# Pancreatic Cancer – Treatment Approaches

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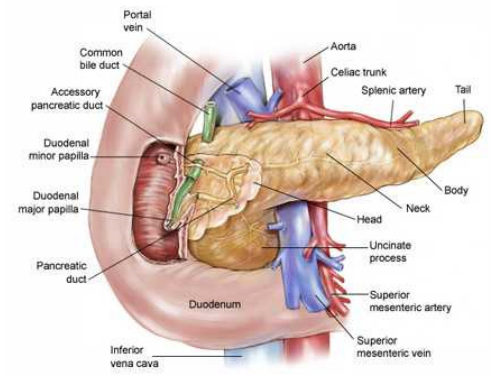
## Disclosures

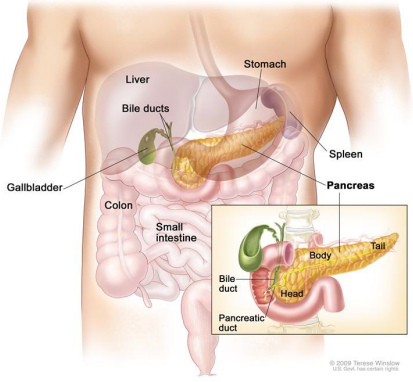
- Consultant or Advisory Role: Celgene, Cook Medical

## Introduction

- This talk highlights clinical staging and treatment approaches for 'pancreatic adenocarcinoma'
- I have used the term 'pancreatic cancer' synonymously with 'pancreatic adenocarcinoma'
- The content of this talk is not applicable to neuroendocrine cancers of the pancreas and other histologic variants

## Pancreas - Anatomy



# Pancreatic Cancer – burden of disease

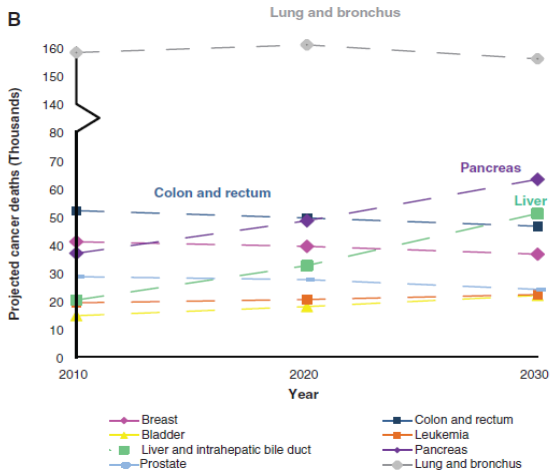
Estimated 46,420 new cases and 39,590 deaths due to pancreatic cancer in 2014

**Estimated Cancer Deaths by Sex in the United States, 2014**

| Men | | | Women | | |
|---|---|---|---|---|---|
| Lung and bronchus | 86,930 | 28% | 26% | 72,330 | Lung and bronchus |
| Prostate | 29,480 | 10% | 15% | 40,000 | Breast |
| Colon and rectum | 26,270 | 8% | 9% | 24,040 | Colon and rectum |
| **Pancreas** | **20,170** | **7%** | **7%** | **19,420** | **Pancreas** |
| Liver | 15,870 | 5% | 5% | 14,270 | Ovary |

