PANCREATIC CANCER ACTION NETWORK®

A Multidisciplinary Approach to Pancreatic Cancer

May 6, 2019

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A Multidisciplinary Approach to Pancreatic Cancer

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Agenda

- Introduction
- Patient presentation – localized pancreatic cancer
  - Diagnostic tests
  - Multidisciplinary treatment
- Patient presentation – metastatic pancreatic cancer
  - Genetic testing for the patient and the tumor
  - Multidisciplinary management
  - Clinical trial participation
- Family members of patients with pancreatic cancer
  - Screening for high-risk individuals

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Introduction

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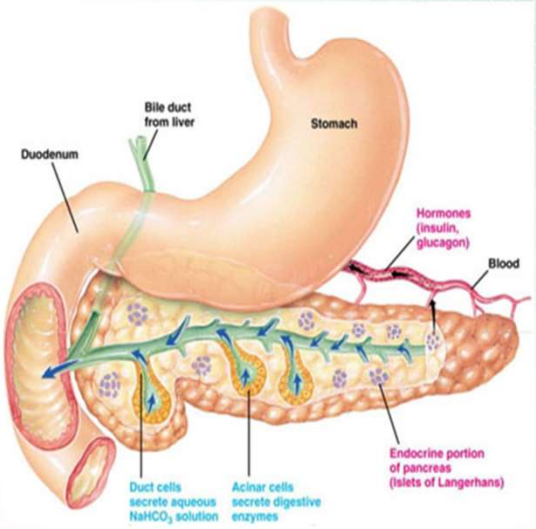
The pancreas

Exocrine cells

Produce enzymes that help with digestion

Endocrine cells

Produce hormones that regulate blood sugar levels:
Insulin - ↓
Glucagon - ↑



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Pancreatic cancer

- ❑ Pancreatic cancer begins when abnormal cells within the pancreas grow out of control and form a tumor
- ❑ More than 95% of pancreatic cancers are **exocrine** tumors also called Pancreatic Ductal AdenoCarcinoma (PDAC)
- ❑ Pancreatic neuroendocrine tumors (PNETs) account for less than 5% of all pancreatic tumors. These can have a very benign or a very malignant behavior but most are indolent / slow growing

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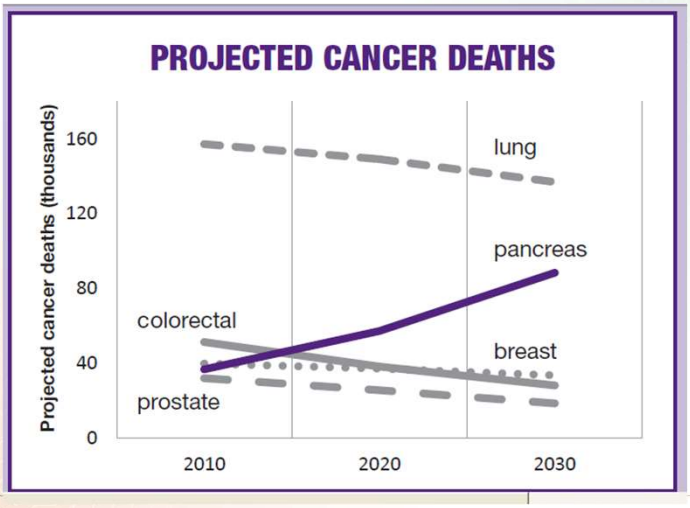
Pancreatic cancer

Pancreatic Cancer Will be 2nd Most Common Cause of Cancer Death By Year 2020



Risk factors for PDAC

Risk factors that ***can*** be changed or avoided

- Cigarette smoking
  - Risk is two times higher than never-smokers
  - 20% - 30% of all PDACs
  - Cigars and smokeless tobacco also a risk factor
- Overweight and obesity
  - Obese people are 20% more likely to develop PDAC

Unclear risk factors, but modifiable

- Diet
  - Animal Products
  - Starch Rich
  - Western
- Alcohol

Risk factors for PDAC

Risk factors that ***cannot*** be changed or avoided

- Family history
- Diabetes
  - Most risk with Type 2 diabetes – adult onset
  - Maybe related to being overweight or obese
  - Unclear if risk with Type 1 (juvenile) diabetes
- Chronic pancreatitis
  - Long-term inflammation of the pancreas (especially in smokers)
  - Most people with pancreatitis never develop PDAC

