Treatments

This section provides links to published papers that relate to the treatment of carcinoid cancer and neuroendocrine tumors reviewed by CCF medical advisors. Treatment categories include:

Surgery

Chemoembolization/Bland Embolization and Radiofrequency Ablation

Anesthesia

Biotherapy (Medical treatments)

Alpha Interferon

Radioisotope Treatment-systemic and targeted (to liver)

Chemotherapy

Surgery

- Long-term survival after pancreatoduodenectomy for pancreatic adenocarcinoma: is cure possible? (Abstract)

Schnelldorfer T, Ware AL, Sarr MG, Smyrk TC, Zhang L, Qin R, Gullerud RE, Donohue JH, Nagorney DM, Farnell MB.

Ann Surg. 2008 Mar;247(3):456-62Division of Gastroenterologic and General Surgery; Mayo Clinic, Rochester, MN 55905, USA.

CONCLUSION: Pancreatoduodenectomy for adenocarcinoma in the head of pancreas can provide long-term survival in a subset of patients, particularly in the absence of lymph node metastasis. One of 8 patients can achieve 10-year survival with a potential for cure. PMID: 18376190 [PubMed - indexed for MEDLINE]

- An aggressive approach leads to long-term survival in patients with pancreatic endocrine tumors (Abstract) for full text CLICK HERE

Fendrich V, Langer P, Celik I, Bartsch DK, Zielke A, Ramaswamy A, Rothmund M Department of Surgery, Philipps-University Marburg, Marburg, Germany. fendrich@med.uni-marburg.de

Ann Surg. 2006 Dec;244(6):845-51; discussion 852-3.

OBJECTIVE: To evaluate the outcome of reoperations in patients with duodenopancreatic neuroendocrine tumors (PETs) in a tertiary referral center.

SUMMARY BACKGROUND DATA: The management of reoperations in PETs is still controversial.

METHODS: A total of 125 patients with PETs that underwent surgery between 1987 and 2004 at our institution were retrospectively evaluated. The diagnosis of PETs was based on clinical symptoms, biochemical tests, and histopathology. Patients with at least one reoperation were analyzed regarding clinical characteristics, pathology, operations, and long-term follow-up.

RESULTS: A total of 33 patients with a median age of 42 years were identified for this study: 13 patients had gastrinomas, 12 patients had nonfunctional islet cell tumors, 6 patients had insulinomas, and 2 patients had vipomas; 24 patients had sporadic NETs, 9 patients had a MEN-1-syndrome; 27 patients had histologically verified malignant tumors; 33 initial operations and 50 reoperations were performed. The initial procedures comprised 27 resections of the primary tumor and 6 explorative laparotomies; 28 of all reoperations were resections of distant metastases, including 15 liver resections; 19 resections of the pancreas or duodenum were performed during reoperations. The overall morbidity and mortality was 45% and 4.8%, respectively. After a median follow-up of 124 months (range, 16-384 months), 27 of 33 patients are still alive, 12 without evidence of disease. All 6 patients with benign tumors are still alive. The 5-, 10-, and actuarial 25-year survival rate for patients with malignant tumors were 81%, 72%, and 36%, respectively. The survival rate was significantly related to the patients age at time of initial operation and better in patients younger than 50 years compared with patients older than 50 years (P = 0.0007), and the presence or development of metastases (none or lymph node metastases versus distant metastases: P = 0.01).

CONCLUSION: We show that an aggressive surgical approach leads to long-term survival in patients with malignant PETs. Although long-term cure can only be achieved in a proportion of patients with malignant PETs, significant long-term palliation can be achieved.

- Surgery increases survival in patients with gastrinoma. (Full text) Norton JA, Fraker DL, Alexander HR, Gibril F, Liewehr DJ, Venzon DJ, Jensen RT.

  CONCLUSION: These results demonstrate that routine surgical exploration increases survival in patients with ZES by increasing disease-related survival and decreasing the development of advanced disease. Routine surgical exploration should be performed in ZES patients.nn Surg. 2006 Sep;244(3): 410-9

- Operative resection of primary carcinoid neoplasms in patients with liver metastases yields significantly better survival

  Babak Givi, SuEllen J. Pommier, Alivia K. Thompson, Brian S. Diggs and Rod Surgery, Volume 140, Issue 6, December 2006, Pages 891-898 Conclusions: Resection of the primary neoplasm is associated with better progression-free survival and overall survival in patients with abdominal carcinoid neoplasms. Therefore, localization and resection of the primary neoplasm should be considered, even among patients in whom the primary neoplasm is asymptomatic.

