Clinical Research Trials for Pancreas Cancer

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What does it take to develop one new cancer drug?

• One billion dollars and 10-15 years
• Drug discovery (5000-10,000 compounds)
• Preclinical laboratory work (250 compounds)
• Clinical trials in humans
• FDA submission and approval
### How have cancer drugs changed?

<table>
<thead>
<tr>
<th>1970-1990’s</th>
<th>2000 and beyond</th>
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<tbody>
<tr>
<td>Cytotoxic</td>
<td>Cytostatic</td>
</tr>
<tr>
<td>Non-specific</td>
<td>More selective</td>
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<tr>
<td>Intravenous toxins</td>
<td>Oral/IV biologics</td>
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<tr>
<td>Highly toxic</td>
<td>Well-tolerated</td>
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<tr>
<td>DNA damaging</td>
<td>Targets the tumor and tumor environment</td>
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Why do we need patient participation in clinical trials?
Recently FDA approved oncology compounds

- Everolimus
- Bendamustine
- Sunitinib
- Sorafenib
- Nilotinib
- Ixabepilone
- Temsirolimus
- Lapatinib
- Velcade
- Imatinib

- Vorinostat
- Rituxan
- Panitumumab
- Lenalomide
- Dasatinib
- Decitabine
- Cetuximab
- Rituximab
- Trastuzumab
- Bevacizumab

- Denosumab
- Pazopanib
- Sipuleucel-T
- Eribulin
- Ofatumumab
- Ipilimumab
- Cabazitaxel
- Crizotinib
<table>
<thead>
<tr>
<th>FDA approved oncology drugs 2012-2013</th>
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<tbody>
<tr>
<td>• Obinutuzumab</td>
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<td>• Pertuzumab</td>
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<tr>
<td>• Nab-paclitaxel</td>
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<tr>
<td>• Afatinib</td>
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<tr>
<td>• Trametinib</td>
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<tr>
<td>• Dabrafenib</td>
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<tr>
<td>• Abiraterone</td>
</tr>
<tr>
<td>• Cabozanitinib</td>
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<tr>
<td>• Vandetanib</td>
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<tr>
<td>• Omacetaxine</td>
</tr>
<tr>
<td>• Regorafenib</td>
</tr>
<tr>
<td>• Bosutinib</td>
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<tr>
<td>• Enzalutamide</td>
</tr>
<tr>
<td>• Ziv-aflibercept</td>
</tr>
<tr>
<td>• Carfilzomib</td>
</tr>
<tr>
<td>• Vismodegib</td>
</tr>
<tr>
<td>• Axitinib</td>
</tr>
<tr>
<td>• Ruxolitinib</td>
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<tr>
<td>• Brentuximab</td>
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<tr>
<td>• Vemurafenib</td>
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</table>
Barriers to Clinical Trial Enrollment

• Access

• Education
  – Patient perceptions
    • “guinea pig”
    • “I don’t want a placebo”
    • “Will my insurance cover this?”
  – MD perceptions
    • Too time intensive
    • Too much paperwork

ONLY ~ 10% of all adult cancer patients participate in clinical trials!
Pancreatic Cancer

Resection

Metastatic

- ADJUVANT THERAPY
  - RTOG 0848
  - HyperAcute Vaccine (CLOSED)

- PALLIATIVE THERAPY
  - Gemcitabine/cisplatin + birinapant

- Locally advanced
  - Gemcitabine/Nab-paclitaxel/XRT
  - FOLFIRINOX and HyperAcute Vaccine
Adjuvant Phase III Trial-RTOG 0848

**FIRST RANDOMIZATION**

1. **STRATIFY**
   - Nodal Status:
     - 1: involved
     - 2: uninvolved
   - CA19-9 result:
     - 1: ≤ 90
     - 2: > 90 – 180
   - Surgical margins:
     - 1: positive (R1)
     - 2: negative (R0)

2. **RANDOMIZE**
   - Arm 1:
     - Gemcitabine x 5 cycles
   - Arm 2:
     - Gemcitabine + Erlotinib x 5 cycles

3. **Evaluate to Confirm No Progression**

If no progression, then:

