Providence

Pancreatic Adenocarcinoma:

"Stigma vs. Fact- Is Pancreatic Cancer Survivable in 2021?"

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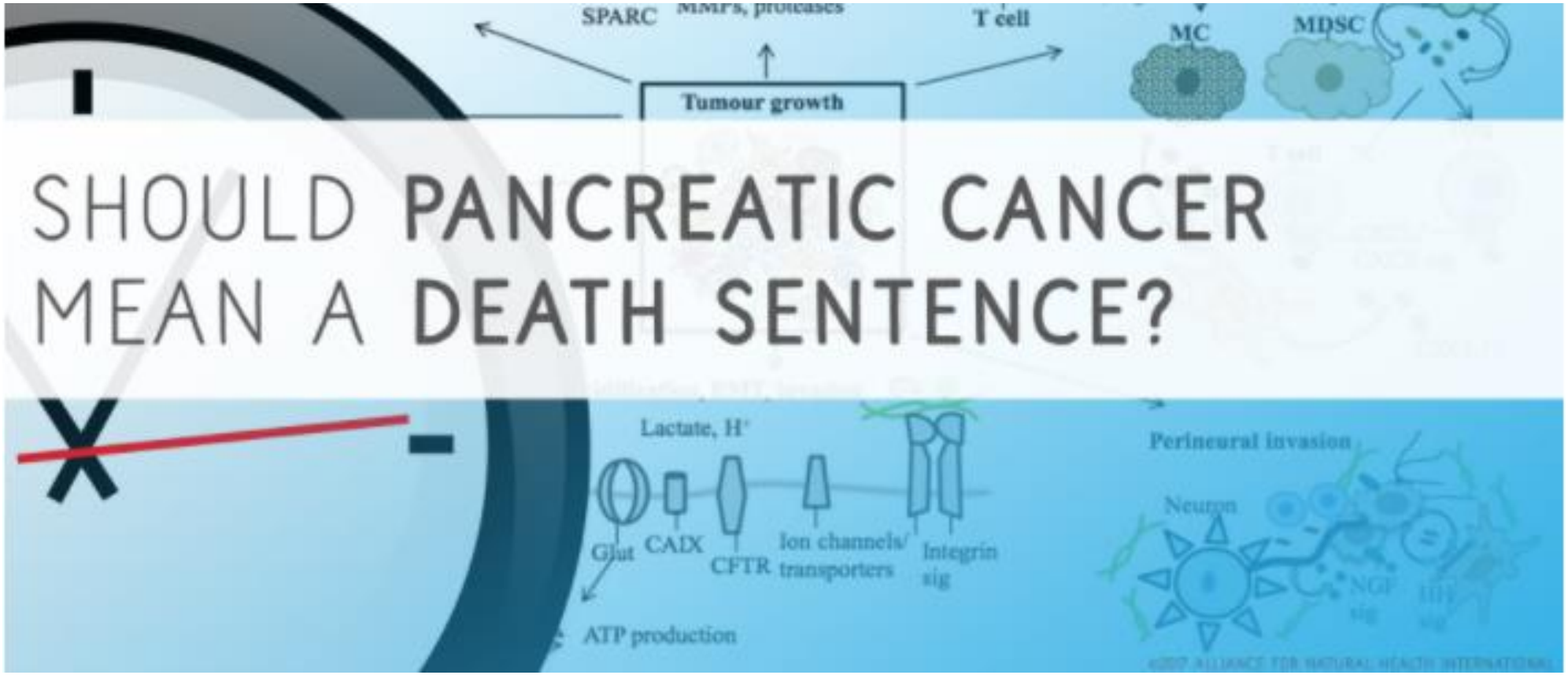
PROVIDENCE PANCREAS AND LIVER SURGERY

