To Treat or Not to Treat: Resection of Primary Pancreatic Neuroendocrine Tumors in the Metastatic Setting

Sarah Wornow BS[1], Daniel M. DePietro MD[1], Robert Roses MD[2], Jennifer Eads MD[3], Michael C. Soulen MD[1]

Divisions of Interventional Radiology[1], Surgical Oncology[2], GI Medical Oncology[3], Abramson Cancer Center, University of Pennsylvania

Introduction

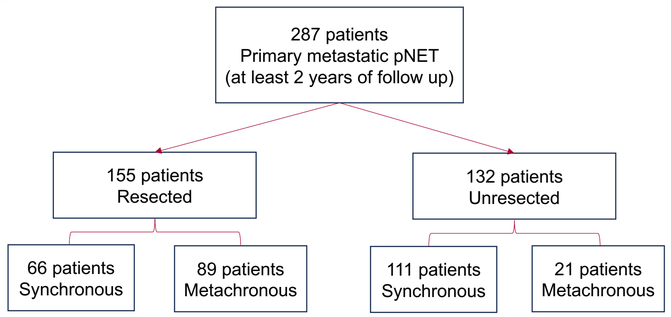
- Surgical resection of the primary tumor is the standard of care for metastatic small bowel neuroendocrine tumors (NETs) and is associated with increased overall survival.[1]
- The benefit of resecting pancreatic NETs (pNETs) in the metastatic setting is unclear.[2-4]
- To better understand pNET treatment outcomes and develop further pancreas-directed therapies, we compared progression and overall survival of a cohort of unresected metastatic pNET patients with patients who underwent resection of their primary tumor.

Purpose: To compare survival outcomes of metastatic pNET patients who underwent resection of their primary tumor to unresected patients.

Materials & Methods

Data Collection

- The healthcare system database was searched to find all patients with metastatic primary pancreatic neuroendocrine tumors and at least 2 years of follow up
- 287 total patients were found and divided into the following groups:



Statistical Analysis

- Kaplan-Meier progression-free survival (PFS) and overall survival (OS) curves were generated for each group and compared using a log-rank test

Results

Result #1: Distal pancreatectomy was the most common type of resection

- Among the 155 patients who underwent resection, the breakdown of resection type is as follows:
  - 54% Distal Pancreatectomy
  - 37% Whipple
  - 9% Enucleation or Partial Resection

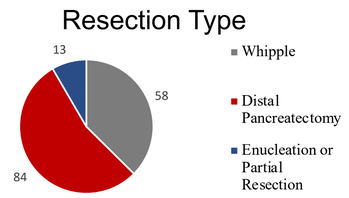


Figure 1: Number of patients by resection type

Result #2: Complications are common post-resection

Major operative complications (31%)

- Infection
- Pancreatic leak
- Fistula
- Bowel obstruction
- DVT/PE
- Cardiac events

Long term morbidity (70%)

- New/worsening diabetes
- Exocrine insufficiency (requiring Creon)

Result #3: Metastatic pNET patients who underwent primary tumor resection had improved survival

- Statistically significant improvements in PFS and OS were observed in patients who underwent resection of the primary tumor ($p < 0.0001$)