- Surgery for Gastrinoma and Insulinoma in MEN 1 (Abstract)

  Norton JA, Fang TD, Jensen RT. Department of Surgery, Stanford University Medical Center, Room H-3591, 300 Pasteur Drive, Stanford, CA 94305-5641, USA. janorton@stanford.edu

  J Natl Compr Canc Netw. 2006 Feb;4(2):148-53. Review

- Surgical treatment of advanced-stage carcinoid tumors: lessons learned. (Abstract)

  For full text Click Here

  Boudreaux JP, Putty B, Frey DJ, Woltering E, Anthony L, Daly I, Ramcharan T, Lopera J, Castaneda W. Department of Surgery, Louisiana State University Health Sciences Center, New Orleans, Louisiana, USA. Ann Surg. 2005 Jun;241(6):839-45; discussion 845-6.

  OBJECTIVE: To evaluate clinical outcomes in a large group of advanced-stage carcinoid

patients (stage IV) following multimodal surgical therapy.

SUMMARY BACKGROUND DATA: Patients with advanced-stage carcinoid have traditionally experienced poor 5-year survival (18%-30%). Few recent series have evaluated a large number of patients treated with aggressive surgical rescue therapy.

METHODS: This single-center retrospective review analyzes the records of 82 consecutive carcinoid patients treated by the same 2 surgeons, from August 1998 through August 2004 with a 3- to 72-month follow-up. RESULTS: Surprisingly, one third of 26 (32%) patients were found to have intestinal obstructions; 10 being moribund at presentation. Mesenteric encasement with intestinal ischemia was successfully relieved in 10 of 12 cases. Five of eighty-two "terminal" patients were rendered free of macroscopic disease. Karnofsky performance scores improved from 65 to 85 ($P < 0.0001$). Two- and four-year survival for patients with no or unilateral liver metastases ($n = 23$) was 89%, while 2- and 4-year survival for patients with bilateral liver disease ($n = 59$) was 68% and 52% ($P = 0.072$), respectively.

CONCLUSION: We think that all patients with advanced-stage carcinoid should be evaluated for possible multimodal surgical therapy. Primary tumors should be resected, even in the presence of distant metastases to prevent future intestinal obstruction. The "wait an The "wait and see" method of management of this slow-growing cancer no longer has merit. We offer an algorithm for the surgical evaluation and management of these patients.

- Surgery for Midgut Carcinoid (Full Text PDF)

  Sutton R, Doran H E et. al

  Endocr Relat Cancer. 2003 Dec;10(4):469-81

  Abstract: Many clinicians prefer to avoid surgery in patients with carcinoid neoplasia, because of its slow growth and relatively favourable prognosis. Nevertheless, the most common cause of death in patients with carcinoid is advanced metastatic disease, and both clinical and epidemiological data indicate that the more effectively the disease is ablated, the more long- lasting the benefit. Multidisciplinary management of patients with carcinoid must consider inherited risk, possible multiple carcinoids and/or synchronous non-carcinoid cancer, and the use of a range of investigations that also evaluate the 10% of patients with carcinoid syndrome±valvular heart disease. Although primary size is correlated with the presence of nodal±liver metastases, carcinoid tumours<1 cm in diameter may be metastatic at presentation, particularly those arising within the small intestine. In the jejunum and ileum, resection of all sizes of carcinoid with local and regional nodes is preferred, to prevent nodal dissemination causing mesenteric ischaemia±infarction. Resection of nodal metastases should be undertaken in those with persistent or recurrent nodal disease if possible. Appendiceal and right colonic carcinoids are most effectively treated by right hemicolectomy with local and regional nodal clearance, as for adenocarcinoma. For most appendiceal carcinoids, however, which are<1 cm in diameter and non-invasive, appendicectomy alone is sufficient. For appendiceal carcinoids 1-2 cm in diameter, histopathological assessment helps to determine the need for hemicolectomy. Liver resection has been followed by prolonged 5-year survival in several series and is recommended in appropriate patients to attempt cure or to debulk metastatic disease. Liver transplantation has had only qualified success in highly selected patients without extra-hepatic disease in whom other therapies have failed.

- Effect of Surgery on the Outcome of Midgut Carcinoid Disease with Lymph Node and Liver Metastases (Full Text PDF)

  By Per Hellman, M.D., Ph.D.1, Tobias Lundström, M.D.1, Ulf Öhrvall, M.D., Ph.D.2, Barbro Eriksson, M.D., Ph.D.3, Britt Skogseid, M.D., Ph.D.3, Kjell Öberg, M.D., Ph.D.3, Eva Tiensuu Janson, M.D., Ph.D.3, and Göran Åkerström, M.D., Ph.D.1

World J Surg 2002 Aug;26(8):991-7

Excellent paper supporting proactive treatment approaches (surgery followed by biotherapy) resulting in increased survival. "We have evaluated survival and tumor-related symptoms in the presence of mesenteric lymph node and liver metastases in relation to surgical procedures in 314 patients . . . Patients who underwent resection for the primary tumor had a longer survival than those with no resection(median survival 7.4 vs. 4.0 years; $p < 0.01$)."

