Management for Resectable, Borderline and Locally Advanced Pancreatic Cancer

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Medical Oncologist
Cross Cancer Institute

Outline

• Review the role of systemic chemotherapy for treatment of
  – Resectable disease
  – Borderline resectable (BR) disease
  – Locally advanced (LAPC) disease

• Explore future directions and upcoming clinical trials
Estimated Cancer Deaths in 2015

<table>
<thead>
<tr>
<th>Site</th>
<th>Percent</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>26.60%</td>
<td>10,900</td>
</tr>
<tr>
<td>Colorectal</td>
<td>12.4%</td>
<td>5,100</td>
</tr>
<tr>
<td>Prostate</td>
<td>10.1%</td>
<td>4,100</td>
</tr>
<tr>
<td>Pancreas</td>
<td>5.6%</td>
<td>2,300</td>
</tr>
<tr>
<td>Bladder</td>
<td>4.0%</td>
<td>1,600</td>
</tr>
<tr>
<td>Esophagus</td>
<td>3.9%</td>
<td>1,600</td>
</tr>
<tr>
<td>Leukemia</td>
<td>3.8%</td>
<td>1,550</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>3.5%</td>
<td>1,450</td>
</tr>
<tr>
<td>Stomach</td>
<td>3.2%</td>
<td>1,300</td>
</tr>
<tr>
<td>Brain/CNS</td>
<td>3.0%</td>
<td>1,250</td>
</tr>
</tbody>
</table>

Pancreatic cancer is the 4th leading cause of cancer death among men and women in Canada (4,600 deaths total)

Prognosis with Respect to Clinical Staging

Observed Survival

<table>
<thead>
<tr>
<th>Stage</th>
<th>Median survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>9.6 months</td>
</tr>
<tr>
<td>II</td>
<td>8.9 months</td>
</tr>
<tr>
<td>III</td>
<td>7.7 months</td>
</tr>
<tr>
<td>IV</td>
<td>2.5 months</td>
</tr>
<tr>
<td>Overall</td>
<td>4.4 months</td>
</tr>
</tbody>
</table>

Pancreatic Cancer Treatment Overview

Diagnosis and stage of pancreatic cancer confirmed

- **Resectable**
  - Distal pancreatectomy (tail)
  - Total pancreatectomy (multifocal)
  - Whipple procedure (head)
  - Adjuvant chemotherapy (usually gemcitabine or 5-FU)

- **Borderline resectable**
  - Interval chemotherapy ± radiotherapy

- **Advanced**
  - Locally advanced
    - Surgery ± venous resection (hepatic portal or superior mesenteric)
  - Metastatic
    - Palliative chemotherapy (gemcitabine, combination, or FOLFIRINOX)

5-FU, 5-fluorouracil; FOLFIRINOX, 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin.

Resectable Pancreatic Cancer
**ESPAC-4: Survival By Treatment**

- **Gemcitabine**
  - Median OS: 25.5 months (95% CI: 22.7-27.9)
  - Median OS: 28.0 months (95% CI: 23.5-31.5)

- **Gemcitabine-Cape
eptabine**
  - HR = 0.62 (95% CI: 0.48-0.99)
  - \( \chi^2(1) = 4.61, p = 0.032 \)

**Survival Rates**

- **Med OS**: 25.5m vs 28m
- **5Yr OS (est)**: 16% vs 29%
- **SAE’s**: 26% vs 24%
- **Gd 3-4 ANC**: 24% vs 38%
- **Gd 3-4 HFS**: - vs 7%

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**ESPAC Trials: 5 Year Overall Survival**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment</th>
<th>No. of pts (N=2012)</th>
<th>5-Year OS (95% CI)</th>
<th>Stratified Log-Rank ( x^2 )</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESPAC-1</td>
<td>5FU/FA</td>
<td>149</td>
<td>21 (14.6 – 28.5) %</td>
<td>7.03</td>
<td>0.030*</td>
</tr>
<tr>
<td></td>
<td>No chemotherapy</td>
<td>143</td>
<td>8.0 (3.8 – 14.1) %</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chemoradiotherapy (5FU/RA)</td>
<td>145</td>
<td>10.8 (6.1 – 17.0) %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESPAC-3</td>
<td>GEM</td>
<td>539</td>
<td>17.5 (14.0 – 21.2) %</td>
<td>0.74</td>
<td>0.390*</td>
</tr>
<tr>
<td></td>
<td>5FU/FA</td>
<td>551</td>
<td>15.9 (12.7 – 19.4) %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESPAC-4</td>
<td>GEM</td>
<td>366</td>
<td>16.3 (10.2 – 23.7) %</td>
<td>4.61</td>
<td>0.032†</td>
</tr>
<tr>
<td></td>
<td>GEMCAP</td>
<td>364</td>
<td>28.8 (22.9 – 35.2) %</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Stratification factor: resection margin status; †stratification factors: resection margin status and country
Summary of Current Standard

