Improved Resection Rates in Locally Advanced Pancreatic Cancer (LAPC) Following EUS-FNI of Large Surface Area Microparticle Paclitaxel (LSAM Pac)

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Overview

• Overview of Pancreatic Cancer

• Background on Large Surface Area Microparticle Paclitaxel (LSAM Pac) Nanopac

• Research Results

• Q/A
Background on Pancreatic Cancer
Pancreatic Cancer - Epidemiology

• Approximately 57,600 people (30,400 men and 27,200 women) will be diagnosed with pancreatic cancer.

• About 47,050 people (24,640 men and 22,410 women) will die of pancreatic cancer.

• Pancreatic cancer accounts for about 3% of all cancers in the US and about 7% of all cancer deaths.
Pancreatic Cancer - Epidemiology

- Most Pancreatic cancer cases are adenocarcinomas
- 7-9% 5 year survival for pancreatic cancer
- High percentage of cases detected in late stage disease
Pancreatic Cancer

- Staging in Pancreatic Cancer is paramount to optimal treatment
  - Only R-0 resection has survival value for surgery
  - Often there are large vessels preventing complete resection
  - 50-80% will reoccur in the first 2 years after resection

- CT scans + EUS for staging
Pancreatic Cancer - Treatment

- Surgery:
  - Whipple
  - Distal pancreatectomy

- Chemotherapy:
  - Gemcitabine + Abraxane
  - Folfirinox

- Radiation:
  - IMRT
  - Cyberknife (SBRT)
Background On Nanopac
Most Patients are not resectable

Of the 55-60k new Panc Ca and Cca Patients/Yr, The Vast Majority Are Not Surgical Candidates

80–85% Pancreatic Ca non-surgical candidates

Opportunity

Microparticulate Production Technology

- Technology
  - Unique non-mechanical process using supercritical CO₂ and sonication to precipitate nanoparticles in a GMP production environment

- Benefits
  - Increased microparticle stability without need for additives or coatings
  - Small particles with large surface area and narrow particle size distribution (majority in 0.8 micron range)

Carbon Dioxide (CO₂) above the critical point (> 72.8 bar, >31°C) is supercritical
- scCO₂ is miscible with organic solvents
- scCO₂ is a poor solvent for paclitaxel
- Mixing paclitaxel in organic solvent with scCO₂ causes NanoPac to precipitate
NanoPac Overview

- Paclitaxel vs LSAM Pac

Unprocessed paclitaxel

LSAM Pac
Background on Large Surface Area Microparticle Paclitaxel (LSAM Pac) Nanopac

- **Nanopac**
  - **Phase Ib**
  - **Now completed Phase IIb**

- The injection of particle coated with Paclitaxel directly into a pancreatic via an endoscopic procedure

- **Goal:** To decrease the tumor size so that the patient can get to surgery for tumor resection or possibly avoid the development of cancer in precancerous lesions
Study Results
The aim of the study was to determine safety and tolerability of NanoPac when injected directly to the lesion, and to assess the impact on the lesion by means of imaging assessments at three and six months following the first injection. [NCT#03077685]

In the second phase subjects received two injections of LSAM Pac directly into their pancreatic lesion via endoscopic ultrasound-guided fine needle injection (EUS-FNI) 4 weeks apart, at 15 mg/mL concentration, in a volume equivalent to 20% of the tumor volume.
Results on Phase II Single Site analysis

- Of the 13 subjects considered non-surgical at study entry at this site, seven (54%) were restaged becoming eligible for surgery following LSAM paclitaxel injections.

- Of the 7, six proceeded to surgery and one opted to receive alternate chemotherapy treatment.

