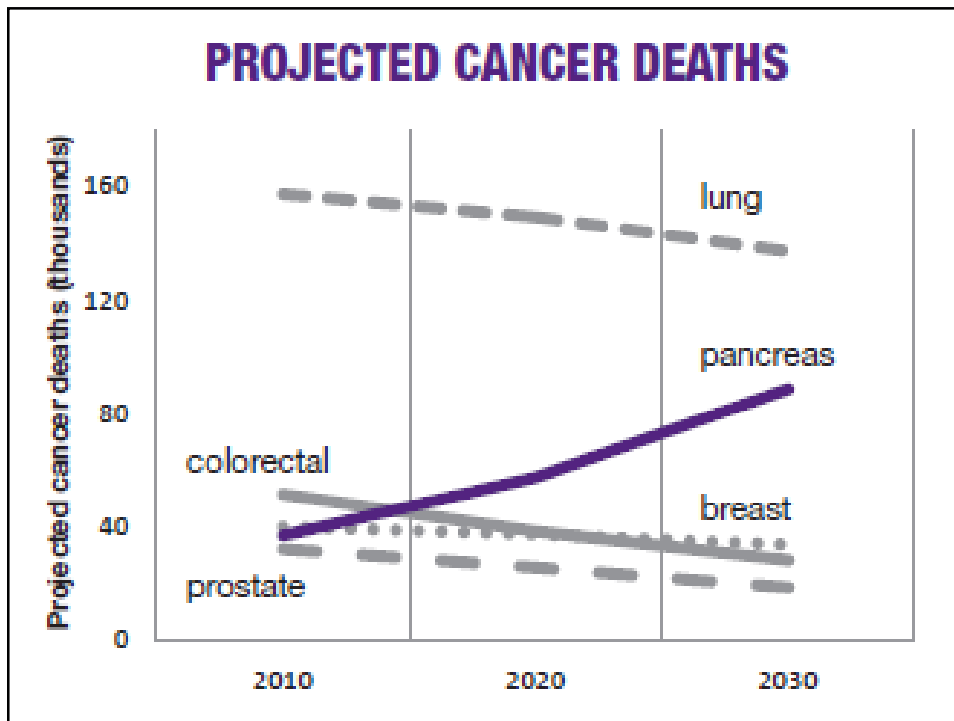


Pancreatic Cancer: FDA Approved Treatments and Clinical Trials

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**Pancreatic cancer
is the
hardest cancer of all to
treat**

**Pancreatic cancer:
Why so difficult to treat?**

- 1) Hard to diagnose / discovered in advanced form
- 2) Drugs not as effective as desired
- 3) Lack of sophisticated/integrated multidisciplinary care
- 4) Patients a little older, sometimes hard to use intensive treatments
- 5) PESSIMISM**

Optimism
A pessimist sees the difficulty
in every opportunity;
an optimist sees the
opportunity in every difficulty.
--Winston Churchill



www.gavatorta.com

PANCREATIC
CANCER

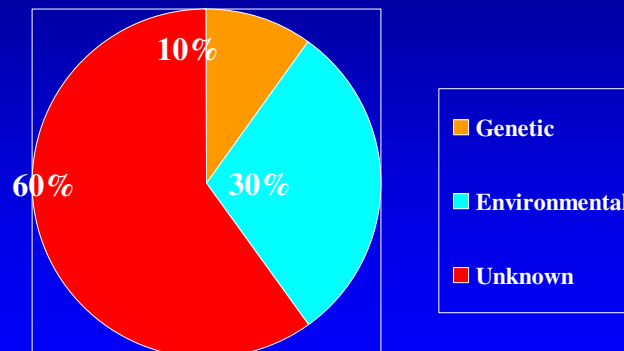
**Challenge Goal:
Double survival by 2020**

ACTION
NETWORK

Pancreatic cancer: Epidemiology

- Lifetime risk approximately 1 in 70
- Incidence slowly rising
- Average age ~65, most patients between 60-80, rare under 40
- Males slightly more common than females
- More common in Afro-Americans, less so in Asian-Americans

Pancreatic cancer: Etiology



Any patient with any combination of...