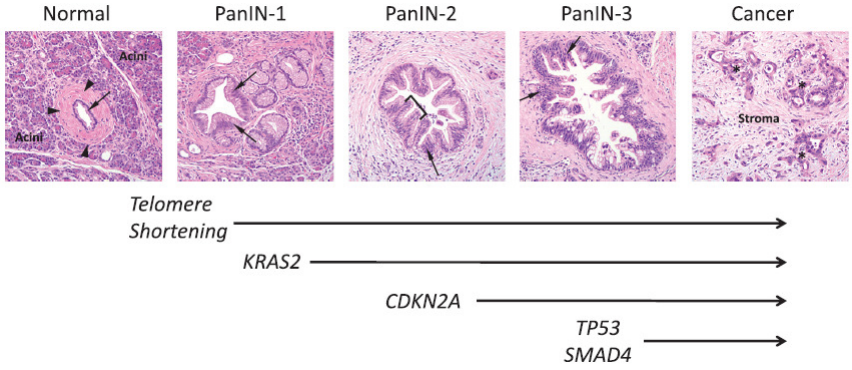
Siegel R et al, 2014

# Pancreatic Cancer is projected to become a major problem

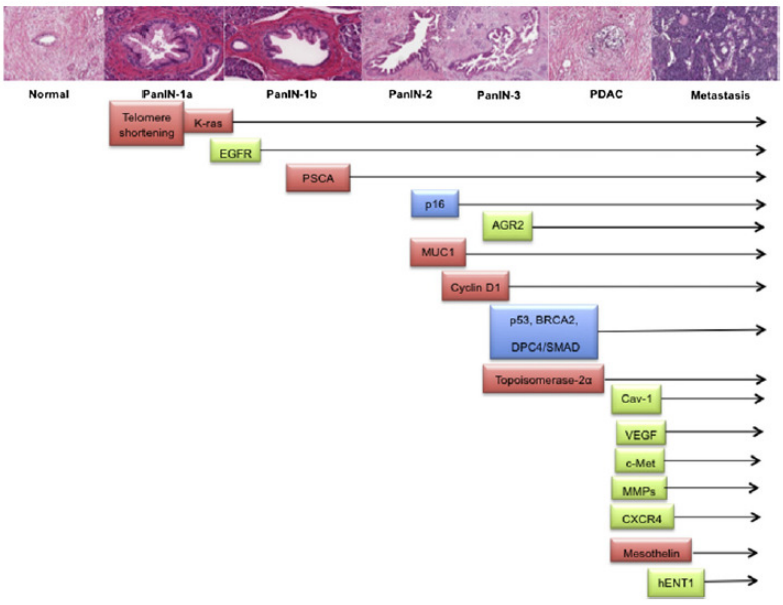



Rahib L et al, 2014

# Evolution of Pancreatic Cancer




Iacobuzio-Donahue et al, 2012




Giovinazzo et al, Surgical Oncology, 2012

## Pancreatic Cancer – Risk factors

- Cigarette smoking
- High body mass and lack of physical activity
  - Diabetes Mellitus
  - High Fat Diet
- Nonhereditary chronic pancreatitis
- Family History
- Hereditary pancreatitis
- Germ-line mutations
- Non-O blood group

## Pancreatic Cancer – Symptoms and Signs

### Symptoms

- Asthenia – 86 %
- Weight loss – 85 %
- Anorexia – 83 %
- Abdominal pain %
- Epigastric pain – 71 %
- Dark urine – 59 %
- Jaundice – 56 %
- Nausea – 51 %
- Back pain – 49 %
- Steatorrhea – 25 %

### Signs

- Jaundice – 55 %
- Hepatomegaly- 39 %
- RUQ mass – 15 %
- Cachexia – 13 %
- Epigastric mass – 9 %
- Ascites – 5 %

## Pancreatic Cancer Imaging

- Triple-phase contrast-enhanced thin-slice (multi-detector row) helical computed tomography (MDCT) with 3 D reconstruction
- Endoscopic Ultrasound (EUS)
- Positron Emission Tomography (PET) scan
- Magnetic Resonance Imaging (MRI)

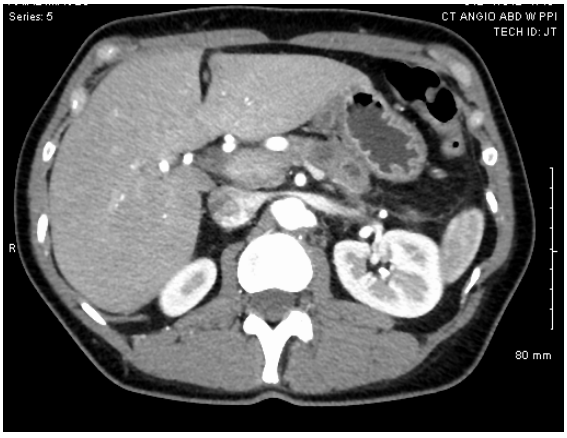
## Pancreatic Cancer - Staging

- T – Tumor size
  - T0 – T4
- N – Lymph node status
  - N0-N1
- M – Metastases
  - M0-M1
- Stages
  - I – IV (based on T, N and M status)