- Five of the six subjects underwent surgery with the same surgeon [Schmidt], and the procedure resulted in successful R0 resections; the sixth subject had surgery resulting in an R1 resection.
<table>
<thead>
<tr>
<th>Subject Number</th>
<th>Stage at Diagnosis</th>
<th>OR Date</th>
<th>Margins</th>
<th>Regional Lymph</th>
<th>Perineural Invasion</th>
<th>Lymph-vascular Invasion</th>
<th>Treatment Effect</th>
<th>Path Stage</th>
<th>INJ Dates</th>
<th>ChemoRT</th>
<th>Chemo RT</th>
<th>Chemo RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>T2NOMO SMA involvement</td>
<td>7-Jun-2019</td>
<td>All Negative</td>
<td>0/14</td>
<td>Present</td>
<td>None Identified</td>
<td>Moderate Response; Fibrosis and necrosis consistent with</td>
<td>pT2N0</td>
<td>8-Jan-2019</td>
<td>Sep-2018</td>
<td>Nov-2018</td>
<td>22-Jan-2019</td>
</tr>
<tr>
<td>005</td>
<td>T2N1M0 Portal Vein and SMV abutment</td>
<td>18-Jun-2020</td>
<td>All Negative</td>
<td>0/10</td>
<td>None Identified</td>
<td>None Identified</td>
<td>Minimal Response</td>
<td>pY1cN0</td>
<td>12-Jun-2019</td>
<td>Apr-2019</td>
<td>Jun-2019</td>
<td>Mar-2020</td>
</tr>
<tr>
<td>006</td>
<td>T4N0M0 Encases the GDA, 180° involvement SMV as it enters the portal confluence. 5-8mm length of abutment/encasement of SMA &lt;180°</td>
<td>30-Jan-2020</td>
<td>All negative</td>
<td>1/15</td>
<td>None Identified</td>
<td>None Identified</td>
<td>Excellent Response</td>
<td>pT1aN1</td>
<td>24-Jun-2019</td>
<td>18-Mar-2019</td>
<td>Oct-2019</td>
<td></td>
</tr>
<tr>
<td>007</td>
<td>T2N0M0 Encasement of GDA; abuts portal vein for 1.9 cm</td>
<td>13-Mar-2020</td>
<td>No evidence of residual tumor</td>
<td>0/41</td>
<td>None Identified</td>
<td>None Identified</td>
<td>Complete Response</td>
<td>pT0N0</td>
<td>7-Oct-2019</td>
<td>28-Feb-2019</td>
<td>Jul-2019</td>
<td>19-Nov-2019</td>
</tr>
<tr>
<td>012</td>
<td>T2N1M0 There is less than 180° of involvement of the hepatic artery &amp; involvement of SMA</td>
<td>6-Apr-2020</td>
<td>SMV and SMA margins positive, Uncinate margin 0.5mm, Pancreatic neck margin extranodal extension identified</td>
<td>8/13</td>
<td>Multiple Foci</td>
<td>Multiple Foci</td>
<td>Focal Necrosis</td>
<td>pT4N2</td>
<td>16-Dec-2019</td>
<td>Sep-2019</td>
<td></td>
<td></td>
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<tr>
<td>013</td>
<td>T4N1M0 Encases entire celiac axis, splenic artery, left gastric artery; involvement of hepatic artery</td>
<td>24-Sep-2020</td>
<td>All Negative</td>
<td>0/32</td>
<td>None Identified</td>
<td>None Identified</td>
<td>Moderate Response (minimal residual cancer)</td>
<td>pT4N0</td>
<td>02-Jan-2020</td>
<td>24-Jun-2019</td>
<td>4-Sep-2019</td>
<td>Jul-2020</td>
</tr>
</tbody>
</table>

**Results on Phase II - Single Site analysis**
# Results on Phase II - Single Site analysis

<table>
<thead>
<tr>
<th>Subject</th>
<th>CA19-9 u/mL Baseline (week 24)</th>
<th>Largest Diameter of Lesion (cm)</th>
<th>% change at week 24</th>
<th>Time from initiating LSAM paclitaxel treatment to surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Week 12</td>
<td>Week 24</td>
<td></td>
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<tr>
<td>001</td>
<td>43 (28)</td>
<td>2.5</td>
<td>1.7</td>
<td>1.9</td>
</tr>
<tr>
<td>005</td>
<td>342 (65.3)</td>
<td>2.8</td>
<td>3.0</td>
<td>2.7</td>
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<tr>
<td>006</td>
<td>132 (36)</td>
<td>2.3</td>
<td>2.1</td>
<td>1.6</td>
</tr>
<tr>
<td>007</td>
<td>25 (44)</td>
<td>2.2</td>
<td>1.1</td>
<td>n/a*</td>
</tr>
<tr>
<td>012</td>
<td>619 (668)</td>
<td>2.6</td>
<td>4.2</td>
<td>n/a*</td>
</tr>
<tr>
<td>013</td>
<td>3 (2)</td>
<td>3.1</td>
<td>3.3</td>
<td>2.3</td>
</tr>
</tbody>
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Questions & Answers