- 1) abdominal pain**
- 2) weight loss**
- 3) jaundice**
- 4) new- onset diabetes, or**
- 5) acute pancreatitis....**

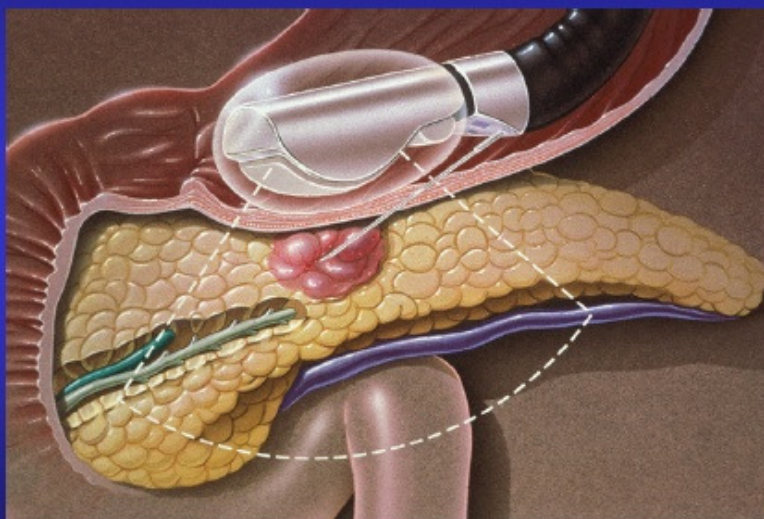
think pancreas cancer!!!

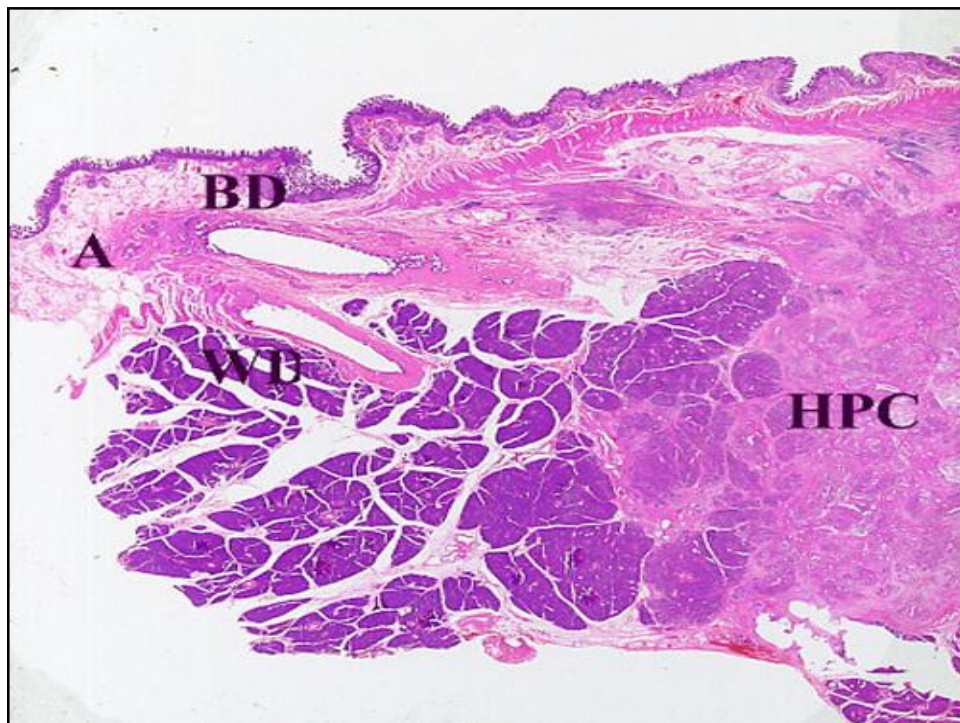
Pancreatic cancer: Keys to diagnosis

1. High “index of awareness”
2. Remember key risks
3. Multiple key clinical features
4. Early sophisticated imaging
5. Repetitive testing

