Outcomes of Locoregional Treatment for Unifocal Progression in Widespread Metastatic Gastroenteropancreatic Neuroendocrine Tumors

Taymeyah E. Al-Toubah, Mauro Cives, Daniel A. Anaya, Heloisa P. Soares, Jonathan R. Strosberg

H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida

Abstract

Background: New systemic treatments have improved the therapeutic landscape for patients with progressive, metastatic GEP-NETs. While drugs such as everolimus are appropriate for patients with widespread disease progression, local treatment approaches may be more appropriate for patients with unifocal progression. Surgical resection, radiofrequency ablation (RFA), hepatic arterial embolization (HAE), or radiation, can control discrete sites of progression, allowing patients to continue their existing therapy, and sparing them toxicities of a new systemic treatment.

Methods: We reviewed records of patients treated at a large referral center to identify patients seen between 1/2014 and 5/2017 with metastatic GEP-NETs who underwent a local treatment for focal progression. Patients undergoing lobar HAE or cytoreductive hepatic surgery were not included. The primary endpoint was time to new systemic therapy. Secondary endpoints included time to any additional intervention (systemic or local), progression free survival, and side effects of treatment.

Results: 59 patients were identified who underwent a form of local treatment for a progressive metastatic tumor in the setting of widespread metastases. 27% underwent resection, 29% RFA, 25% external beam radiation, and 19% selective HAE. With a median follow-up of 17 months, 19 patients (32.2%) eventually progressed to the extent that they received salvage systemic treatment. 6 patients (10.2%) progressed and received further local treatment. Median time to new systemic treatment was 42 months (95% CI, 9.7-74.3 months). Median time to any additional intervention was 21 months (95% CI, 11.4-30.6 months). 4 patients died, all of whom had progressed and received further systemic treatment.

Conclusions: We identified a large cohort of patients with metastatic GEP-NETs who underwent a local treatment for unifocal progression in the setting of widespread metastases. Control of local sites of progression enabled the majority of patients to remain on their existing systemic treatment and avoid potential toxicities associated with salvage systemic therapy.

Demographics and Baseline Therapies

Gender, n (%)	
Female	24 (40.7%)
Male	35 (59.3%)
Primary tumor site, n (%)	
Cecum	1 (1.7%)
Pancreas	29 (49.2%)
Rectum	1 (1.7%)
Small Intestine	25 (42.4%)
Stomach	1 (1.7%)
Unknown	2 (3.4%)
Grade, n (%)	
High	2 (3.4%)
Intermediate	16 (27.1%)
Low	38 (64.4%)
Unknown	3 (5.1%)
Site of metastasis treated, n (%)	
Bone	1 (1.7%)
Liver	42 (71.2%)
Lung	2 (3.4%)
Lymph Node	6 (10.2%)
Ovary	6 (10.2%)
Peritoneum	2 (3.4%)
Adverse Events, n (%)	
No*	46 (78.0%)
Yes	13 (22.0%)
Baseline Systemic Therapies, n (%)	
Yes	47 (79.6%)
• Somatostatin Analogs (SSA)	40 (67.8%)
• SSA + cytotoxic chemotherapy	2 (3.4%)
• SSA + everolimus	1 (1.7%)
• Everolimus	2 (3.4%)
• Cytotoxic chemotherapy	2 (3.4%)
No	12 (20.4%)

*14 (23.7%) patients reported resolution of pre-existing symptoms and better QoL post locoregional treatment

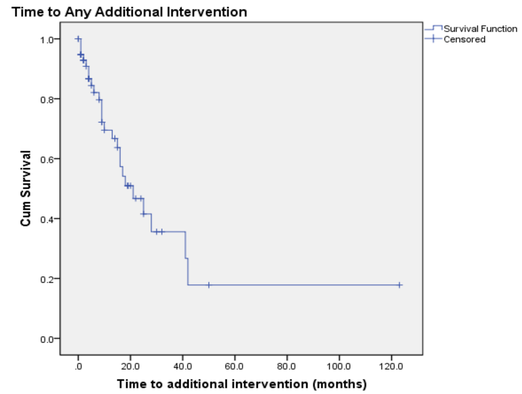
Post Recurrence Therapies

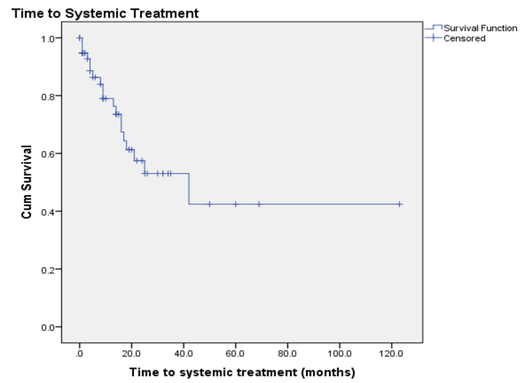
19 patients (32.2%) received systemic therapy upon recurrence

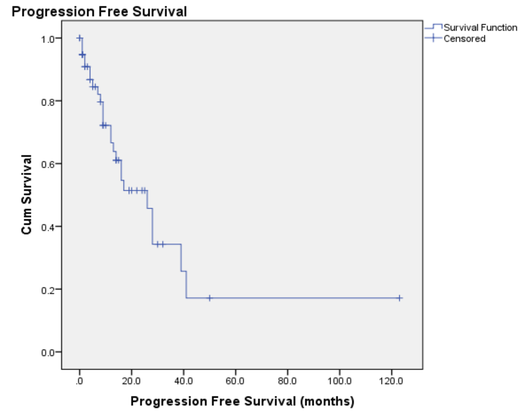
12 (20.3%) patients had previously been on systemic therapy
- Sunitinib – 3 patients
- Everolimus – 2 patients
- Avastin – 1 patient
- Cytotoxic chemotherapy – 4 patients
- High Dose Octreotide – 1 patient
- PRRT – 1 patient

7 (11.9%) patients were not on any prior continuous systemic therapy
- SSA – 1 patient
- Immunotherapy – 1 patient
- Cytotoxic chemotherapy – 2 patients
- Everolimus – 2 patients
- Avastin – 1 patient

Adverse Event	n (%)	Duration
Vomiting	2 (3.4%)	5 days post procedure
Infection	1 (1.7%)	2 weeks
Pain	6 (10.2%)	Intermittent
Diarrhea	3 (5.1%)	Intermittent
Skin irritation	1 (1.7%)	Intermittent







	Type of Locoregional Treatment				Totals
	Surgical Resection	Embolization	RFA	Radiation	
Subsequent Intervention, n (%)					
No	10 (62.5%)	4 (36.4%)	12 (70.6%)	8 (53.3%)	**34 (57.6%)**
Yes	6 (37.5%)	7 (63.6%)	5 (29.4%)	7 (46.7%)	**25 (42.4%)**
Systemic treatment, n (%)	6 (37.5%)	6 (54.5%)	3 (17.6%)	4 (26.7%)	**19 (32.2%)**

	Median (months)	95% CI (months)
Time to Additional Intervention	21	11.4 – 30.6
Time to Systemic Treatment	42	9.7 – 74.3
PFS (n=25)	26	16.7 – 35.3