Progress in Pancreatic Cancer

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Anatomy of the pancreas

Pancreatic tumor types

- Ductal adenocarcinoma (>85%)
- Acinar cell carcinoma
- Pancreatic Neuroendocrine Tumor
- Cystic neoplasms
- Other- Lymphoma

Biology and treatment vary widely. Only a Biopsy can determine the type.
**Why is it so hard to treat?**

- No adequate screening test
- High incidence of metastatic disease at presentation
- Aggressive biology and clinical course
- Relative lack of effective systemic therapies
- Lack of understanding of the biology
Risk Factors

- Age
- Smoking (2X)
- Family History (2-3X)
- Chronic inflammation (pancreatitis)
- Obesity
- Race (higher in African-Americans)
- Diabetes mellitus (2X)
- Diet (high animal fat and red meats)

Familial syndromes
(May be suspected with 1st degree relatives, others with pancreatic cancer or other cancers)

- Hereditary Breast and Ovarian cancer (BRCA2)
- Peutz-Jeghers
- Familial melanoma syndrome
- Lynch syndrome
- Hereditary pancreatitis

Accounts for ~ 10% of cases
Personalized Cancer Care

• Creation of a treatment plan which is specific to the individual patient
• Takes into account unique tumor and patient factors
• The ability to personalize therapy increases with knowledge of the biology of the cancer.

Tumor Factors

• Stage (size, spread to nodes or organs)
• Resectability (Curable vs. Incurable)
• Available treatment options
• Likelihood of response to treatment
Patient Factors

• Symptoms
• Age
• Other medical problems
• Organ function (liver, kidneys)
• Functional capacity
• Nutritional status

Multi-disciplinary Cancer Care

Cancer is complex, many providers participate
Cancer care is a “team sport”

• Surgery
• Radiation Medicine
• Medical Oncology
• Gastroenterology
• Palliative medicine
• Radiology
• Pathology

• Nutrition
• Psychosocial support
• Oncology Nursing
• Genetics
• Pain specialists (anesthesia)
• Physical therapy
Medical Oncologist’s Role

• New diagnosis: to help decide the optimal first intervention (surgery, chemotherapy, chemotherapy + radiation)
• After resection: to give therapies to reduce the risk of recurrence
• If the disease spreads: to give therapy to prolong survival and to manage symptoms related to the cancer, while maximizing quality of life

Stage

• TNM classification (Stage I-IV)
  T= tumor extent
  N= lymph nodes involved
  M= distant spread (metastases)
• Determined by imaging (CT, PET), endoscopic and surgical staging
• Determines best treatment
Treatment Options

- Surgery
- Radiation therapy
- Chemotherapy
- Nutrition support
- Social and psychological support
- Symptom management

Standard of Care

- Determined by large studies in humans done over several years
- Evolves over time based on new trials
- Leads to consensus guidelines
- Varies based on the stage of disease
- Defines the best known therapy at the time
- NCCN
Clinical Trials

• Foundation for the advancement of cancer care
• Necessary to get new drugs approved for general use
• May involve randomization between one or the other treatment
• May or may not result in a “better” drug or treatment
• Positive trials can result in a change in the standard of care
Clinical Trials

- Participation is voluntary
- Careful consideration of the possible toxicities and possible individual benefits
- Potential for benefit of future patients
- Options vary from institution to institution
- Phases I, II, III, IV
Surgery

- Pancreaticoduodenectomy (Whipple)
- Operative mortality <2-3% in major surgical centers

Surgery

- Distal pancreatectomy with splenectomy
Adjuvant Therapy

Adjuvant therapy

- Treatment given after surgery to reduce the risk of recurrence and improve the chance of long-term survival
- Survival and risk of recurrence can be improved.
- Options:
  - Chemotherapy
  - Chemotherapy + Chemoradiation
  - Clinical trials (vaccine trials in process)
Radiation therapy

- High energy x-rays delivered to a local area to kill cancer cells
- Given with low dose chemotherapy, “radiation sensitizer”
- May reduce the risk of local recurrence
- The impact on overall survival is less certain.
- Daily therapy (M-F) for 5-6 weeks

Neoadjuvant Therapy
Neoadjuvant therapy

- Treatment prior to possible surgical resection
- Many patients can’t have upfront resection due to vascular involvement
- Allows chemotherapy and/or radiation to penetrate tumor better
- Chemotherapy allows for early treatment of occult spread of disease

Options for Neoadjuvant therapy

- Chemotherapy
- Chemoradiation
- Chemotherapy + chemoradiation
- Clinical trial (OHSU vaccine trial)
Treatment of Advanced disease

Chemotherapy

• Drugs which kill or slow the growth of rapidly dividing cells
• Affects normal and cancer cells
• May be intravenous (IV) or by mouth
• Systemic therapy
• Usually given in an outpatient clinic
• Side effects are drug and dose specific
Chemotherapy side effects

- Fatigue
- Low blood counts
- Increased risk of infection
- Anemia
- Hair loss
- Nausea and vomiting
- Diarrhea or constipation
- Loss of appetite
- Neuropathy, cold sensitivity
- Infertility

Gemcitabine

- No confirmed objective responses
- Clinical benefit response: 23.8% in Gem arm, 4.8% in 5-fu arm
- Median survival 5.65 vs. 4.41 mos
Gemcitabine + X Chemo

- Gemcitabine has been combined with many other active cytotoxic agents:
  - 5-fu
  - Cisplatin
  - Docetaxel
  - Oxaliplatin
  - Irinotecan

>10 yrs of randomized trials, no study showed survival was better compared to Gem alone
Until NOW…

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FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer

- mOS 11.1 vs. 6.8 mos
- 1 yr survival 48 vs. 20%

- Overall Survival
  - Hazard ratio, 0.57 (95% CI, 0.45–0.73)
  - P=0.001 by stratified log-rank test
Increased Survival in Pancreatic Cancer with nab-Paclitaxel plus Gemcitabine

mOS 8.5 vs. 6.7 mos
1 yr survival 35 vs. 22%
Future Advances

*Early detection*
- Imaging for high risk individuals
- Blood test

*Localized disease*
- Incorporating more active systemic therapies
- Adding immunotherapies (vaccines, other modulators)

*Advanced disease*
- Many biologic therapy trials ongoing
- Immunotherapies

Conclusions

- Pancreatic cancer remains a challenge.
- Advances in detection and treatment are still needed.
- Numerous studies incorporating new agents are ongoing.
- Enrollment in clinical trials is crucial for progress.