

National Cancer Institute

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Pancreatic Neuroendocrine Tumors (Islet Cell Tumors) Treatment (PDQ®)

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General Information About Pancreatic Neuroendocrine Tumors (Islet Cell Tumors)

Incidence and Mortality

They are uncommon cancers with about 1,000 new cases per year in the United States.[1] They account for 3% to 5% of pancreatic malignancies and overall have a better prognosis than the more common pancreatic exocrine tumors.[1,2] Five-year survival is about 55% when the tumors are localized and resected but only about 15% when the tumors are not resectable.[2] Overall 5-year survival rate is about 42%.[1]

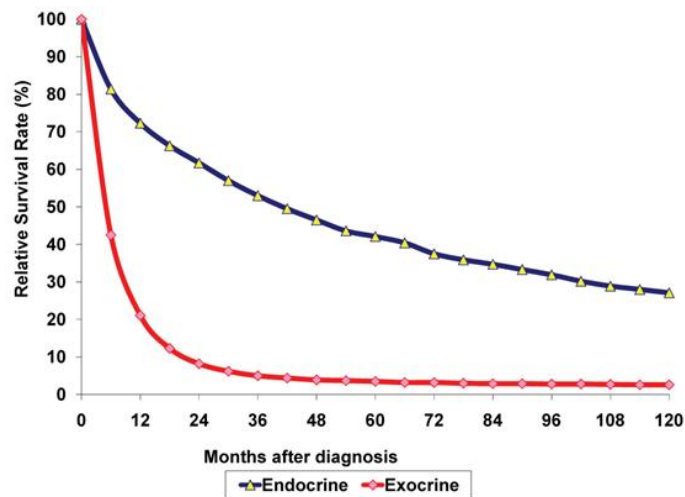


Figure 1. Cancer of the Pancreas: Relative Survival Rates (%) by Histologic Subtype, Ages 20+, 12 SEER Areas, 1988-2001. Key, C. Ch 7: Cancer of the pancreas. In: Ries LAG, Young JL, Keel GE, et al. (eds). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program, NIH Pub. No. 07-6215, Bethesda, MD, 2007.

Pathogenesis

Tumors of the endocrine pancreas are a collection of tumor cell types collectively referred to as pancreatic neuroendocrine tumors (NETs). These tumors originate in islet cells. Although they may be similar or identical in histologic appearance to carcinoid tumors of the gastrointestinal tract, differences in their underlying biology and likely differences in response to therapeutic agents suggest that they should be treated and investigated as a distinct entity.[3]

Most pancreatic NETs are sporadic, but some occur as part of the autosomal dominant multiple endocrine neoplasia type-1 (MEN-1) inherited syndrome consisting of tumors of the anterior pituitary, parathyroid, and endocrine pancreas glands, which results from the inactivation of the tumor suppressor gene *Menin* located on chromosome 11q13.[4] When part of the MEN-1 syndrome, there may be multiple pancreatic tumors.

Islet tumors may either be functional (produce one or more active hormones) or nonfunctional.[4] The functional tumors, which usually present with symptoms of hormone hypersecretion, include:

- Gastrinoma.
- Insulinoma.
- Glucagonoma.
- Somatostatinoma.
- VIPoma.

Prognostic Factors

Most islet cell cancers are functional, but about 15% are nonfunctional, with presentations similar to the

far more common exocrine adenocarcinomas of the pancreas.[5-7] Because of the presence of several cell types in the pancreatic islets (alpha, beta, delta, A, B, C, D, E, F), the term, islet cell tumors, refers to at least five distinct cancers that, when functional, produce unique metabolic and clinical characteristics. The clinical manifestations in functional tumors may result from the distinctive metabolic effects of the polypeptide(s) secreted by the cancer cells rather than from tumor bulk or metastatic disease. Functional tumors may even be too small to be detected by conventional imaging techniques.

