Team Oncobusters
Steve Jobs, Alex Trebek, Are You Next? The Battle Against Pancreatic Cancer!!

14-18 Age Group

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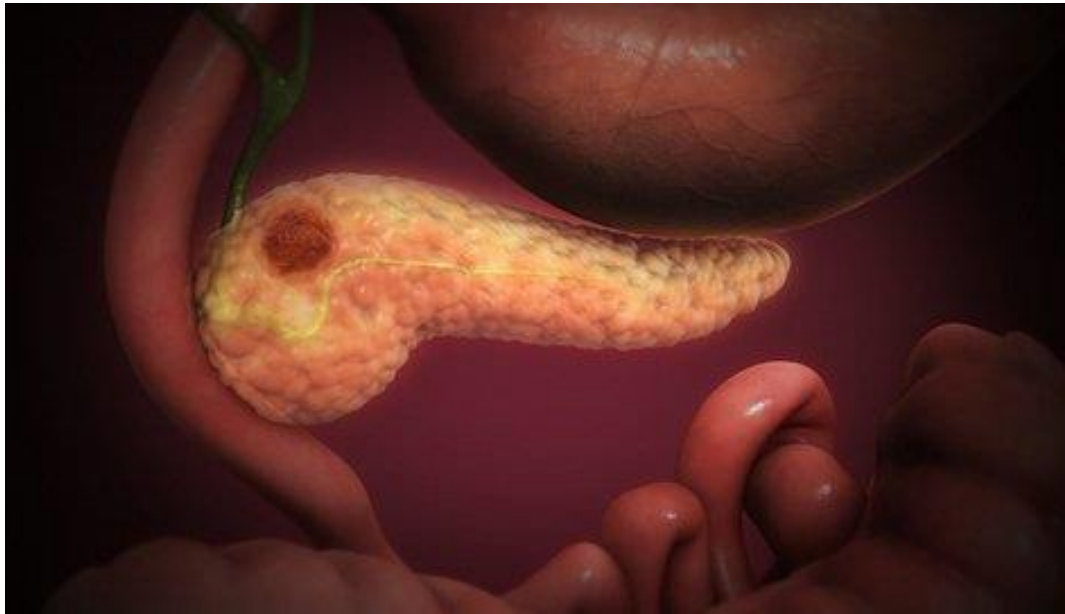
Abstract

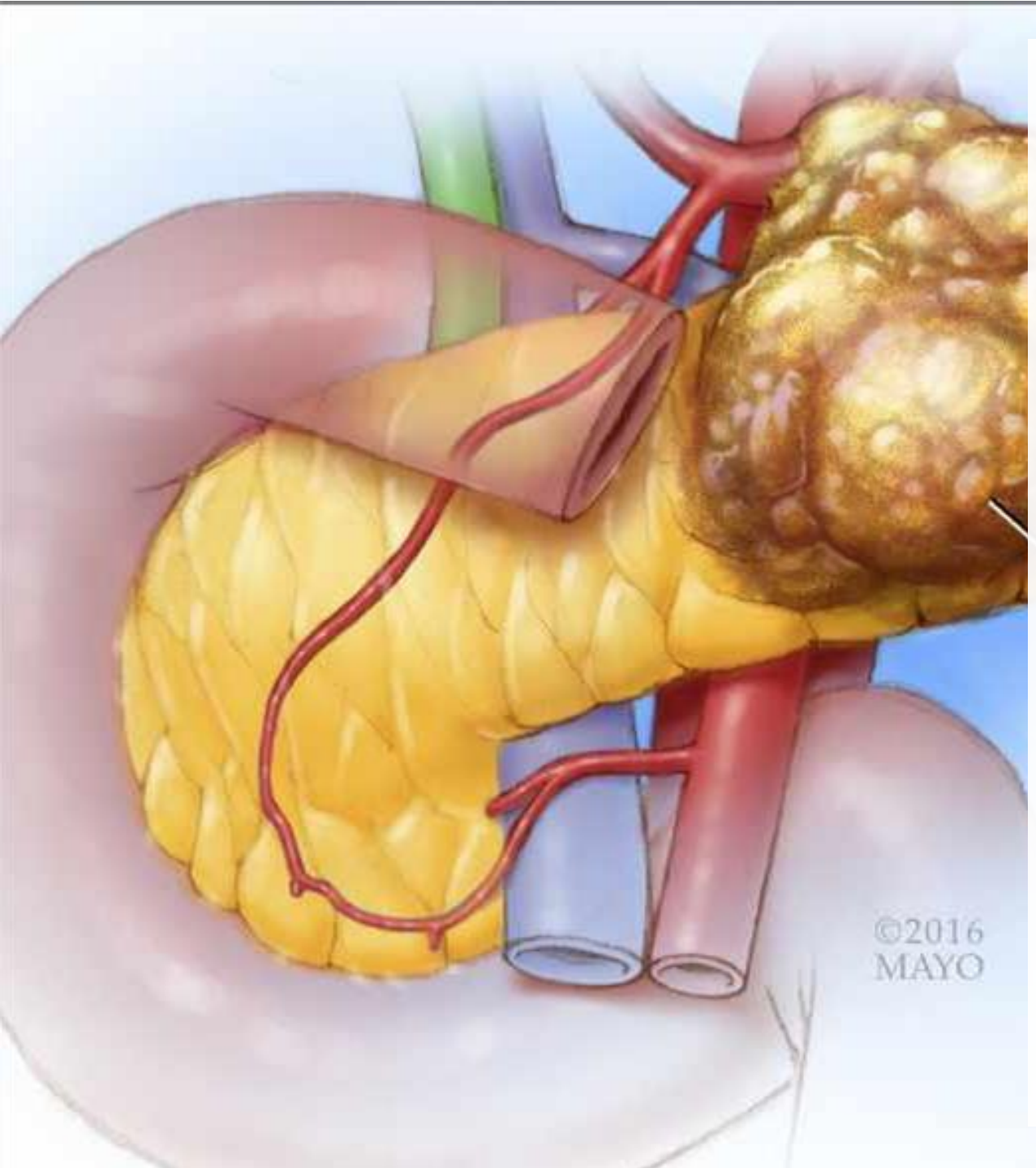
This presentation will cover many characteristics of pancreatic cancer, with an emphasis on the treatment avenues, risk factors, and genetics of this cancer. We will also explore the prevalence and survival rates of pancreatic cancer in the United States, and worldwide, and use this as a model to predict future trends. This research and presentation is aimed at educating the public on how to detect pancreatic cancer, the current methods for tumor resection and cancer treatment, and what things you can do now to prevent yourself from getting this cancer. We hope that people walk away knowing about the seriousness of pancreatic cancer and what they can do to lead a healthy life. Over the course of our research, we have read over research papers from trusted sources, such as NCBI and ASCO, and we have referenced information from trusted sites such as PubMed, American Cancer Society, and Mayo Clinic. This research was done mainly to uncover more information about the biology and characteristics of various tumors, the specific gene mutations and cell signaling pathways used, and to learn about the future of pancreatic cancer in terms of treatment options. Even though pancreatic cancer is the 11th leading cancer in the United States, it has one of the highest death rates for a cancer. By analyzing gene changes and family heredity closer, we can hopefully detect this cancer in the early stages, and then use advanced laparoscopy and radiation therapies to treat the tumor. There is still a long line ahead, but if we continue our research, we can combat this cancer!

