Progress in Pancreatic Cancer

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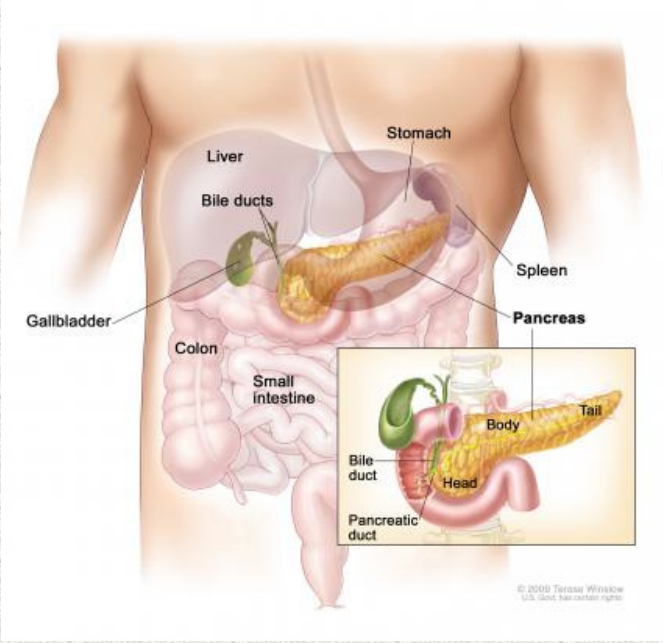
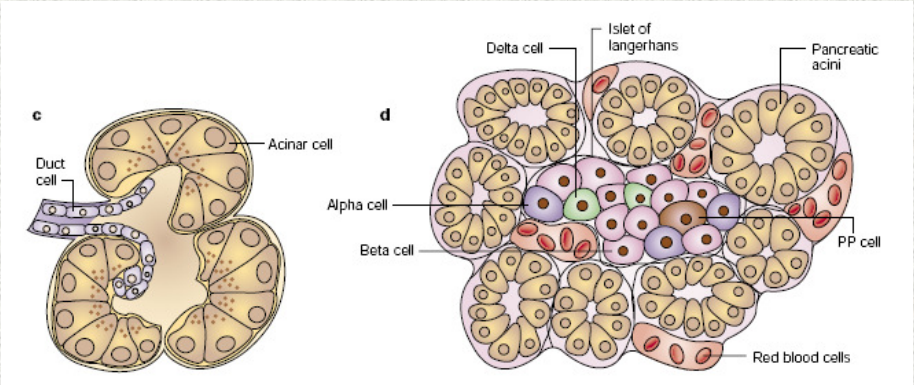


Anatomy of the pancreas



DePinho, Nature Reviews, 2002

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.

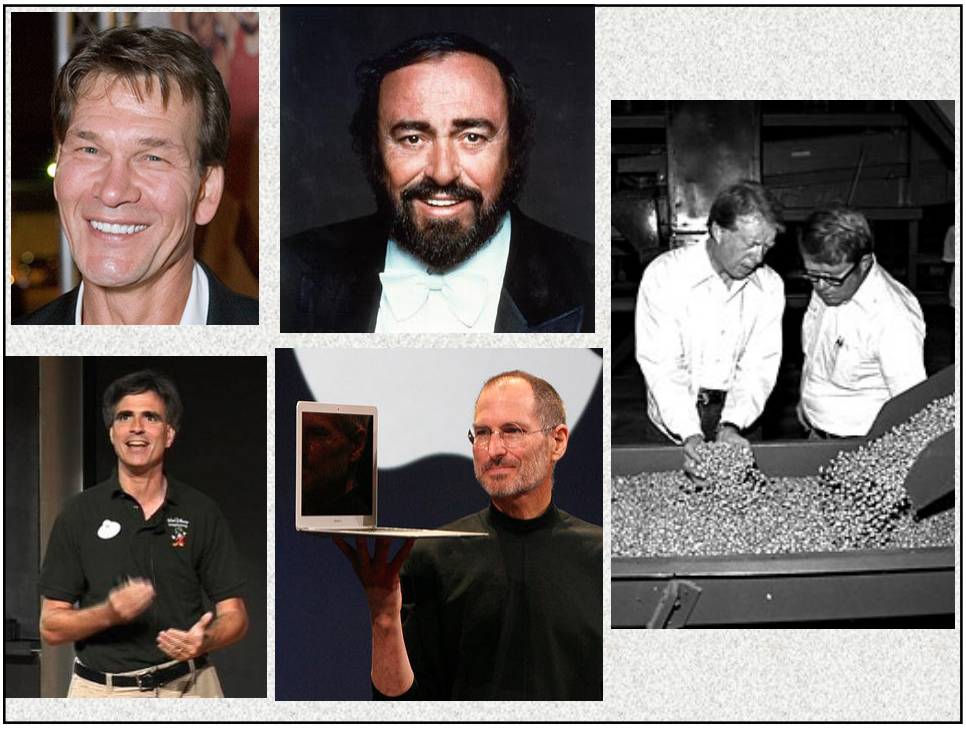
Leading New Cancer Cases and Deaths – 2014 Estimates