**You don't have
pancreatic cancer
unless
a biopsy proves you
do**

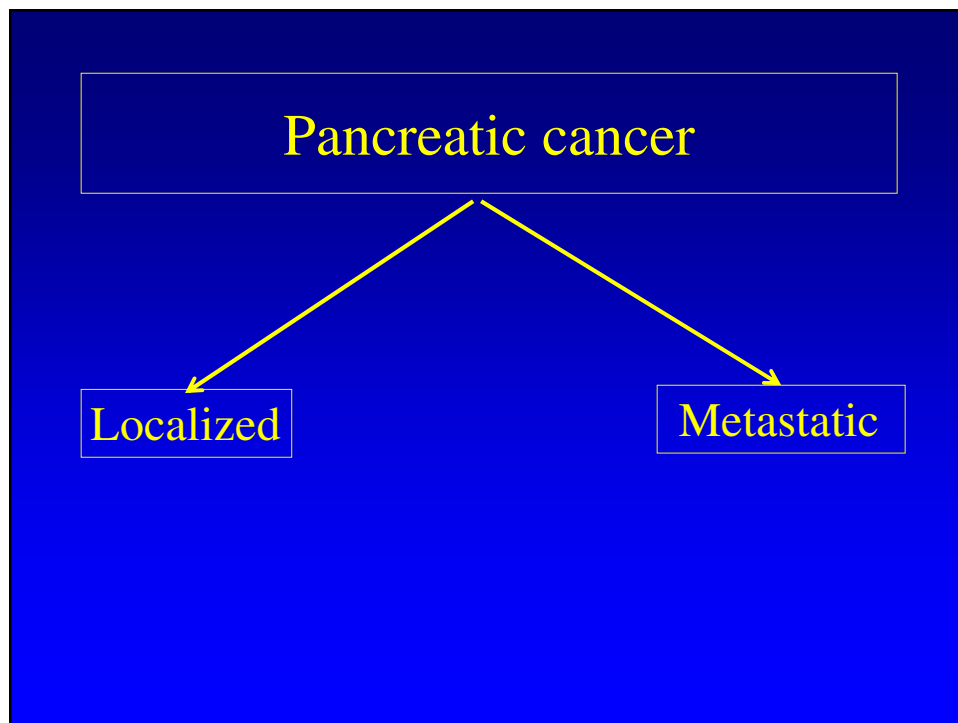
EUS-FNA





Pancreatic cancer: Standard evaluation

- History and Physical Examination
- CBC/diff/plt/chemistry panel
- CA19.9
- Chest imaging
- CT scan of abdomen using special imaging techniques for pancreas detail



Is it RESECTABLE ????

- Pancreatic cancer:
Frequently of extent**
- Localized
Resectable 15%
 - Not immediately resectable 35%
 - Metastatic 50%

Pancreatic cancer: Goals of therapy

- Quality of life
- Quantity of life
- A chance for a cure

**Complete resection of
pancreatic cancer is
usually necessary, but
usually not sufficient for a
permanent cure**

Pancreatic cancer: Key quality of life issues

- Pain
- Depression
- Diabetes
- Weight loss
- Nausea/vomiting, stomach dysfunction (GOO)
- Biliary obstruction/infection
- Thromboembolism
- Other medical problems

Pancreatic Cancer: FDA Approved Treatments

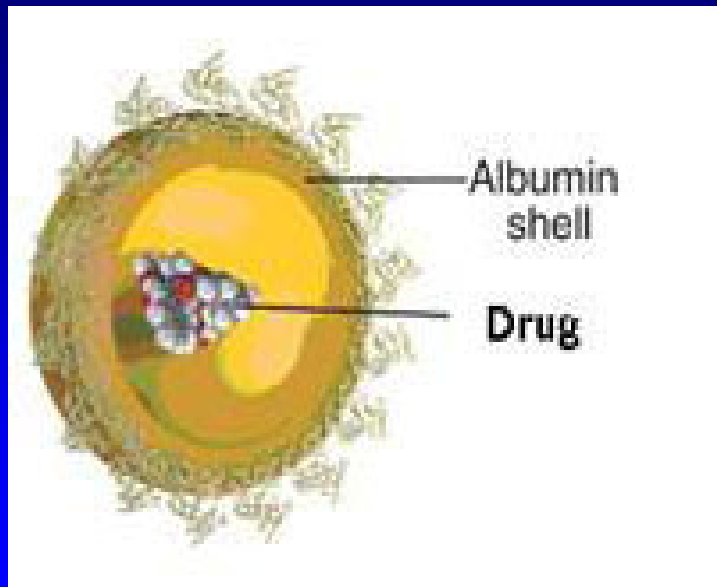
Metastatic pancreatic cancer: Options for treatment