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Patient presentation: Localized pancreatic cancer

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Patient 1

65 year-old male

- ❑ Smoker for 40 years
- ❑ Weight loss of 20 pounds unintentionally
- ❑ Indigestion not relieved with antacids
- ❑ Now with dark urine and yellow eyes over the last 2 days

Laboratory results:

Bilirubin	8.3 mg/dL
Alkaline Phosphatase	365 U/L
AST	67 U/L
ALT	126 U/L
CA19-9	350 U/mL

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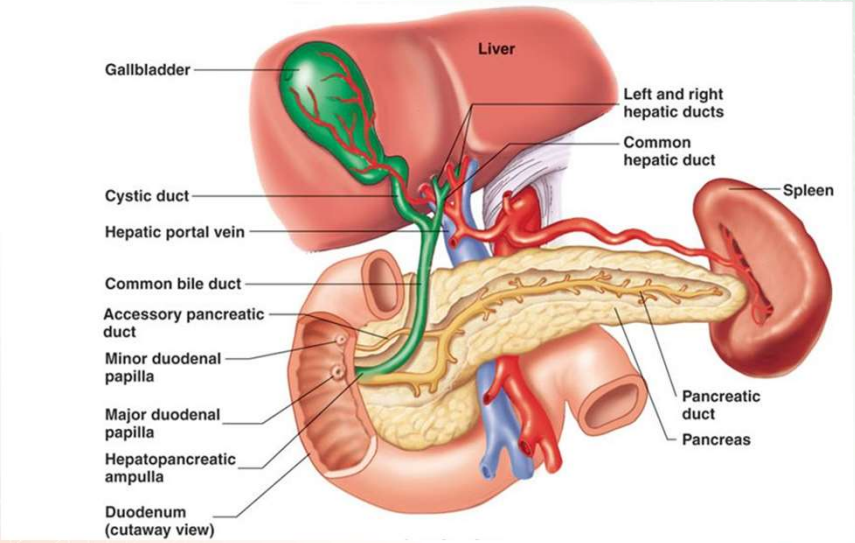
Pancreas anatomy basics



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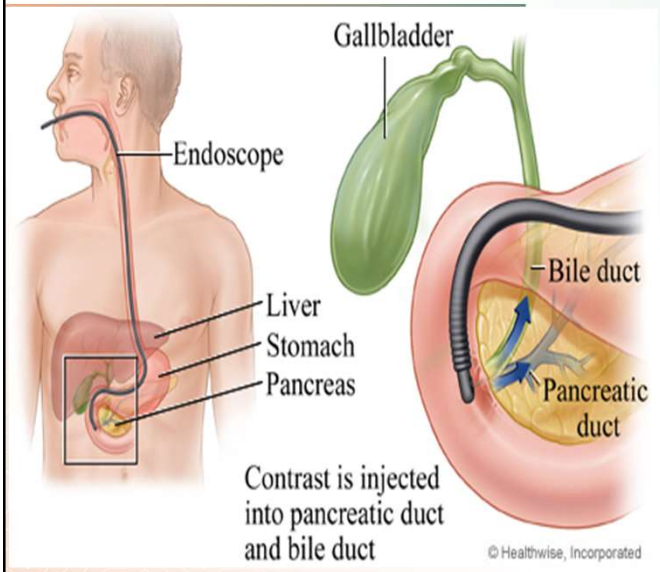
ERCP



Biopsies, or samples of the tumor, can be obtained

Pictures taken show if the pancreatic or bile ducts are narrowed or blocked by a tumor

If bile duct is blocked a small plastic or metal stent, can be placed into a blocked bile duct to keep it open and allow bile to flow

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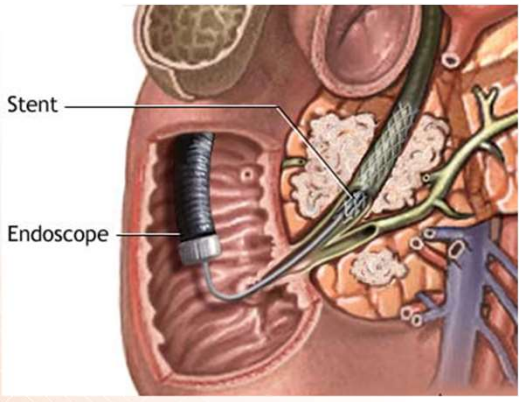
ERCP