Nonfunctional tumors tend to present at later clinical stages with symptoms attributable to mass effect or metastases.[4] Although nonfunctional tumors do not produce specific clinical syndromes, they may secrete inactive amine and peptide products such as the following:

- Neurotensin.
- Alpha-subunit of human chorionic gonadotropin (alpha-hCG).
- Neuron-specific enolase.
- Pancreatic polypeptide.
- Chromogranin A.

Diagnosics

The frequent long delays between initial symptoms and diagnosis and the varied effects of the polypeptides secreted often necessitate involvement of multiple surgical and medical subspecialties. Surgery is the only curative modality. Surgery is often used even in the setting of metastatic disease to alleviate the symptoms of hormonal hypersecretion.[4] Effective palliation may be achieved because of the slow-growing nature of the majority of these tumors and the potential use of antihormonal pharmacologic therapy (e.g., cimetidine in the ulcer-producing Zollinger-Ellison syndrome). In patients with indolent, slow-growing metastatic islet cell tumors, the best therapy may be careful observation, and no treatment until palliation is required. In patients with MEN-1 in which 85% have pancreatic islet cell tumors, 90% have hyperparathyroidism, and 65% have pituitary tumors, and they are less likely to be cured by pancreatic resection than are patients with sporadic islet cell tumors. With the exception of pain relief from bone metastases, radiation therapy has a limited role in this disease.

Tumor localization and staging studies include imaging with computed tomography (CT) with or without magnetic resonance imaging (MRI), and endoscopic ultrasound. In addition, somatostatin-receptor scintigraphy and single-photon emission CT may be useful adjuncts. However, somatostatin-receptor scintigraphy has diminished utility in localizing insulinomas versus other pancreatic NETs, since insulinomas often have a low density of somatostatin receptors.[4] If the noninvasive tests do not reveal a tumor, but clinical suspicion remains high, more invasive and technically demanding tests, such as selective arteriography or selective arterial stimulation (with a secretagogue specific for the suspected tumor type), may be useful.[7]

Some of the tumor types have unique characteristics that require specific approaches in their diagnosis and initial evaluation.

Gastrinoma

Diagnosis is dependent on elevated serum gastrin and elevated gastric acid levels. Provocative testing

with calcium and secretin shows considerable overlap, and the value of these tests is limited. Zollinger-Ellison syndrome (ZES) is a syndrome of unrelenting peptic ulcer disease, diarrhea, and gastric hyperacidity, associated with a gastrin-producing tumor. (Refer to the Diarrhea section in the PDQ summary on Gastrointestinal Complications for more information.) It accounts for less than 1% of all peptic ulcer disease. About 15% to 35% of gastrinomas are associated with the MEN-1 syndrome and up to 50% are malignant. Up to 33% of gastrinomas have liver metastases.[4]

Diagnostic tests:

1. BAO:MAO \geq 0.6 (Basal Acid Output:Maximal Acid Output).
2. Overnight AO \geq 100 mmol.
3. BAO \geq 10 mmol/hr.
4. Serum gastrin 10 times normal or >500 pg/mL (the accuracy of gastrin assays may vary widely).
5. Secretin test: 1 unit/kg IV rapid injection: Positive = 100% increase in gastrin within 10 minutes; 2 units/kg: Positive = 100% increase over baseline.
6. Elevated human chorionic gonadotropin levels.

Insulinoma

Insulinomas are far more likely to be benign than malignant. Only 10% are multiple, and only 10% are malignant. About 5% to 8% are associated with MEN-1 syndrome.[4] The clinical manifestations are those of hypoglycemia, which results from inappropriate secretion of insulin by the tumor. Fasting hypoglycemia (<40 mg/dL) associated with an elevated insulin level (in the absence of exogenous administration of insulin) is pathognomonic. Measurement of plasma proinsulin may be helpful for diagnosing insulin-secreting carcinomas. These tumors are usually slow-growing tumors and, when localized to the pancreas or regional lymph nodes, can be cured with pancreatic resection.