	Resected	Unresected
Median PFS (months)	38.1	8.5
Median OS (months)	190	45.6

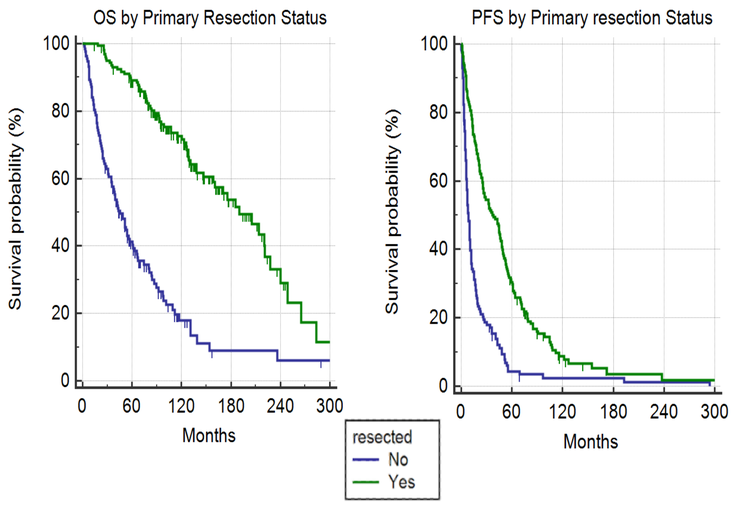


Figure 2: OS and PFS of resected and unresected metastatic pNET patients

Result #4: Patients with synchronous metastases who underwent resection showed significantly improved survival

- Statistically significant improvements in PFS and OS were observed in patients who underwent resection of the primary tumor ($p < 0.001$)

	Resected	Unresected
Median PFS (months)	20	8
Median OS (months)	47	38

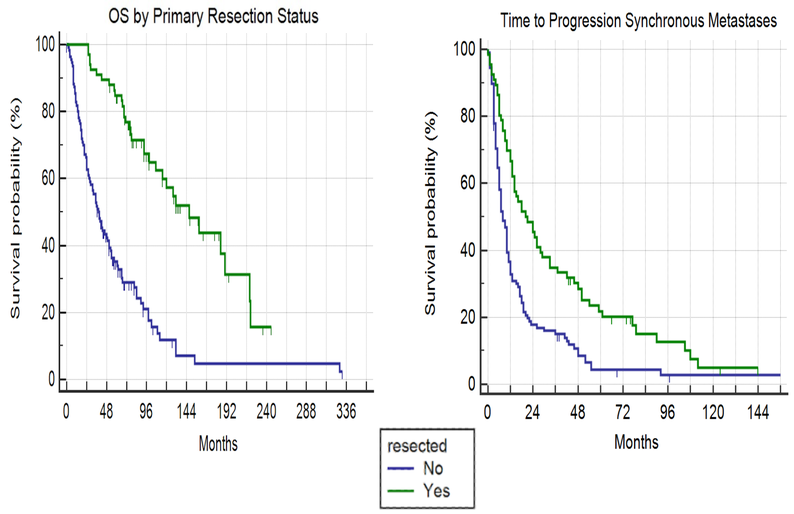


Figure 3: OS and PFS of resected and unresected synchronous metastatic pNET patients

References

1 Howe, James R et al. "The Surgical Management of Small Bowel Neuroendocrine Tumors: Consensus Guidelines of the North American Neuroendocrine Tumor Society." *Pancreas* vol. 46,6 (2017): 715-731. doi:10.1097/MPA.0000000000000846
2 Fujimori, Nao et al. "Natural history and clinical outcomes of pancreatic neuroendocrine neoplasms based on the WHO 2017 classification; a single-center experience of 30 years." *Pancreatology : official journal of the International Association of Pancreatology (IAP) ... [et al.]* vol. 20,4 (2020): 709-715. doi:10.1016/j.pan.2020.04.003
3 Franko, Jan et al. "Non-functional neuroendocrine carcinoma of the pancreas: incidence, tumor biology, and outcomes in 2,158 patients." *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract* vol. 14,3 (2010): 541-8. doi:10.1007/s11605-009-1115-0
4 Bilimoria, Karl Y et al. "Clinicopathologic features and treatment trends of pancreatic neuroendocrine tumors: analysis of 9,821 patients." *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract* vol. 11,11 (2007): 1460-7; discussion 1467-9. doi:10.1007/s11605-007-0263-3

Conclusions

- Resection of the primary tumor in patients with metastatic pNETs is associated with considerable improvements in PFS and OS
- Post-pancreatectomy short- and long-term morbidity is common
- Multivariate analyses incorporating tumor grade, type of resection, and other therapies are underway
- These data provide a basis for designing trials of pancreas-directed therapies in the metastatic pNET setting