

# ADVANCES IN PANCREAS CANCER

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Pancreas cancer is one of the most common malignancies worldwide. It is considered the fourth cause of cancer deaths. It seems as if the incidence of pancreatic cancers is increasing. This is true despite the advances in CT scanning, MRI's, surgical care and as well chemotherapy. Few patients can undergo resection of the pancreas cancer. The vast majority of patients - estimated at more than 75% - are not suitable for surgical removal.

Overall about 5% of patients with pancreas cancer live five years with standard therapy. That makes new treatment options most important. Early diagnosis is seldom an issue.

Local symptoms often include pain, jaundice (yellowing of the skin due to bile deposited there), obstruction of the gastrointestinal tract and malnutrition. In the past, studies suggested that chemotherapy/radiation administered after surgery gave better results than surgery alone. Other studies have evaluated chemotherapy/radiation prior to surgery. Many people receive only chemotherapy and sometimes radiation. Once cancer travels beyond the pancreas, surgery is not generally used.

A relatively new chemotherapeutic drug called Gemcitabine has been used and has shown activity in patients with pancreas cancer. In fact, Gemcitabine has been shown to be superior to 5FU - both to improve symptoms and survival. Of course, each new chemotherapy drug holds promises for better results and less toxicity.

Recently, continuous infusion Gemcitabine with Mitomycin C and external beam radiation was used for patients with locally advanced unresectable carcinoma of the pancreas. The point was to determine the maximum dose of Gemcitabine given weekly as a 24-hour infusion with a fixed of Mitomycin C as a bolus and to determine toxicity of the regimen and to find the anti-tumor effectiveness.

Kornek et al recently reported on this study in the International Journal of Radiation Oncology Biology Physics. Patients were enrolled in this study between January 1997 and August 1998. Patients had biopsy of the pancreas to confirm the diagnosis as well as CT scans and angiography to show its unresectability. Patients were excluded if they had distant metastases or serious co-morbid disease or other cancers.

The regimen included four weekly cycles of Mitomycin C at 8mg/m<sup>2</sup> given as intravenous bolus on Day One and Gemcitabine given intravenously as a 24-hour infusion on Days One, Eight and Fifteen. Gemcitabine started at a dose of 100mg/m<sup>2</sup> and increased to 160mg/m<sup>2</sup>.

If patients had stable disease, they were given up to six cycles while patients with progressive disease were removed from the study.

The radiation consisted of photon treatments using three or four fields with a daily fraction dose of 1.8 Gray for five days a week for a total dose of 45 Gray. Gray is a measurement of radiation exposure. This would represent five-day a week treatment for five weeks. The target of cancer was included with approximately 1-1/2cm to 3cm margins.

Fifteen patients were enrolled consisting of eight women and seven men. Their median age was 62 years. The cancer was in the head of the pancreas in 9 patients; in the head extending to the body in 2 patients, in the body of the pancreas in 3 patients, and in the tail of the pancreas in 1 patient.

The size of the cancer ranged from 2 to 9cm with a median size of 4cm. Nine patients (60%) had

pain at the beginning of treatment, with 60% also having impaired function at commencement of treatment. Time from diagnosis to the start of treatment was 4 weeks with a range of 2 to 7 weeks. Thirteen patients completed this combined modality treatment. Two patients refused further treatment after the first course.

Toxicity included that affecting the blood counts or gastrointestinal tract. Radiation was completed for 13 patients with 2 patients refusing after three and four weeks. The median dose was 45 Gray, which was the prescribed dose.

Time to progression was 5.5 months with a range of 2 to 12 months. The first site of cancer recurrence was in the liver in 7 patients, the liver and lungs in 3 patients, and the liver and peritoneal surfaces in 2 patients. The peritoneal surface is the lining of the abdominal cavity. Twenty percent developed local recurrence. The median survival of the population was 8.3 months with a one-year survival of 13.3%.

Responding to an issue of why new treatments are being developed for pancreas cancer, the authors stated, "Disappointing results with surgery, chemotherapy and radiation therapy used separately for Stage II and III pancreatic cancer have stimulated clinical trials of combined modality therapy in these patients. Many of these studies demonstrated that both radiation and chemotherapy are necessary to achieve optimal results. The first clinical trials investigating combined chemo, radiotherapy in locally advanced pancreatic carcinomas used 5FU given either as bolus injection or as continuous infusion during irradiation. Higher doses of infusional 5FU and the combination with Leucovorin, Mitomycin C, or Cisplatin seemed to result in better therapeutic outcome, however in view of the reported long-term results of several contemporary trials, further improvements are certainly warranted."

The strategy at Radiosurgery New York has been to use stereotactic body radiosurgery in an attempt to maximize tumor dose. Our tumor control rate is 94% meaning 94% of the cancers in the pancreas have been controlled with no further progression. This is an enviable number. We have been able to treat both newly diagnosed as well as patients with a recurrent pancreatic cancer within the pancreas or elsewhere. It is a treatment option that can be considered in select patients. Our expert panel of physicians meets on multiple occasions each week to prospectively evaluate candidates into our program.

Fractionated stereotactic radiosurgery can be utilized in new or recurrent cancers – even after radiation, chemotherapy and/or surgery. Our local control rates are high. Comparison data seems to show an improved survival versus chemotherapy. Of course, our best results are seen when we treat so-called respectable pancreas cancers – not by surgery but by radiosurgery. Prognosis decreases when the cancer is advanced, yet we have high control rates even in the face of unresectable pancreas cancer. These cancers often spread to the liver through the blood stream. We try to offer intrusive treatment before this occurs. In select situations, we have treated both the pancreas and the metastases. For the pancreas, some chose to receive chemotherapy and concurrent fractionated radiosurgery. Each person is unique and we prefer to discuss these issues at length. Risk, benefits and alternatives are discussed.

Our data managers continue to evaluate all patients who have gone through the program to determine effectiveness and survival benefits.

We have established a hot line at 212-CHOICES and e-mail address: [gil.lederman@rsny.org](mailto:gil.lederman@rsny.org). There are also monthly seminars on brain, body and prostate cancer treatment. We invite your participation. We encourage you to learn as much as you can. We also will ask that you send in copies of films, reports, pathology for review by our panel of experts.