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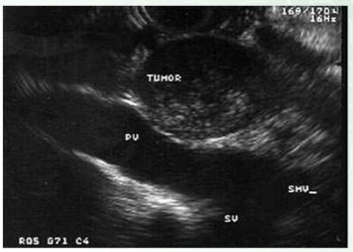
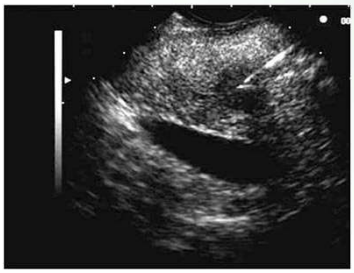
EUS

- Detailed ultrasound pictures of the pancreas, bile duct and digestive tract
- Allows determination of:
  - Size and location of a tumor in the pancreas
  - Tumor spread to nearby lymph nodes
  - Invasion of nearby blood vessels
- Main use is to obtain a biopsy - fine-needle aspiration (FNA) or fine-needle biopsy (FNB)
- Also used for celiac plexus block (a type of nerve block) for pain relief





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Pancreatic protocol CT scan

- **CT scans are used to:**
  - Detect the presence of a tumor
  - Determine the size and location of a tumor
  - Determine if the tumor has metastasized, or spread to other tissues
  - See the relationship of the tumor to surrounding blood vessels
  - Guide a biopsy
  - Help plan for surgery or radiation therapy
  - Determine whether the tumor is responding to treatment
- **Pancreatic protocol CT scan**
  - This is a special technique of doing the scan with “thin slices” through the pancreas to get better resolution pictures of the tumor and the blood vessels

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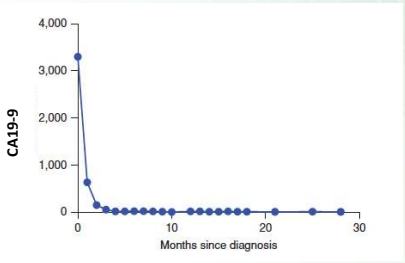
PET/CT scan

- PET/CT scanning combines two imaging tests into one procedure
- Images detect tissues that are using more glucose
  - Cancer cells use glucose at a faster rate than normal cells
  - Pancreatitis, infections, surgeries, and other diseases may change the way cells use glucose
  - Could produce false-positive results
- A PET/CT is not a substitute for a high-quality, contrast-enhanced pancreas protocol CT scan

Serum CA19-9 level

- CA 19-9 is a protein released by pancreatic tumor cells and measured in blood
- Elevated in many patients with pancreatic cancer – can be used to track the response to treatment or raise suspicion for relapse
- About 15% do not secrete these antigens - level can be normal even with PDAC
- Many conditions can cause elevation of CA 19-9
  - Other cancers
  - Jaundice
  - Pancreatitis
  - Cirrhosis
- **Cannot be used as a screening or diagnostic test for PDAC**



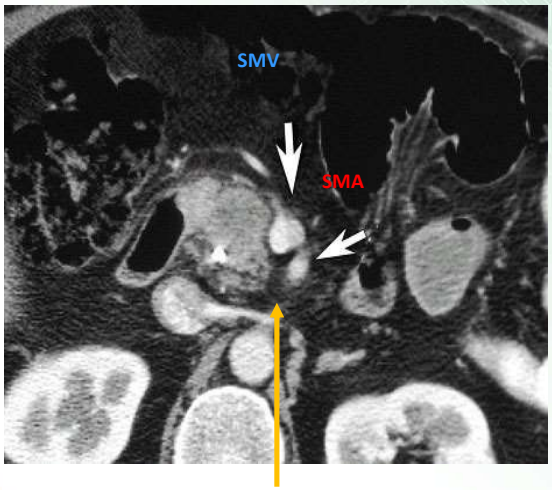
Back to patient 1

ERCP - placement of a stent in the distal common bile duct

EUS - 1.5cm mass in the head of the pancreas; biopsy - adenocarcinoma

Pancreatic protocol CT - done after the ERCP and shows the stent. This scan also confirmed that there was no interface between the tumor and the super mesenteric artery or vein

There were no visible lymph nodes or other metastases seen on the CT scan.