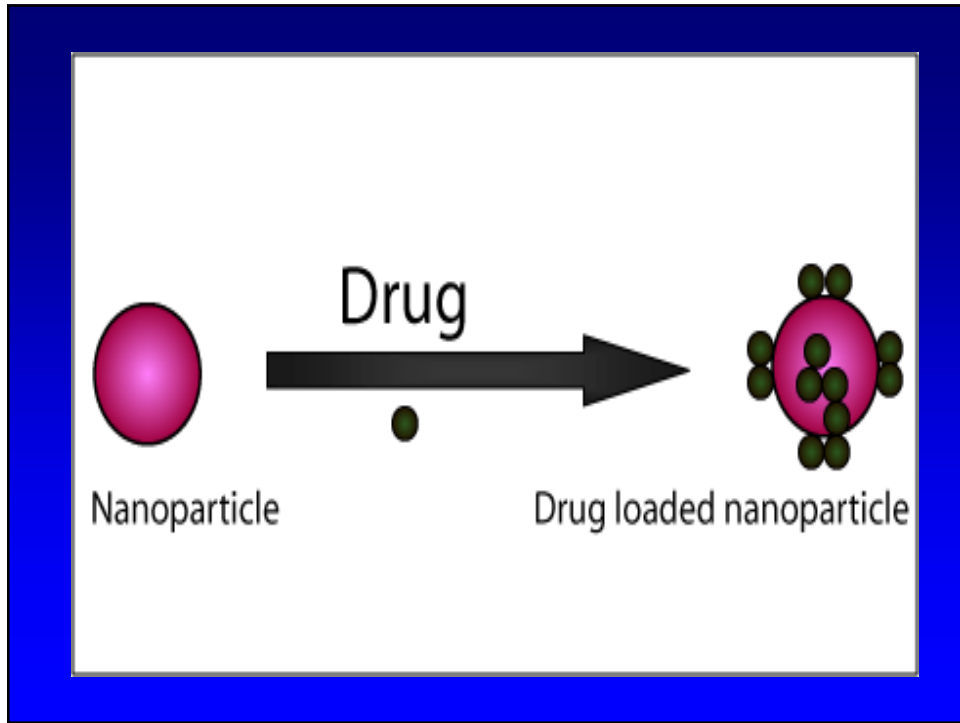
- 1. Supportive care** (especially if function limited)
- 2. Chemotherapy** - gemcitabine- based (e.g. gemcitabine/nab-paclitaxel) or fluoropyrimidine-based (e.g. FOLFIRINOX)
- 3. Clinical trial**

Pancreatic cancer: Commonly used drugs - 2014

- **GEMCITABINE**
- **5-FU**
- **Erlotinib**
- **Capecitabine**
- **Nab-Paclitaxel**
- **Cisplatin**
- **Oxaliplatin**
- **Irinotecan**
- **Docetaxel**

What is better than gemcitabine ??





Gem/nab-paclitaxel in metastatic pancreatic cancer

(von Hoff. NEJM 2013)

- 861 patients, randomized phase III
- Response rate more than 3x higher than gemcitabine
- Time to progression ~50% longer than gemcitabine
- Overall survival ~ 1/3 longer than gemcitabine
- Easier to take than FOLFIRINOX for most patients
- ? Can SPARC protein predict who will respond better

Folfirinox vs.gemcitabine

(Conroy et.al. NEJM 2011)

- 342 patients, randomized phase III
- Response rate nearly 3x higher than gemcitabine
- Time to progression 2x higher than gemcitabine
($p < .00001$)
- Overall survival 50% longer than gemcitabine
- But.....
- Harder, more expensive to use, side effects greater