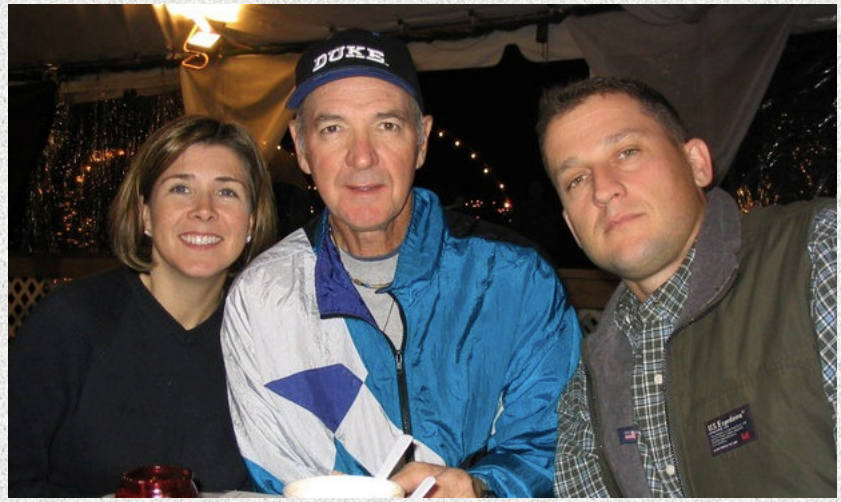
Estimated New Cases*		Estimated Deaths	
Male	**Female**	**Male**	**Female**
Prostate 233,000 (27%)	Breast 232,670 (29%)	Lung & bronchus 86,930 (28%)	Lung & bronchus 72,330 (26%)
Lung & bronchus 116,000 (14%)	Lung & bronchus 108,210 (13%)	Prostate 29,480 (10%)	Breast 40,000 (15%)
Colon & rectum 71,830 (8%)	Colon & rectum 65,000 (8%)	Colon & rectum 26,270 (8%)	Colon & rectum 24,040 (9%)
Urinary bladder 56,390 (7%)	Uterine corpus 52,630 (6%)	Pancreas 20,170 (7%)	Pancreas 19,420 (7%)
Melanoma of the skin 43,890 (5%)	Thyroid 47,790 (6%)	Liver & intrahepatic bile duct 15,870 (5%)	Ovary 14,270 (5%)
Kidney & renal pelvis 39,140 (5%)	Non-Hodgkin lymphoma 32,530 (4%)	Leukemia 14,040 (5%)	Leukemia 10,050 (4%)
Non-Hodgkin lymphoma 38,270 (4%)	Melanoma of the skin 32,210 (4%)	Esophagus 12,450 (4%)	Uterine corpus 8,590 (3%)
Oral cavity & pharynx 30,220 (4%)	Kidney & renal pelvis 24,780 (3%)	Urinary bladder 11,170 (4%)	Non-Hodgkin lymphoma 8,520 (3%)
Leukemia 30,100 (4%)	Pancreas 22,890 (3%)	Non-Hodgkin lymphoma 10,470 (3%)	Liver & intrahepatic bile duct 7,130 (3%)
Liver & intrahepatic bile duct 24,600 (3%)	Leukemia 22,280 (3%)	Kidney & renal pelvis 8,900 (3%)	Brain & other nervous system 6,230 (2%)
All sites 855,220 (100%)	All sites 810,320 (100%)	All sites 310,010 (100%)	All sites 275,710 (100%)

