CPI-613 is a novel agent that selectively targets the altered mitochondrial enzyme function of tumor cells, causing apoptosis, necrosis, and autophagia (1). Results assessing clinical efficacy of CPI-613 translated from animal xenograft models to patients with Stage IV pancreatic cancer are presented.

**Introduction / Background**

**Animal Studies:** Efficacy of CPI-613 (25 mg/kg), according to tumor growth inhibition and prolongation of survival, was assessed in C1D1-NuNu mice with pancreatic tumor xenografts generated by inoculation of BxPC-3 human pancreatic tumor cells. Results were compared to Gemzar® (50 mg/kg, MTD [2] and non-treated control. Test agents were given intraperitoneally 1x weekly for 4 weeks.

**Clinical Studies:** The efficacy (assessed according to overall survival) of CPI-613 + Gemzar® was evaluated in patients with Stage IV pancreatic cancer. CPI-613 (70-320 mg/m²) was given 2x weekly, whereas Gemzar® (1,000 mg/m²) was given 1x weekly. Both drugs were administered IV on a 3-weeks-on-1-week off treatment cycle.

**Methods**

**Results**

**Animal Studies**

Tumor Growth Inhibition: Both CPI-613 and Gemzar® suppressed tumor growth when compared to control (Figure 1). Tumor growth inhibition of both agents occurred not only during treatment, but also for at least 4 weeks post treatment. Tumor growth inhibition was greater for CPI-613 than Gemzar®.

**Clinical Studies**

There were 6 patients with Stage IV pancreatic cancer treated with CPI-613+Gemzar® combination (see Table A). The CPI-613+Gemzar® combination was well-tolerated by all 6 patients.

**Figure 1:** Tumor growth inhibition induced by 4 doses of CPI-613, and to a lesser degree, by Gemzar®, when compared to control in treatment of C1D1-NuNu mice with pancreatic xenograft. n=10/group. * = P<0.05; ** = P<0.01, compared to control.

**Results (cont'd.)**

**Survival in Treatment-Naive Patients with Metastatic Pancreatic Cancer Treated with CPI-613 + Gemzar®**

**Table A:** Patients with Stage IV pancreatic cancer treated with CPI-613+Gemzar® combination

<table>
<thead>
<tr>
<th>ID</th>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>Ethnicity</th>
<th>Chemotherapy Prior to Study Participation</th>
<th>Dose*</th>
<th>C-G T&lt;sub&gt;x&lt;/sub&gt; (months)</th>
<th>D-x (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>106</td>
<td>52</td>
<td>M</td>
<td>Hispanic</td>
<td>None</td>
<td>None</td>
<td>70</td>
<td>4.0 (still alive)</td>
<td>4.1</td>
</tr>
<tr>
<td>110</td>
<td>43</td>
<td>F</td>
<td>Caucasian</td>
<td>None</td>
<td>None</td>
<td>75</td>
<td>7.4 (still alive)</td>
<td>-</td>
</tr>
<tr>
<td>113</td>
<td>59</td>
<td>F</td>
<td>African-American</td>
<td>None</td>
<td>None</td>
<td>195</td>
<td>6 (still alive)</td>
<td>24 (still alive)</td>
</tr>
<tr>
<td>107</td>
<td>62</td>
<td>M</td>
<td>Caucasian</td>
<td>Gemzar®</td>
<td>Gemzar® (50 mg/kg)</td>
<td>105</td>
<td>6.8</td>
<td>9.8</td>
</tr>
<tr>
<td>111</td>
<td>78</td>
<td>F</td>
<td>African</td>
<td>5-FU, Gemzar®, FOLFIRINOX, Monotherapy</td>
<td>150</td>
<td>6.0 (still alive)</td>
<td>11.3</td>
<td></td>
</tr>
<tr>
<td>101</td>
<td>65</td>
<td>M</td>
<td>Caucasian</td>
<td>Gemzar®+Tarceva, Xeloda, +Chelaplatin</td>
<td>320</td>
<td>2.25 (still alive)</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

*CPI-613 was given in combination with Gemzar® (1,000 mg/m²).

**Summary and Conclusion**

1. Only four weekly administrations of CPI-613 provide long-term anti-tumor efficacy in mice with human pancreatic carcinoma xenografts, as reflected by inhibition of tumor growth and prolongation of survival.

2. CPI-613, when used in combination with Gemzar®, also exhibited long-term anti-tumor activities (prolonged survival) in patients with Stage IV pancreatic cancer.

3. Therefore, CPI-613 exhibits efficacy against pancreatic cancer in animal models, which appears translational to patients with Stage IV disease. Further clinical evaluation in this patient population is warranted.

**References**


**Figure 2:** Prolongation of survival induced by 4 doses of CPI-613, and to a lesser degree by Gemzar®, when compared to control treatment.

**Figure 3:** Dose-related prolongation of survival induced by 1,000 mg/m² of Gemzar® and various doses of CPI-613 in patients with Stage IV pancreatic cancer who had not received any prior chemotherapy.

Translational Assessment of the Efficacy of CPI-613 Against Pancreatic Cancer in Animal Models Vs. Patients With Stage IV Disease

Avi Retter MD,1 Claudia Maturo MS,2 Karen Hoffman MD,1 John Luddy MS,2 Robert Rodriguez BSc,2 Robert Shorr PhD,2 King Lee PhD 2

1 Eastchester Center for Cancer Care, Bronx, NY; 2 Cornerstone Pharmaceuticals, Inc., Cranbury, NJ