- Hepatic surgery for metastatic gastrointestinal neuroendocrine tumors (Full text PDF)

  Que FG, Sarmiento JM, Nagorney DM. Mayo Clinic and Mayo Foundation, Rochester, MN 55905, USA Cancer Control 2002 Jan-Feb;9(1):67-79

  An EXCELLENT review of the role of cytoreductive hepatic surgery for metastatic Gastroinstestinal Pancreatic Neuroendocrine tumors that has been authored by the surgical group at the Mayo Clinic of Rochester. In the light of their own extensive experience these authors review the world literature on this subject and their conclusions add further impetus to the currentshift towards a more ggressive approach utilizing surgery and multimodality therapy.

- Hepatic surgery for metastases from neuroendocrine tumors (Abstract)

  This link is to an abstract on PubMed.

  Sarmiento JM, Que FG.

  Division of Gastroenterologic and General Surgery, Mayo Clinic, Mayo Foundation, 200 First Street SW, Rochester, MN 55905, USA. sarmiento.juan@mayo.edu

  Surg Oncol Clin N Am. 2003 Jan;12(1):231-42.

  Review ". . . The authors have learned over time that patients with valvular disease are not good candidates for surgery. These patients develop right-sided heart failure with an increase in the central venous pressure. This condition can result in massive hemorrhage during the liver resection because of the difficulty in controlling backbleeding from the hepatic veins [26]. Correction of valvular disease is warranted for safe liver resection. The authors' current policy is to rule out valvular disease in every patient with carcinoid tumors and repair the valves prior to hepatic resection when indicated [27]. This policy clearly has decreased the complication rate. . . ."

- Surgical treatment of neuroendocrine metastases to the liver: a plea for resection to increase survival (Abstract)

  This link is to an abstract on PubMed.

  Sarmiento JM, Heywood G, Rubin J, Ilstrup DM, Nagorney DM, Que FG.

  Division of Gastroenterologic and General Surgery, Mayo Clinic, Rochester, MN 55905, USA.

  J Am Coll Surg. 2003 Jul;197(1):29-37

  CONCLUSION: Hepatic resection for metastatic neuroendocrine tumors is safe and achieves symptom control in most patients. Debulking extends survival, although recurrence is expected. Hepatic resection is justified by its effects on survival and quality of life.

Chemoembolization/Bland Embolization and Radiofrequency Ablation (RFA)

- Prolonged survival after hepatic artery embolization in patients with midgut carcinoid syndrome (Full Text PDF)

  Swärd C, Johanson V, Nieveen van Dijkum E, Jansson S, Nilsson O, Wängberg B, Ahlman H, Kölby L on April 10, 2009 in British Journal of Surgery

  Conclusion: Hepatic Arery Embolization is safe, provides good control of hormonal symptoms, and prolongs survival in biochemically responsive patients. It is a valuable palliative option for patients with midgut carcinoid syndrome due to liver metastases and can be repeated in patients with a favourable response to the first procedure. Copyright (c) 2009 British Journal of Surgery Society Ltd. Published by John Wiley & Sons, Ltd.PMID: 19358175 [PubMed - as supplied by publisher]

- Chemoembolization and Bland Embolization of Neuroendocrine Tumor Metastases to the Liver (Full text)

  Ruutiainen AT, Soulen MC, Tuite CM, Clark TW, Mondschein JI, Stavropoulos SW, Trerotola SO. J Vasc Interv Radiol. 2007 Jul;18(7):847-55 Conclusions: Chemoembolization was not associated with a higher degree of toxicity than bland embolization. Chemoembolization demonstrated trends toward improvement in TTP, symptom control, and survival. Based on these results, a multicenter prospective randomized trial is warranted.

- Ablative Therapies for Liver Metastases of Digestive EndocrineTumors (Full text PDF)

  By D O'Toole, F Maire and P Ruszniewski Endocrine-Related Cancer, December 2003 Volume 10, Issue 4 Abstract: Hepatic metastases are frequently encountered in patients with digestive endocrine tumors and their presence plays an important role in quality of life and overall prognosis. Surgery is the treatment method of choice for hepatic metastases but this is frequently impossible due to disease extent. Systemic chemotherapy is offered to patients with diffuse and/or progressive liver metastases but results are disappointing especially in patients with metastases from midgut origin. In the latter patients with carcinoid syndrome, somatostatin analogues are frequently initially effective but their efficacy wanes due to disease progression and development of tachyphylaxis. Other therapeutic options in the treatment of hepatic metastases are locoregional strategies where vascular occlusion induces ischemia in these highly vascular tumors using either surgical or radiological techniques. Available methods include surgical ligation of the hepatic artery, transient hepatic ischemia or sequential hepatic arterialization. Trans-catheter arterial chemoembolization has proven effective in terms of long palliation and objective tumor responses. Other treatments aimed at regional destruction either alone or in combination with surgery include radiofrequency ablation and cryotherapy. The latter are usually important adjuncts to surgery and are usually reserved for limited disease.