What is Pancreatic Caner???

- The pancreas is a **gland** located behind the stomach. (1)
- It produces **digestive juices and hormones** which regulate blood sugar levels and aid in digestion. (1)
- **Exocrine** pancreatic cells produce the digestive juices, and **endocrine** pancreatic cells produce the hormones. (1)
- The majority of pancreatic cancers start in the **exocrine cells**. (1)
- **Pancreatic cancer** is a disease in which malignant cancer cells form in the tissues of the pancreas. The tumor is named based on the region in the pancreas where it forms.
- This specific form of cancer is rarely detected in the early stages (1)
- It is the **11th most common cancer** in the United States, but causes a significant number of deaths each year. (2)

(32)





Signs and Symptoms

- Usually do not occur until disease is **advanced.**
- Include
  - **Pain in the upper abdomen** that radiates to your back
  - Loss of appetite or unintended weight loss
  - Depression
  - New-onset **diabetes**
  - **Glucose Intolerance**
  - Blood clots
  - Fatigue
  - Yellowing of your skin and the whites of your eyes (**jaundice**)
  - **Steatorrhoea**: This is the passing of fatty stools. They noticeably float in water due to high fat levels. (3) + (4)

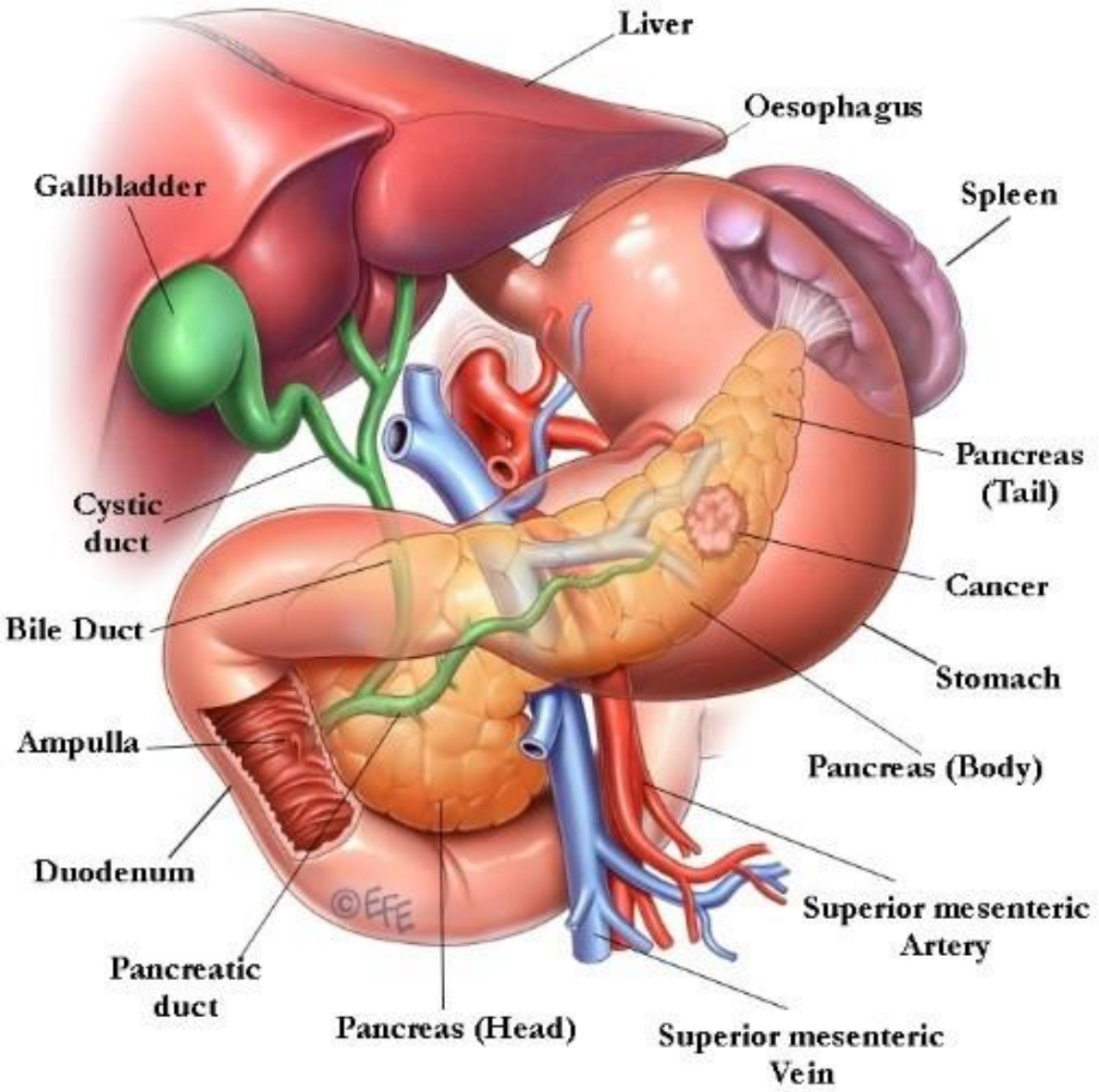
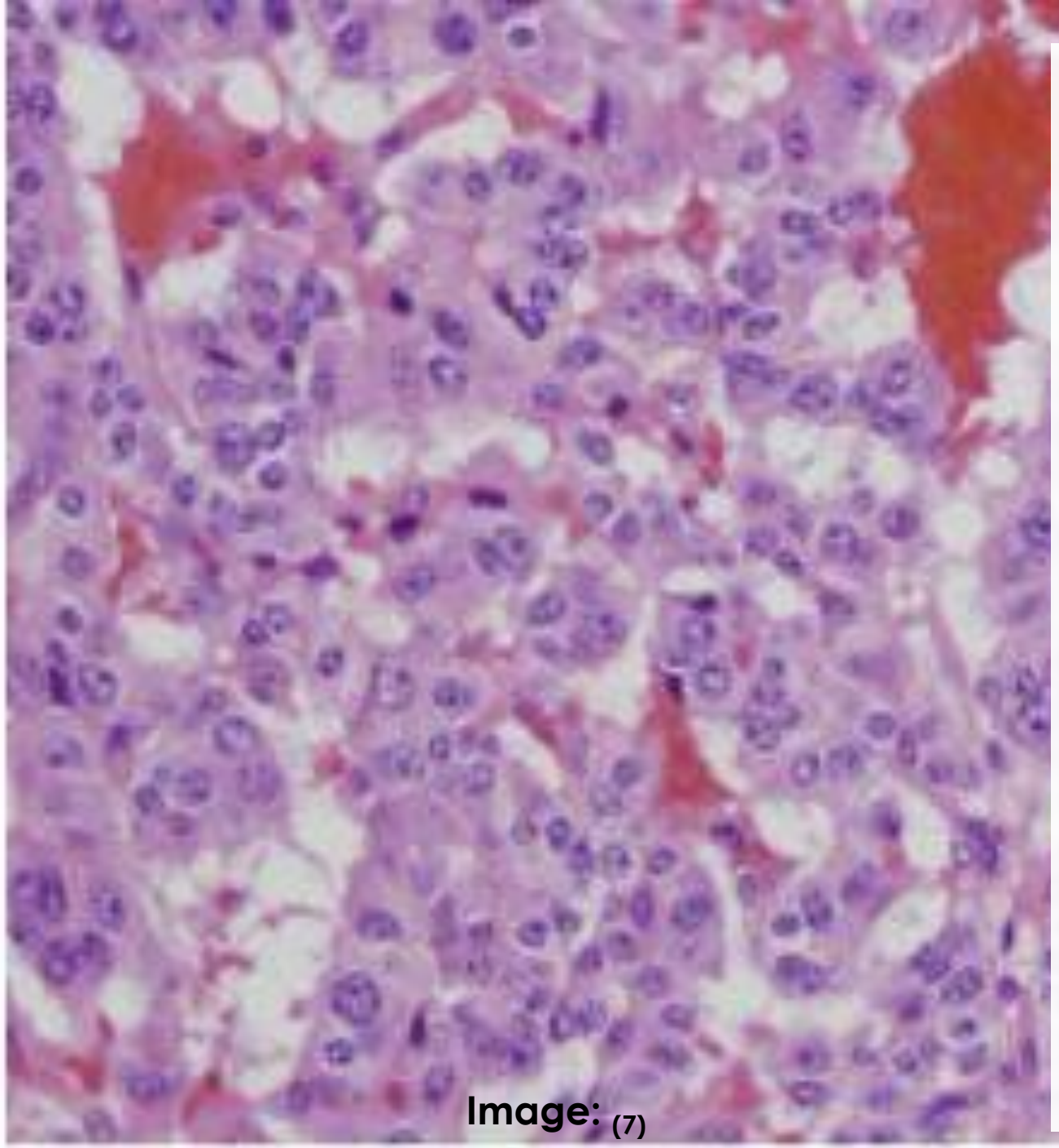