10/8/2021

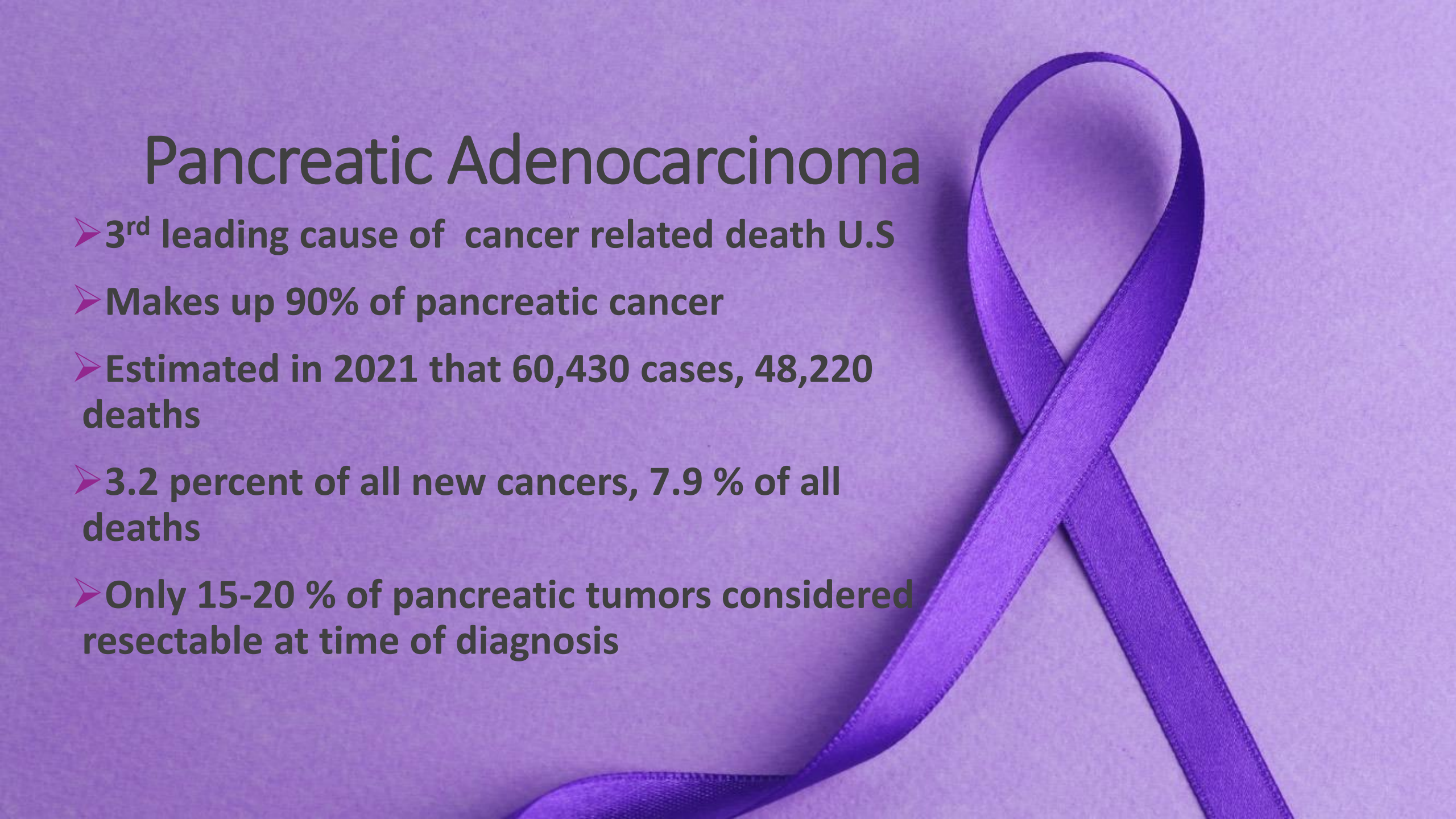
Objectives

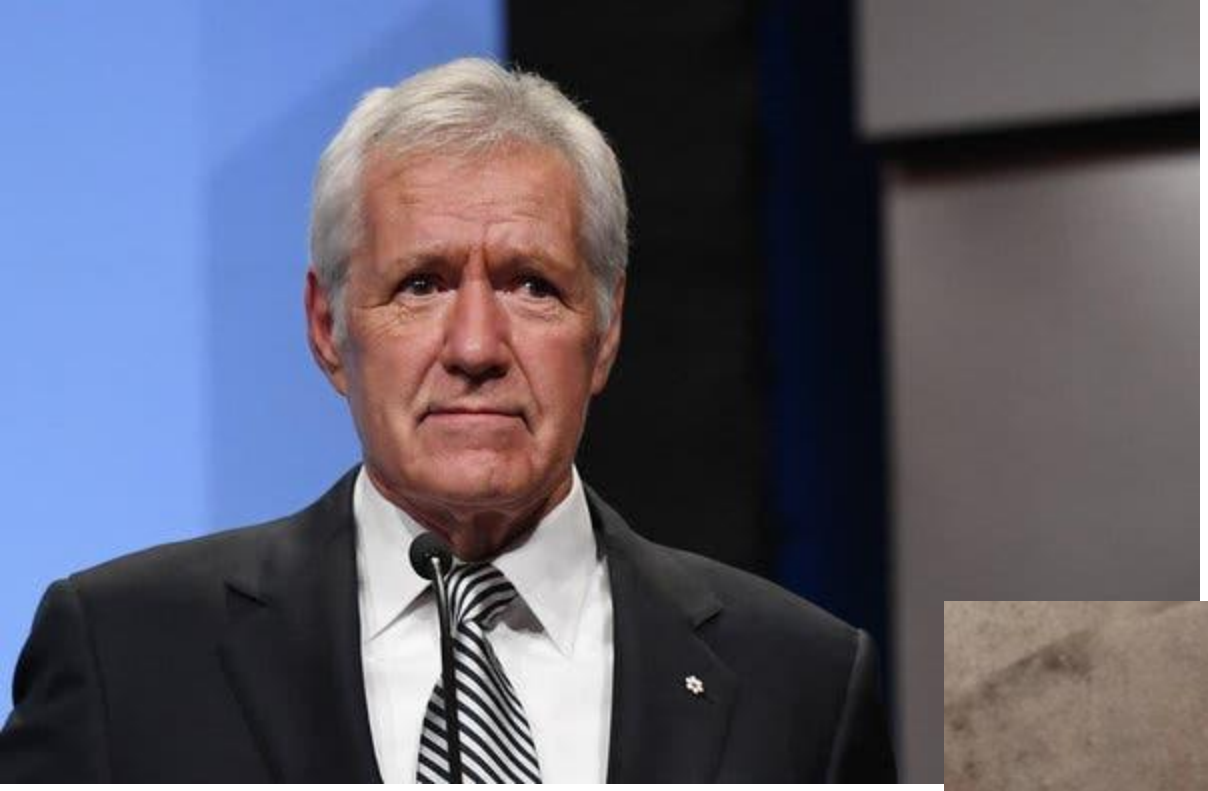
- Pancreatic Cancer Statistics
- Diagnosis/Work up
- Treatment options
- Advantages of a neoadjuvant approach


SPARC
MMPs, proteases
T cell
MC
MDSC
Tumour growth
SHOULD PANCREATIC CANCER
MEAN A DEATH SENTENCE?
Lactate, H+
Glut
CAIX
CFTR
Ion channels/
transporters
Integrin
sig
ATP production
Perineural invasion
Neuron
NGF
sig

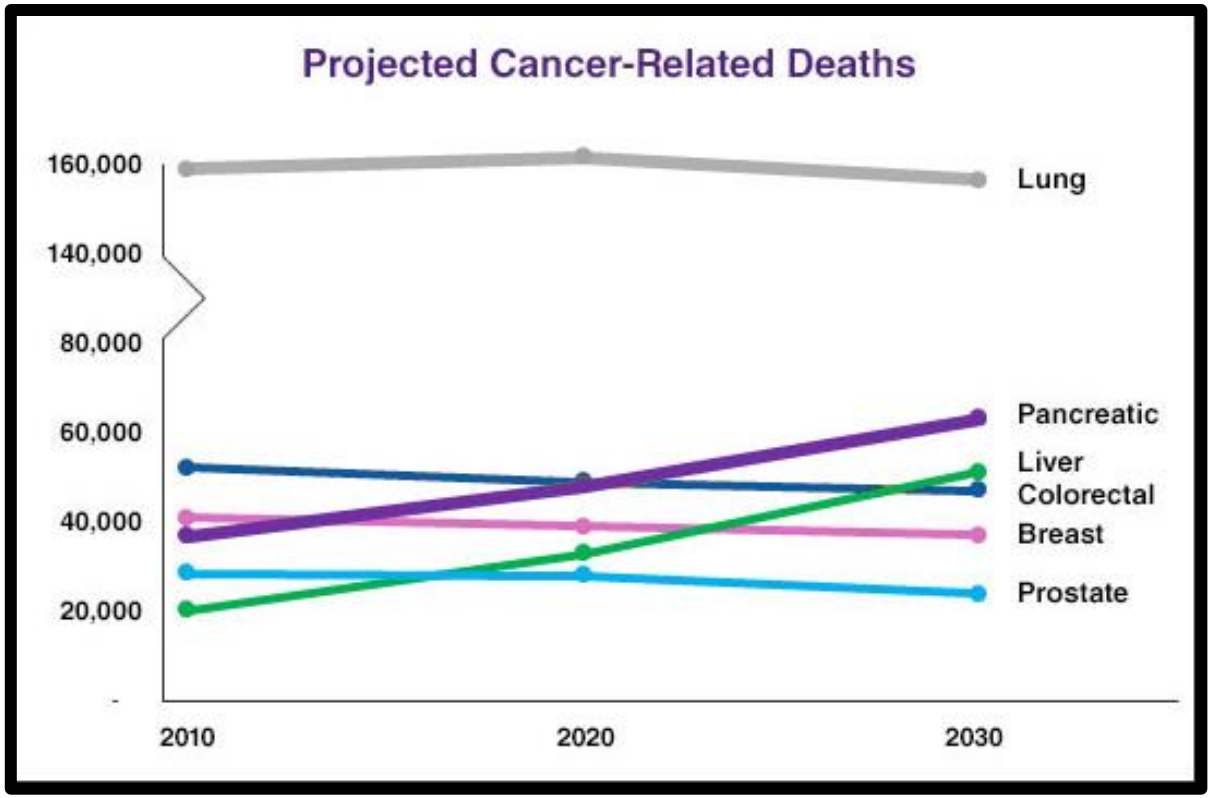
Pancreatic Adenocarcinoma

- 3rd leading cause of cancer related death U.S
- Makes up 90% of pancreatic cancer
- Estimated in 2021 that 60,430 cases, 48,220 deaths
- 3.2 percent of all new cancers, 7.9 % of all deaths
- Only 15-20 % of pancreatic tumors considered resectable at time of diagnosis





Cancer Trends in US by 2030

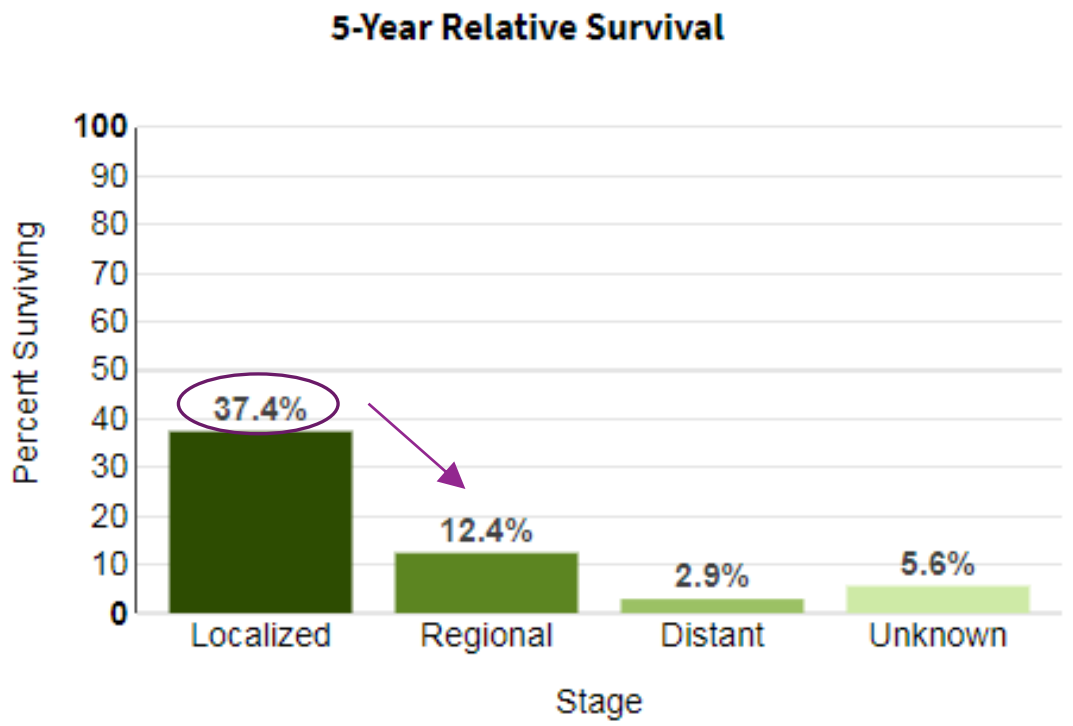


Rahib et al. Projecting Cancer Incidence and Deaths to 2030: The unexpected Burden of Thyroid, Liver, and Pancreas Cancers in U.S. Cancer Research. May 19, 2014 pg 1-9.