- Outcome of Hepatic Artery Chemoembolization (HACE) in the treatment of Metastatic Carcinoid of the Liver.

  By Warner RRP, Nowakowski F, Mitty H.A. et.al. The Mount Sinai School of Medicine. NYC

  Presented at SIR 2003.

  The Annual Meeting of the Society of Invasive Radiology, Salt Lake City, March 31, 2003

  Journal of Vascular Invasive Radiology

Abstract: The Authors reported on outcome in 62 Carcinoid Syndrome (CS) patients treated with HACE when combined in sequential multimodality regime with other therapies (Surgery, Biotherapy, Chemotherapy, Radio Frequency Ablation etc.) Patients were followed up to 14 years. When compared with the outcome in a historical control group of 91 untreated CS patients reported by Davis, Moertel and Mc Ilrath, The Mayo Clinic, in 1973* the treated patients had a median survival from onset of symptoms of more than 3 fold longer (10,75 years vs 3.2 years) These findings support the contention that HACE has a definite survival benefit in addition to its generally acknowledged palliation benefit as part of multi-modality treatments.

*Ref. The Malignant Carcinoid Syndrome . Davis Z, Moertel C.G, McIlrath, D.C.; Surg.,Gyn.,Onc. Oct 1973 Vol 137

- Chemoembolization fo Hepatic Malignancies (Full text PDF)

  By Michael C. Soulen, MD Associate Professor of Radiology & Surgery, University of Pennsylvania, Philadelphia, PA.

- Painful Metastases Involving Bone: Feasibility of Percutaneous CT-and IS-guided Radio-frequency Ablation (Full text HTML)

  By Callstrom MR, Charboneau JW, Goetz MP, Rubin J, Wong GY, Sloan JA, Novotny PJ, Lewis BD, Welch TJ, Farrell MA, Maus TP, Lee RA, Reading CC, Petersen IA, Pickett DD.

  Department of Radiology, Mayo Clinic, 200 First St SW, E2, Rochester, MN 55905, USA.

  Radiology 2002 Jul;224(1):87-97

  Conclusion: "RF ablation of painful osteolytic metastases is safe, and the relief of pain is substantial."

Anesthesia (Special Considerations During Surgery for Neuroendocrine Tumors)

- Perianaesthetic risks and outcomes of abdominal surgery for metastatic carcinoid tumours (Full text PDF)

  By Kinney MA, Warner ME, Nagorney DM, Rubin J, Schroeder DR, Maxson PM, Warner MA. Br J Anaesth. 2001 Sep;87(3):447-52.

- Anesthesia for patients with carcinoid syndrome (Abstract)

  This link is to an abstract on PubMed.

  Vaughan DJ, Brunner Mct on PubMed. D.

  Int Anesthesiol Clin. 1997 Fall;35(4):129-42.

  ". . . Carcinoid syndrome, although rare, can create serious problems to the anesthetist, both by the nature and variability of clinical manifestations and by the complications that can occur peroperatively. . . . The severity of symptoms does not predict the severity of perioperative complications, so that patients with minor preoperative symptoms may have significant intraoperative complications. . . .The keys to successful anesthetic management of

patients with carcinoid syndrome are good communication between endocrinologist, anesthetist, and surgeon and preoperative optimization of the patient. . . .Octreotide has largely replaced the use of other drugs both for symptomatic control and acute treatment of the symptoms associated with carcinoid syndrome. . . ."

- Octreotide treatment of carcinoid hypertensive crisis (Abstract)

  For full text article contact the Carcinoid Cancer Foundation 888-722-3132

  Warner RR, Mani S, Profeta J, Grunstein E.

  Mt Sinai J Med. 1994 Sep;61(4):349-55."

  ". . .We suggest that hypertensive as well as hypotensive carcinoid crises respond to octreotide and that this agent should be considered for prophylactic and emergency use in all carcinoid syndrome patients prior to and during anesthesia and surgery."

Biotherapy (Somatostatin Analogues)

- New Study First to Confirm Sandostatin LAR(R) Depot Controls Tumor Growth in Patients With Rare Gastrointestinal Tumors (PDF Full Text)

  "In recent years, a growing body of evidence has suggested that Sandostatin LAR provides antitumor effects, but theseare the first data to confirm this effect from a well-designed, prospective, placebo-controlled study," said David Epstein,President & CEO of Novartis Oncology.