Image: (5)

Wait, there are many forms of PC?

- **Adenocarcinoma -** this is cancer of the exocrine cells that line the pancreatic ducts. More than 95% of pancreatic cancers are this type.
  - Interfere with the drainage of bile from the bile ducts, causing jaundice.
- **Cystic Tumors -** tumors that form in the fluid filled sacs in the pancreas. Most are benign.
- **Acinar Cell Cancers -** tumors that form on the ends of the pancreatic ducts in the cells that produce enzymes.
- **Sarcomas -** tumors that form in the connective tissue that bonds together the pancreatic cells. This is very rare.
- **Ampullary Cancers -** cancer that develops in the ampulla of Vater. (3)



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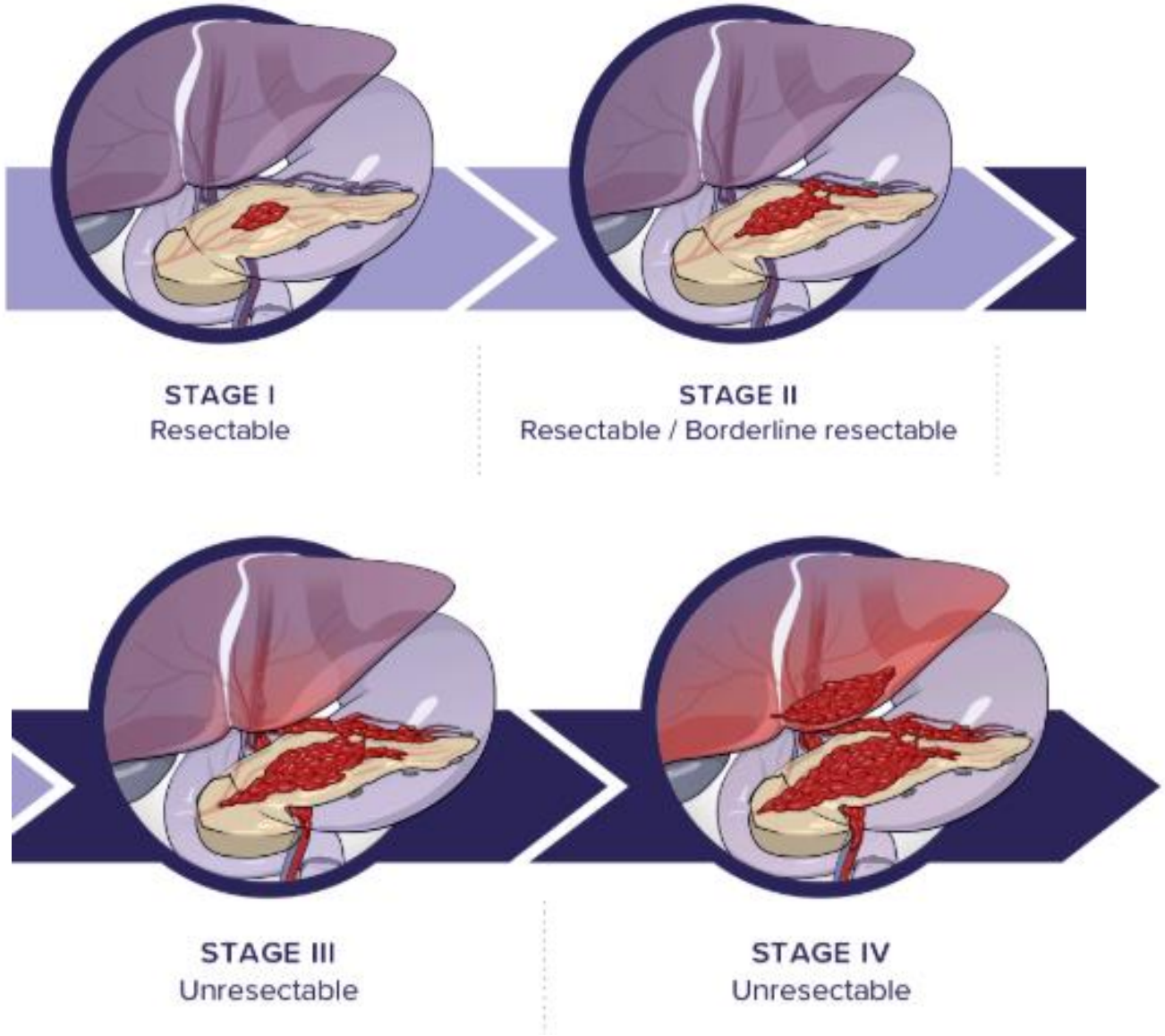
Pancreatic Neuroendocrine Tumors

- **7%** of pancreatic cancers. Disrupt hormone secretion.
- Can be **functioning** or **non functioning**.
- **Insulinoma** - Insulin
- **Glucagonoma** - Glucagon
- **Gastrinoma** – Gastric Acid
- **Somatostatinoma** – Somatostatin (controls cell proliferation and hormone activity)
- **VIPomas** – Vasoactive Intestinal Peptide (controls secretion of water, salts, enzymes, and gastric acid during digestion. Works with smooth muscles.
- **Ppomas** – Pancreatic Polypeptide (6)



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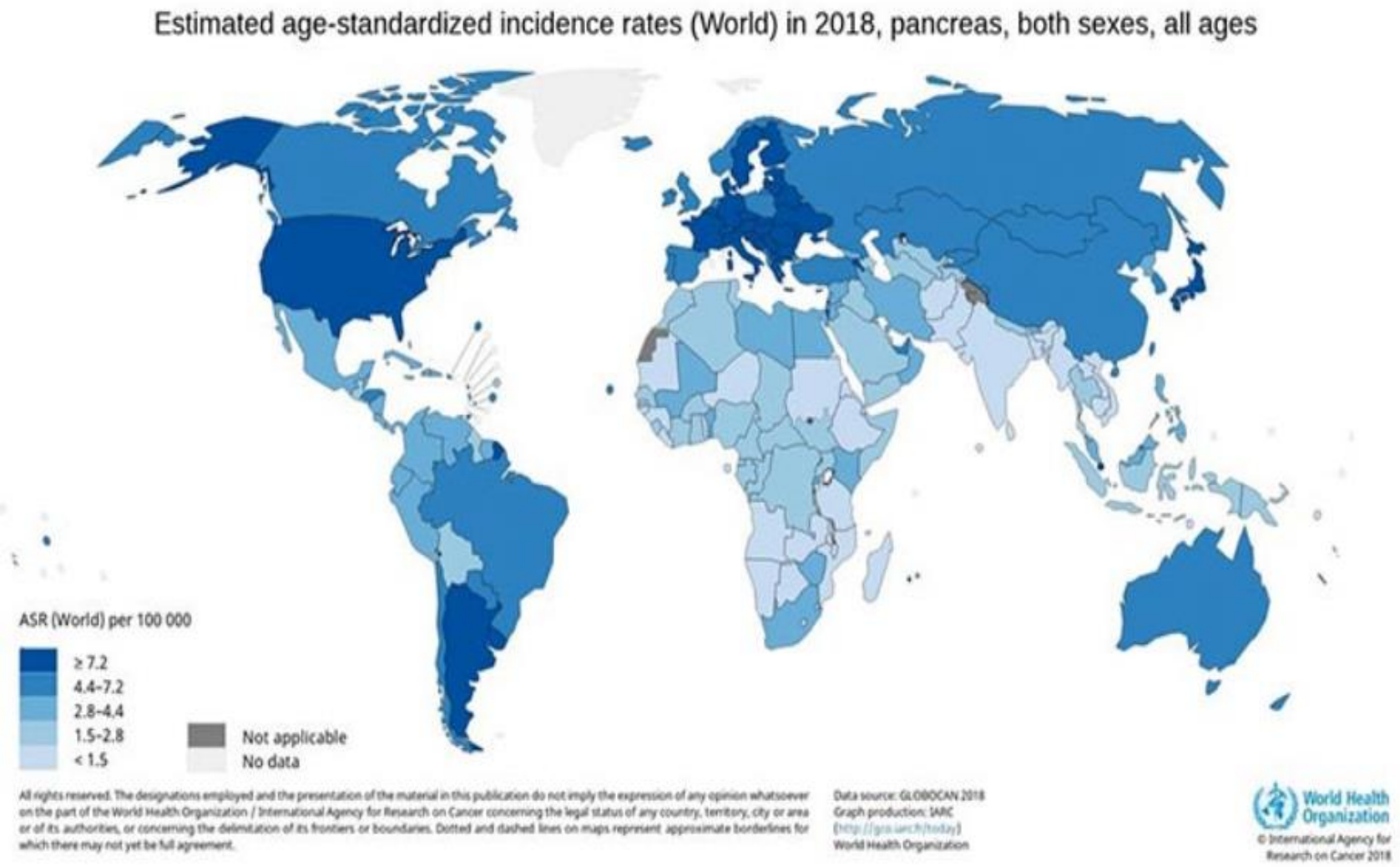
Pancreatic Cancer Stages

