 was likely related to PRRT and unlikely to disease.

CONCLUSION: 177Lu-DOTATATE is generally well tolerated. Caution is needed in patients with high tumor burden in the liver or peritoneum, intestinal luminal compression by tumor, or with mesenteric ischemia from underlying tumor.

Table 1. Treatment-related adverse events leading to treatment discontinuation

ID#	AE (grade)	Onset of AE (approx)	Predisposing factor(s)
1	Edema, limbs (G3) Blood Bilirubin increased (G2)	2 days after dose #2 2 wks after dose #2	Extensive liver metastases and hypoalbuminemia
2	Duodenal obstruction* (G3)	6 wks after dose #1	Baseline grade 2 duodenal obstruction*
3	Duodenal obstruction* (G3)	5 days after dose #1	Large mesenteric mass inseparable from duodenum
4	GI, other: Small bowel enteritis (G3) Visceral arterial ischemia (G4)	2 wks after dose #1 8 wks after dose #1	Symptomatic mesenteric mass with worsening abdominal pain
5	Generalized edema (G3) Blood bilirubin increased (G3)	4 days after dose #1 1-5 wks after dose #1	Extensive liver metastases with portal hypertension, hypoalbuminemia
6	Bone pains, Myalgias (G3) Fatigue (G3)	<24 hours of dose #1 2 wks after dose #1	Extensive bone and liver metastases
7	Neutrophil count decreased (G4)	3 wks after dose #1 and #2 8 wks after dose #3	Extensive bone and bone marrow metastases Grade 3 neutropenia pre-PRRT

Table 1 (continued)

8	Small bowel obstruction (G3)	1 day after dose #3	Extensive peritoneal carcinomatosis
9	^ALT increase, #AST increase (G3) ^ALT increase, #AST increase (G3) (Imaging showed cholelithiasis and choledocholithiasis)	2 wks after dose #1 9 wks after dose #3	None (Baseline imaging showed no gallstones)

*Extrinsic compression by tumor ^Alanine aminotransferase, #Aspartate aminotransferase