Pancreatic cancer 5 year survival

*Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 18 Regs Research Data, Nov 2011-2017*

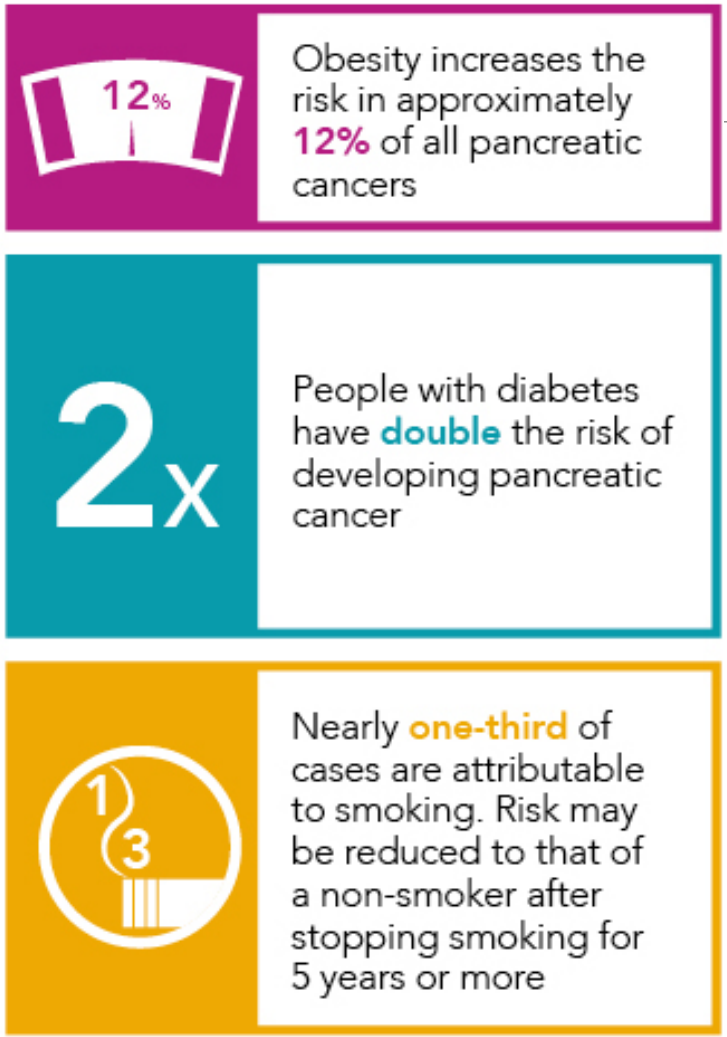
5- year Survival Based on Type of Disease



*Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 9 Regs Research Data, Nov 2018 Sub (1975-2016)*

Risk factors

- Obesity
- Smoking
- Chronic pancreatitis
- Diabetes or pre-diabetes
- Genetic disorders: Familial pancreatitis, Peutz-Jeghers syndrome, melanoma-pancreatic cancer syndrome, Lynch syndrome, BRCA1/2 mutation, Fanconi anemia, ATM mutations, MEN1
- Mucinous cystic neoplasms or IPMN



Pancreatic Cancer Action. Causes of pancreatic cancer. Pancreaticcanceraction.org/about-pancreatic-cancer/causeas-and –risks

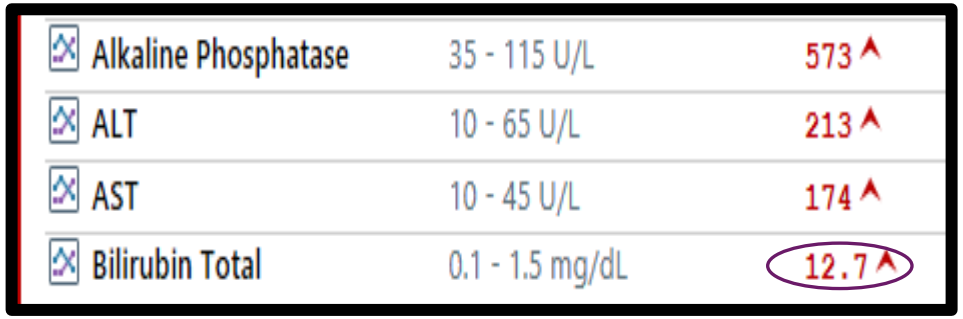
Presentation and Diagnosis

Case Study

63-year-old male comes to your outpatient clinic for concerns of itching and change of color of skin. He has lost about 15 lbs in last week. Denies fever, chills, nausea, and vomiting

Diagnostic Work-Up

- LABS
  - CBC, COMPR, INR
- IMAGING
  - CT ABD/PELVIS



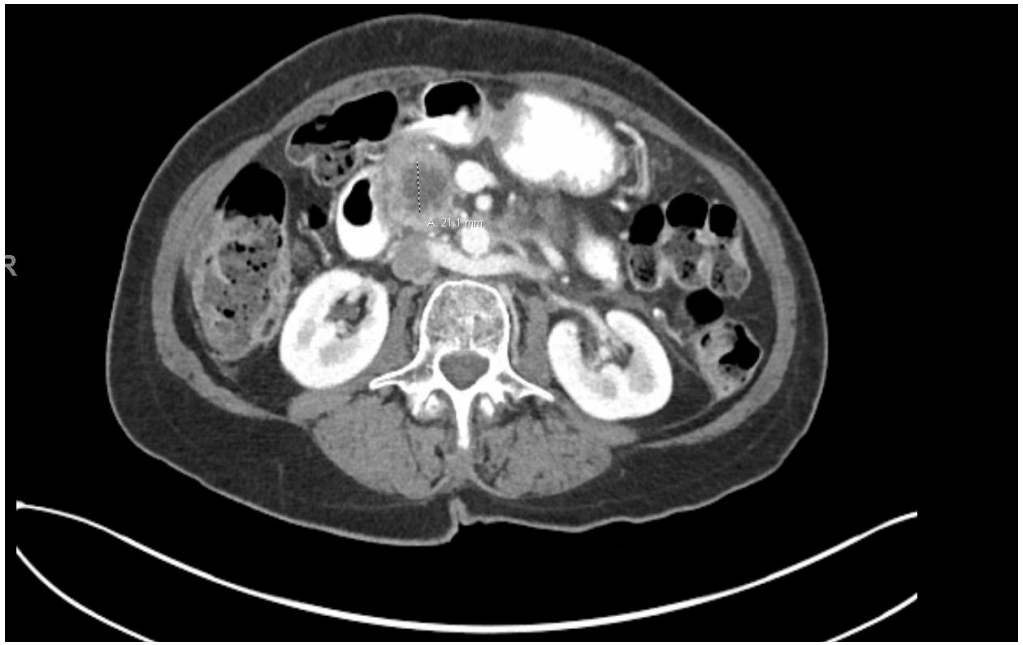
Alkaline Phosphatase	35 - 115 U/L	573 ^
ALT	10 - 65 U/L	213 ^
AST	10 - 45 U/L	174 ^
Bilirubin Total	0.1 - 1.5 mg/dL	12.7 ^

CT Scan Abdomen/Pelvis

Shows a 2.1 cm mass in head of pancreas.

No signs of vascular involvement

What is a complete work up for pancreas cancer?

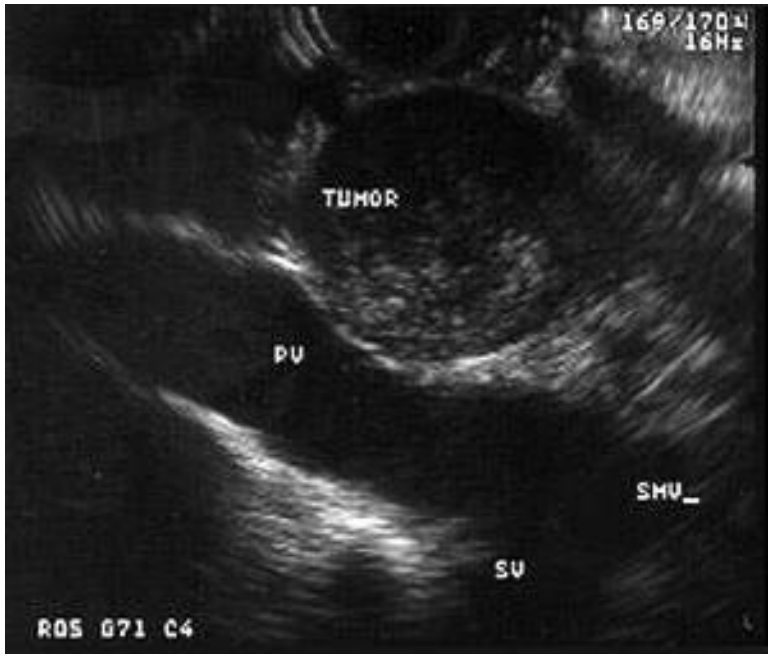


Diagnosis/ Staging Work -up

WORK UP

- CT Pancreas protocol CT
  - MRI/Multiphase
- CT chest w/o contrast
- EUS/ERCP
- Biopsy
  - Tissue is the issue
- **REFERRAL to HPB SURGERY**
- REFERRAL to Medical Oncology