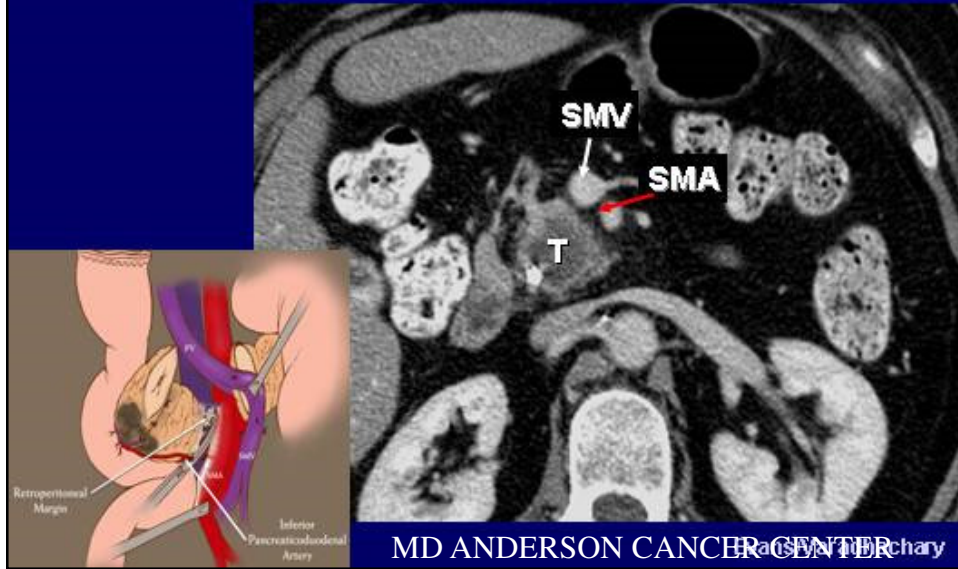
Pancreatic cancer: Issues in metastatic disease

1. More effective therapy
2. Therapy for less vigorous patients
3. Therapy after gemcitabine and 5-FU-based treatments have failed
4. Personalized therapy

Pancreatic cancer: Types of new drugs

- Chemotherapy
- Targeted therapy
- Anti-stem-cell therapy
- Anti-stromal therapy
- Immunotherapy