• GEMCAP is now an option for resected pancreatic adenocarcinoma
  – CA 19-9 eligibility limitation; post op CT;
  – Node positive 80%; R1 rates high 60%
• Results of APACT and PA.6 are eagerly anticipated
  – *nab*-Paclitaxel and Gemcitabine vs. Gemcitabine for 6 cycles (24 wks)
  – Gemcitabine for 6 cycles (24 wks) vs. mFOLFIRINOX (no 5-FU bolus) for 12 cycles (24 wks)
• Role of neoadjuvant chemotherapy is being investigated

Borderline Resectable and Locally Advanced Pancreatic Cancer (LAPC)
Pancreatic Cancer: Determining Resectability

- **Borderline Resectable**
  - High likelihood of an incomplete resection has prompted interest in strategies to “downstage” the tumor using neoadjuvant therapy

- **Locally Advanced Unresectable**
  - Unresectable due to tumor invasion into adjacent structures
**Enrollment— Intergroup definition**

Radiographic interface between tumor and one or more of the following vessels:

<table>
<thead>
<tr>
<th>Potentially Resectable</th>
<th>BORDERLINE RESECTABLE</th>
<th>Locally Advanced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portal V</td>
<td>TVI* &lt; 180°</td>
<td>TVI ≥ 180° and / or reconstrucable occlusion</td>
</tr>
<tr>
<td>Superior Mesenteric A</td>
<td>No TVI</td>
<td>TVI &lt; 180°</td>
</tr>
<tr>
<td>Hepatic A</td>
<td>No TVI</td>
<td>Reconstructable short-segment TVI of any degree</td>
</tr>
<tr>
<td>Celiac Trunk</td>
<td>No TVI</td>
<td>TVI &lt; 180°</td>
</tr>
</tbody>
</table>

*TVI, tumor-vascular interface

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**Summary of Phase III Trials in LAPC**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Median OS (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRT</td>
<td>Radiation Alone</td>
</tr>
<tr>
<td>Radiation vs. radiation + 5-FU + MMC¹</td>
<td>8.4</td>
</tr>
<tr>
<td>Radiation vs. radiation + 5-FU²</td>
<td>9.3–9.7</td>
</tr>
<tr>
<td>Gemcitabine vs. gemcitabine + radiation³</td>
<td>11.1</td>
</tr>
<tr>
<td>Radiation + 5-FU vs. cisplatin vs. gemcitabine⁴</td>
<td>8.6</td>
</tr>
<tr>
<td>Radiation + 5-FU vs. radiation + 5-FU + TNFerade⁵</td>
<td>10.0 vs. 10.0 (with TNFerade)</td>
</tr>
<tr>
<td>Gemcitabine ± erlotinib → gem ± erlotinib vs. gemcitabine ± erlotinib → gemcitabine ± erlotinib + radiation⁶</td>
<td>15.2</td>
</tr>
</tbody>
</table>

Most recent randomized phase III trials demonstrated no survival benefit from the addition of chemoradiation to chemotherapy in this setting

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**LAPC Treatment Strategies**

- **Chemoradiotherapy vs. chemotherapy**
  - Two separate meta-analyses of trials concluded that there was no survival benefit (GREATER TOXICITY) for chemoradiotherapy\(^1,2\)

- **Chemoradiotherapy after initial chemotherapy**
  - Period of initial disease control with chemotherapy alone may allow the selection of patients without occult micrometastatic disease\(^3,4\)

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**Hammel (LAP07): Induction Chemotherapy Followed by Chemotherapy or Chemoradiation**

Histologically confirmed LAPC
PS 0 - 2
No prior radiation or chemotherapy
N = 442