ENDOSCOPIC ULTRASOUND MAGING



Additional Labs

CA19-9

- Tumor marker for pancreaticobiliary cancer
- Falsely elevated in hyperbilirubinemia
- Prognosticator for prognosis
- Used to assess chemotherapy response
- Not elevated in all pancreas cancers

HEMOGLOBIN A1C

- 1 in 4 people diagnosed with pancreas cancer were first diagnosed with diabetes
- 25-50% of patients developed pancreas cancer between 6-36 months of diagnosis

Bellehaninna et al. The clinical utility of serum CA 19-9 in the diagnosis, prognosis, and management of pancreatic adenocarcinoma. Journal of Gastrointestinal oncology June 2012 Vol 3(2)
Savatore et al. Pancreatic cancer and Diabetes: A two –way relationship in the perspective of diabetologist. International Journal of Surgery. Sept 2015 (21) pg 572-577

Liver and Pancreas Tumor Board

- Weekly meetings
- Diverse group of participants
- Oncologist, Radiologist, Interventional GI, Interventional IR, Surgeons
- GI pathologist

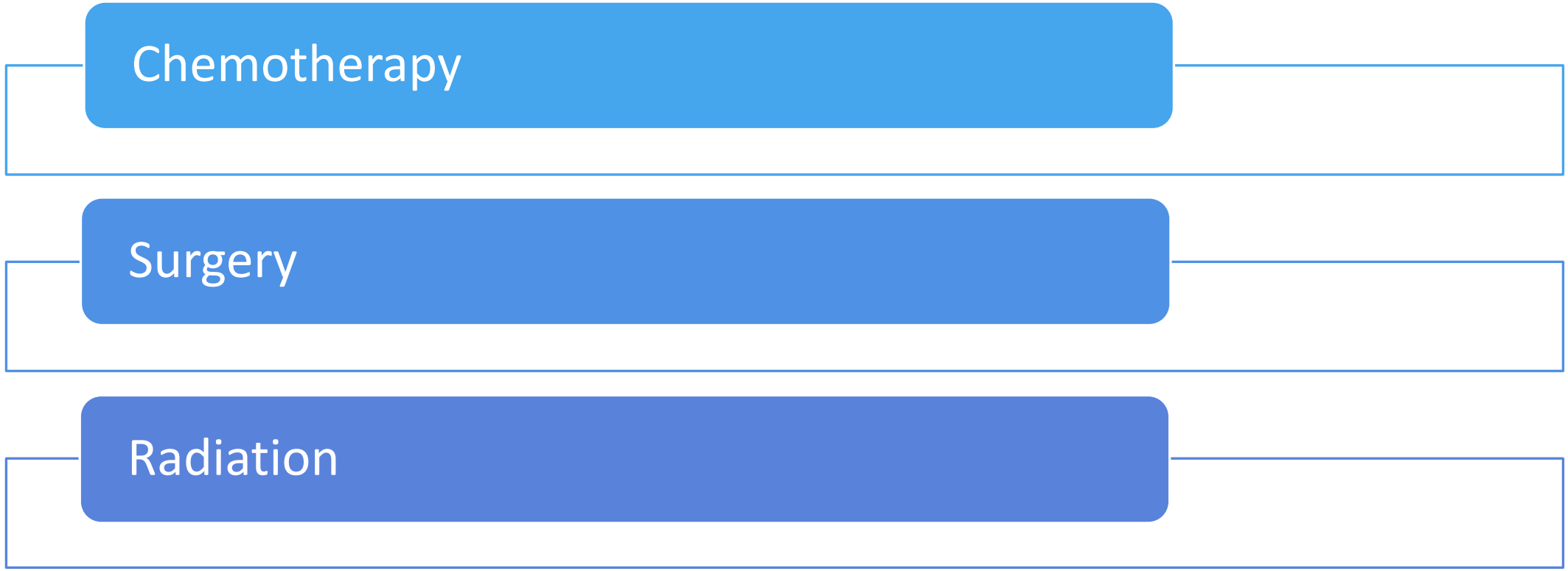
Accessing additional resources

Prehabilitation

- Physical Therapist dedicated to prehabilitation in cancer patients
- Neoadjuvant patients participate
- Home Health option
- Nutritionist