- **-Stage 0** – The cancer is confined to the top layers of the Pancreatic duct cells. It has not spread to deeper tissues, distant nodes, or distant sites outside of the pancreas. Carcinoma in situ
- **-Stage I** – A tumor that is 2-3 centimeters long and has not spread to other parts of the body.
- **Stage IIA:** The tumor is larger than 4 cm and extends beyond the pancreas (arteries, veins, lymph nodes). Has not spread to other body parts.
- **Stage III:** A tumor that has spread to regional lymph nodes, nearby arteries and veins, or confined to the pancreas **Stage IV:** Any tumor that has spread to other parts of the body. (8)



- The average lifetime risk of pancreatic cancer is about **1 in 64.**
- Globally, the **incidence** of pancreatic cancer is 5.5 per 100,000 for men and 4.0 per 100,000 for women (11)

Survival Statistics:

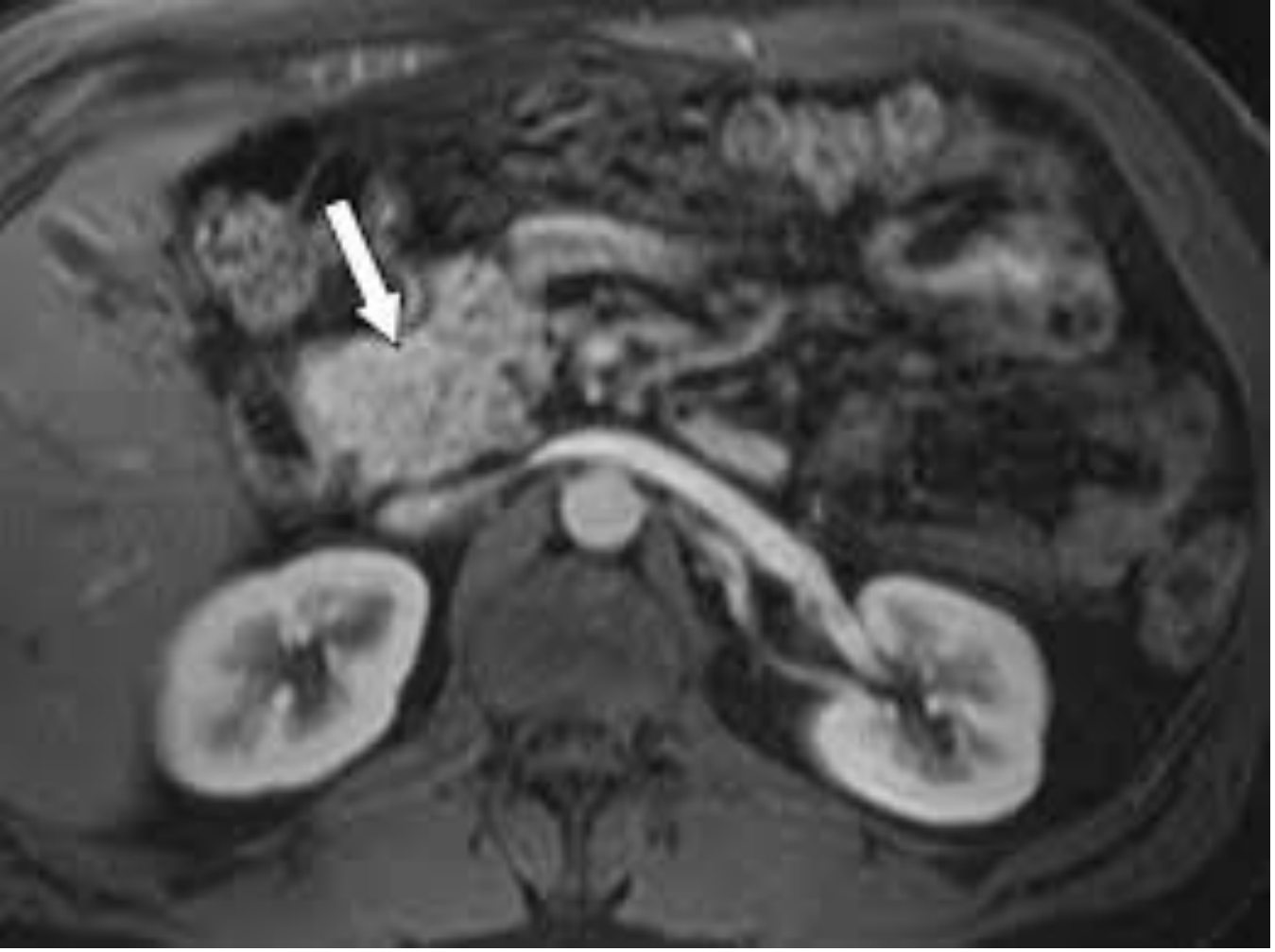
- About **56,770 people** (29,940 men and 26,830 women) will be diagnosed with pancreatic cancer.
- About **45,750 people** (23,800 men and 21,950 women) **will die** of pancreatic cancer.
- Pancreatic cancer accounts for about **3% of all cancers in the US** and about **7% of all cancer deaths.** (10)

Image: (16)

Risk Factors

Image: (15)

- **Tobacco Use-** About **25%** of pancreatic cancers are thought to be caused by cigarette smoking. Use of Cigars or other tobacco products can also increase risk of developing Pancreatic Cancer.
- **Race**- African Americans are **23-52%** more likely to develop pancreatic cancer than whites. Not only is pancreatic cancer more common among African Americans, but African Americans are more often diagnosed with advanced, and therefore, inoperable cancer.
- **Being Obese:**
  - Obese people (body mass index [BMI] of 30 or more) are about 20% more likely to develop pancreatic cancer.
  - Heavy alcohol use can cause chronic pancreatitis and cirrhosis, which can lead to pancreatic cancer.
- Most people with PC also have an **insufficient amount of pancreatic enzymes.** Consuming foods with lipase, protease and amylase can keep the pancreas relatively healthy.
  - Pineapple, papaya, mango, honey, banana, avocado, and ginger
  - Pancreatic Enzyme Supplement
- **Age**- Almost all patients diagnosed with Pancreatic Cancer are **45 or older**. About 2/3 are at least 65.
- **Gender**- It is slightly more common in **men than in women**. Men use tobacco more than women, which raises the risk of them developing PC. (12), (13), (14)



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Why is it diagnosed late?