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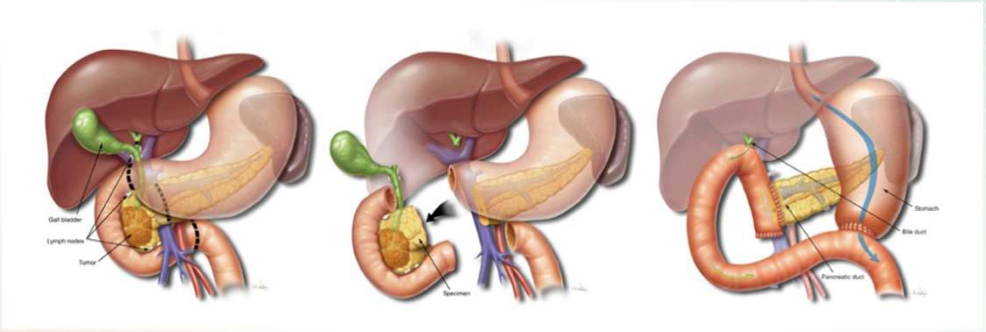
The Whipple



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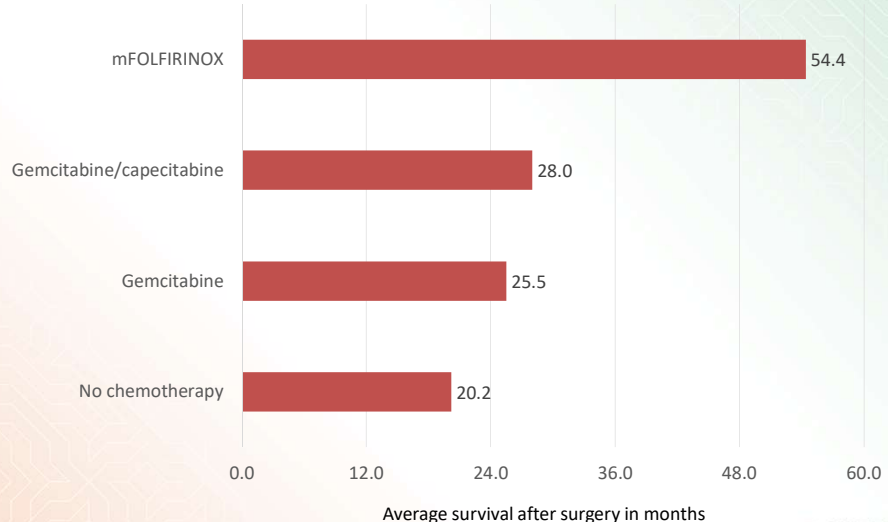
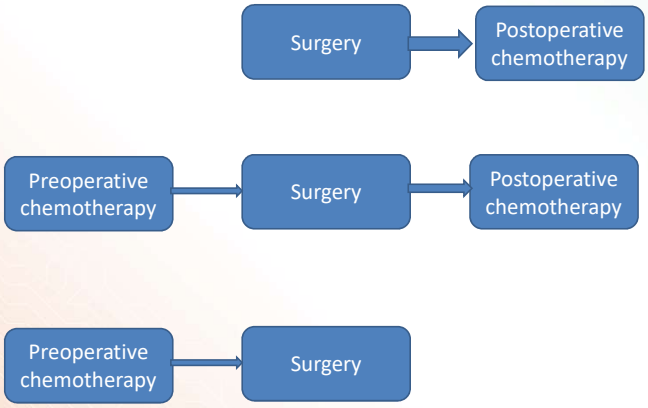
Patient 1 Pathology Result

- ❑ The patient underwent a whipple procedure (pancreaticoduodenectomy)
- ❑ The tumor was 1.8cm in size
- ❑ All the resection margins were negative (clean)
- ❑ All 22 lymph nodes resected were negative
- ❑ The pathologic stage was T3 N0 (stage IIA)
- ❑ The patient was referred to medical oncology 4 weeks post-operatively

Options for post-operative "adjuvant" chemotherapy



What about pre-operative "neoadjuvant" chemo?



