Pancreatic Cancer
Treatment Approaches & Options

Pancreatic Cancer Action Network
OUMC

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Pancreatic Cancer
Where are we?

- Estimated 2016 data
- 3% of cancer cases
- 7% of cancer deaths
- 53,070 new cases in 2010
- 41,780 deaths in 2010
- Median survival < 6 months
- < 4% overall 5-year survival

Am Cancer Soc 2016
Pancreatic Cancer
Where were we?

1970’s

- Nihilism prevailed
- Mortality rates for resection high
- Results of therapy poor
- No effective adjuvant therapy
- No neoadjuvant therapy

“Pancreatic cancer the dismal disease”
- Fitzgerald PJ. Arch Pathol Lab Med; 1976

“The advantages of bypass over radical pancreaticoduodenectomy in the treatment of pancreatic cancer”
- Crile G. Surg Gyneco Obstet; 1970
Pancreatic Cancer
Where are we?

Contemporary Results for Resected Patients

- Median, 1 year and 5 year survival
  - 21.3 months
  - 76%
  - 23%
- 30/90 day operative mortality
  - 0.7%
  - 1.7%

Treatment Options
Non-metastatic Disease

- Locally resectable
  - Surgery first
  - Neoadjuvant therapy, then surgery
- Borderline resectable or locally advanced
  - Neoadjuvant therapy
  - Chemo or chemo/rad
Neoadjuvant Therapy

Rationale in resectable patients
- Avoid delay in post-op chemoradiation
- Identify patients with aggressive disease
- Identify patients too frail for operation
- Increase R0 resections
- Improve survival

Neoadjuvant therapy

Rationale in locally advanced patients
- Render resectable
- Improve survival
Neoadjuvant Therapy
Locally Advanced Disease

Duke study
- 111 patients
- Radiation therapy and 5Fu based chemotherapy
- 39 responders, 2 complete pathologic responses
- 72% R0 resections
- 70% node negative resections
- Median survival >16 months

Oncol 2001

Stanford study
- 15 “marginally resectable” pts studied
- Radiation therapy and 5FU based chemo
- 9/15 resected
- R0 resection in all, 7/9 N0
- 2 complete responses
- Median survival 30 months

J Gastrointest Surg 2001
Neoadjuvant Therapy
Resectable Disease
Prospective Randomized Phase II Study
- Multi-center
- Surgery first vs chemo/radiation
- Trial accrual halted early (reason unclear)
- 73 patients
- Neoadjuvant therapy well tolerated
- Minimal overall differences in outcomes

Neoadjuvant Therapy
Resectable at presentation
- 5% of patients will not undergo operation after neoadjuvant therapy
- 2% of patients will progress locally
- 14% of patients will have metastatic disease identified on re-staging
- Overall 21% of operable patients will not get operation
  - Good?
  - Bad?
  - Goff, SL and Chabot JA. The Cancer Journal 2012
Neoadjuvant Therapy
Resectable Disease

Resectable at presentation
- 77% of patients taken to OR resectable
- R0 resection achieved in 88%
- Data doesn’t allow comparisons of overall survival with or without neoadjuvant therapy

Value unclear
- Probably best in T3, N1 patients?
- No good data
Surgical Therapy

SECOND OPERATION

END STAGE

Retroperitoneal
Area to be drained.

Trimble’s Procedure

Fig. 1. Normal topography of the upper abdomen.
Trimble’s Procedure

Pyloric Preservation

Division of r. gastric a

Pylorus

Division of gastroepiploic vessels

Area resected

FIG. 1. Area of pancreas and duodenum resected. Ligation of right gastric and gastroepiploic vessels to preserve the vascular arcade on lesser and greater curvature of the stomach with an intact blood supply to pylorus and first portion of duodenum.
Pyloric Preservation

- Initially recommended for pancreatitis
- Less extensive resection
- No difference in cancer survival
- Fewer long-term GI side effects
- Now standard operation for cancer

