Conclusions

First in Human Phase 1 Study of Paclitaxel-Eluting PTM-101 in Subjects with Borderline Resectable or Locally Advanced Pancreatic Cancers

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Background

Improvements in the treatment of pancreatic cancer have been very limited, in part due to the inability to deliver chemotherapy to the tumor at efficacious concentrations for prolonged duration. PTM-101 is a proprietary flexible absorbable film that enables sustained, high-dose administration of paclitaxel directly to the peritoneal area, maximizing anti-tumor potency and reducing the severe side effects typically seen with systemic administration of paclitaxel. PTM-101 was designed to easily integrate with well-established laparoscopic procedures that can be used for peritoneal placement and deliver drug directly onto the tumor for up to 6 weeks.

Precinical animal studies suggest that PTM-101 results in significantly enhanced drug levels (>100 fold higher) in the tumor, compared with comparable systemic paclitaxel dosing, leading to tumor reduction and survival benefit. In a murine orthotopic patient-derived xenograft model, PTM-101 had a much greater impact on limiting tumor growth and proliferation compared with IV infusion of an equivalent dose of paclitaxel (e.g., smaller tumor volume, extended OS, inhibition of metastasis). [1]

Method

This first in human study was conducted at a single site in Australia to assess the safety, toxicity, and surgical feasibility of administration of PTM-101 containing 100mg of paclitaxel. PTM-101 was sutured directly onto the pancreatic surface overlying the tumor by a surgical oncologist using well-established laparoscopic equipment during a disease-staging assessment. Once in place on the anterior surface of the pancreas, and for the duration of treatment, PTM-101 will release paclitaxel via a surgical/oncologist-tunable, absorbable film that enables sustained, high-dose administration of paclitaxel concentrations for prolonged duration. PTM-101 is a proprietary flexible biomaterial with an absorbable film that enables sustained, high-dose administration of paclitaxel concentrations for prolonged duration.

Approximately 3 weeks after PTM-101 placement, all participants began standard of care therapy with mFOLFIRINOX. This study enrolled 3 subjects that had treatment naïve, borderline resectable or locally advanced, pancreatic cancer.  It delivers chemotherapy directly to the site of the tumor.

Demographics

Table 1: Product and/or Procedure Related Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>N (3)</th>
</tr>
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<tbody>
<tr>
<td>Partial Response (PR)</td>
<td>0</td>
</tr>
<tr>
<td>Locally Advanced (LA)</td>
<td>0</td>
</tr>
<tr>
<td>Overall</td>
<td>1.3%</td>
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Two out of three subjects treated with PTM-101, in addition to FOLFIRINOX, had substantial volume reduction of 40% or more. Median overall volume reduction of ~20% was observed with similar patient populations having been reported. 

Conclusions

This study provided important evidence that PTM-101 is a surgically viable treatment, with favorable safety and tolerability. Additional key study findings include:

- No systemic paclitaxel exposure was measured.
- Tumor size reduction occurred in all 3 subjects, with a >40% reduction in two of the three patients.
- The reduction in anterior/posterior tumor size, along with the reduction in tumor volume for 2 of 3 subjects prior to systemic neoadjuvant chemotherapy, suggests a clinical signal of anti-tumor activity for PTM-101 for the treatment of pancreatic cancer. Additional studies are being planned at higher doses of paclitaxel with the intent of demonstrating the potential for PTM-101 to be a first-line adjunct to systemic neoadjuvant therapy in treatment naive, borderline resectable or locally advanced pancreatic cancer.

References