  EAST HANOVER, N.J., Jan. 13, 2009, PRNewswire -- Sandostatin LAR$^{(R)}$ Depot (octreotide acetate suspension for injection) demonstrated antitumor benefit in patients with metastatic neuroendocrine tumors (NETs) of the midgut,according to interim data presented today at the 2009 Gastrointestinal Cancer Symposium of the American Society of Clinical Oncology.

  - Data show significant 66% reduction in risk of disease progression versus placebo

  - Sandostatin LAR more than doubled time without tumor growth for a median of 14 months compared to six months on placebo

  - Results support Sandostatin LAR as first treatment after surgery in certain patients with newly diagnosed neuroendocrine tumors (NETs)

- Clinical Value of Monitoring Plasma Octreotide Levels During Chronic Octreotide Long-Acting Repeatable Threapy in Carcinoid Patients (PDF Full Text)

  Woltering EA, Salvo VA, O'Dorisio TM, Lyons J 3rd, Li G, Zhou Y, Seward JR, Go VL, Vinik AI, Mamikunian P, Mamikunian G.

  Department of Surgery, Louisiana State University Health Sciences Center, New Orleans, LA, USA. ewolte@lsuhsc.edu Pancreas. 2008 Jul;37(1):94-100.

  Abstract

  CONCLUSIONS: Current plasma octreotide values are significantly lower than previously reported for 30-, 60-, and 120-mg/mo LAR doses. Serial plasma octreotide value measurements should be used to determine if increasing symptoms or tumor growth are associated with suboptimal drug dosing.

- Effect of octreotide LAR dose and weight on octreotide blood levels in patients with neuroendocrine tumors. (Abstract)

  Woltering EA, Mamikunian PM, Zietz S, Krutzik SR, Go VL, Vinik AI, Vinik E, O'Dorisio TM, Mamikunian G.

  Pancreas. 2005 Nov;31(4):392-400.

  Access to full text with permission from the authors.

  Conclusion: Frequent measurement of octreotide levels may be useful to guide octreotide therapy in patients with poorly controlled symptoms or those patients experiencing tumor growth.

  "In patients experiencing tumor growth, independent of their symptom control, the clinician may choose to increase octreotide doses in the hope that this will further suppress tumor progression. Whereas the antitumor effect of octreotide remains controversial and may be dose-dependent, the safety profile of octreotide is well established and is not dose-dependent. This safety profile allows the clinician a great deal of latitude in choosing an appropriate octreotide dose."

- Discussion on the utility of various routes of administration of octreotide acetate (Full text access with permission of the author)

  By: Eugene A. Woltering MD FACS

  The James D. Rives Professor of Surgery and Neurosciences

  Louisiana State University Health Sciences Center, New Orleans LA 70065 March 2005

  The drug octreotide acetate is part of a class of drugs known as somatostatin analogs (This class of drugs includes octreotide, lanreotide and most recently, vapreotide). All of these drugs can be given subcutaneously (SC), intravenously (pump based therapy) or by depot injections of a slow release form of the compound (LAR).

- An important note: The only somatostatin analogue currently available in the US is octreotide (trade name Sandostatin [sc] and [LAR]), manufactured by Novartis. In the rest of the world, three types of somatostatin analogues are available -- octreotide, lanreotide and vapreotide. Lanreotide (trade names Somatuline, Autogel) is manufactured by Ipsen. Vapreotide (trade name Sanvar SR) is manufactured by H3 Pharma.

- Beford Laboratories™ Shipping octreotide acetate injection

  BEDFORD, OH – (April 4, 2005) – Bedford Laboratories™, a division of Ben Venue Laboratories Inc., announced that it began shipping Octreotide Acetate Injection on April 4, 2005. This generic product is equivalent to Sandostatin® shortacting sc by Novartis. LAR version is currently not available

The following information regarding octreotide (Sandostatin), of special interest for the medical professional, is made available from the Novartis Pharmaceuticals Corporation website.

- Somatostatin receptor targeting for tumor imaging and therapy.

This link is to an abstract on PubMed. A full text version can be purchased trough the NY Academy of Sciences.

Grotzinger C, Wiedenmann B.

Charite Medical School, Campus Virchow Hospital, Department of Internal Medicine, Division of Hepatology and Gastroenterology, 13353 Berlin, Germany

Ann N Y Acad Sci. 2004 Apr;1014:258-64. Review.

- Neuroendocrine tumors--somatostatin receptor expression and somatostatin analog treatment

  Janson ET, Oberg K.

  Department of Medical Sciences, University Hospital, Uppsala, Sweden.

  Cancer Chemotherapy and Biological Response Modifiers . 2003;21:535-46. Chapter 25.

- Somatostatin and Somatostatin Analogues: Diagnostic and Therapeutic Uses

  This link is to an abstract in Pub Med. Full text of this volume is available to subscribers of the Current Opinion on Oncology or by per-article payment.