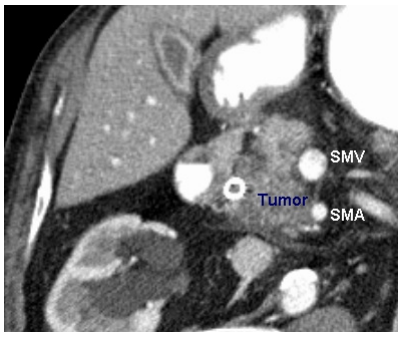
## Pancreatic Cancer Clinical Staging

- Resectable pancreatic cancer
- Borderline resectable pancreatic cancer
  - Katz A
  - Katz B
  - Katz C
- Locally advanced pancreatic cancer
- Metastatic pancreatic cancer

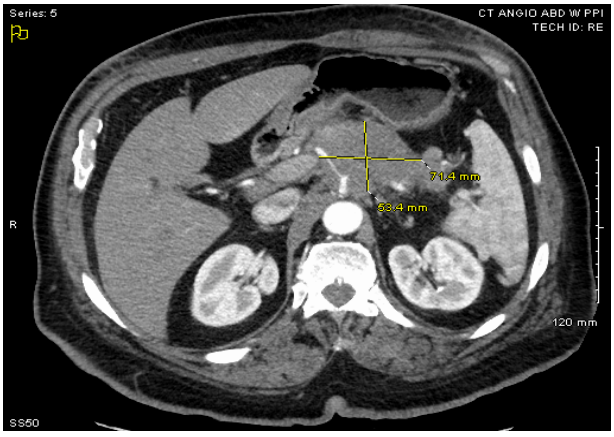
## Resectable pancreatic cancer



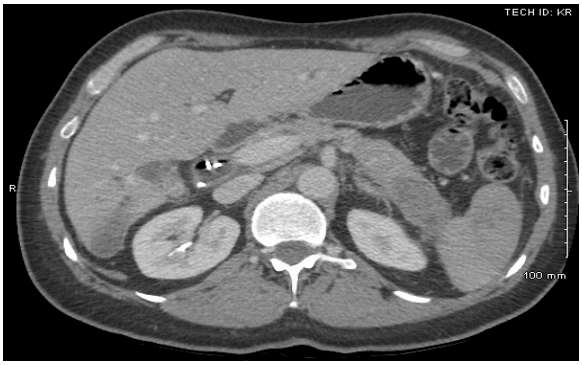
## Borderline resectable pancreatic cancer




## Locally advanced pancreatic cancer



## Metastatic pancreatic cancer




## Cancer Concepts/Terminology

- Resectable, borderline resectable, locally advanced and metastatic pancreatic cancer
- Synchronous/Metachronous
- Concept of metastases/micro-metastases
- Systemic therapy = Chemotherapy (cytotoxics) & biologic/targeted agents
- Adjuvant therapy/Neo-adjuvant therapy
- Response Rate (RR)

## Principles of Cancer Therapy

- Goals of Therapy – Curative Intent or Palliative
- Treatment modalities offered are often locoregional and/or systemic
- Treatments offered depends on stage of cancer and patterns of recurrence/mode of metastases
- Disease recurrence can be a result of metachronous primary or locoregional/distant metastases

## Principles of Cancer Therapy

- Cancer stage usually correlates with survival
  - Biology trumps everything else
- Clinical staging may or may not be equal to pathologic staging
  - clinical staging has limitations
- Scans don't tell the complete story
- Stage IV = metastases = palliative intent therapy with rare exceptions
- Not all stage IV cancers are equal

## Principles of treatment

- Resectable and borderline resectable pancreatic cancer patients are treated with a curative intent
- Locally advanced and metastatic pancreatic cancer patients are treated with a palliative intent
- Surgery offers the only chance for cure but only 15 to 20% of patients have resectable disease at initial diagnosis
- Reported 5-yr survival rates following surgery (PD) for node-negative and node-positive disease are 25-30% and 10 %, respectively
- Therefore, surgery is essential but not sufficient for cure

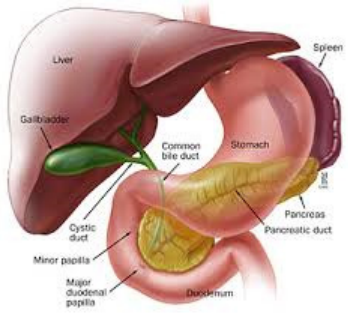
## Pancreatic Cancer – components of treatment