*Excludes basal and squamous cell skin cancers and in situ carcinoma except urinary bladder.

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




DUKE

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)

Risk Factors

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

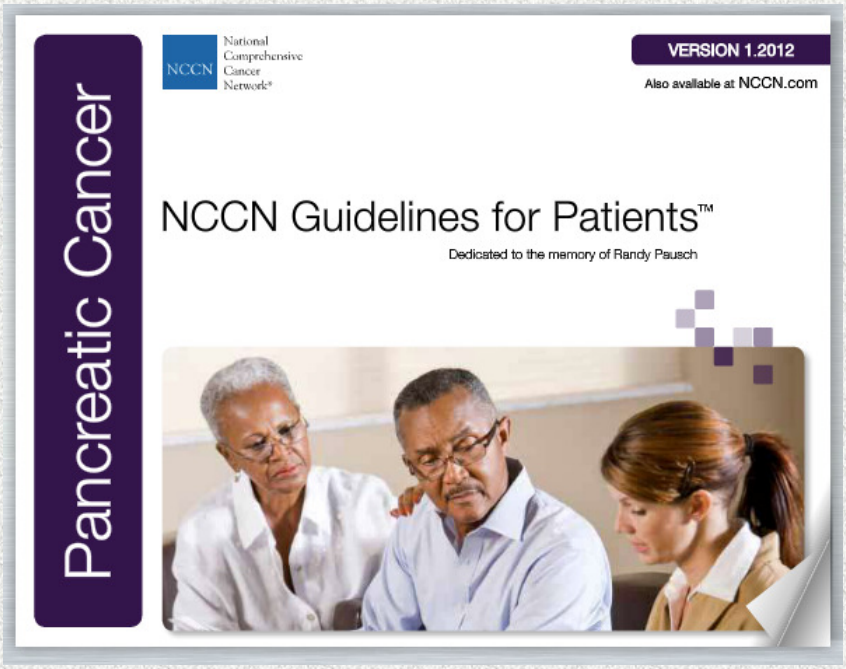
- TNM classification (Stage I-IV)
  - T= tumor extent
  - N= lymph nodes involved
  - M= distant spread (metastases)
- Determined by imaging (CT, PET), endoscopic and surgical staging
- Determines best treatment

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 (http://www.nccn.org/patients/patient_guidelines/pancreatic/index.html)