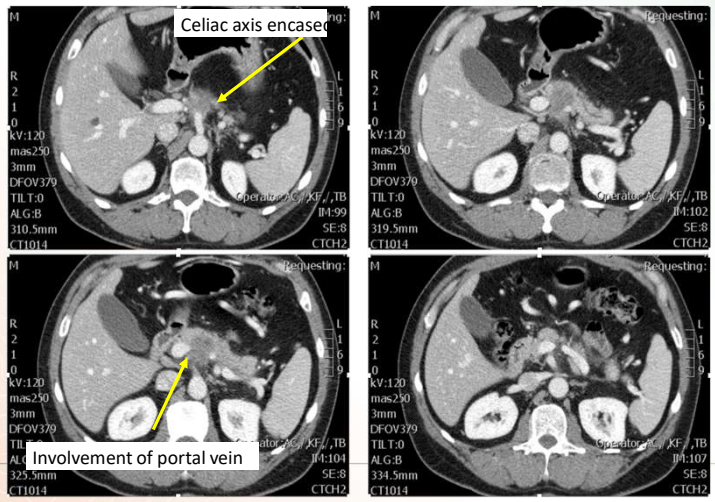
What if the tumor is "borderline resectable"?

- ❑ Pancreatic cancers which can be technically resected, but which can be expected to have a higher than average incidence of positive margins (and therefore less favorable prognosis)
- ❑ Should be treated with neoadjuvant (preoperative) chemotherapy

What about unresectable tumors?

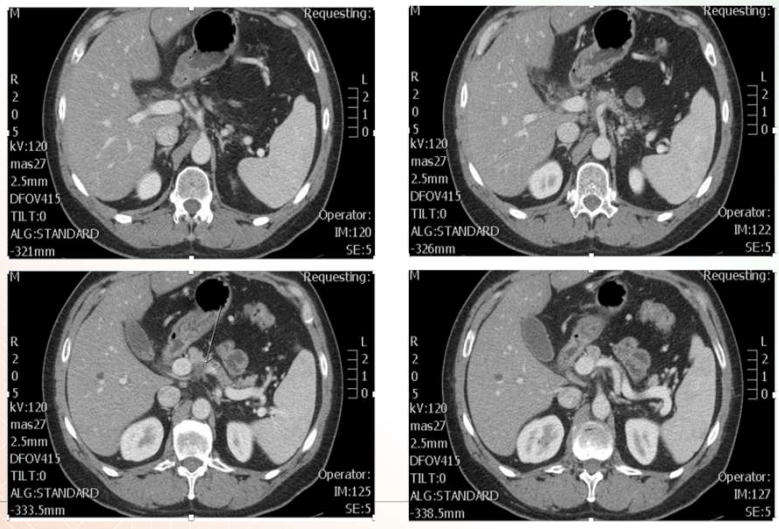
45 year-old male coming in with back pain

- ❑ CA19-9 = 1213
- ❑ EUS/biopsy confirmed PDAC



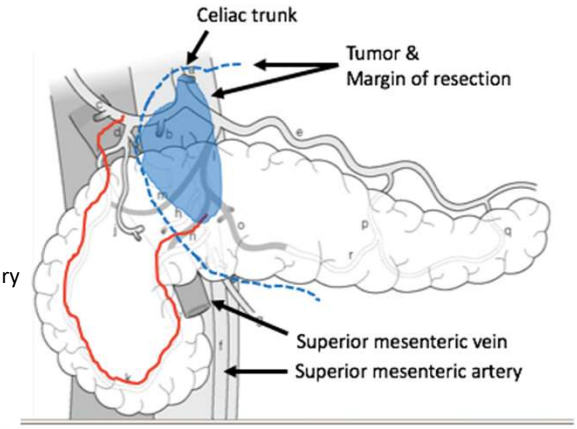
Patient 2

- ❑ Treated with FOLFIRINOX for 10 cycles then radiation therapy
- ❑ CA19-9 level came down from 1213 to 22