The approach to management depends on carefully performed preoperative localization studies and the findings at exploratory laparotomy. In a retrospective case series of 30 patients with 32 pancreatic insulinomas, the combination of preoperative dual-phase thin-section multidetector CT and endoscopic sonography correctly identified and localized all of the tumors.[8] These tests, with or without MRI, have replaced older, more invasive, and technically challenging tests, such as percutaneous transhepatic portal venous sampling and arterial stimulation with venous sampling except for unusual circumstances in which the imaging tests are unsuccessful.[4,9]

Glucagonoma

Glucagonoma is the third most common endocrine-secreting islet cell tumor. About 75% of glucagonomas are malignant.[4] Necrolytic migratory erythema, hyperglycemia, and venous thrombosis comprise a virtually diagnostic triad. A serum glucagon level greater than 1000 pg/mL confirms the diagnosis. These tumors tend to be large and easily visible on CT scan. Somatostatin receptor scintigraphy scanning may be a useful adjunct in detecting metastases.

Miscellaneous islet cell tumors

These tumors are rare but have defined clinical syndromes associated with specific production of polypeptide hormone production by islet cell tumors. Because of their rarity and similar approaches to

management, they are grouped in the section on treatment. Miscellaneous tumors include the following:

- VIPoma (Verner-Morrison Syndrome) is characterized by watery diarrhea, hypokalemia, and achlorhydria.

A serum vasoactive intestinal peptide (VIP) greater than 200 pg/mL is diagnostic.[4] These tumors can generally be easily localized by CT scan. Somatostatin receptor scintigraphy scanning may be a useful adjunct in detecting metastases.

- Somatostatinoma.

These tumors are particularly rare. They often present with diarrhea, steatorrhea, diabetes, and/or gallstones. Decreased pancreatic secretion of enzymes and bicarbonate accounts for the diarrhea and steatorrhea. Somatostatin-mediated inhibition of cholecystokinin leads to gallstone formation. Somatostatin also inhibits insulin, producing hyperglycemia. The diagnosis is made by a fasting serum somatostatin level greater than 100 pg/mL. CT scan, MRI, and endoscopic ultrasound can usually help localize and stage the tumor. Most of these tumors are malignant and have metastases at diagnosis.

Related Summaries

- Gastrointestinal Carcinoid Tumors Treatment
- Pancreatic Cancer Treatment

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Cellular Classification of Pancreatic Neuroendocrine Tumors (Islet Cell Tumors)

Table 1. Endocrine Tumors of the Pancreas

Enlarge

Islet Cells	Secreted Active Agent	Tumor and Syndrome
Alpha	Glucagon	Glucagonoma (diabetes, dermatitis)
Beta	Insulin	Insulinoma (hypoglycemia)
Delta	Somatostatin	Somatostatinoma (mild diabetes); diarrhea/steatorrhea; gallstones
D	Gastrin	Gastrinoma (peptic ulcer disease)
A -> D	VIP and/or other undefined mediators	WDHA
	5-HT	
	ACTH	
	MSH	
		Carcinoid
		Cushing syndrome
		Hyperpigmentation
Interacinar Cells	Secreted Active Agent	Tumor and Syndrome
F	Pancreatic polypeptide	Multiple hormonal syndromes
EC	5-HT	Carcinoid

ACTH = adrenocorticotropin; MSH = melanocyte-stimulating hormone; VIP = vasoactive intestinal peptide; WDHA = watery diarrhea, hypokalemia, and achlorhydria; 5-HT = serotonin.