1. **STRATIFY**
2. **RANDOMIZE**
   - Arm 1: gemcitabine
   - Arm 2: gemcitabine + erlotinib

**SECOND RANDOMIZATION**

For Non-Progressing Patients

1. **RANDOMIZE**
   - Arm 3:
     - 1 cycle of chemotherapy
   - Arm 4:
     - 1 cycle of chemotherapy followed by RT with either capecitabine or 5-FU

**Principle Investigator:** Adam Berger, MD
HyperAcute®-Pancreas immunotherapy

Adjuvant therapy (Gemcitabine alone or with 5-FU chemoradiation) with or without HyperAcute®-Pancreas (algenpantucel-L) immunotherapy in subjects who have undergone surgical resection

Principal Investigator: Harish Lavu, MD
HyperAcute® Technology

α(1,3)GT gene introduced into human cancer cells using viruses

Selected human lung cancer cell lines

Selected human pancreatic cancer cell lines
Locally Advanced Unresectable Pancreatic Adenocarcinoma
Gemcitabine and Nab-Paclitaxel as a Promising Combination

- Gemcitabine and Nab-Paclitaxel IV weekly x 3 with 1 week off

Patients with metastatic pancreas cancer receiving this doublet did better than the group receiving gemcitabine alone.

vonHoff et al ASCO, 2013
# Upcoming Gem/Paclitaxel Trial for Locally Advanced Pancreas Cancer

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<tbody>
<tr>
<td>Gem</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Nab-paclitaxel</td>
<td><strong>III</strong></td>
<td><strong>III</strong></td>
<td></td>
<td><strong>II</strong></td>
<td><strong>III</strong></td>
<td><strong>III</strong></td>
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<tr>
<td>CRT</td>
<td></td>
<td></td>
<td>30 Gy 3Gy/fx</td>
<td></td>
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Principal Investigator: Voichita Bar-Ad, MD
FOLFIRINOX as a Promising Regimen

5-Fluorouracil
Oxaliplatin
Leucovorin
Irinotecan
IV every 2 weeks

Patients with metastatic pancreas cancer did better than the group receiving gemcitabine alone.

Open Trial of FOLFIRINOX With or Without HyperAcute®-Pancreas Immunotherapy Trial for Locally Advanced Pancreas Cancer
Study Schema

FOLFIRINOX (SOC) + HAPA

CT scan → If new distant disease then salvage GEM +/- HAPA

Chemoradiation + HAPA

CT scan

Surgically Resectable

Surgery

Adjuvant SOC (Gem) + HAPA

SD

Progressed +/- Mets

FOLFIRINOX + HAPA Continues

Salvage Gem + HAPA

Surgically Unresectable

Surgically Resectable

Surgery

Adjuvant SOC (Gem)

SD

Progressed +/- Mets

FOLFIRINOX Continues

Salvage Gem

Surgically Unresectable

Chemoradiation

CT scan
Metastatic Pancreas Cancer
Programmed cell death is called apoptosis.

Cancer cells circumvent apoptosis and continue to grow.

TL32711 or birinapant, antagonizes the cancer cells’ inhibitors of apoptosis and can make the chemotherapy work better at killing cancer cells.
<table>
<thead>
<tr>
<th>Dose Level</th>
<th>TL32711 (iv)</th>
<th>Gemcitabine (iv) once weekly x 2 weeks (Day 1 and 8)</th>
<th>Cisplatin (iv) once every 3 weeks (Day 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>17 mg/m^2</td>
<td>1000 mg/m^2</td>
<td>75 mg/m^2</td>
</tr>
<tr>
<td>A1</td>
<td>22 mg/m^2</td>
<td>1000 mg/m^2</td>
<td>75 mg/m^2</td>
</tr>
<tr>
<td>A2</td>
<td>26 mg/m^2</td>
<td>1000 mg/m^2</td>
<td>75 mg/m^2</td>
</tr>
<tr>
<td>A3</td>
<td>35 mg/m^2</td>
<td>1000 mg/m^2</td>
<td>75 mg/m^2</td>
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</table>
“Enrollment in a clinical trial is the best management for patients with cancer”

National Comprehensive Cancer Network Guidelines
TEAMWORK!

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Edith Mitchell, MD
Mony Pillai, MD