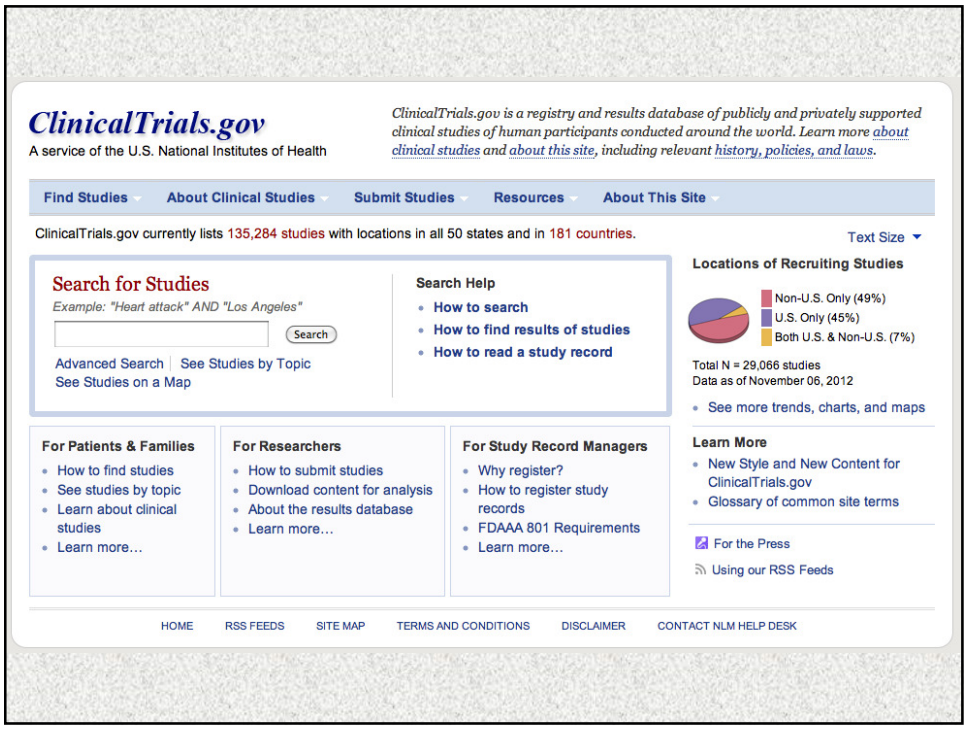


Clinical Trials

- 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

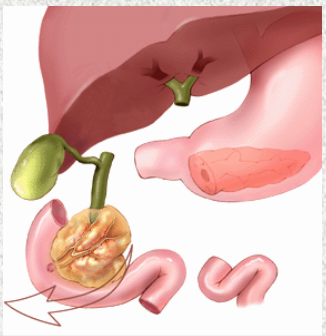
Clinical Trials

- 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

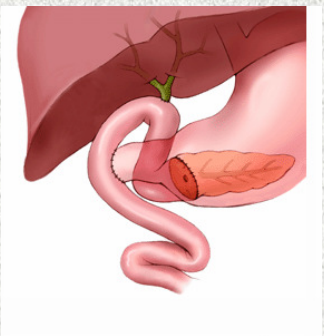


Surgery

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



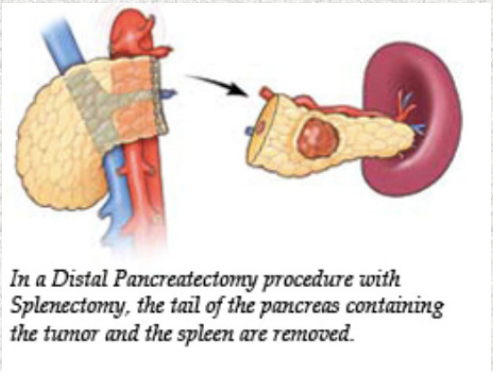
Organs removed during a Whipple



Most common anatomy after Whipple

Surgery

- Distal pancreatectomy with splenectomy



In a Distal Pancreatectomy procedure with Splenectomy, the tail of the pancreas containing the tumor and the spleen are removed.

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

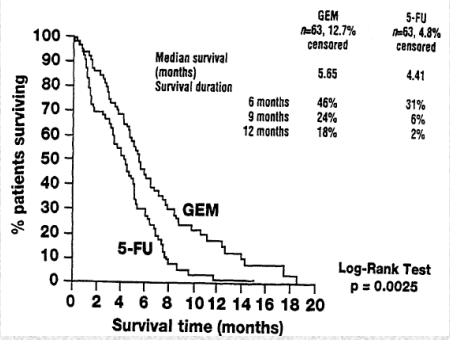
- Drugs which kill or slow the growth of rapidly dividing cells
- Affects normal and cancer cells
- May be intravenous (IV) or by mouth
- Systemic therapy
- Usually given in an outpatient clinic
- Side effects are drug and dose specific