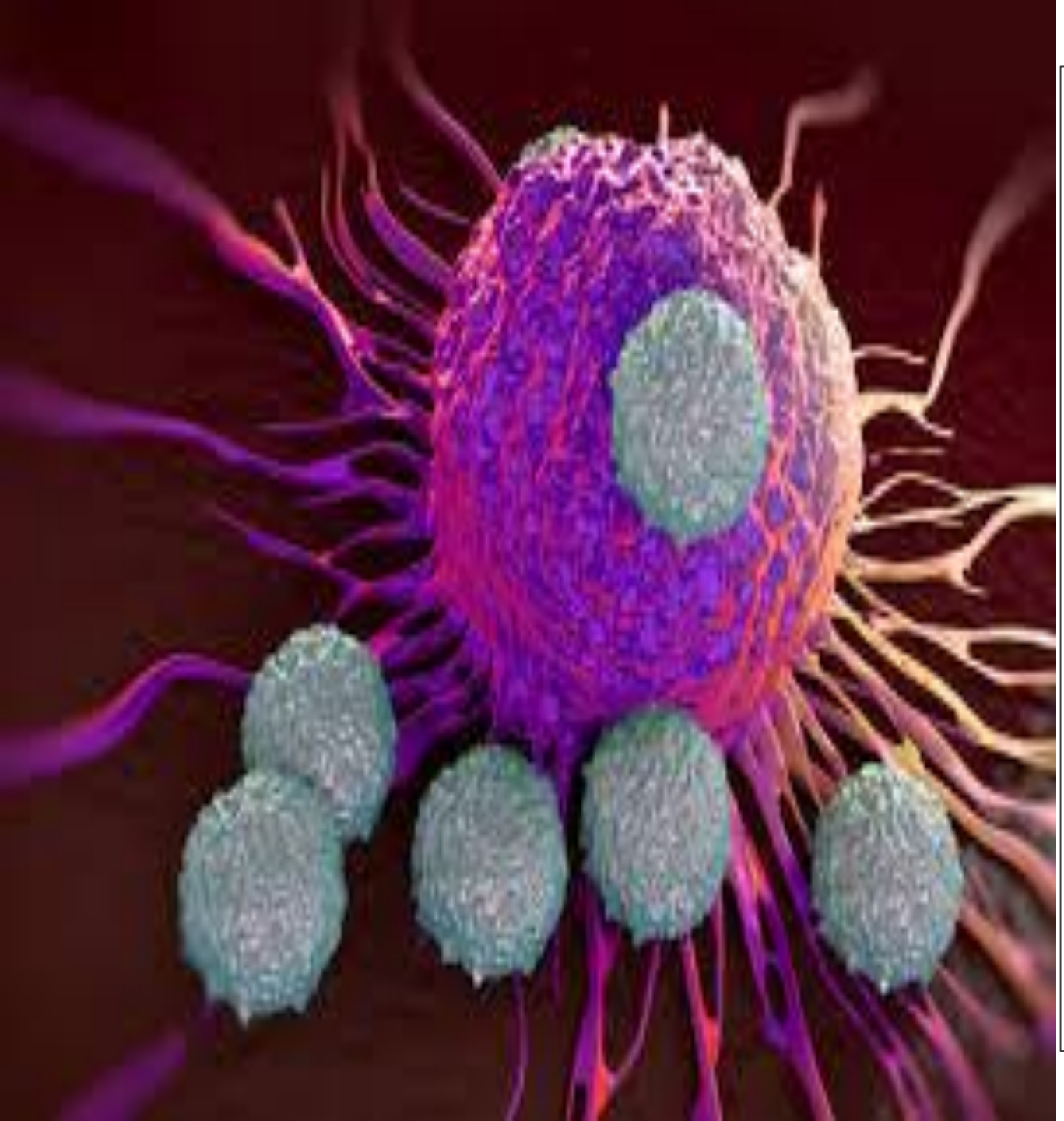
"Due to a **lack of early detection methods**, patients are typically diagnosed at a late stage, with a five-year survival rate of <5%. Surgical resection remains the only curative treatment, but fewer than 20% of patients qualify as candidates" (Wang, Huang & Sun, 2017)

(17)

(18)

Current Treatment Modules (chemo)

- **Chemotherapy:**
- Capecitabine (Xeloda); Erlotinib (Tarceva), a type of Targeted therapy; Fluorouracil (5-FU); Gemcitabine (Gemzar); Irinotecan (Camptosar); Leucovorin (Wellcovorin); Nab-paclitaxel (Abraxane); Nanoliposomal irinotecan (Onivyde); Oxaliplatin (Eloxatin)
- **First-line chemotherapy:** This is generally the first treatment used for people with either locally advanced or metastatic pancreatic cancer.
- **Second-line chemotherapy:** When treatment does not work or stops working to control cancer growth, the cancer is called refractory.
- **Off-label use:** This refers to a drug being given for a condition not listed on its label. This means that it is not being given for the condition(s) that the drug is specifically approved for by the FDA. (19)