Procedure

- Diagnostic laparoscopy
- Subtotal distal pancreatectomy with splenectomy
- Celiac artery axis and common hepatic artery resection
- Portal vein resection with primary repair



- Outcome
  - **Complete pathologic response**
  - **All margins negative**
  - **All 12 lymph nodes negative**

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Patient presentation: Metastatic pancreatic cancer

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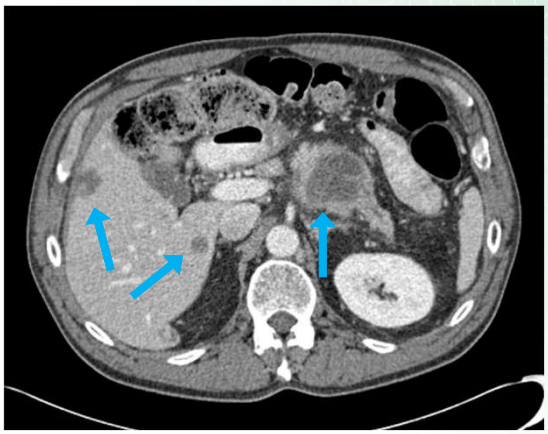
Patient 3

66 year-old male with worsening left upper abdominal pain. He went to his local emergency room where a CT scan was performed.

The CT showed a mass in the pancreas as well as liver lesions which were very suspicious for metastatic PDAC

CA19-9 level was 10, 824

A liver biopsy confirmed adenocarcinoma



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Symptom management in PDAC

- Patients with newly diagnosed metastatic PDAC usually are very symptomatic
- Early referral to palliative care for symptom management is encouraged
- Common problems:
  - Cancer-related pain
    - Opioids and celiac plexus block
  - Weight loss
    - Consult an oncology dietician
    - Start pancreatic enzyme replacement therapy
  - Depression
    - Consult a psychologist or psychiatriast

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Patient 3

- Other pertinent history:
  - He is of Ashkenazi Jewish descent
  - His mother had breast cancer in her 80's
  - His maternal grandfather also had breast cancer
- This history triggered germline genetic testing:
  - He was found to have the Ashkenazi Jewish founder **mutation in BRCA2** denoted 6174delT
- Tumor (somatic) genetic testing (next generation sequencing) was also performed:

Microsatellite status MS-Stable §	***RAD21*** amplification §
Tumor Mutational Burden 3 Muts/Mb §	***RNF43*** R117fs*39
BRCA2 S1982fs*22	***SMAD4*** Y276fs*24
KRAS G12D	***TP53*** V216M

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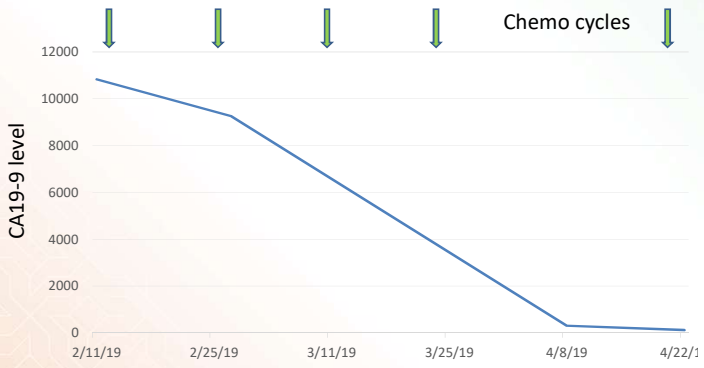
Patient 3

- Treatment course: Started mFOLFIRINOX chemotherapy
  - Pain improved
  - Appetite improved
  - Energy level improved