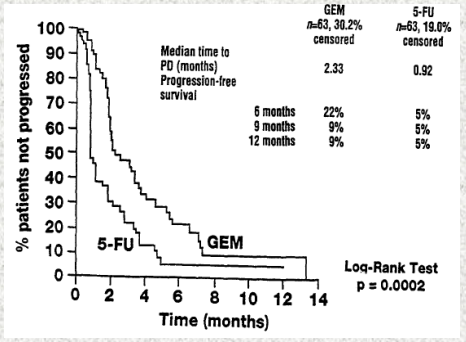
Chemotherapy side effects

- 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

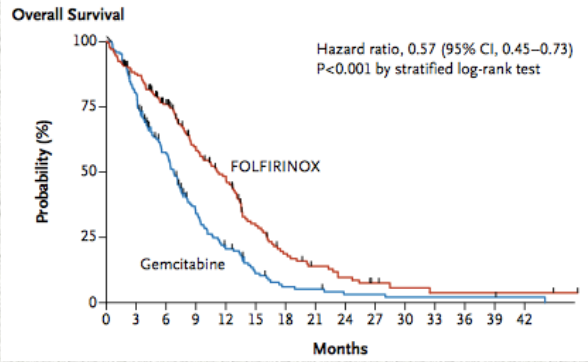
- Gemcitabine has been combined with many other active cytotoxic agents:
  - 5-fu
  - Cisplatin
  - Docetaxel
  - Oxaliplatin
  - Irinotecan……

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

Until NOW…

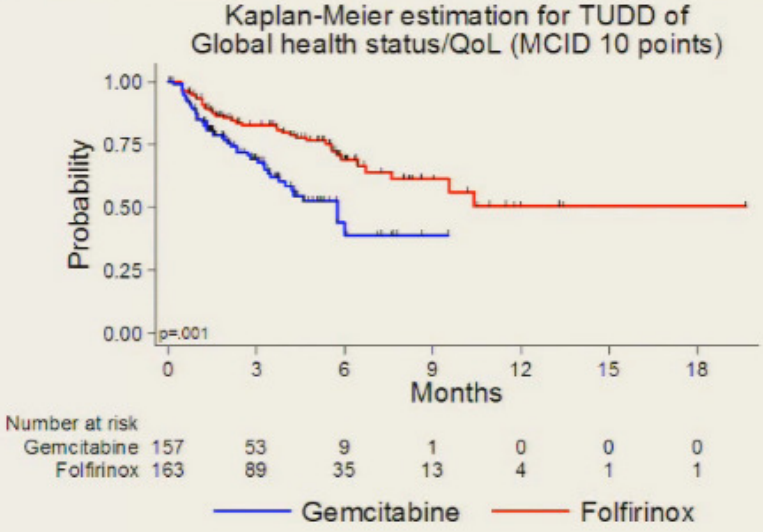
ORIGINAL ARTICLE

FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer



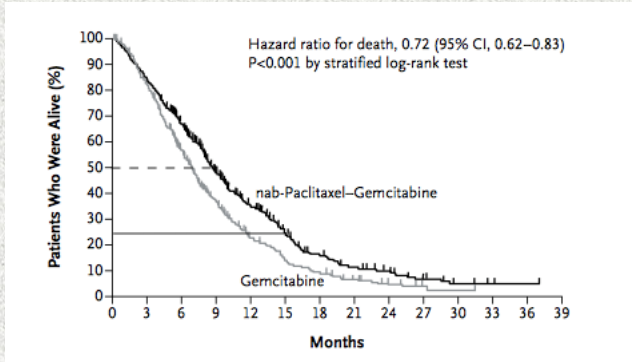
mOS 11.1 vs. 6.8 mos
1 yr survival 48 vs. 20%

Time to definitive QoL degradation



ORIGINAL ARTICLE

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.