  By de Herder WW, Lamberts SW.

  Current Opinion Oncology, 2002 Jan;14(1):53-7.

Alpha Interferon

- Prospective, Randomized, Multicenter Trial on the Antiproliferative Effect of Lanreotide, Interferon Alfa, and Their Combination for Therapy of Metastatic Neuroendocrine Gastroenteropancreatic Tumors—The International Lanreotide and Interferon Alfa Study Group

  By Siegbert Faiss, Ulrich-Frank Pape, Michael Böhmig, Yvonne Dörffel, Ulrich Mansmann, Werner Golder, Ernst Otto Riecken, and Bertram Wiedenmann

  J Clin Oncol 21:2689-2696. 2003 by American

  Society of Clinical Oncology.

- Treatment of Malignant Endocrine pancreatic tumors with a combination of alpha-interferon and somatostatin analogs (Abstract)

  This link is to an abstract on PubMed. A full text version can be purchased at Humana Press.

  Fjallskog ML, Sundin A, Westlin JE, Oberg K, Janson ET, Eriksson B.

  Med Oncol 2002;19(1):35-42

  "Somatostatin analogs and alpha-interferon induce good responses as single drugs in the treatment of endocrine pancreatic tumors. We examined the efficacy and tolerability of the combination of alpha-interferon and somatostatin analogs in 16 patients with metastatic endocrine pancreatic tumors. . . ."

- Randomized clinical trial of the effect of interferon alpha on survival in patients with disseminated midgut carcinoid tumours. (Abstract)

  This link is to an abstract on PubMed. A full text version can be purchased trough Interscience Wiley Co.

  Kolby L, Persson G, Franzen S, Ahren B. Br J Surg. 2003 Jun;90(6):687-93.

  "Conclusion:

  Addition of IFN- to octreotide may retard tumour growth in patients with midgut carcinoid tumours".

Radiosotope Treatments -- Systemic and Targeted (to liver)

- Radioembolization with selective internal radiation microspheres for neuroendocrine liver metastases

King J, Quinn R, Glenn DM, Janssen J, Tong D, Liaw W, Morris DL.

Department of Surgery, University of New South Wales, St. George Hospital, Sydney, New South Wales, Australia.

Cancer. 2008 Sep 1;113(5):921-9.

CONCLUSIONS: In this open study of 34 patients, the results demonstrated that radioembolization with (90)Y resin microspheres can achieve relatively long-term responses in some patients with nonresectable NETLMs.

- Radioembolization for Unresectable Neuroedocrine Hepatic Metastases Using Resin ^{90} Y-Microspheres: Early Results in 148 Patients

  Kennedy AS, Dezarn WA, McNeillie P, Coldwell D, Nutting C, Carter D, Murthy R, Rose S,Warner RR, Liu D, Palmedo H, Overton C, Jones B, Salem R.

  American Journal of Clinical Oncology. Volume 31. Number 3, June 2008

  Abstract

  CONCLUSION: Radioembolization with ^{90}Y-Microspheres to the whole liver, or lobe with single or multiple fractions are safe and produce high response rates, even with extensive tumor replacement of normal liver and/or heavy pretreatment. The acute and delayed toxicity was very low without a treatment related grade 4 acute event or radiation induced liver disease in this modest-sized cohort. The significant objective response suggests that further investigation of this approach is warranted.

- 90Y Radioembolization for metastatic neuroendocrine liver tumors: preliminary results from a multi-institutional experience. (Abstract)

  Rhee TK, Lewandowski RJ, Liu DM, Mulcahy MF, Takahashi G, Hansen PD, Benson AB 3rd,Kennedy AS, Omary RA, Salem .

  Ann Surg. 2008 Jun;247(6):1029-35

CONCLUSION: Yttrium-90 (Y) radioembolization of metastatic NET is a viable therapy with acceptable toxicity. Further investigation is warranted.

- Treatment With the Radiolabeled Somatostatin Analog [177Lu-DOTA0,Tyr3]Octreotate: Toxicity, Efficacy, and Survival

  Dik J. Kwekkeboom, Wouter W. de Herder, Boen L. Kam, Casper H. van Eijck, Martijn van Essen, Peter P. Kooij, Richard A. Feelders, Maarten O. van Aken, Eric P. Krenning

  Department of Nuclear Medicine, Erasmus Medical Center, Dr Molewaterplein 40, 3015 GD Rotterdam, the Netherlands. d.j.kwekkeboom@erasmusmc.nl

  J Clin Oncol. 2008 May 1;26(13):2124-30.