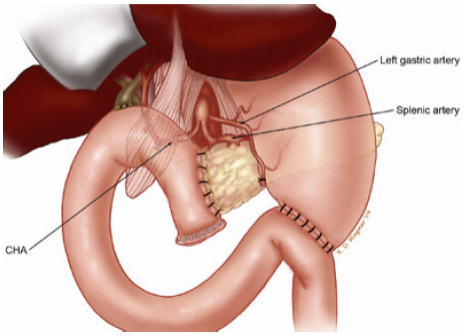
- Surgery
- Chemotherapy (CT) – systemic treatment
  - Offers local/regional benefit and systemic benefit
- Radiotherapy (RT)
  - Offers local/regional benefit
- Surgery, chemotherapy and radiotherapy are essential for curing pancreatic cancer
- The optimal sequence of these treatment modalities is still evolving

# Curative Intent Treatment

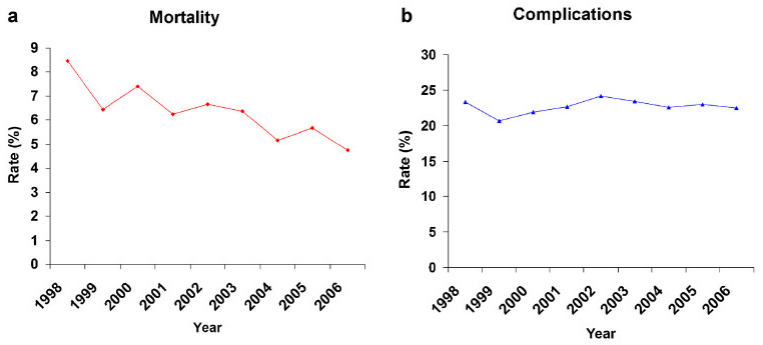
Resectable and Borderline Resectable Pancreatic Cancer