**Efficacy by R2**

<table>
<thead>
<tr>
<th></th>
<th>CT</th>
<th>CRT</th>
<th>HR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS, median, months</td>
<td>16.4</td>
<td>15.2</td>
<td>1.03</td>
<td>0.83</td>
</tr>
<tr>
<td>PFS, median, months</td>
<td>11.8</td>
<td>12.5</td>
<td>0.9</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Similar rates of grade 3/4 AEs, except for nausea with chemoradiotherapy (6% vs. 0%; \( P < 0.01 \))

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* Patients receiving erlotinib at R1 had maintenance with erlotinib after protocol completion.
AE, adverse event; CRT, chemoradiation therapy; CT, chemotherapy; HR, hazard ratio; LAPC, locally advanced pancreatic cancer; OS, overall survival; PFS, progression-free survival; PS, performance status; qw 3/4, first 3 of 4 weeks; R, randomization.

Hammel (LAP07): Induction Chemotherapy Followed by Chemotherapy or Chemoradiation

Overall Survival by Random 2 Status

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Event</th>
<th>Censor</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>133</td>
<td>110</td>
<td>24</td>
<td>15.4</td>
</tr>
<tr>
<td>Chemoradiotherapy</td>
<td>24</td>
<td>15.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HR = 95% CI = 1.03 (0.79; 1.34)

logrank p = 0.8295

0, confidence interval; HR, hazard ratio.

LAP07 Further Analyses

- At the time of analysis, 238 had tumour progression
  - 96 (50.5%) locoregional
  - 97 (49.5%) metastatic
- In the CRT arm, patients had significantly less local tumour progression compared to the RT arm
  - 34% vs. 65% (P < 0.001)
- Median time without treatment was longer in the CRT arm
  - 159 vs. 96 days (P = 0.05)
- 4% (18/442) of patients underwent surgical resection
  - 6 before second randomization, 12 after protocol completed
  - R0: 11, R1: 6, unknown: 1

CRT, chemoradiation therapy; R, radical Neglect; RT, radiation therapy.
Hammel P. Oral presentation at: WGOG 2015.
Chemotherapy in LAPC

- ACCORD and MPACT trials excluded locally advanced patients
  - Only included metastatic pancreatic cancer patients
  - There is an ongoing phase II trial evaluating nab-paclitaxel plus gemcitabine in LAPC patients: LAPACT

- Limited data in locally advanced setting, mostly from institutional case series
  - Larger trials are missing and needed

ClinicalTrials.gov: NCT02301145.

PRODIGE 4/ACCORD 11: Overall Survival

<table>
<thead>
<tr>
<th>Median OS, Mos</th>
<th>FOLFIRINOX</th>
<th>Gemcitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>0.57 (95% CI: 0.45-0.73)</td>
<td></td>
</tr>
<tr>
<td>Stratified log rank test</td>
<td>$P &lt; .0001$</td>
<td></td>
</tr>
</tbody>
</table>

Patients at Risk, n
- Gemcitabine: 171 134 89 48 28 14 7 6 3 3 2 2 2
- FOLFIRINOX: 171 146 116 81 62 34 20 13 9 5 3 2 2

Conroy T, et al. ASCO 2010. Abstract 4010. Reprinted with permission. RR 31.6 vs. 9.4%
### Studies of LAPC Patients Treated with FOLFIRINOX

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Stage</th>
<th>n</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase II^1</td>
<td>LAPC Metastatic</td>
<td>11</td>
<td>ORR: 27% LAPC; 26% metastatic</td>
</tr>
<tr>
<td>Registry at 3 US institutions^2</td>
<td>LAPC Metastatic</td>
<td>18</td>
<td>21% of LAPC patients underwent surgical resection</td>
</tr>
<tr>
<td>Retrospective analysis, single US institution^3</td>
<td>LAPC Metastatic</td>
<td>16</td>
<td>8% of LAPC patients underwent surgical resection</td>
</tr>
<tr>
<td>Retrospective analysis, single US institution^4</td>
<td>LAPC Metastatic</td>
<td>12</td>
<td>8% of LAPC patients underwent surgical resection</td>
</tr>
<tr>
<td>Retrospective analysis, Borderline/LAPC</td>
<td>Borderline</td>
<td>34</td>
<td>86% underwent surgical resection (R0)</td>
</tr>
<tr>
<td>Retrospective analysis, single Canadian institution^5</td>
<td>LAPC Metastatic</td>
<td>36</td>
<td>11% of LAPC patients underwent surgical resection</td>
</tr>
<tr>
<td>Prospective database^6</td>
<td>LAPC</td>
<td>77</td>
<td>36% underwent surgical resection (R0)</td>
</tr>
</tbody>
</table>

Disease control rate (DCR), FOLFIRINOX, 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin; LAPC, locally advanced pancreatic cancer; ORR, overall response rate; PD, progressive disease; PR, partial response; R, resection margin; SD, stable disease.