Stage Information for Pancreatic Neuroendocrine Tumors (Islet Cell Tumors)

Note: The American Joint Committee on Cancer has published the 7th edition of the *AJCC Cancer Staging Manual*, which for the first time incorporates pancreatic neuroendocrine tumors in the same staging

system as pancreatic exocrine tumors.[1] The classification of these tumors as benign versus malignant is not always consistent, so the AJCC recommends that all pancreatic neuroendocrine tumors be staged using this system and reported to cancer registries. It also recommends that the protocol developed by the College of American Pathologists for endocrine pancreatic tumors be used to examine and stage specimens.[2]

Definitions of TNM

The American Joint Committee on Cancer has designated staging by TNM classification to define pancreatic neuroendocrine tumors (islet cell tumors).[1]

Table 2. Primary Tumor (T)^a

Enlarge

TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
Tis	Carcinoma <i>in situ</i> . ^b
T1	Tumor limited to the pancreas, ≤2 cm in greatest dimension.
T2	Tumor limited to the pancreas, >2 cm in greatest dimension.
T3	Tumor extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery.
T4	Tumor involves the celiac axis or the superior mesenteric artery (unresectable primary tumor).

^aReprinted with permission from AJCC: Exocrine and endocrine pancreas. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 241-9.

^bThis also includes the "PanInIII" classification.

Table 3. Regional Lymph Nodes (N)^a

Enlarge

NX	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis.
N1	Regional lymph node metastasis.

^aReprinted with permission from AJCC: Exocrine and endocrine pancreas. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 241-9.

Table 4. Distant Metastasis (M)^a

Enlarge

M0	No distant metastasis.
M1	Distant metastasis.

^aReprinted with permission from AJCC: Exocrine and endocrine pancreas. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 241-9.

Table 5. Anatomic Stage/Prognostic Groups^a

Enlarge

Stage	T	N	M
0	Tis	No	Mo
IA	T1	No	Mo
IB	T2	No	Mo
IIA	T3	No	Mo
IIB	T1	N1	Mo
	T2	N1	Mo
	T3	N1	Mo
III	T4	Any N	Mo
IV	Any T	Any N	M1

^aReprinted with permission from AJCC: Exocrine and endocrine pancreas. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 241-9.

Histologic Grade (G)^a

A two-, three-, or four-grade system may be used. If a grading system is not specified, generally the following system is used:

Table 6. Histologic Grading System^a

Enlarge

GX	Grade cannot be assessed.
G1	Well differentiated.
G2	Moderately differentiated.
G3	Poorly differentiated.
G4	Undifferentiated.

G = grade

^aReprinted with permission from AJCC: Exocrine and endocrine pancreas. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 241-9.

Current Clinical Trials

Check for U.S. clinical trials from NCI's list of cancer clinical trials that are now accepting patients with islet cell carcinoma. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

General information about clinical trials is also available from the NCI Web site.

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Treatment Option Overview

Localized Disease

If technically and medically feasible, primary management of endocrine tumors of the pancreas involves surgical resection with curative intent. Given the rare nature of these tumors, surgical approaches are based upon case series and expert opinion rather than randomized controlled trials.[1] The surgical options listed below are based on retrospective series from single reporting centers.[2-4][Level of evidence: 3iiD or 3iiiD]

Adjuvant therapy has no proven benefit and is, therefore, investigational. There have been no well-controlled trials of adjuvant therapy after complete tumor resection.[5]

Surgical Cytoreduction for Metastases

Surgery plays a role even in the setting of metastatic disease. The symptoms of metastatic functional pancreatic neuroendocrine tumors (NETs) may be ameliorated by the reduction of overall tumor burden through surgical debulking.

The liver is a common site of metastasis from pancreatic NETs. Because of the slow growth rate of many NETs, liver metastases are often resected when technically feasible. Resection of all grossly visible liver metastases can be associated with long-term survival and, in the case of symptomatic hormonally functional tumors, symptom relief.[6] Most symptoms from functional tumors respond to this form of surgical debulking. How much of the favorable survival rates is attributable to patient selection factors is not known (e.g., underlying patient condition, extent of metastases, slow doubling time, and so forth).