Resectable Pancreatic Cancer

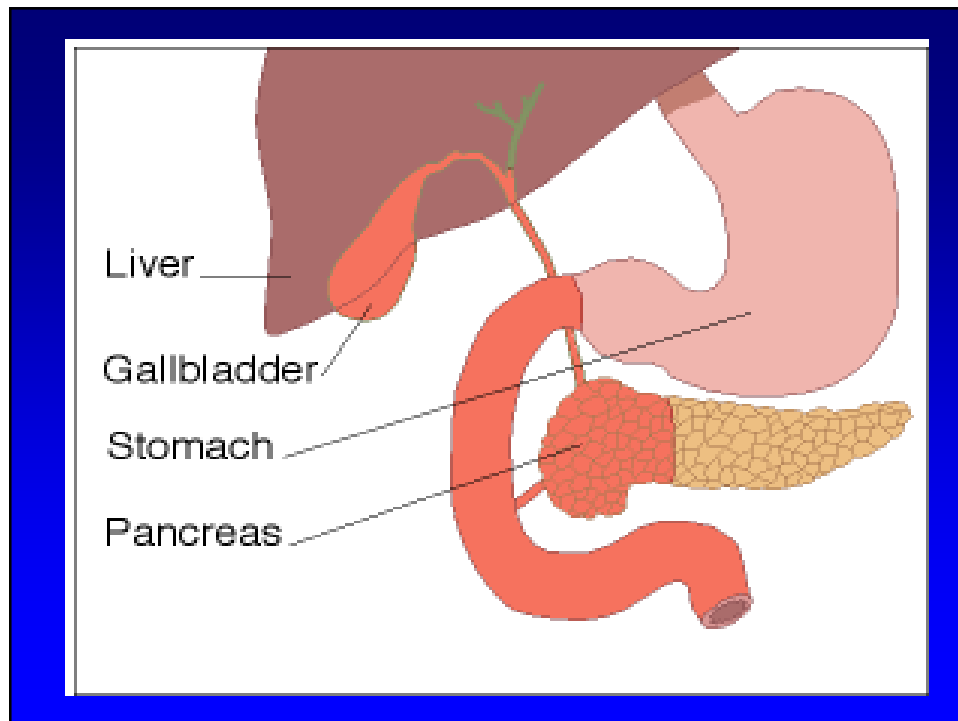


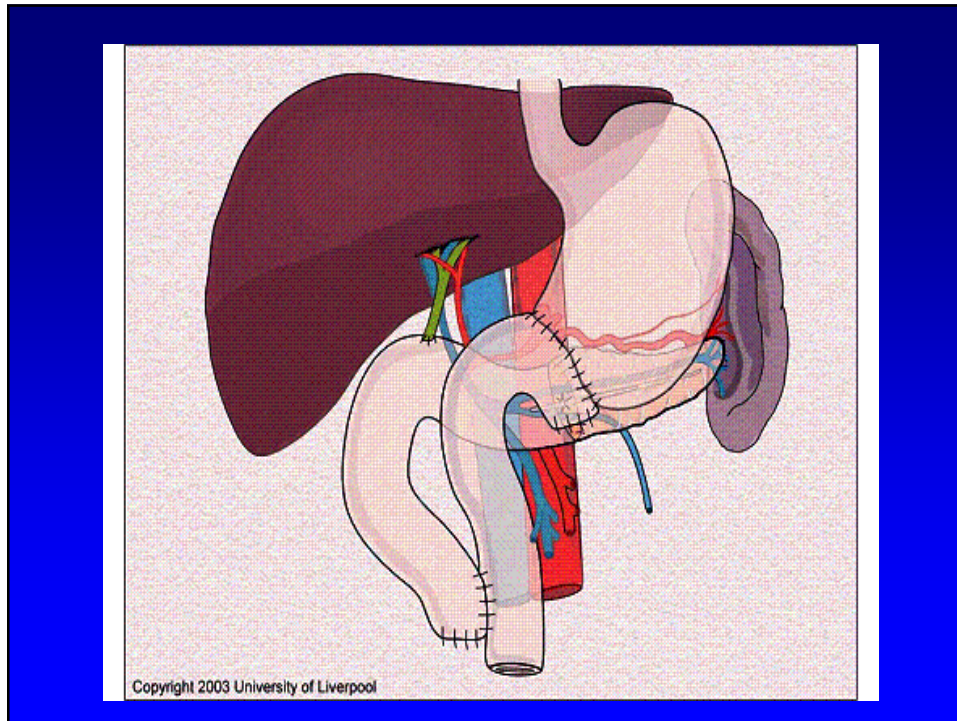
You need an experienced surgeon !

Pancreatic cancer: Surgical volume and outcome

(Birkmeyer NEJM 2002)