### Systematic review of FOLFIRINOX in patients with locally unresectable pancreatic cancer

- Rombouts S et al, ASCO 2016
  - Median OS 8.9-25 months
  - Resection rate 28%

- Suker M at al, Lancet Oncology 2016
  - Median OS 24.2 months
**Resectability post FOLFIRINOX**

- 40 patients received neoadjuvant FOLFIRINOX as initial treatment for LAPC/BR

- Post treatment clinical imaging:
  - 19 LAPC
  - 9 BR

- Despite post-FOLFIRINOX imaging suggesting unresectability, 92% had R0 resection

- FOLFIRINOX treated arm had longer operative times and more blood loss, but lower operative mortality

- FOLFIRINOX treated group had significantly less node positivity and perineural invasion


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**Gemcitabine and nab-Paclitaxel**

<table>
<thead>
<tr>
<th></th>
<th>nab-P + Gem</th>
<th>Gem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients at Risk</td>
<td>431/430</td>
<td>430</td>
</tr>
<tr>
<td>Time (months)</td>
<td>0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45</td>
<td>0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45</td>
</tr>
</tbody>
</table>

**OS, months**

<table>
<thead>
<tr>
<th>Events/n</th>
<th>Median (95% CI)</th>
<th>75th Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>nab-P + Gem: 380/431</td>
<td>8.7 (7.89 - 9.69)</td>
<td>14.8</td>
</tr>
<tr>
<td>Gem: 394/430</td>
<td>6.6 (6.01 - 7.20)</td>
<td>11.1</td>
</tr>
</tbody>
</table>

HR 0.72
95% CI, 0.620 - 0.825
P < 0.0001

Studies of LAPC Patients Treated with \textit{nab}-Paclitaxel/Gemcitabine Regimens

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Stage</th>
<th>n</th>
<th>Treatment</th>
<th>Results</th>
</tr>
</thead>
</table>
| Retrospective analysis, single US institution\(^1\) | Borderline/ LAPC | 13 | nab-Paclitaxel + gemcitabine | • 23% (3/13) underwent surgical resection (R0)  
• PR: 69% (9/13)  
• SD: 23% (3/13)  
• PD: 8% (I/13) |
| Retrospective analysis, 2 Australian clinics\(^2\) | Borderline LAPC | 8  | nab-Paclitaxel + gemcitabine or carboplatin | 26% (6/23) underwent surgical resection (R0, 2 R1)  
PR: 69% (9/13)  
SD: 23% (3/13)  
PD: 8% (1/13) |
| Retrospective analysis, single US institution\(^3\) | LAPC | 13 | nab-Paclitaxel + gemcitabine ± CRT | 38% (5/13) underwent surgical resection post-CRT R0 and 1 pre-CRT R0  
PR: 36% (4/11)  
SD: 55% (6/11)  
PD: 9% (1/11) |
| Pilot study in Germany\(^4\) | LAPC | 8  | nab-Paclitaxel (2 cycles) followed by FOLFIRINOX (2 cycles) | 37% (3/8) underwent surgical resection (R0)  
PR: 63% (5/8)  
SD: 37% (3/8) |
| Phase I study in Japan\(^5\) | LAPC | 14 | nab-Paclitaxel + gemcitabine concurrently with RT | 14% (2/14)  
PR: 43% (6/14)  
PD: 29% (4/14) |

CRT, chemoradiation therapy; FOLFIRINOX, 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin; LAPC, locally advanced pancreatic cancer; PD, progressive disease; PR, partial response; R, resection margin; RT, radiation therapy; SD, stable disease.