## Surgery for pancreatic cancer

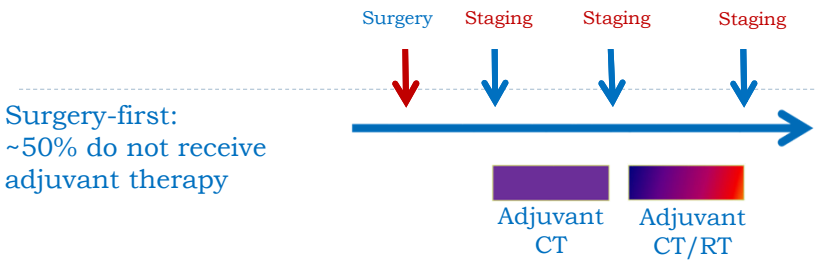


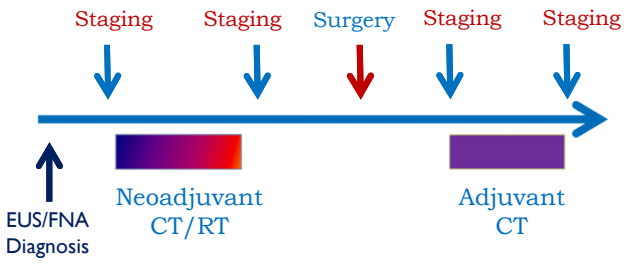
# A complex surgery




Simons et al, 2009

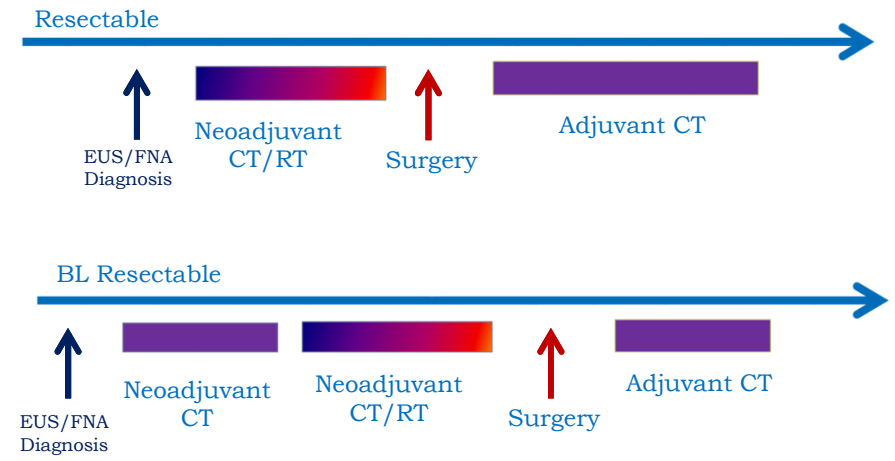



Surgery-first:
~50% do not receive adjuvant therapy




Neoadjuvant ~30% do not receive surgery

## Neoadjuvant Treatment Sequencing




## Palliative Treatment

Locally Advanced & Metastatic Pancreatic Cancer

## Metastatic Pancreatic Cancer (MPC): Landmarks

- **1996:** Gemcitabine improved survival compared to 5-FU
- **2005:** Gemcitabine + Erlotinib improved survival compared to Gemcitabine
- **2010:** FOLFIRINOX (FFX) improved survival compared to Gemcitabine
- **2013:** *nab*-Paclitaxel + Gemcitabine (*Nab*-P/G) improved survival compared to Gemcitabine

## Principles of treatment

- Locally advanced pancreatic cancer
  - 4 months of chemotherapy → Chemo-radiotherapy
- Metastatic pancreatic cancer
  - Chemotherapy
- Role of Clinical Trials cannot be emphasized enough

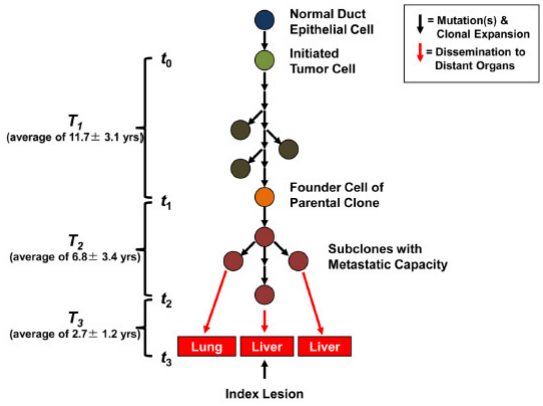
## Supportive Care

- Venous thromboembolism (VTE)
  - Low molecular weight heparin/warfarin
- Biliary Obstruction
  - Plastic/Metal stent
  - Percutaneous Drain
- Exocrine Pancreatic Insufficiency
- Cancer related Cachexia
- Diabetes Management

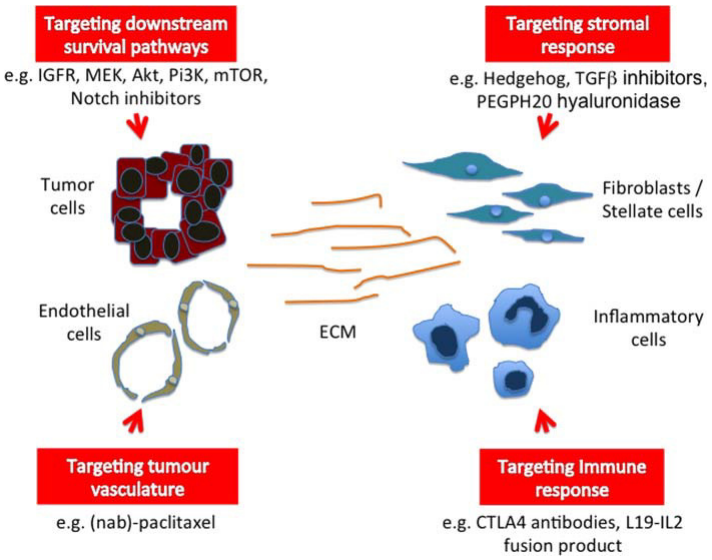
## Treatment of Pancreatic Cancer

What are the challenges?

# Challenges - evolution




Yachida et al, 2010




Michl et al, Gut, 2012

# Multidisciplinary Team

Clinical Team

- Surgical Oncology
- Medical Oncology
- Radiation Oncology
- Gastroenterology
- Radiology
- Interventional Radiology
- Pathology
- Palliative Care/Pain Clinic

Supportive Team

- Nutrition
- Diabetes management team
- Psychosocial support
- Genetic Counseling
- Oncology Nursing
- Physical/Occupational Therapy