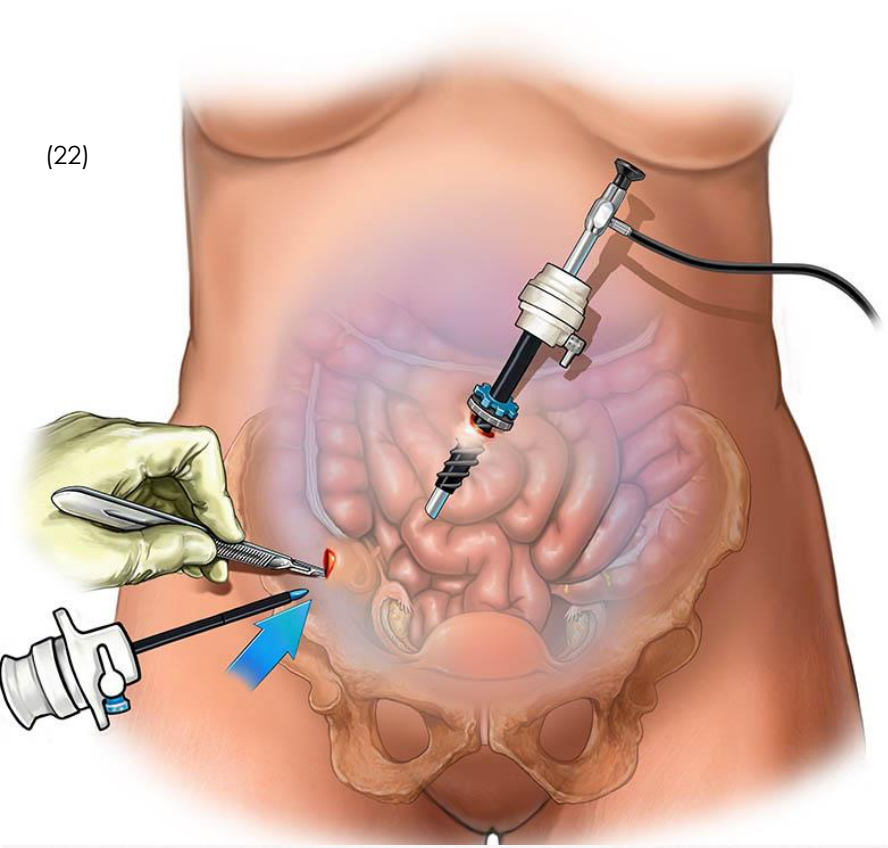


Current Treatment Modules:

- Immunotherapy
- Cancer vaccines are used which are created from various sources such as pancreatic cancer cells, bacteria, or a person's specific tumor cells.
- Use PD-1 antibodies
- CTLA-4 antibodies are also being used as another immune checkpoint inhibitors but aren't as effective for PC patients, except for those with tumors that have high microsatellite instability.
- Adoptive immunotherapy is also being tested, where researchers collect and modify a person's T cells
- Targeted Therapy
- Erlotinib and gemcitabine is the only targeted therapy approved for PC treatment. (19), (20)

Image: (21)

Current Treatment Modules (surgery)



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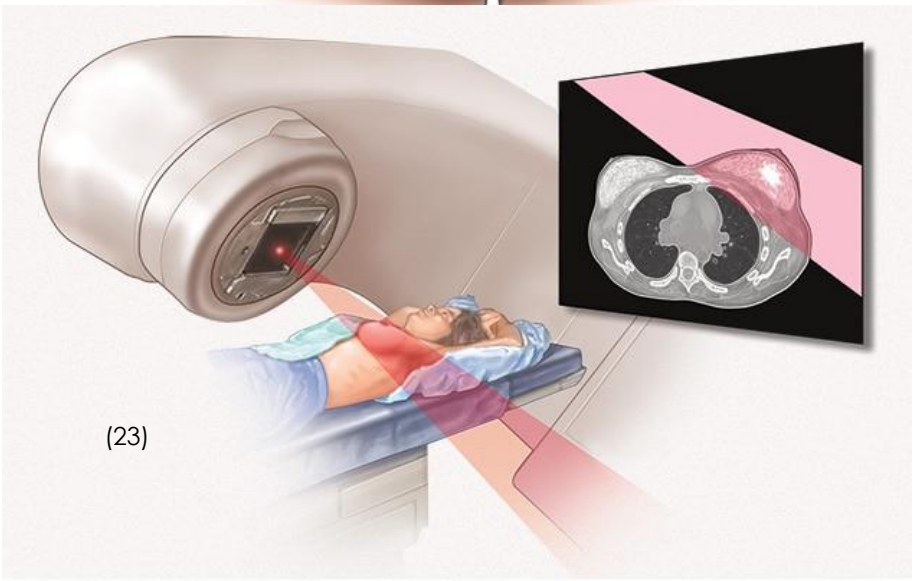

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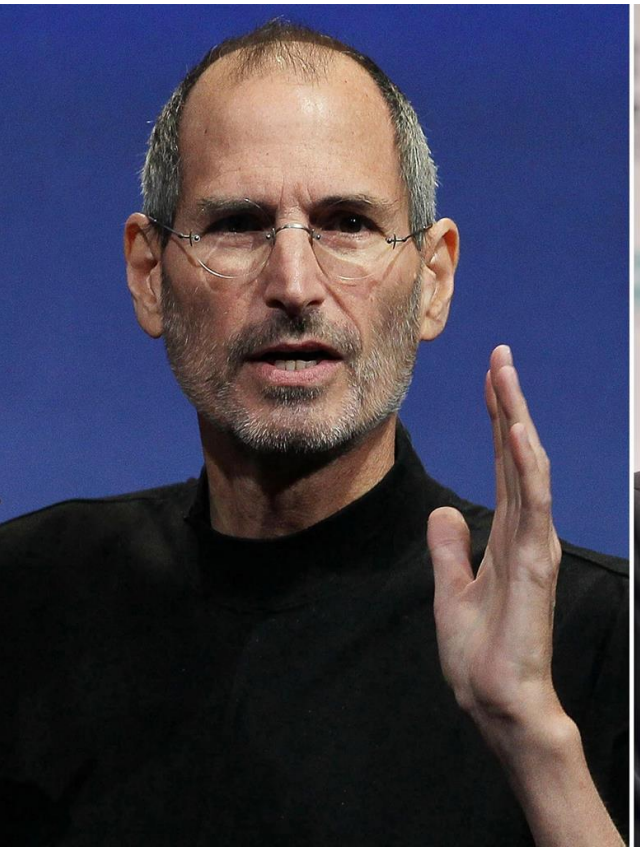
- Cancer Stem Cells
- **Surgery:**
- **Laparoscopy** can be performed to view if the cancer has spread to other parts of the abdomen. Done by making small holes in the abdomen and passing a camera through.
- **Whipple Procedure** is performed if the cancer is located at the head of the pancreas.
- **Distal Pancreatectomy** performed if the cancer is located at the tail of the pancreas.
- Total **Pancreatectomy performed** only if the cancer is located in many areas
- **Radiation Therapy:**
- **External-beam radiation therapy** is the type of radiation therapy used most often for pancreatic cancer.
- **Proton beam therapy** is a type of external-beam radiation therapy that uses protons rather than x-rays.
- **Stereotactic body radiation** (SBRT) or Cyberknife includes higher doses in a short amount of time (19), (20)