**Expert Recommendation:**

**Patients With Locally Advanced Disease**

- Although there is only randomized evidence for Abraxane/gemcitabine for patients with metastatic disease, it is reasonable to extrapolate to patients with locally advanced disease based on available data with other regimens

- The pCODR Expert Review Committee (pERC) recommended funding Abraxane/gemcitabine for the first-line treatment of patients with locally advanced unresectable or metastatic adenocarcinoma of the pancreas

- Recommend to send to trial if possible

*Expert opinion of steering committee.*

**pERC Meeting:** pCODR Pan-Canadian Oncology Drug Review. 2014

ClinicaTrials.gov: NCT02301143, NCT02043730, NCT02125136.
### First-Line Treatment Options for LAPC

<table>
<thead>
<tr>
<th>Performance Status</th>
<th>Agent(s)</th>
<th>NCCN Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good Good</td>
<td>Chemotherapy</td>
<td>Category 2A</td>
</tr>
<tr>
<td></td>
<td>Clinical trial preferred</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FOLFIRINOXa (5-fluorouracil, leucovorin, irinotecan, and oxaliplatin)</td>
<td>Category 2A</td>
</tr>
<tr>
<td></td>
<td>Gemcitabine</td>
<td>Category 2A</td>
</tr>
<tr>
<td></td>
<td>Gemcitabine + nab-paclitaxel or other gemcitabine-based combinations</td>
<td>Category 2A</td>
</tr>
<tr>
<td>Chemoradiation in selected patientsb</td>
<td>Induction chemotherapy followed by 5-FU or gemcitabine-based chemoradiation</td>
<td>Category 2A</td>
</tr>
<tr>
<td></td>
<td>Upfront fluoropyrimidine (5-FU or capecitabine)-based chemoradiation</td>
<td>Category 2A</td>
</tr>
<tr>
<td>Poor</td>
<td>Gemcitabine</td>
<td>Category 1</td>
</tr>
<tr>
<td></td>
<td>OR Palliative and best supportive care</td>
<td></td>
</tr>
</tbody>
</table>

*Recommendations for FOLFIRINOX and gemcitabine + nab-paclitaxel are based on extrapolations from randomised trials in patients with metastatic disease.

Chemoradiation should be reserved for patients who do not develop metastatic disease while receiving systemic chemotherapy. Based on preliminary data from the LAP07 trial, there is no clear survival benefit with the addition of conventional chemoradiation following gemcitabine monotherapy. Chemoradiation may improve local control and delay the need for resumption therapy.

5-FU, 5-fluorouracil; FOLFIRINOX, 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin; LAPC, locally advanced pancreatic cancer; NCCN, National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology, Pancreatic Adenocarcinoma, v2. 2015.

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**Borderline resectable (BLR)**

- No large, prospective studies
- Standard approach remains undefined
- CT ➔ CRT (borrowed from LAPC)
  - CT > CRT *(Chauffert B, Ann Oncol, 2008)*
  - CRT > CT *(Loehrer PJ, JCO, 2011)*
  - CT ➔ CRT > CT *(Huguet F, JCO, 2007; Krishnan S, Cancer 2007)*
  - CT ➔ CRT = CT *(Hammel P, ASCO 2013, Abstract #4003)*
Preoperative mFOLFIRINOX followed by chemoradiation for borderline resectable PDAC
Initial results from Alliance Trial A021101

Matthew H.G. Katz, Qian Shi, Syed Ahmad, Joe Herman, Robert Marsh, Eric Collisson, Lawrence Schwartz, Robert Martin, William Conway, Mark Truty, Hedy Kindler, Andrew M. Lowy, Tanios Bekai-Saab, Philip Philip, Dana Cardin, Noelle LoConte, Alan Venook

Presented By Matthew Katz at 2015 ASCO Annual Meeting

Standard treatment for BLR PDAC is based on consensus

![Diagram]

- **CTX**: Cytotoxic effect on systemic disease
- **CXRT**: Sterilization of surgical margins (R0)
- **Time**: Selection of tumor biology and patient physiology for surgery

*Provides an opportunity to understand and impact the natural history of the disease*

Presented By Matthew Katz at 2015 ASCO Annual Meeting
Treatment Schema

- Real-time centralized review of all radiographic studies and enrollment criteria
- Prospective QC of all treatment modalities

Treatment Overview

- Initiated mFOLFIROINOX
  - N = 22
- Initiated Cape-XRT
  - n = 21 (95%)
- Pancreatectomy
  - n = 15 (68%)
- Initiated Gemcitabine
  - n = 10 (45%)
- Completed all protocol treatment
  - n = 9* (41%)

*1 pt stopped at cycle 7 (first cycle of neoadjuvant chemo)
RECIST Response

Best Response:
CR: 2 (9%)
PR: 4 (18%)
SD: 14 (64%)
PD: 2 (9%)