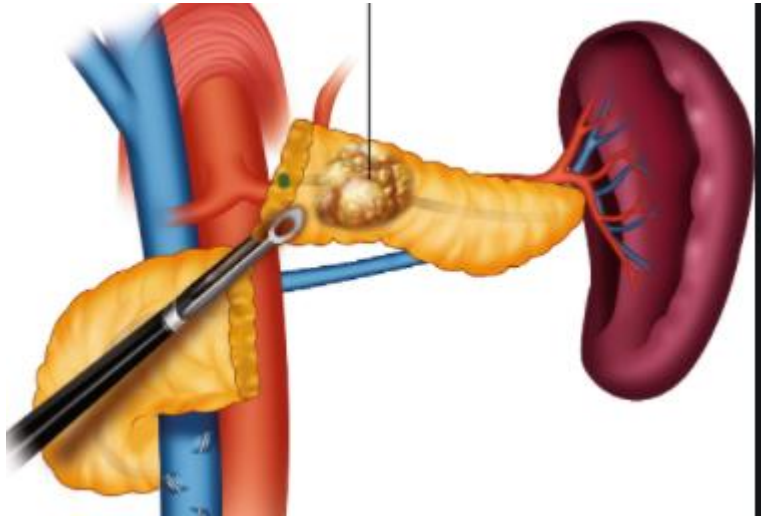
Treatment: Combo Meal Deal

Treatment algorithm for pancreas cancer



Surgery

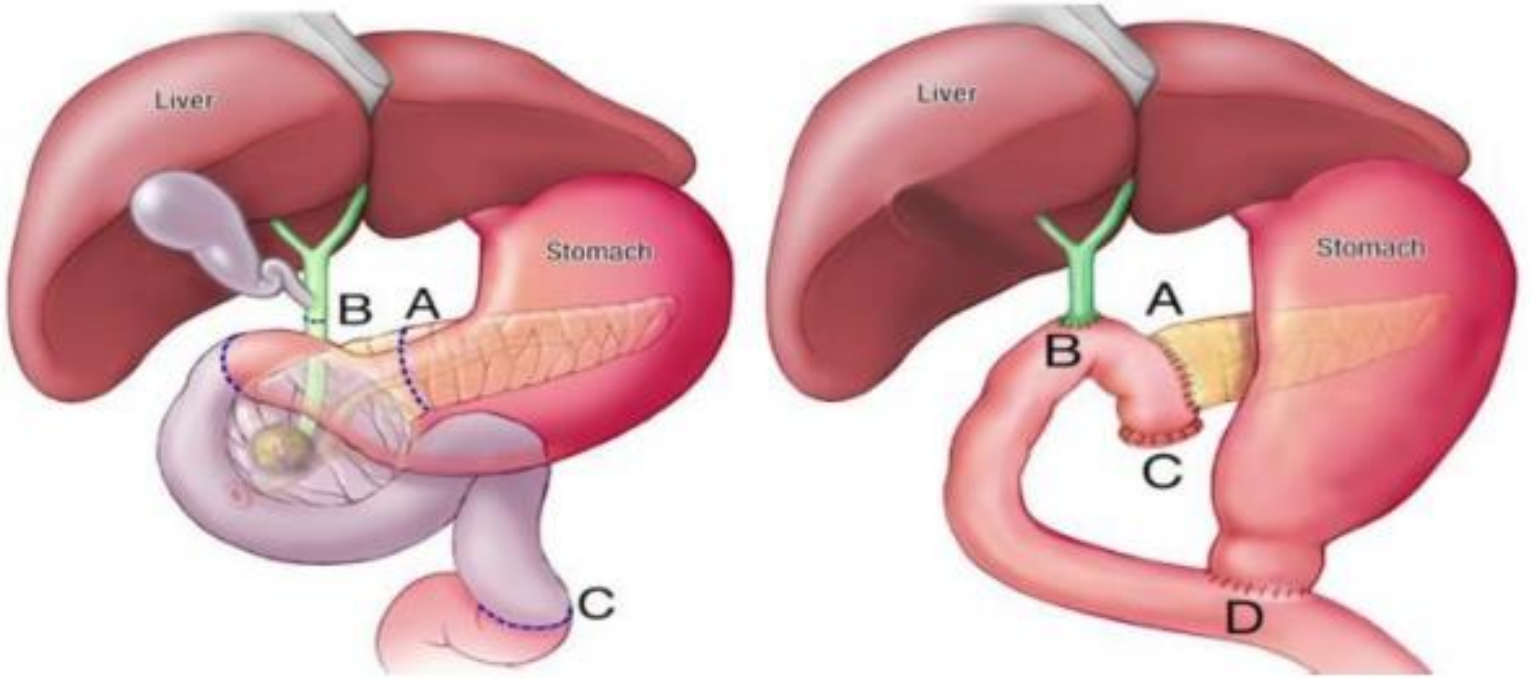
Distal pancreatectomy and splenectomy



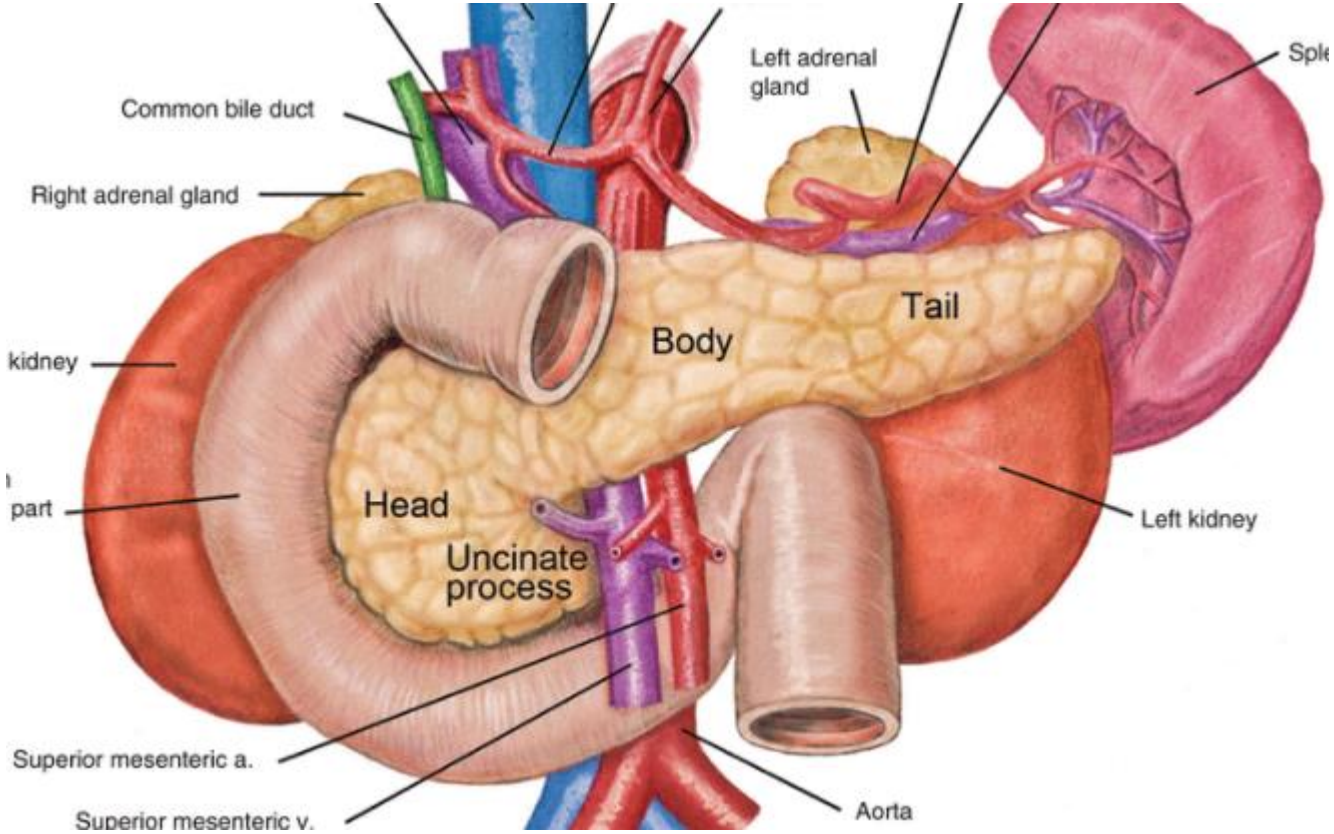
- 20-25% of all pancreas cancers
- Only about 10% of all distal/body tumors are resectable
- Lack early symptoms
- Worse prognosis
- Require splenic vaccinations
  - HIB, Meningococcus, Pneumococcus

Surgery

Pancreaticoduodenectomy (Whipple Procedure)



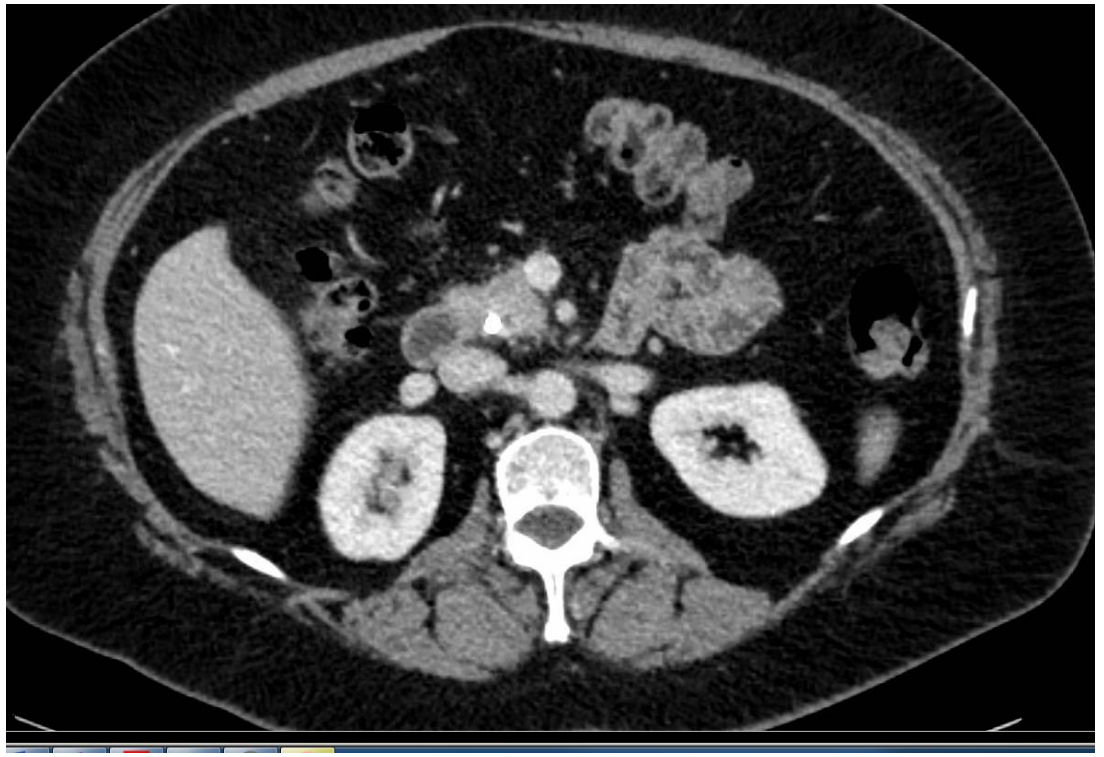
Defining resectability



Classification of Resectability

RESECTABLE

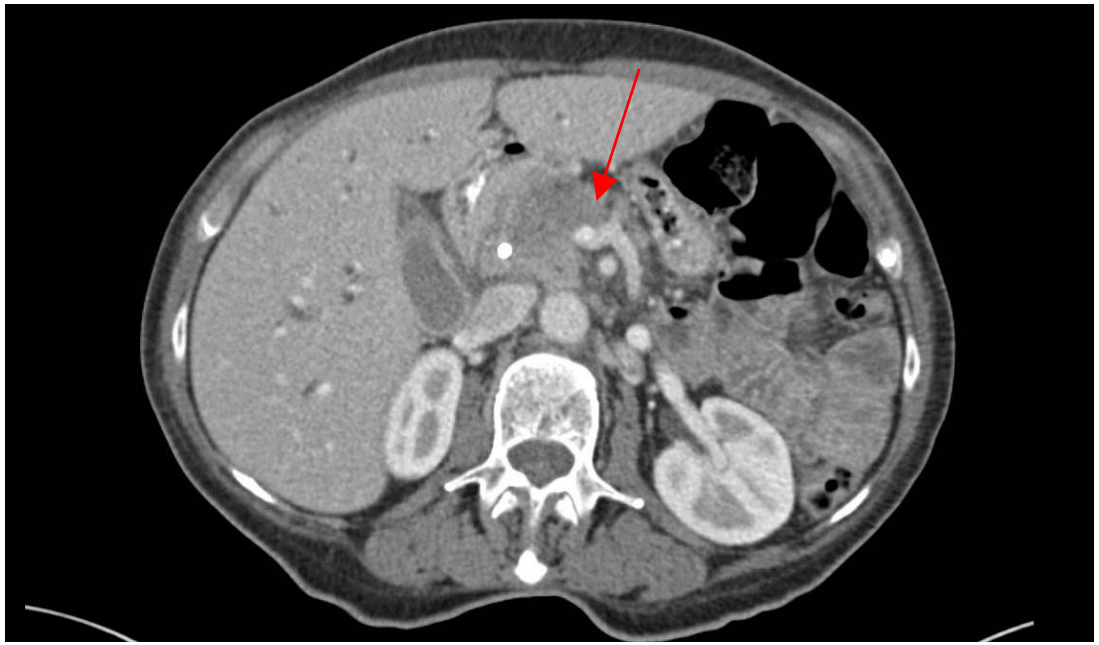
- Normal tissue plane between SMA and SMV
- No involvement CHA or celiac axis
- No metastatic/extrahepatic disease