Famous Figures with Pancreatic Cancer



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Steve Jobs

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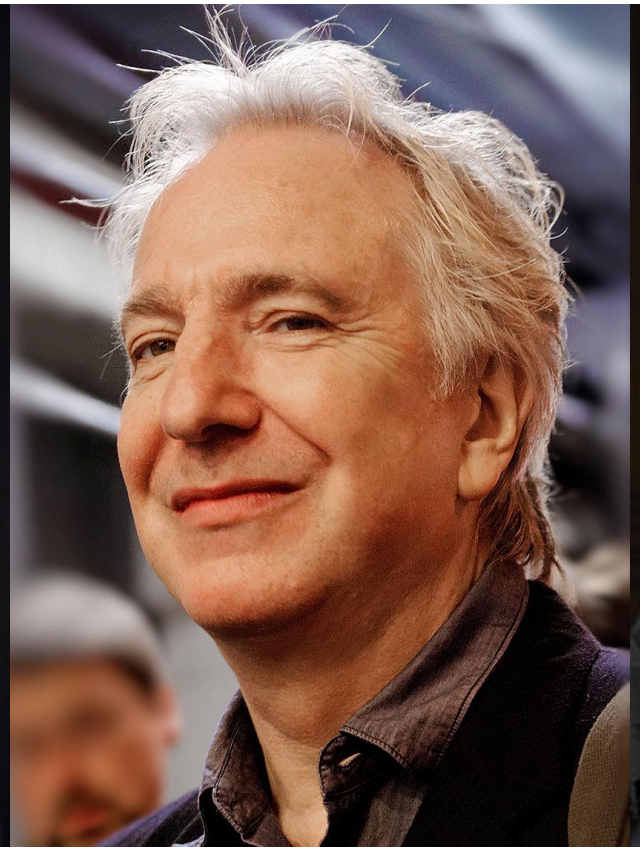
Alex Trebek



Alan Rickman

(26)

Ruth Bader Ginsburg

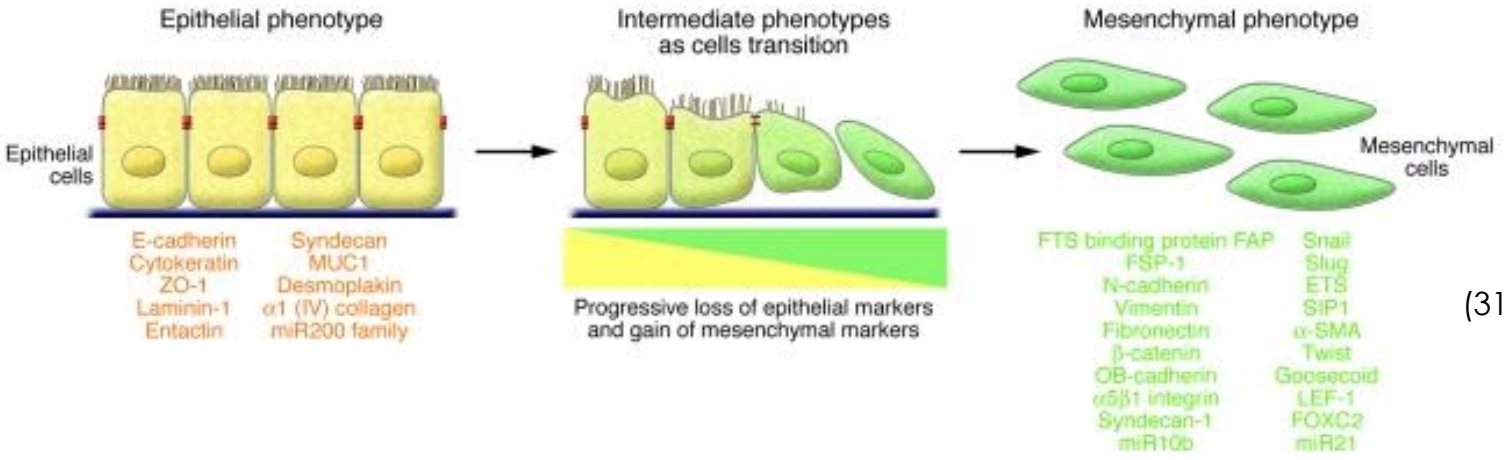
Genetics of Pancreatic Cancer

- Selective mutations of ***BRCA2***, and to a lesser extent, ***BRCA1***, have been associated with familial pancreatic cancer.
  - Common in Ashkenazi Jews. (28)
- Mutations in **exon 11** (nucleotides 3035–6629) in *BRCA2*—the so-called ovarian cancer cluster region (27)
- A polymorphic **stop codon** in the coding region of *BRCA2 (K3326X)* was shown in a large case–control study to be significantly more prevalent in individuals with FPC. (28)
- In addition, many pancreatic cancers include several genetic mutations of the oncogene ***KRAS***, which is integrated in signaling pathways of various receptor kinases such as *EGFR* and *IGFR-I*. (28)
- Several pancreatic tumors show several mutations in several **tumor suppressor genes**, including *p53, DPC4, p16,* and *BRCA2*. (28)
- In a whole-genome sequencing study of 24 pancreatic tumors, an average of **63 genetic alterations** were detected per cancer, mostly point mutations. (28)

(29)

Epithelial-Mesenchymal Transition

- During EMT, epithelial cells **become motile** after undergoing defined molecular changes, and becoming a **mesenchymal cell**. This process is **reversible.**
- During tumorigenesis, EMT may increase the motility and invasiveness of cancer cells
- During EMT, the following occurs to cause cancer cells to be able to **break away and move to other parts of the body**:
  - Disassembly of cell-cell contacts
  - Cytoskeletal modification
  - Changes in gene expression
  - Gain of motility
- The activation of Snail, ZEB, and bHLH family transcription factors m ediates the transition from epithelial to mesenchymal gene expression.
- Tight junctions, adherens junctions, and desmosomes are disassembled during this process. (30)



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