A variety of alternative approaches to the management of liver metastases have been reported, including gel-foam embolization or transarterial chemoembolization,[7] radioembolization with radioactive microspheres,[8-10] radiofrequency ablation, cryoablation, and percutaneous alcohol ablation. These alternative approaches have been reviewed.[11]

Results from surgical resection series appear to be more favorable than with these techniques, and surgery is considered to be the standard approach to resectable liver metastases. However, there are no high-quality studies comparing the various approaches. A systematic review of evidence comparing liver resection versus other treatments for patients with resectable liver neuroendocrine metastases found no

randomized trials, or even quasi-experimental, cohort, or case-control studies in which the patient population given the alternative therapies was similar enough to the surgery group to draw reliable conclusions.[12] The evidence for resection of all grossly visible liver metastases derives solely from case series.[Level of evidence: 3iiD or 3iiiD]

In most cases, liver metastases are not completely resectable. Cytoreductive surgery, with or without radiofrequency ablation or cryoablation, has been used to palliate symptoms. A systematic review found no randomized or quasi-randomized trials comparing cytoreductive surgery to other palliative approaches such as chemotherapy or tumor product inhibitors.[13] The evidence for surgical cytoreduction of unresectable liver metastases is restricted to case series [Level of evidence: 3iiD or 3iiiD], and interpretation of outcomes may be strongly affected by patient selection factors.

Systemic Therapy for Advanced and Metastatic Disease

Somatostatin analogs may be effective in reducing the symptoms of functional tumors.[14]

Chemotherapy using drugs such as the following, either alone or in combination, has been shown to have antitumor effects, but evidence is weak or conflicting regarding the impact of chemotherapy on overall survival:[15-17]

- Streptozocin.
- Doxorubicin.
- 5-fluorouracil.
- Chlorozotocin.
- Dacarbazine.
- Temozolomide.

More recently, a variety of systemic agents have shown biologic or palliative activity, including:[5,18]

- Tyrosine kinase inhibitors (e.g., sunitinib).
- Temozolomide.
- Vascular endothelial growth factor pathway inhibitors.
- Mammalian target of rapamycin inhibitors (e.g., everolimus).

Nearly all of the evidence of activity derives from case series.[Level of evidence 3iiiDiv] However, there are ongoing placebo-controlled randomized trials of everolimus [19] and sunitinib [20] that have been reported in abstract form showing an increase in progression-free survival in each case.[Level of evidence 1iDiii]

Favorable responses have been reported in patients with advanced progressive pancreatic NETs after treatment with several radiolabeled somatostatin analogs in which the analogs octreotide, octreotate, lanreotide, or edotreotide are stably attached to the radionuclides ¹¹¹Indium, ⁹⁰Yttrium, or ¹⁷⁷Lutrium. [21-23] The relative efficacy of these various compounds is unknown. Study designs have been limited to case series with tumor response, biochemical response, or symptom control as the measure of efficacy. [Level of evidence 3iiiDiv]

As noted in each of the clinical situations, there is a paucity or absence of high-level evidence, and a need

for randomized controlled trials.[5]

Current Clinical Trials

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Gastrinoma

The approach to treatment often depends on the results of preoperative localization studies and findings at exploratory laparotomy. At exploration, 85% of these tumors are found in the gastrinoma triangle with 40% on the surface of the pancreas and 40% outside of the pancreas. Only 15% are found within the substance of the pancreas. Percutaneous transhepatic venous sampling may occasionally provide accurate localization of single sporadic gastrinomas. Resection (enucleation of individual tumors, if technically feasible), and even excision of liver metastases, is associated with long-term cure or disease control.[1]

Standard treatment options:

1. Single lesion in head of the pancreas:[2-5]
 - Enucleation.
 - Parietal cell vagotomy and cimetidine.
 - Total gastrectomy (rarely used with the advent of current therapies).
2. Single or multiple lesions in the duodenum:[2-5]
 - Pancreatoduodenectomy.
3. Single lesion in body/tail of the pancreas:[2-5]
 - Resection of body/tail.
4. Multiple lesions in pancreas:[2-5]
 - Resection of body/tail and, if residual disease is present,
 - Parietal cell vagotomy and cimetidine, or
 - Total gastrectomy (rarely used with the advent of current therapies).
5. No tumor found:
 - Parietal cell vagotomy and cimetidine.
 - Total gastrectomy (rarely used with the advent of current therapies).

