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
Challenge Goal:
Double survival by 2020

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

--Winston Churchill

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PANCREATIC CANCER
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

- Genetic: 10%
- Environmental: 30%
- Unknown: 60%
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.
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

Pancreatic cancer

- Localized
- Metastatic
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)

<table>
<thead>
<tr>
<th># cases/year</th>
<th>mortality</th>
</tr>
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<tbody>
<tr>
<td>&lt;1</td>
<td>16.2%</td>
</tr>
<tr>
<td>1-2</td>
<td>14.4%</td>
</tr>
<tr>
<td>3-5</td>
<td>10.9%</td>
</tr>
<tr>
<td>&gt;16</td>
<td>3.9%</td>
</tr>
</tbody>
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![Pancreatic anatomy](image)
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??

Locally advanced

Borderline resectable or “downstageable"

Non-downstageable
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
THANK YOU!!!!