Classification of Resectability

BORDERLINE

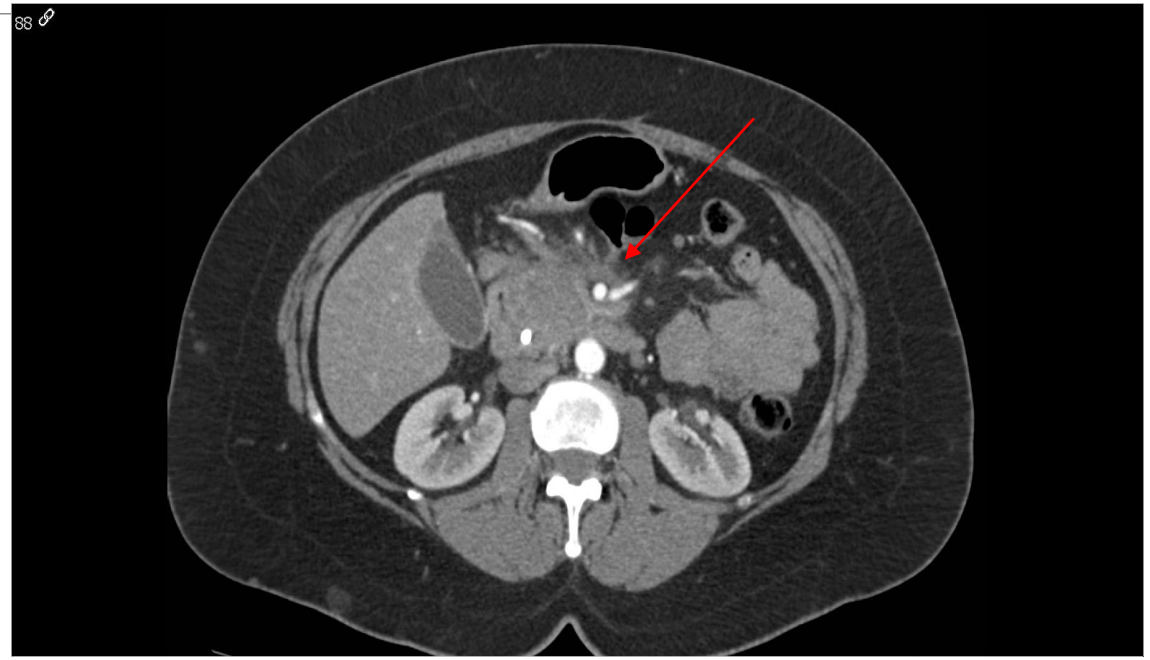
- SMV abutment or encasement amendable to reconstruction
- SMA abutment ≤ 180°
- Common hepatic artery abutment or short-segment encasement



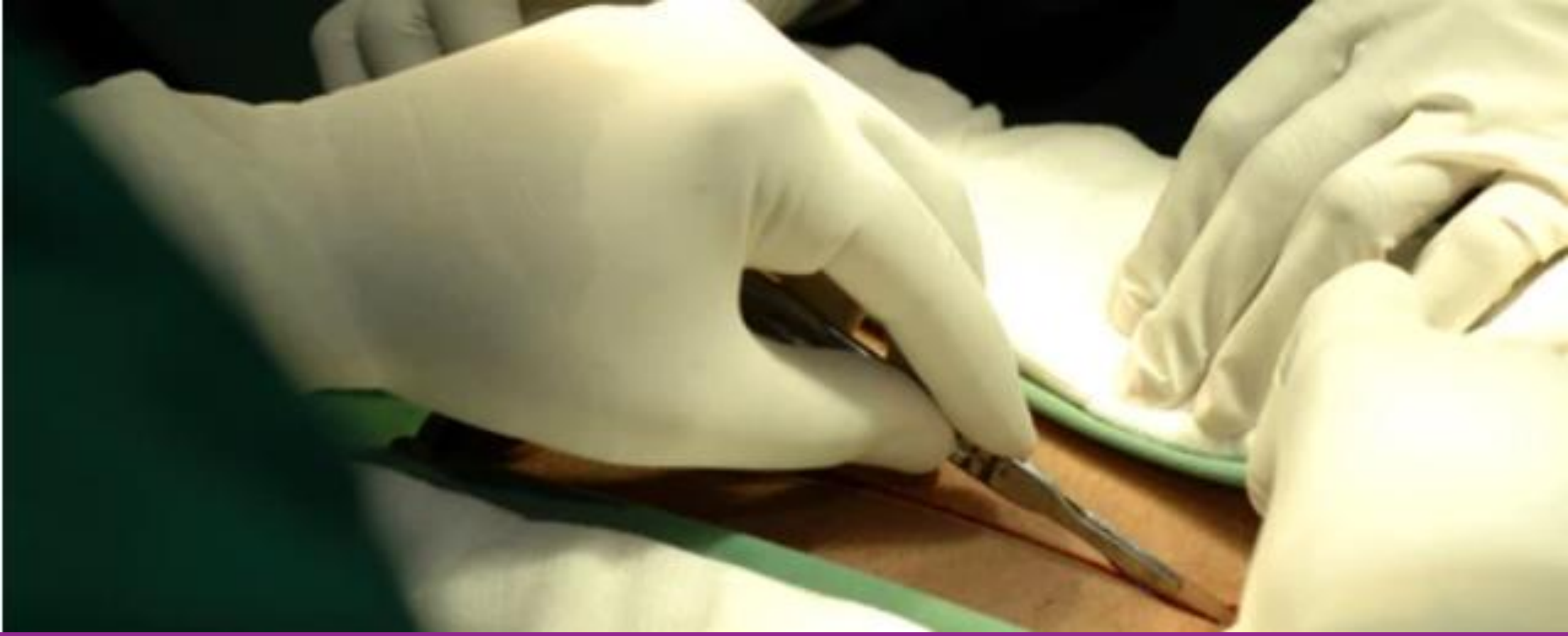
Classification of Resectability

LOCALLY ADVANCED

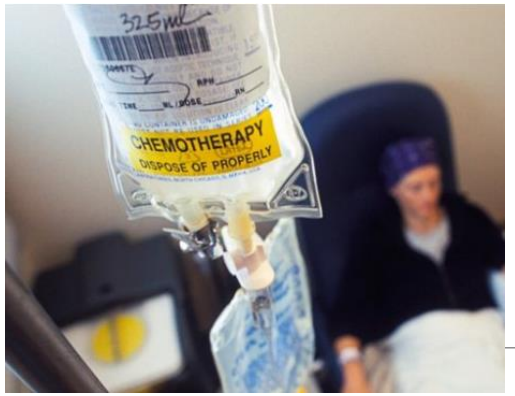
- Surgically unresectable
- SMA tumor incasement >180°
- SMV/Portal vein involvement not allowing for reconstruction
- Celiac access involvement



Kluger et Al. Resection of Locally Advanced Pancreatic Cancer without Regression of Arterial Encasement After Modern-Era Neoadjuvant. Journal of Gastrointesitnal Surgery. Feb 2018 (22) 2. pp 235-241.



TO CUT IS TO CURE…… Right??



Chemotherapy Options

FOLFIRINOX

- Oxaliplatin, irinotecan, fluorouracil, and leucovorin
- Side effects: neutropenia, diarrhea, thrombocytopeina, vomiting neuropathy
- Showed advantage overall of 11 months compared to 6.8 months gem alone

GEM/NAB-PACLITAXEL

- Gemcitabine and albumin bound paclitaxel
- Side effects: Neutropenia, fatigue, alopecia, nausea
- Median overall survival 8.5 months gem/nab-paclitaxel vs 6.7 months gem alone

Von Hoff et al. Increased survival in Pancreatic Cancer with nab Paclitaxel plus Gemcitabine. New England Journal 2013; 369: 1691-1703
Conroy et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N England Journal 2011; 364: 1817-1825

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2021
Pancreatic Adenocarcinoma

