JS-5  Treatment of Locally Unresectable Pancreatic Cancer with Chemoradiotherapy
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The standard treatment for unresectable pancreatic cancer has traditionally used the combination of radiation (RT) and 5FU, with radiation portals including both the tumor and regional lymph nodes. The introduction of gemcitabine (Gem) offered the opportunity to improve the outcome of treatment. Gem was shown to be superior to 5FU in the treatment of metastatic disease. The discovery that Gem is also a potent radiation sensitizer made it logical to assess the combination of Gem and RT. Early studies using low dose (40 mg/m2) gem twice a week with RT, or gem with standard RT doses and portals, produced only modest results and, in some cases, substantial toxicity. We have developed an approach using full dose (1000 mg/m2) gem given on a chemotherapeutic schedule with conformal radiation, which was well tolerated and produced median survivals in the range of one year (1). When clinical trials suggested that gem-cisplatin was a promising combination, we extended our laboratory studies to assess gem + cisplatin + RT. We then designed a clinical trial of this combination, using a novel and more efficient clinical trial design (2). Although this trial produced a median survival of 13 months, there was significant toxicity (3). More recently, we have evaluated the combination of gem + oxaliplatin + RT in the laboratory and in a clinical trial (4). Our recent laboratory studies are focused on improving outcome by adding either a Chk 1 inhibitor or an EGFR inhibitor to gem-RT, and our most recent clinical trial is exploring whether toxicity can be decreased using IMRT. We are optimistic that the outcome of treatment of unresectable pancreatic cancer is improving through the rational use of multi-modality therapy.
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JS-6  Current Status in Japan Regarding Chemoradiotherapy for Pancreatic Cancer
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Pancreatic cancer is a virulent disease and a major leading cause of cancer-related mortality worldwide. Chemoradiotherapy is a treatment choice for both locally advanced disease and as an adjuvant therapy for resectable disease. In this presentation, the current status of this treatment modality in Japan is discussed.
Resectable disease
There is no consensus regarding the optimal management of patients following resection of pancreatic cancer, and the approach is different in the US and in other regions. In Japan, randomized controlled trials (RCTs) have been conducted to examine the effectiveness of systemic chemotherapy including 5-FU-based regimens and gemcitabine monotherapy, although none of them succeeded in showing any significant survival advantage for adjuvant chemotherapy.
Locally advanced disease
For patients with locally advanced disease, chemoradiotherapy has been accepted as standard because the results of RCTs in the 80’s to 90’s demonstrated a survival advantage for concurrent radiotherapy and bolus 5-FU injection. In attempts to improve the efficacy of the treatment, numerous trials using modified chemoradiotherapeutic approaches have been conducted. In an attempt to optimize radiosensitization and/or enhance the chemotherapeutic effect, various agents including protracted 5-FU, cisplatin, gemcitabine, and S-1 have been examined. To intensify local tumor control, specialized radiotherapy techniques, including intraoperative radiotherapy and hyperfractionation radiotherapy have been investigated.
Since the introduction of gemcitabine in 2001 in Japan, there have been many arguments for and against radiotherapy as a partner with chemotherapy. A Japan Clinical Oncology Group (JCOG) phase II study is being conducted to evaluate the activity of gemcitabine monotherapy for locally advanced disease.
Chemoradiotherapy has been investigated intensively, but its situation as a standard therapy is controversial in Japan.