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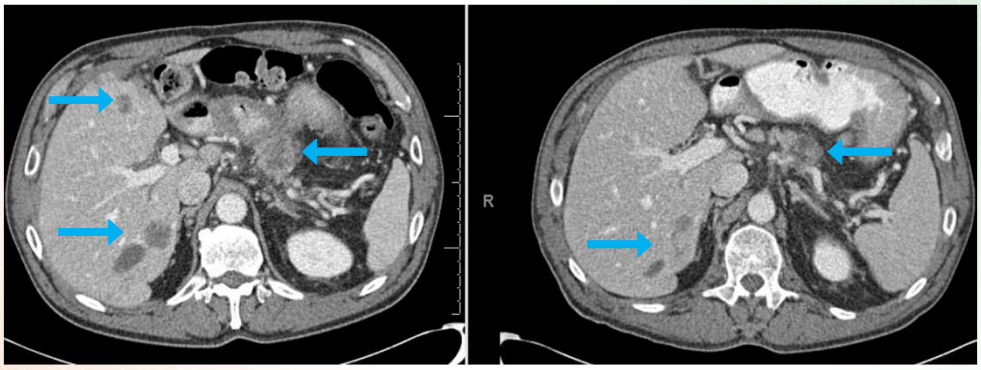
Patient 3

Treatment course: Started mFOLFIRINOX chemotherapy



Pre-treatment CT scan showing pancreatic mass and liver lesions

Post-treatment CT scan showing Significant shrinkage of the pancreatic Tumor as well as the liver lesions

Chemotherapy selection

FOLFIRINOX		Gemcitabine/Abraxane
Three	**Chemo drugs**	Two
Every 2 weeks	**Schedule**	Three weeks on and one week off
4-6 hours on first day followed by a 2-day infusion pump	**Duration**	One hour infusion weekly
Uncommon	**Hair loss**	Very common
Common	**Nausea**	Uncommon
Very frequent	**Diarrhea**	Uncommon
Always	**Cold sensitivity**	Rare
Common	**Fatigue**	Common

Chemotherapy selection

FOLFIRINOX		Gemcitabine/Abraxane
May be better in patients with BRCA or other similar gene mutations	**Biomarker**	No biomarker
Can improve quality of life and prolong survival	**Effectiveness**	Can improve quality of life and prolong survival
Not recommended	**Elderly/frail patients**	Can be given with dose and schedule modifications

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Clinical trial participation

Pancreatic cancer patients who participate in clinical research have better outcomes. Every treatment available today was approved through a clinical trial. The Pancreatic Cancer Action Network strongly recommends clinical trials at diagnosis and during every treatment decision.

What are clinical trials?

Clinical trials are research studies that investigate new treatments or new combinations of treatments. Pancreatic cancer clinical trials are necessary to determine whether new treatments developed in the laboratory are beneficial to people living with pancreatic cancer. The Food and Drug Administration (FDA) reviews and analyzes data from successful clinical trials to determine whether an experimental treatment should be approved for a specific disease or disorder, such as pancreatic cancer.

In the fight against pancreatic cancer, clinical trials often provide the best treatment options, and they give patients early access to cutting-edge treatments that can lead to progress in research, improved treatment options and better outcomes.

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Screening for high-risk individuals

Who Should Have Germline Genetic Testing?

- ❑ Family history of pancreas cancer
- ❑ Young age at diagnosis of pancreas cancer

- ❑ Recent National Comprehensive Cancer Network guidelines
  - ➢ Consider for all patients with a personal history of pancreatic cancer *after* counselling
  - ➢ Clinical value still being determined

- ❑ Panel testing includes many cancer susceptibility genes
  - ➢ Identifies 1 or more so-called deleterious variants that are only weakly associated with cancer risk
  - ➢ Interpretation can be challenging for practitioners
  - ➢ Anxiety for patients

Inherited genetic syndromes and PDAC

< 10% of PDACs

- **Hereditary breast and ovarian cancer syndrome -** *BRCA1* or *BRCA2* genes
- **Familial atypical multiple mole melanoma (FAMMM) syndrome** - *p16/CDKN2A* gene
- **Familial pancreatitis** -*PRSS1* gene
- **Lynch syndrome** (H*ereditary non-polyposis colorectal cancer*) - *MLH1* or *MSH2* genes
- **Peutz-Jeghers syndrome** - *STK11* gene
- **Von Hippel-Lindau syndrome** - *VHL* gene

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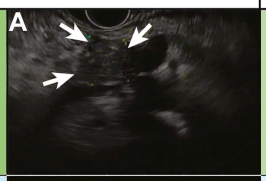
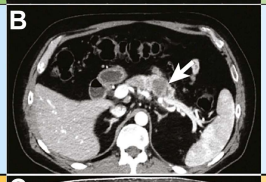
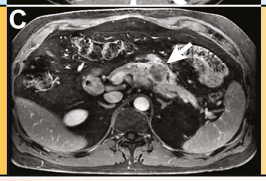
Who Gets Pancreas Screening?