NCCN Guidelines Index
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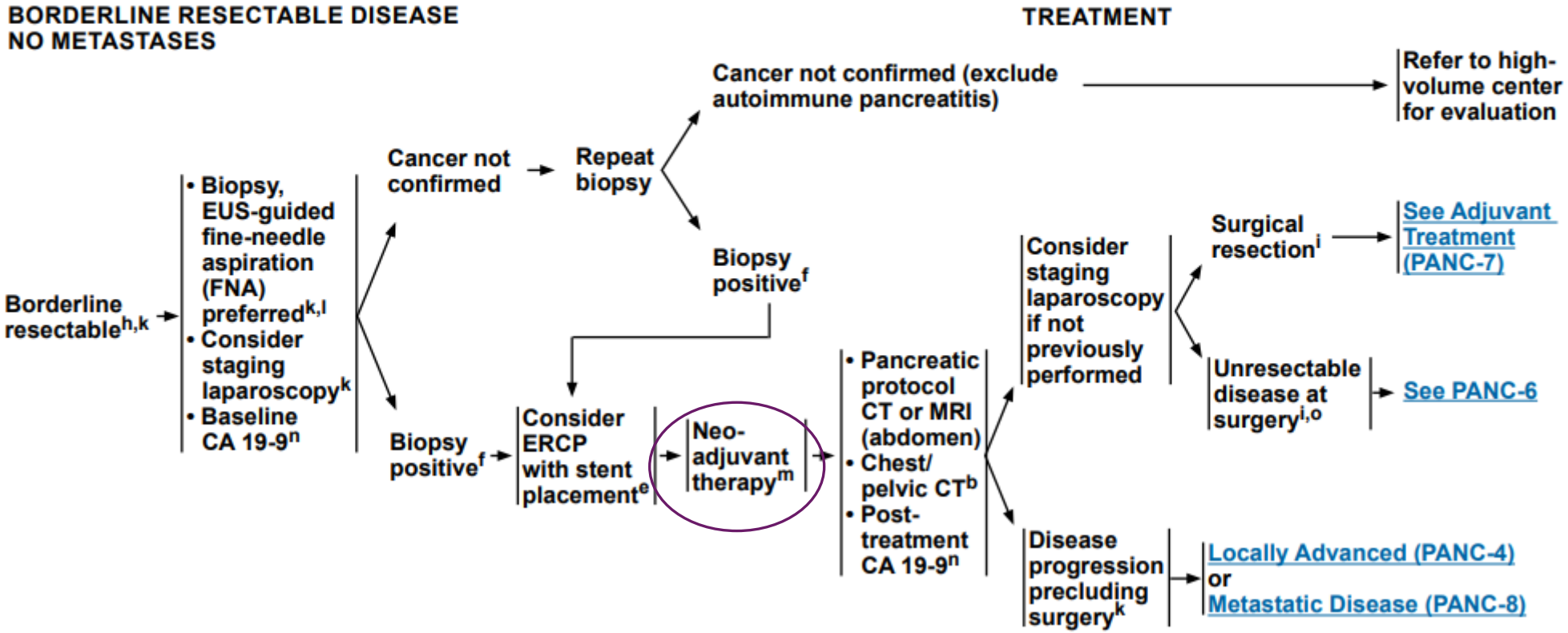
Discussion



ORIGINAL ARTICLE

FOLFIRINOX or Gemcitabine as Adjuvant Therapy for Pancreatic Cancer

Thierry Conroy, M.D., Pascal Hammel, M.D., Ph.D., Mohamed Hebbar, M.D., Ph.D., Meher Ben Abdelghani, M.D., Alice C. Wei, M.D., C.M., Jean-Luc Raoul, M.D., Ph.D., Laurence Choné, M.D., Eric Francois, M.D., Pascal Artru, M.D., James J. Biagi, M.D., Thierry Lecomte, M.D., Ph.D., Eric Assenat, M.D., Ph.D., et al., for the Canadian Cancer Trials Group and the Unicancer-GI–PRODIGE Group*

PRODIGE 24

- First randomized control trial to show that FOLFIRINOX offers longer survival adjuvant treatment compared to gemcitabine in resected patients
- Median follow- up 33.6 months
- Median disease free survival 21.6 months FOLFIRINOX group and 12.8 months gemcitabine
- Median overall survival was 54.4 months and 35 months gemcitabine group

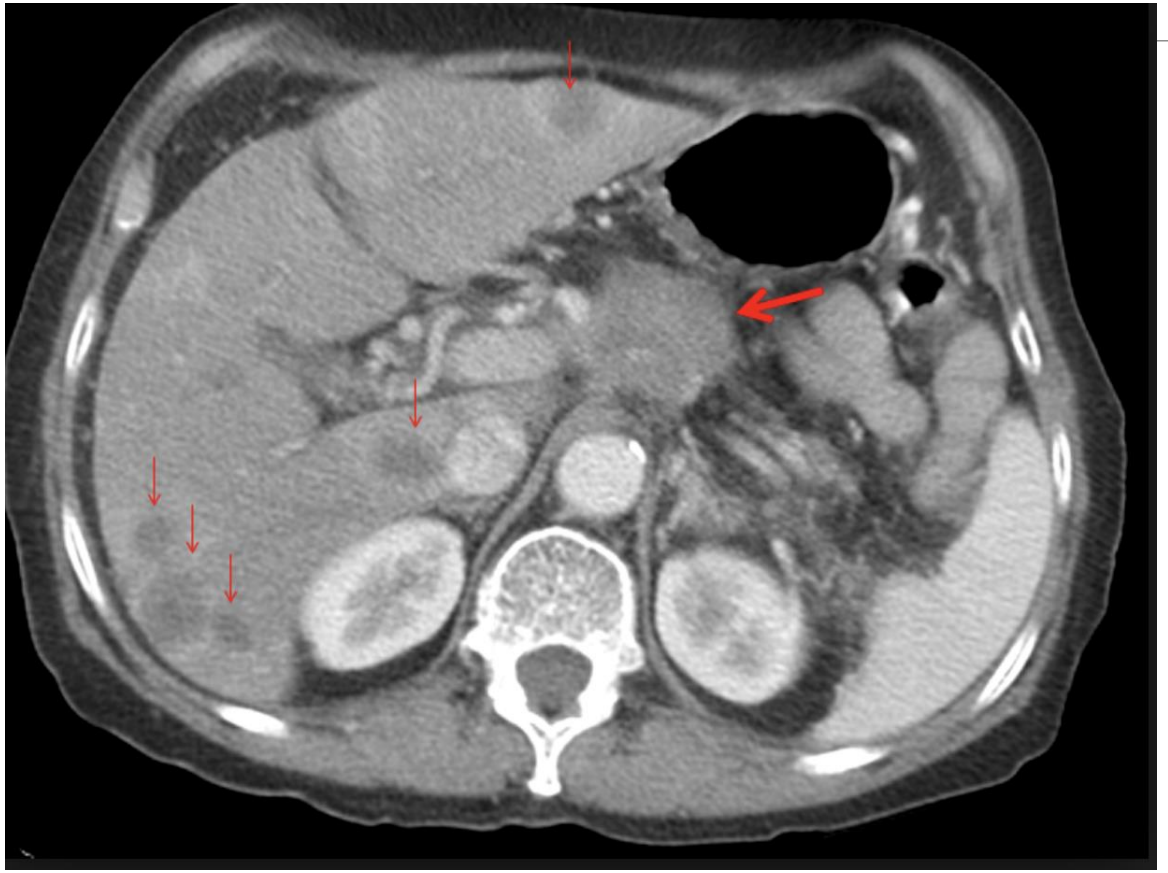
Conroy et al. FOLFIRINOX or Gemcitabine as Adjuvant Therapy for Pancreatic Cancer. N Engl J Med 2018; 379:2395-2406

Why Neoadjuvant Chemotherapy?

- To increase R0 resection rates
- Ensure patients receive **ALL** chemotherapy
- Determine biology of tumor
- Treat micrometastatic disease

Raufi et al. Neoadjuvant Treatment for Pancreatic Cancer. Semin Oncol. 2019 Feb; 46(1):19-27

Biology of disease



- This is a systemic disease
- Patients will need chemotherapy
- Recent trial showed that 17-34% people progressed on neoadjuvant therapy
- Another study showed that giving neoadjuvant therapy increases likelihood of receiving all components of care

K. Tang et al. Neoadjuvant therapy for patients with borderline resectable pancreatic cancer: a systematic review and meta-analysis of response and resection percentages. Pancreatology 16(1) Jan 2016. 28-37
Piperdi et al. Neoadjuvant strategy for pancreatic adenocarcinoma increases likelihood of receiving all components of care: lessons from a single-institution database. HPB 2010; 12:204-10
Katz et a. Borderline resectable pancreatic cancer: The importance of this emerging stage of disease. Am Coll Surg. May 2018 (206)5: 833-848

Does Neoadjuvant Chemotherapy Effect Outcome of Resection?