<u># cases/year</u>	<u>mortality</u>
<1	16.2%
1-2	14.4%
3-5	10.9%
>16	3.9%





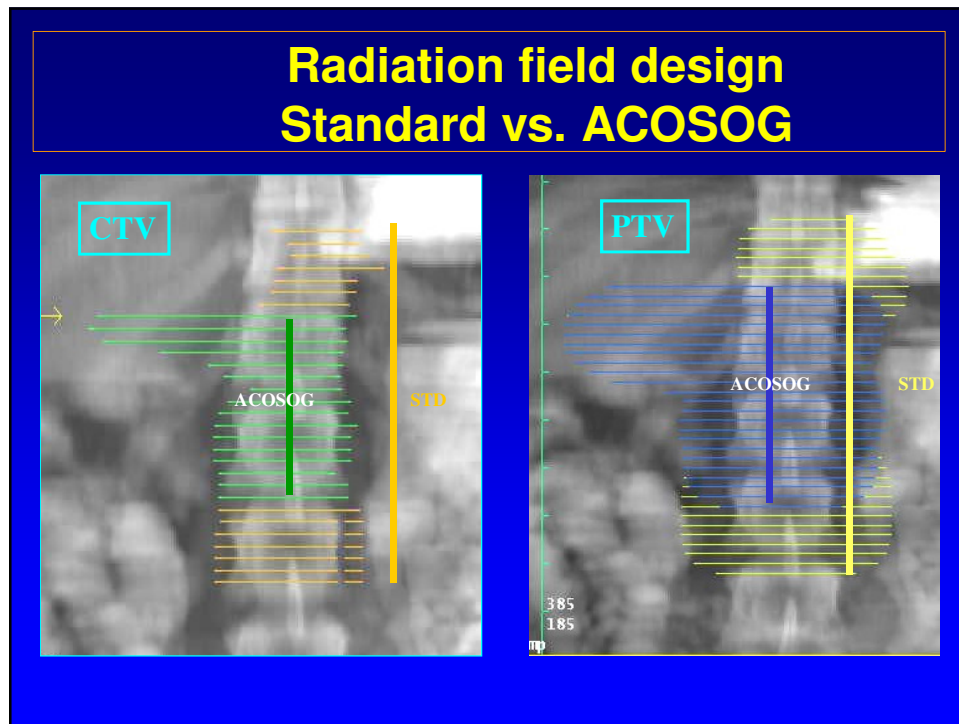
**However, even when
pancreatic cancer is removed or
localized, it has usually (about
90% of the time) already spread
(i.e. a systemic disease),
thus it is not if systemic
therapy (i.e. drugs) should be
given....
...but how**

Pancreatic cancer: Treatment of resected disease

- **Observation** – probably not a good option for patients willing able to take therapy
- **Chemotherapy only**- gemcitabine or 5FU/LV for 6 months is the standard of care
- **Chemotherapy / XRT**- patients with high risk of local recurrence, good in experienced centers
- **Clinical trial**

Resected pancreatic cancer: The ESPAC 3 trial (Neoptolemos et.al. JAMA 2010)

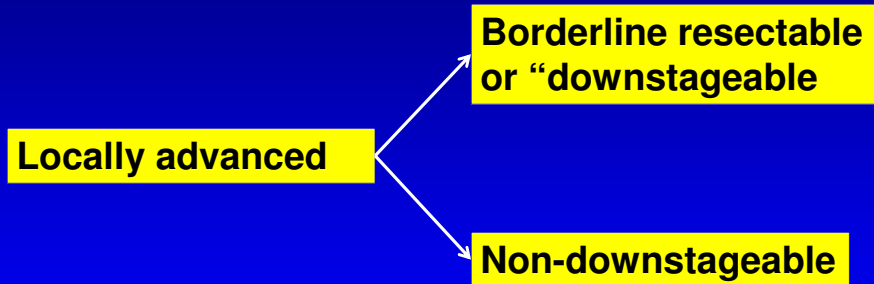
- 1088 pts, randomized phase III
- 5FU/LV vs gemcitabine
- No diff median survival
- No diff 2-year overall survival
- Complications higher with 5FU/LV ($p < .001$)



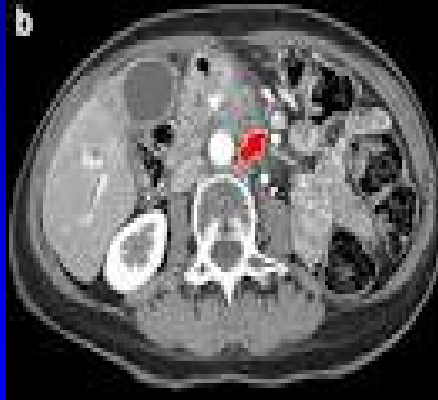
Pancreatic cancer: Issues in resectable disease

1. ??? Radiation
2. Better chemotherapy
3. Neoadjuvant therapy
4. Better radiotherapy
5. Immunotherapy

IS IT RESECTABLE???
DOWNSTAGEABLE??