6. Liver metastases:[6-13]

- Liver resection where possible.
- Radiofrequency ablation or cryosurgical ablation.
- Chemoembolization of liver.

7. Metastatic disease or disease refractory to surgery and cimetidine:[14-23]

- Chemotherapy
- Somatostatin analogue therapy.

Patients with hepatic-dominant disease and substantial symptoms caused by tumor bulk or hormone-release syndromes may benefit from procedures that reduce hepatic arterial blood flow to metastases (hepatic arterial occlusion with embolization or with chemoembolization). Such treatment may also be combined with systemic chemotherapy in selected patients. Treatment with proton pump inhibitors or H₂ blocking agents may aid in control of peptic symptoms.

In the era of proton pump inhibitors and H₂ blocking agents, the potentially lethal hyperacidity and hypersecretory states induced by excessive gastrin production can usually be controlled. In a series of 212 patients with Zollinger-Ellison syndrome (ZES), no patients died of causes related to acid hypersecretion. Of those patients, only 2.3% had been subjected to total gastrectomy, and the cohort upon which the report was based had a long median follow-up period of 13.8 years. Although 32% of the patients died during the course of the study, only 50% of the 67 deaths were attributable to ZES-related causes. Those causes were mainly liver metastases with progressive anorexia and cachexia (67%) or secondary endocrine tumors consequent to MEN-1 syndrome. The development of bone or liver metastases (especially diffuse liver disease) or of ectopic Cushing syndrome during the study period predicted for decreased survival times.[24]

Current Clinical Trials

Check for U.S. clinical trials from NCI's list of cancer clinical trials that are now accepting patients with gastrinoma. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

General information about clinical trials is also available from the NCI Web site.

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Insulinoma

Curative surgical excision, by open laparotomy or laparoscopy, is the treatment of choice when possible. The open surgical approach is used if the tumor is suspected to be malignant, since en bloc

lymphadenectomy is performed for malignant tumors without distant metastases. Intraoperative ultrasound aids the localization of tumor extent and the relationship to other anatomic structures.[1]

Standard treatment options:

1. Single, small lesion in head or tail of pancreas:[1-4]
 - Enucleation, if feasible.
2. Large lesion in the head of the pancreas that is not amenable to enucleation:[1-4]
 - Pancreaticoduodenectomy.
3. Single, large lesion in body/tail:[1-4]
 - Distal pancreatectomy.
4. Multiple lesions: occur in 10%, often in association with multiple endocrine neoplasia syndrome type 1 (MEN-1):[1-4]
 - Distal pancreatectomy with enucleation of tumors in the head of the pancreas.
5. Metastatic lesions: lymph nodes or distant sites:[5-12]
 - Resect when possible.
 - Consider radiofrequency or cryosurgical ablation, if not resectable.
6. Unresectable:[13-22]
 - Combination chemotherapy.
 - Pharmacologic palliation: diazoxide 300 to 500 mg/day.
 - Somatostatin analogue therapy.

Patients with hepatic-dominant disease and substantial symptoms caused by tumor bulk or hormone-release syndromes may benefit from procedures that reduce hepatic arterial blood flow to metastases (hepatic arterial occlusion with embolization or with chemoembolization).[6,8-12] Such treatment may also be combined with systemic chemotherapy in selected patients.

Current Clinical Trials

Check for U.S. clinical trials from NCI's list of cancer clinical trials that are now accepting patients with insulinoma. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

General information about clinical trials is also available from the NCI Web site.