2 CR → 2 CR → 2 res.
2 PR → 2 PR → 2 res.
16 SD → 11 SD → 9 res.*
2 PD**
3 PD

Surgery and pathology

<table>
<thead>
<tr>
<th>Pancreatectomy (N=15)</th>
<th>N</th>
<th>%*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portal V resection</td>
<td>12</td>
<td>80</td>
</tr>
<tr>
<td>Hepatic A resection</td>
<td>4</td>
<td>27</td>
</tr>
</tbody>
</table>

* Among 15 patients who underwent pancreatectomy

<table>
<thead>
<tr>
<th>Pathologic variable</th>
<th>N</th>
<th>%*</th>
<th>%**</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0</td>
<td>14</td>
<td>64</td>
<td>93</td>
</tr>
<tr>
<td>N0</td>
<td>10</td>
<td>46</td>
<td>67</td>
</tr>
<tr>
<td>&lt; 5% residual cells</td>
<td>7</td>
<td>32</td>
<td>47</td>
</tr>
<tr>
<td>pCR</td>
<td>2</td>
<td>9.1</td>
<td>13</td>
</tr>
</tbody>
</table>

* Among patients who initiated mFOLFIROX (n = 22)
** Among patients who underwent pancreatectomy (n = 15)
Upcoming Clinical Trials

RT00 1251
A PHASE II RANDOMIZED TRIAL EVALUATING THE ADDITION OF HIGH OR STANDARD INTENSITY RADIATION TO GEMCITABINE AND NAB-PACLITAXEL FOR LOCALLY ADVANCED PANCREATIC CANCER

SCHEMA (7/5/14)

STEP 1 REGISTRATION
Gemcitabine + nab-Paclitaxel x 3 cycles (total of 9 doses)

Central SMA4 testing
Mandatory submission of cell block or core biopsy
NOTE: Tumor tissue must be received and central review completed before STEP 2 randomization can occur

CT/MRI of abdomen/pelvis for restaging

STEP 2 REGISTRATION: for non-progressing patients

Stratify: CA19-9 (< 1 vs. 2 to 90 vs. > 90; SMA4 intact vs. loss vs. undetermined)

RANDOMIZE

Arm 1
Gemcitabine + nab-Paclitaxel x 1 cycle (4 weeks)
63.0 Gy in 28 fractions (IMRT), capecitabine
Gemcitabine + nab-Paclitaxel until progression

Arm 2
Gemcitabine + nab-Paclitaxel x 1 cycle (4 weeks)
50.4 Gy in 28 fractions (3D-CRT or IMRT),
capcitabine
Gemcitabine + nab-Paclitaxel until progression

Arm 3
Gemcitabine + nab-Paclitaxel until disease progression
No chemotherapy
LAPACT: Phase II Trial of \(nab\)-Paclitaxel + Gemcitabine in Patients with LAPC

**Schema**

**LAPC**
- (Non-metastasis, unresectable)
- Age \(\geq 18\) years
- Planned \(N = 110\)

**Induction phase**
- \(nab\)-P 125 mg/m\(^2\) qw 3/4
- + Gem 1000 mg/m\(^2\) qw 3/4
- \(\times 6\) cycles (28 days/cycle)

**Primary objective**
- TTF in induction therapy followed by investigator’s choice of treatment

**Secondary objectives**
- DCR after the first 6 cycles
- ORR
- PFS and OS
- Safety profile
- Quality of life

**Exploratory objective**
- Changes in circulating nucleic acids correlate with response

**Follow-up period**
- Continue \(nab\)-P + Gem until PD or toxicity
- Chemoradiotherapy
- Surgical intervention


Celgene data on file; ClinicalTrials.gov: NCT02301143.
Locally Advanced Chemotherapy Trials

- GAP trial (phase II)
  - Abraxane/gemcitabine vs. Gem alone in locally advanced unresectable pancreatic cancer

- NEOLAP (Phase II)
  - Abraxane/gemcitabine followed by Abraxane/gem vs. FOLFIRINOX as neoadjuvant chemotherapy in locally advanced pancreatic cancer

Borderline Resectable/LAPC

- Multidisciplinary assessment critical
- Close communication with surgeons
- If unresectable, FOLFIRINOX and Gemcitabine + Abraxane are available options
- Consider clinical trial
Pancreatic cancer represents one of the most aggressive cancers to treat. This latest research evidence is giving that small window of hope that treatment options are coming down the pipeline.