- Appropriate age
- Carriers of a germline mutation in a pancreatic cancer susceptibility gene
- Multiple blood relatives with pancreatic cancer
  - At least 1 first-degree and 1 second-degree relative with pancreatic cancer

	Who should be screened?
	Statements
A1	Individuals with three or more affected blood relatives, with at least one affected FDR, should be considered for screening.
A2	Individuals with at least two affected FDRs with PC, with at least one affected FDR, should be considered for screening once they reach a certain age.
A3	Individuals with two or more affected blood relatives with PC, with at least one affected FDR, should be considered for screening.
A4	All patients with Peutz–Jeghers syndrome should be screened, regardless of family history of PC.
A5	*p16* carriers with one affected FDR should be considered for screening.
A6	*BRCA2* mutation carriers with one affected FDR should be considered for screening.
A7	*BRCA2* mutation carriers with two affected family members (no FDR) with PC should be considered for screening.
A8	*PALB2* mutation carriers with one affected FDR should be considered for screening.
A9	Mismatch repair gene mutation carriers (Lynch syndrome) with one affected FDR should be considered for screening.

Canto M. International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer. Gut. 2013.

How Do We Screen?

		Advantages for early detection	Disadvantages for early detection
Endoscopic ultrasound (EUS)		• Highest sensitivity and specificity • Provides excellent resolution for small lesions • Can be used with FNA for diagnosis	• Not practical for routine screening • Can be dependent on technical expertise
Computed tomography (CT)		• High sensitivity and specificity • Generally standardized and available • Can be relatively easy to interpret	• Exposes patient to radiation • Requires iodine contrast, which can cause reaction in some patients
Magnetic resonance imaging (MRI)		• High sensitivity and specificity • Provides good soft tissue contrast • Does not expose patient to radiation	• Less standardized than CT • Can be difficult to do for patients with certain medical devices, claustrophobia, or allergies to gadolinium

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Gastroenterology 2019 156, 2024-2040DOI: (10.1053/j.gastro.2019.01.259)

Cancer of the Pancreas Screening

- ❑ Cancer of the Pancreas Screening
  - ➢ Baseline EUS followed by EUS, MRI, or CT
- ❑ 16-year follow-up study of individuals at high-risk for PDAC
- ❑ Most PDACs detected during surveillance (9/10) were resectable
- ❑ Most (85%) of these patients survived for 3 years

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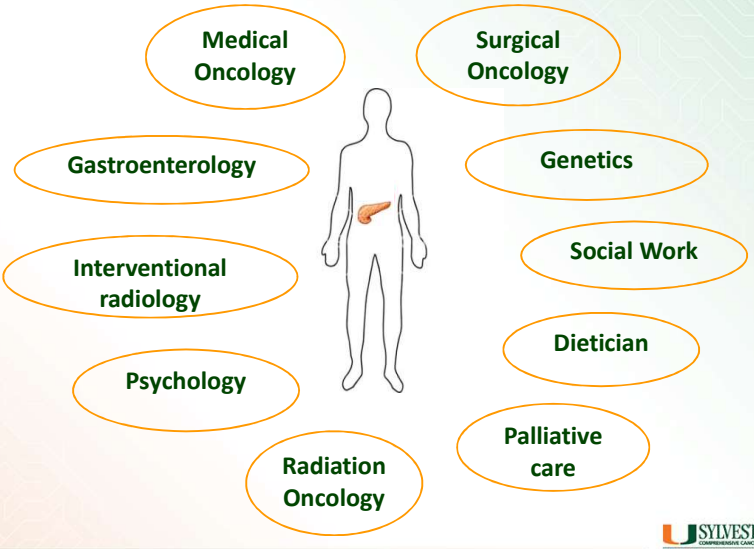
Gastroenterology 2019 156 (7).

Summary



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Thank You

Questions?

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Thank you for your participation.

If you have questions, please contact
Patient Central at
877-2-PANCAN or e-mail patientcentral@pancan.org.

www.pancan.org

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