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Glucagonoma

As with the other pancreatic neuroendocrine tumors, the mainstay of therapy is surgical resection, and extended survival is possible even when the disease is metastatic. Resection of metastases is also a

consideration when feasible.[1]

Standard treatment options:

1. Single, small lesion in head or tail of pancreas:[1-4]
 - Enucleation, if feasible.
2. Large lesion in the head of the pancreas that is not amenable to enucleation:[1-4]
 - Pancreaticoduodenectomy.
3. Single, large lesion in body/tail:[1-4]
 - Distal pancreatectomy.
4. Multiple lesions:[1-4]
 - Enucleation, if feasible.
 - Resect body and tail otherwise.
5. Metastatic disease: lymph nodes or distant sites:[5-12]
 - Resect when possible.
 - Consider radiofrequency or cryosurgical ablation, if not resectable.
6. Unresectable disease:[13-22]
 - Combination chemotherapy.
 - Somatostatin analogue therapy. Necrotizing erythema of glucagonoma may be relieved in 24 hours with somatostatin analogue, with nearly complete disappearance within 1 week.

Patients with hepatic-dominant disease and substantial symptoms caused by tumor bulk or hormone-release syndromes may benefit from procedures that reduce hepatic arterial blood flow to metastases (hepatic arterial occlusion with embolization or with chemoembolization).[6,8-12] Such treatment may also be combined with systemic chemotherapy in selected patients.

Current Clinical Trials

Check for U.S. clinical trials from NCI's list of cancer clinical trials that are now accepting patients with glucagonoma. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

General information about clinical trials is also available from the NCI Web site.

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Miscellaneous Islet Cell Tumors

VIPoma

Immediate fluid resuscitation is often necessary to correct the electrolyte and fluid problems that occur as a result of the watery diarrhea, hypokalemia, and achlorhydria that patients experience. Somatostatin analogs are also used to ameliorate the large fluid and electrolyte losses. Once patients are stabilized, excision of the primary tumor and regional nodes is the first line of therapy for clinically localized disease. In the case of locally advanced or metastatic disease, where curative resection is not possible, debulking and removal of gross disease, including metastases, should be considered to alleviate the characteristic manifestations of VIP overproduction.[1] (Refer to the Treatment Option Overview section of this summary for information about the remaining principles of therapy.)

Somatostatinoma

Complete excision is the therapy of choice, if technically possible. However, metastases often preclude curative resection, and palliative debulking can be considered to relieve symptoms.[1] (Refer to the Treatment Option Overview section of this summary for information about the remaining principles of therapy.)

Other Pancreatic Neuroendocrine Tumors

For these very rare tumors, complete surgical excision is the only curative option when technically possible, and debulking or somatostatin analogs are used for palliation of symptoms if the tumor is functional. (Refer to the Treatment Option Overview section of this summary for information about the remaining principles of therapy.)

Current Clinical Trials

Check for U.S. clinical trials from NCI's list of cancer clinical trials that are now accepting patients with islet cell tumor. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

General information about clinical trials is also available from the NCI Web site.

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Recurrent and Progressive Pancreatic Neuroendocrine Tumors

There is no established therapy for pancreatic neuroendocrine tumors that recur or progress after prior therapy.[1] Deciding on further treatment depends on many factors, including:

- The specific cancer.
- Prior treatment.
- Site of recurrence.
- Individual patient considerations.

Attempts at re-resection of local tumors that have recurred or metastatic lesions may offer palliation,

when technically feasible. Intra-arterial chemotherapy is a consideration for patients with liver metastases. Patients with hepatic-dominant disease and substantial symptoms caused by tumor bulk or hormone-release syndromes may benefit from continuous-infusion intra-arterial chemotherapy or procedures that reduce hepatic arterial blood flow to metastases (hepatic arterial occlusion with embolization or with chemoembolization).[2-7] Such treatment may also be combined with systemic chemotherapy. A variety of systemic agents have shown biologic or palliative activity,[1,8] including:

- Somatostatin analogs.
- Radiolabeled somatostatin analogs.[9-11]
- Tyrosine kinase inhibitors (e.g., sunitinib).
- Temozolomide.
- Vascular endothelial growth factor pathway inhibitors.
- Mammalian target of rapamycin inhibitors (e.g., everolimus).

Current Clinical Trials

Check for U.S. clinical trials from NCI's list of cancer clinical trials that are now accepting patients with recurrent islet cell carcinoma. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

General information about clinical trials is also available from the NCI Web site.