Pancreatic Cancer Treatment Approaches & Options

- Adjuvant therapy
- GI tumor study group studies
- Interferon based therapy
- Folfirinox
- Gemcitabine/nab-Paclitaxel
Adjuvant Therapy

GITSG
- Radiation therapy 4000cGy
- 5-fluorouracil
- Prolongs median survival (11 v 20 mo)
- Increases 2 yr survival (18 % v 43%)
- Cancer 1987;59:2006-2010

Adjuvant Therapy

Interferon-based therapy
- Radiation therapy 4500 – 5000 cGy
- Interferon 3 mil units qod X 5 wks
- Continuous infusion 5FU
- Bolus cisplatin
Adjuvant Therapy

Virginia Mason Clinic study

- Prospective, nonrandomized v GITSG
- Improved 2 yr survival (84% v 54%)
- Significant toxicity in interferon group
- No one has duplicated this work


FOLFIRINOX

Medical treatment of pancreatic cancer: New hopes after 10 years of gemcitabine

It is finally a trial assessing the efficacy of a combination chemotherapy without gemcitabine: the FOLFIRINOX regimen, reported this year (2010), that has shown for the first time a significant improvement in progression free and overall survivals.

Isabelle Trouilloud*, Olivier Dubreuil, Tarek Boussaha, Céline Lepère, Bruno Landi, Aziz Zaanan, Jean-Baptiste Bachet, Julien Taleb

Clinics and Research in Hepatology and Gastroenterology (2011) 35, 364—374
FOLFIRINOX

- Oxaliplatin 85mg/m2
- Irinotecan 180mg/m2
- Leucovorin 400mg/m2, day 1
- 5-FU 400mg/m2 bolus day 1 and 2
- 400mg/m2 46 h CI biweekly

Note: FOLFIRINOX is the first regimen without gemcitabine that has shown a significant improvement in OS and PFS together with a higher RR than gemcitabine alone.

Gemcitabine/Abraxane

- Palliative Therapy
- Nab-paclitaxel 125mg/meter^2 BSA
- Gemcitabine 1000mg/meter^2 BSA

Compared to Gemcitabine alone
- Improved overall survival, progression-free survival and response rate

Pancreatic Cancer
Treatment Approaches & Options

Adjuvant Therapy
- Need better agents
- Need protocols using newer agents
- Much room for improvement

Pancreatic Cancer
Treatment Approaches & Options

Unresectable patients
- Palliation of jaundice and pain
  - Metallic stents
  - Splanchnic nerve blockade
- Chemotherapy
  - Folfirinox
  - Gemcitabine/nab-Paclitaxel
- Radiation therapy
Pancreatic Cancer
Treatment Approaches & Options

What is needed?

- Health services research
- Clinical trials
- Basic research

Health Services Research

- Education of physicians and patients
- Development of patient registries
- Advocacy
Pancreatic Cancer
Where are we?

Case Report

- 61 yr old male
- Early July/02 – abdominal pain
- Late July/02 – jaundice
- Late July - CT scan, mass in head of pancreas, no metastatic disease or local extension

Late July-October 25, 30 lb wt loss
- MRI – pancreatic head mass
- PET – Pancreatic head mass
- ERCP – Double duct sign
- Percutaneous bxs X2 inconclusive
Pancreatic Cancer
Where are we?

Case Report

- 10/31/02 Laparotomy, locally advanced, unresectable head of pancreas mass
- FNA at operation – Adenocarcinoma
- Biliary bypass done

Clinical trials

Neoadjuvant trials

- Study newer agents
- Role of radiation therapy
- Multi-center trials
Pancreatic Cancer
Where are we?

Clinical trials

Adjuvant trials
- Study newer agents
- Multi-center trials

Basic research

- Genetics
- Proteomics
- Imaging
- Active NIH program
Pancreatic Cancer
Where are we?

NIH
- Examples of NIH success
  - Breast
- Role in pancreatic cancer
  - Fund research
  - Focus programs
  - HIV

Pancreatic Cancer
Treatment Approaches & Options

Summary
- Increasingly common disease
- Basic research critical
- Clinical research critical
- NIH must play an active role