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>
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<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
FDA approved oncology drugs 2012-2013

- Obinutuzumab
- Pertuzumab
- Nab-paclitaxel
- Afatinib
- Trametinib
- Dabrafenib
- Abiraterone
- Cabozanitinib
- Vandetanib
- Omacetaxine
- Regorafenib
- Bosutinib
- Enzalutamide
- Ziv-aflibercept
- Carfilzomib
- Vismodegib
- Axitinib
- Ruxolitinib
- Brentuximab
- Vemurafenib
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

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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**

- **Nodal Status:**
  - 1: involved
  - 2: uninvolved

- **CA19-9 result:**
  - 1: $\leq 90$
  - 2: $> 90 - 180$

- **Surgical margins:**
  - 1: positive (R1)
  - 2: negative (R0)

**Randomize**

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

**Evaluate to Confirm No Progression**

**SECOND RANDOMIZATION**

For Non-Progressing Patients

**Randomize**

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

If no progression, then:

- 1. Arm 1: gemcitabine
- 2. Arm 2: gemcitabine + erlotinib

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.
# Upcoming Gem/Paclitaxel Trial for Locally Advanced Pancreas Cancer

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<tbody>
<tr>
<td>Gem</td>
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<td>11</td>
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<tr>
<td>Nab-paclitaxel</td>
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<tr>
<td>CRT</td>
<td></td>
<td></td>
<td>30 Gy 3Gy/fx</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

Chemoradiation + HAPa

CT scan

Surgically Resectable

Surgery

Adjuvant SOC (Gem) + HAPa

Surgically Unresectable

SD

Progressed +/- Mets

FOLFIRINOX + HAPa Continues

Salvage Gem + HAPa

If new distant disease then salvage GEM +/- HAPa

FOLFIRINOX (SOC) ALONE

CT scan

Chemoradiation

CT scan

Surgically Resectable

Surgery

Adjuvant SOC (Gem)

Surgically Unresectable

SD

Progressed +/- Mets

FOLFIRINOX Continues

Salvage Gem

Salvage Gem
Metastatic Pancreas Cancer
Birinapant

- 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.
### Gemcitabine/Cisplatin + TL 327811 (Birinapant)
Pancreas Cancer

#### Table 1b: Dose escalation scheme of TL32711 in combination with gemcitabine plus cisplatin (Part A2) (each cycle is 21 days)

<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>
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<tbody>
<tr>
<td>A1</td>
<td>17 mg/m²</td>
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<td>once weekly x 2</td>
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<tr>
<td>A2</td>
<td>22 mg/m²</td>
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<td></td>
<td>once weekly x 2</td>
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<tr>
<td>A3</td>
<td>26 mg/m²</td>
<td>1000 mg/m²</td>
<td>75 mg/m²</td>
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<td>once weekly x 2</td>
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<tr>
<td>A2</td>
<td>35 mg/m²</td>
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<tr>
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<td>once weekly x 2</td>
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Principal Investigator: Nancy Lewis, MD
“Enrollment in a clinical trial is the best management for patients with cancer”

National Comprehensive Cancer Network Guidelines