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Changes to This Summary (03/07/2014)

The PDQ cancer information summaries are reviewed regularly and updated as new information becomes available. This section describes the latest changes made to this summary as of the date above.

General Information About Pancreatic Neuroendocrine Tumors (Islet Cell Tumors)

Editorial changes were made to this section.

This summary is written and maintained by the PDQ Adult Treatment Editorial Board, which is editorially independent of NCI. The summary reflects an independent review of the literature and does not represent a policy statement of NCI or NIH. More information about summary policies and the role of the PDQ Editorial Boards in maintaining the PDQ summaries can be found on the About This PDQ Summary and PDQ NCI's Comprehensive Cancer Database pages.

About This PDQ Summary

Purpose of This Summary

This PDQ cancer information summary for health professionals provides comprehensive, peer-reviewed, evidence-based information about the treatment of pancreatic neuroendocrine tumors (islet cell tumors).

It is intended as a resource to inform and assist clinicians who care for cancer patients. It does not provide formal guidelines or recommendations for making health care decisions.

Reviewers and Updates

This summary is reviewed regularly and updated as necessary by the PDQ Adult Treatment Editorial Board, which is editorially independent of the National Cancer Institute (NCI). The summary reflects an independent review of the literature and does not represent a policy statement of NCI or the National Institutes of Health (NIH).

Board members review recently published articles each month to determine whether an article should:

- be discussed at a meeting,
- be cited with text, or
- replace or update an existing article that is already cited.

Changes to the summaries are made through a consensus process in which Board members evaluate the strength of the evidence in the published articles and determine how the article should be included in the summary.

The lead reviewers for Pancreatic Neuroendocrine Tumors (Islet Cell Tumors) Treatment are:

- Russell S. Berman, MD (New York University School of Medicine)
- Franco M. Muggia, MD (New York University Medical Center)

Any comments or questions about the summary content should be submitted to Cancer.gov through the Web site's Contact Form. Do not contact the individual Board Members with questions or comments about the summaries. Board members will not respond to individual inquiries.

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Some of the reference citations in this summary are accompanied by a level-of-evidence designation. These designations are intended to help readers assess the strength of the evidence supporting the use of specific interventions or approaches. The PDQ Adult Treatment Editorial Board uses a formal evidence ranking system in developing its level-of-evidence designations.

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For more information, U.S. residents may call the National Cancer Institute's (NCI's) Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) Monday through Friday from 8:00 a.m. to 8:00 p.m., Eastern Time. A trained Cancer Information Specialist is available to answer your questions.

Chat online

The NCI's LiveHelp® online chat service provides Internet users with the ability to chat online with an Information Specialist. The service is available from 8:00 a.m. to 11:00 p.m. Eastern time, Monday through Friday. Information Specialists can help Internet users find information on NCI Web sites and answer questions about cancer.

Write to us

For more information from the NCI, please write to this address:

NCI Public Inquiries Office
9609 Medical Center Dr.
Room 2E532 MSC 9760
Bethesda, MD 20892-9760

Search the NCI Web site

The NCI Web site provides online access to information on cancer, clinical trials, and other Web sites and organizations that offer support and resources for cancer patients and their families. For a quick search, use the search box in the upper right corner of each Web page. The results for a wide range of search terms will include a list of "Best Bets," editorially chosen Web pages that are most closely related to the search term entered.

There are also many other places to get materials and information about cancer treatment and services. Hospitals in your area may have information about local and regional agencies that have information on finances, getting to and from treatment, receiving care at home, and dealing with problems related to cancer treatment.

Find Publications

The NCI has booklets and other materials for patients, health professionals, and the public. These publications discuss types of cancer, methods of cancer treatment, coping with cancer, and clinical trials. Some publications provide information on tests for cancer, cancer causes and prevention, cancer statistics, and NCI research activities. NCI materials on these and other topics may be ordered online or printed directly from the NCI Publications Locator. These materials can also be ordered by telephone from the Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237).