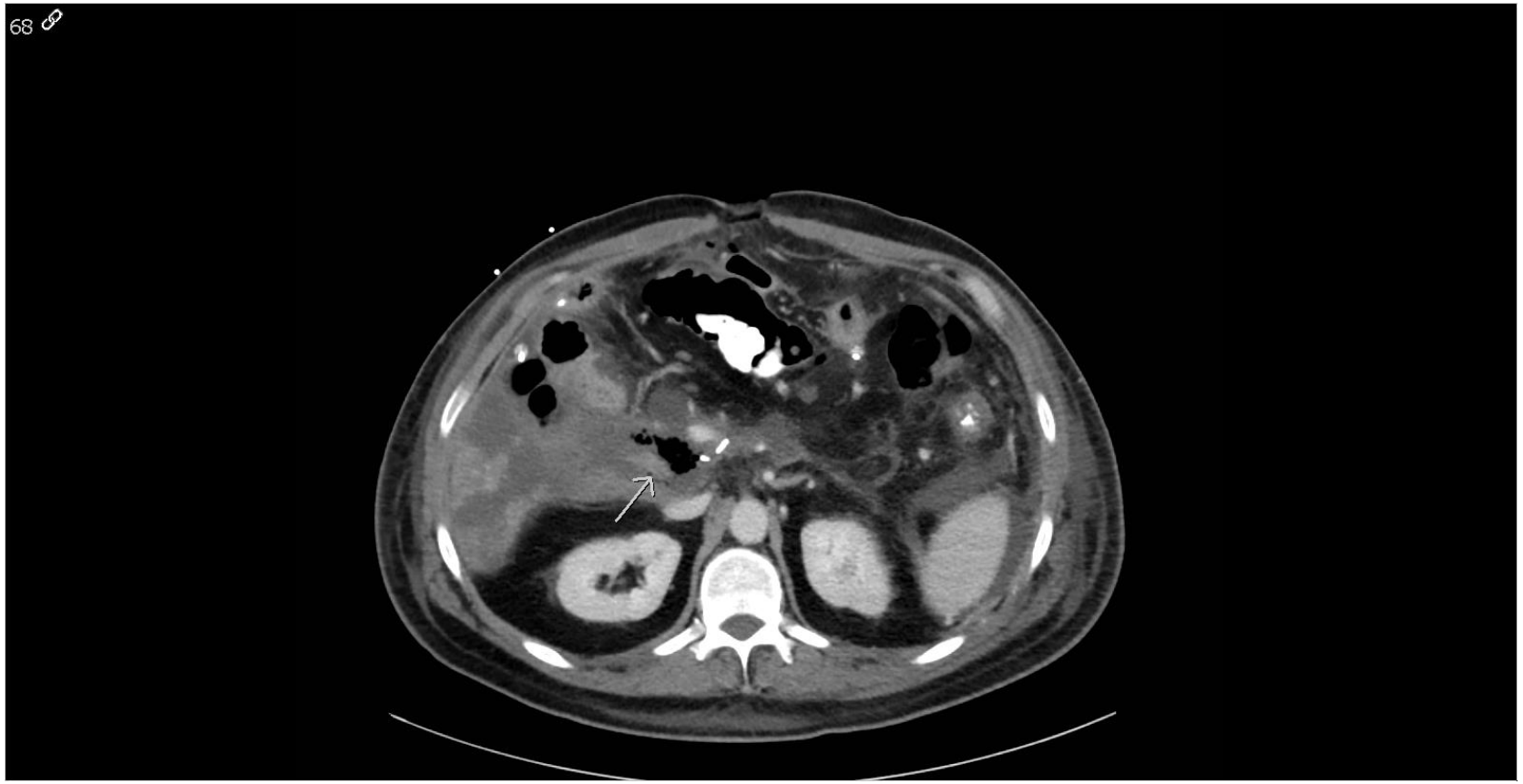
- Prospective study 2012-2014 MGH
- Patients with locally advanced/ borderline disease
- 40 patient with FOLFIRINOX and 87 no neoadjuvant
  - 92% of patients had R0 resection with FOLFIRINOX
  - Significant decrease in nodal positivity
  - Perineural invasion also decreased
  - Decrease in CA 19-9
  - Decrease Tumor Size

Pathological Features of Study Population

	No Neoadjuvant (N = 87)	FOLFIRINOX (N = 40)	*P*
Stage			<0.001
I	4 (5%)	10 (25%)	0.006
IIa	15 (17%)	16 (40%)	
IIb	68 (78%)	14 (35%)	
Median size of tumor on pathology (cm)	3.2 (1.5–10.7)	2.5 (0.1–5.5)	
N+	69 (79%)	14 (35%)	<0.001
R0	75 (86%)	35 (92%)	0.550
Lymphatic invasion	61 (70%)	14 (35%)	<0.001
Perineural invasion	83 (95.4%)	29 (72.5%)	<0.001

Ferrone et al. Radiologic and Surgical Implications of Neoadjuvant Treatment with FOLFIRINOX for Locally Advanced and Borderline Resectable Pancreatic cancer. Ann Surg. 2015 Jan: 261(10: 12-17

Complications…..will occur



Complications after surgery

- 20-40% of patients will have a complication after surgery
- Goal of adjuvant therapy is to get patients on therapy 2 months after surgery
- 20-30% of patients will never make it to adjuvant therapy due to complication, prolonged recovery, early recurrence or refusal

Klinkenbijl et al. Adjuvant radiotherapy and 5-fluorouracil after curative resection of cancer of the pancreas and periampullary region: phase III trial of EORTC GI cancer cooperative group. Ann Surg 1999: 230:776-82
Yeo et al. Pancreaticoduodenectomy for pancreatic adenocarcinoma postoperative adjuvant chemoradiation improves survival a prospective, single institution experience. Ann Surg 1997. 225:621-33

Major Complications Independently Increase Long-Term Mortality After Pancreatoduodenectomy for Cancer

Authors | Authors and affiliations

M. Sandini, K. J. Ruscic, C. R. Ferrone, M. Qadan, M. Eikermann, A. L. Warshaw, K. D. Lillemoe,

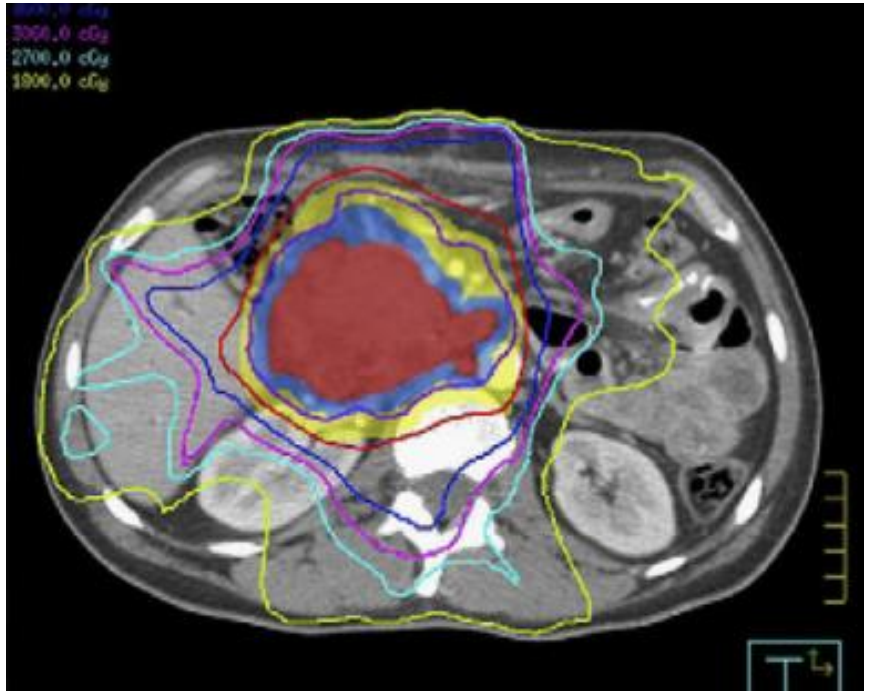
Carlos Fernández-del Castillo

- Retrospective single institution
- 616 patients
- 81.7% whipple, 18.3% distal pancreatectomy
- Overall complication 57.5%
- Likelihood of receiving adjuvant therapy was 43.9% if major complication occurred vs 68.5% if not ($p<0.001$)
- Multivariate analysis for whipple showed complication was a independently associated worse overall survival (HR 1.37, 95% CI (1.01-1.86)

Sandini M et al. Major complications Independently Increase Long Term Mortality after Pancreaticoduodenectomy for cancer. J Gastrointestinal Sur. 2018 pp1-7

To radiate or not to radiate?

- Data is controversial
- Role in non-resectable disease/locally advanced
- Positive margins
- Recurrence



Neoptolemos et al. A randomized Trial of chemoradiotherapy and chemotherapy after resection of Pancreatic cancer. N Engl J Med 2004; 350:1200-1210

Conclusion

- Overall survival is dependent on stage of tumor
- Pancreas cancer is increasing in our population and knowing the treatment work up is essential
- Surgical resection with chemotherapy offers the only chance at cure
- Chemotherapy and neoadjuvant chemotherapy is having an increasing role in pancreas cancer and overall survival

Resources for patients

PANCREATIC CANCER ACTION NETWORK®

PanCAN's vision is to create a world in which all patients with pancreatic cancer will thrive.

Our Statement on Diversity and Inclusion from PanCAN's CEO

Thank you!

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