  PURPOSE: Despite the fact that most gastroenteropancreatic neuroendocrine tumors (GEPNETs) are slow-growing, median overall survival (OS) in patients with liver metastases is 2 to 4 years. In metastatic disease, cytoreductive therapeutic options are limited. A relatively new therapy is peptide receptor radionuclide therapy with the radiolabeled somatostatin analog [(177)Lu-DOTA(0),Tyr(3)]octreotate. Here we report on the toxicity and efficacy of this treatment, performed in over 500 patients.

  PATIENTS AND METHODS: Patients were treated up to a cumulative dose of 750 to 800 mCi (27.8-29.6 GBq), usually in four treatment cycles, with treatment intervals of 6 to 10 weeks. Toxicity analysis was done in 504 patients, and efficacy analysis in 310 patients. RESULTS: Any hematologic toxicity grade 3 or 4 occurred after 3.6% of administrations. Serious adverse events that were likely attributable to the treatment were myelodysplastic syndrome in three patients, and temporary, nonfatal, liver toxicity in two patients. Complete and partial tumor remissions occurred in 2% and 28% of 310 GEPNET patients, respectively. Minor tumor response (decrease in size > 25% and < 50%) occurred in 16%. Median time to progression was 40 months. Median OS from start of treatment was 46 months, median OS from diagnosis was 128 months. Compared with historical controls, there was a survival benefit of 40 to 72 months from diagnosis.

  CONCLUSION: Treatment with [(177)Lu-DOTA(0),Tyr(3)]octreotate has few adverse effects. Tumor response rates and progression-free survival compare favorably to the limited number of alternative treatment modalities. Compared with historical controls, there is a benefit in OS from time of diagnosis of several years.

- Quality of Life in Patients With Gastroenteropancreatic Tumors Treated With [177Lu-DOTA0,Tyr3]octreotate

  Jaap J.M. Teunissen, Dik J. Kwekkeboom, Eric P. Krenning

  From the Department of Nuclear Medicine, Erasmus Medical Center, Rotterdam, The Netherlands

  Address reprint requests to Jaap J.M. Teunissen, Department of Nuclear Medicine, Erasmus Medical Center, Dr Molenwaterplein 40, 3015 GD Rotterdam, The Netherlands; e-mail: j.teunissen@erasmusmc.nl

  Jul 1 2004: 2724-2729

  PURPOSE: To evaluate the quality of life (QoL) in patients with metastatic somatostatin receptor positive gastroenteropancreatic tumors treated with [177Lu-DOTA0,Tyr3] octreotate (177Lu-octreotate) therapy.

  PATIENTS AND METHODS: Fifty patients who had been treated with 600 to 800 mCi of

177Lu-octreotate and had a follow-up of at least 3 months were studied. The patients completed the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire C30 before therapy and at follow-up visit 6 weeks after the last cycle. Overall QoL and specific QoL domains of both the total group of patients and subgroups according to treatment outcome were analyzed. Twenty-four patients had regression, 19 had stable disease, six had progressive disease, and one had nonassessable disease status. Analysis of variance was used for statistical comparison.

RESULTS: A significant improvement in the global health status/QoL scale was observed after therapy with 177Lu-octreotate ($P < .01$). The score increased significantly six weeks after therapy to a mean of 78.2, up from 69.0 (scale range, 0 to 100). Furthermore, significant improvement was observed in the role, emotional, and social function scales. The symptom scores for fatigue, insomnia, and pain were significantly decreased. Patients with proven tumor regression most frequently had an improvement of QoL domains. Unexpectedly, patients with progressive disease also indicated an improvement in their global health/QoL score.

CONCLUSION: 177Lu-octreotate therapy significantly improved the global health/QoL and several function and symptom scales in patients with metastasized gastroenteropancreatic tumors, but especially in those patients with proven tumor regression.

Authors' disclosures of potential conflicts of interest are found at the end of this article.

- Erasmus MC Lutetium 177 Treatment*

  Moleculare RadioTherapy (Website with contact information)

  Information about the Receptor therapy given to patients in the Netherlands. . . Read More

  How to Reach us Click Here

  Postal address
  P.O. box 2040 3000 CA Rotterdam, NL

  Street address
  Dr. Molewaterplein 40 3015 GD Rotterdam, NL

  Direct dial +31-10-4635963
  Fax number +31-10-4635997

  Comment: Head of Department
  Prof. Dr. Eric.P. Krenning

- Systemic radioisotope treatment now available in the US.

  "High Dose Indium-111 Pentetreotide (Octreotide) Therapy in Somatostatin Receptor Expressing Neuroendocrine Neoplasms."