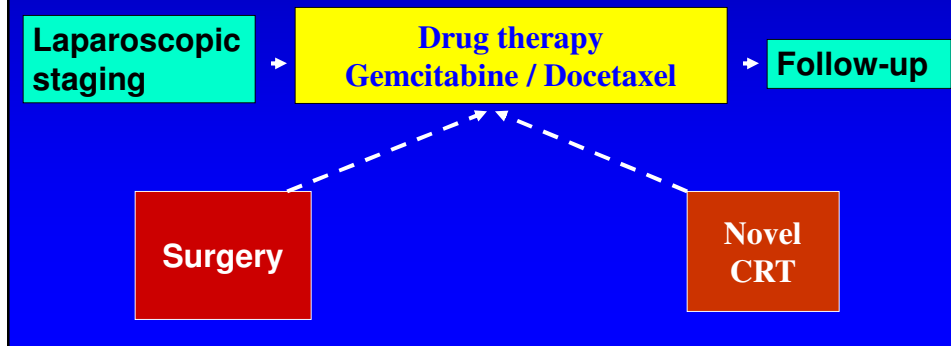
Borderline resectable pancreatic cancer



Borderline resectable pancreatic cancer: possible protocol designs

1. Chemo → Surgery → Chemo
2. CRT → Surgery → Chemo
3. Chemo → CRT → Surgery → Chemo
4. Chemo → Surgery → Chemo → CRT

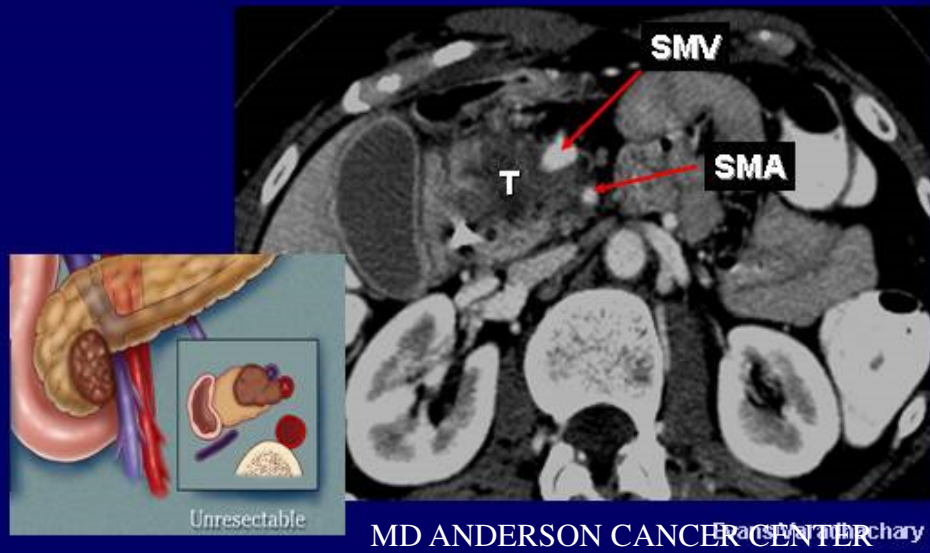
**Pancreatic cancer:
“downstaging” borderline resectable
disease
VM phase II trial**



**Borderline resectable pancreatic cancer:
Virginia Mason methodology
(Rose et.al. Ann Surg Oncol 2014)**

- 76 patients- phase II trial
- ~85% completed 6 months of chemotherapy
- ~75% receive surgery and/or chemoradiation
- ~ 50% successfully had their tumors removed
- Survival ~ 2x literature standard
- Patients with tumors successfully removed surviving as long as patients who are initially resectable

Locally Advanced Pancreatic Cancer



Pancreatic cancer: Treatment of locally advanced disease

- Supportive care
- Chemotherapy only
- Chemotherapy / XRT
- Clinical trial
- but , different expectations than in resectable disease

Locally advanced pancreatic cancer: Results to date

- Chemotherapy seems to be the best first therapy
- Mixed results as to whether chemoradiation adds to chemotherapy
- Chemoradiation very rarely produces long-term survival

Pancreas cancer: 2014

- **OPTIMISM!!!**
 - Better drugs
 - Improved multidisciplinary care
 - Earlier diagnosis
 - Personalized treatment strategies with reduced therapeutic toxicity



“The future ain’t
what it used to be.”
—Yogi Berra