  High-dose 111In-Pentetreotide (~500 mCi/patient) is now offered in the U.S. for therapy in somatostatin receptor expressing neuroendocrine tumors. This is based on the Investigational New Drug (IND) application filed with FDA. Using this innovative method of cancer therapy, a somatostatin receptor analog (called Pentetreotide) is labeled with a high dose of a radioactive element called Indium-111. Pentetreotide will carry Indium-111 to the site of the tumor and attaches to the receptor site located on the cell membrane. The next step is internalization of the compound into the cell cytoplasm and next to the cell nucleus. Radioactivity is then deposited in this region and causes damage to the DNA molecules located in the nucleus of the cancer cells. The net effect will be initial dysfunction of the

tumor cells, followed by prevention of further tumor growth and leading to cell death.

This therapy can be applied to the category of neuroendocrine tumors which include Carcinoid, Islet Cell Carcinoma of the Pancreas, Oat Cell Carcinoma of the Lung, and Medullary Thyroid Carcinoma.

The principle investigator of this program is Dr. Ebrahim S. Delpassand and the project is in collaboration with Excel diagnostic Imaging Clinics, St. Luke's Episcopal Hospital and RadioIsotope Therapy of America (RITA) Foundation in Houston.

For further information regarding this treatment, you can contact Ms. Christiane Assir clinical coordinator of the project at: 713-341-3239. cassir@exceldiagnostics.com

- Treatment of patients with gastro-entero-pancreatic (GEP) tumours with the novel radiolabelled somatostatin analogue [(177)Lu-DOTA(0),Tyr(3)]octreotate (Abstract)

  This link is to an abstract on PubMed. A full text version can be purchased from SpringerLink.

  By Kwekkeboom DJ, Bakker WH, Kam BL, Teunissen JJ, Kooij PP, De Herder WW, Feelders RA, Van Eijck CH, De Jong M, Srinivasan A, Erion JL, Krenning EP

  CONCLUSION:(partial). . . in view of the high success rate of therapy with (177)Lu-octreotate and the absence of serious side-effects, we advocate its use in patients with GEP tumours without waiting for tumour progression.

- Radiolabeled Somatostatin Analog [177Lu-DOTA0,Tyr3]Octreotate in Patients With Endocrine Gastroenteropancreatic Tumors.

  Kwekkeboom DJ, Teunissen JJ, Bakker WH, Kooij PP, de Herder WW, Feelders RA, van Eijck CH, Esser JP, Kam BL, Krenning EP.

  J Clin Oncol. 2005 Apr 20;23(12):2754-62.

  This link is to an abstract on PubMed. A full text version can be purchased from Journal of Clinical Oncology http://www.jco.org

  CONCLUSION Treatment with (177)Lu-octreotate results in tumor remission in a high percentage of patients with GEP tumors. Serious side effects are rare. The median time to progression compares favorably with chemotherapy. Results are better in patients with a limited tumor load. Therefore, early treatment, even in patients who have no progressive disease, may be better.

- Results from Clinical Trials of Systemic treatment with Y90, LU-177 and 111-In

  Overview of Results of Peptide Receptor Radionuclide Therapy with 3 Radiolabeled Somatostatin Analogs (PDF Full text)

  Kwekkeboom DJ, Mueller-Brand J, Paganelli G, Anthony LB, Pauwels S, Kvols LK, O'dorisio TM, Valkema R, Bodei L, Chinol M, Maecke HR, Krenning EP. J Nucl Med. 2005 Jan;46 Suppl 1:62S-6S .

  Conclusion: The results obtained with [(90)Y-DOTA(0),Tyr(3)] octreotide and [(177)Lu-DOTA(0),Tyr(3)] octreotate are very encouraging in terms of tumor regression. Also, if kidney protective agents are used, the side effects of this therapy are few and mild, and the duration of the therapy response for both radiopharmaceuticals is more than 2 y. These data compare favorably with those for the limited number of alternative treatment

approaches.

Radioisotope Treatment with LU -177 available in the Netherlands

For information about this treatment and contact information visit the following website: http://www.prrt.nl/index.php?lang=en

Chemotherapy

- Fluorouracil, Doxorubicin, and Streptozocin in the Treatment of Patients With Locally Advanced and Metastatic Pancreatic Endocrine Carcinomas (Abstract)

  This link is to a review of the article. The full text requires a subscription to Journal of Clinical Oncology Online.

  Kouvaraki MA, Ajani JA, Hoff P, Wolff R, Evans DB, Lozano R, Yao JC.

  J Clin Oncol. 2004 Dec 1;22(23):4710-9.

  "The role of systemic chemotherapy in the management of pancreatic endocrine carcinoma (islet cell carcinoma, PEC) is and area of considerable controversy. Response rates reanges from 6% to 69% have been reported for streptozocin-based chemotherapy. We restrospectively studied 84 patients with locally advanced or metastatic PEC who had been treated with fluorouracil, doxorubicin, and streptozocon (FAS) to determine the objective response rate duration of pf progression-free survival (PPS), and duration of overall survival (OS)."

fordoctors.jpg

Source URL: http://www.carcinoid.org/physician/treatments