Abstract # 5424

Development of a Novel Implantable Drug Product for the Local Treatment of Pancreatic Adenocarcinoma

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Background

Local control of non-metastatic pancreatic ductal adenocarcinoma (PDAC) remains a major challenge. Although potent drugs are available to treat cancers like PDAC, dose and schedule are often limited due to systemic toxicities and reduce the potential efficacy of these drugs. To address this challenge, PanTher is developing a new class of drugs that directly and continuously administer high-doses of chemotherapeutic agents exclusively to the tumor site. Our lead program, PTM-101, was developed to treat localized PDAC.

PTM-101 is a proprietary flexible absorbable film that enables sustained, high-dose administration of paclitaxel directly to the peritumoral area, maximizing anti-tumor activity and reducing the severe side effects typically seen with systemic administration of paclitaxel. It is a multilayer polymeric formation, with a drug eluting layer that provides sustained administration of the drug and a backbone layer that ensures unidirectional release (Figure 1). The drug product is fully absorbed in 90 days. PTM-101 was designed to easily integrate with well-established laparoscopic procedures that can be used for peritumoral placement on the anterior surface of the pancreas (Figure 2) and deliver drug directly to the tumor site for up to 6 weeks.

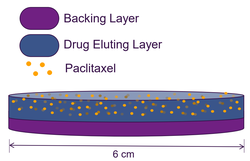

Figure 1. Illustration of PTM-101 key structural features

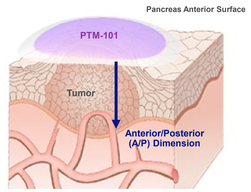

Figure 2: Schematic representing placement of PTM-101 overlaying a tumor and anterior/posterior dimension visualization

Methods

A study was conducted using three cadaveric abdomens to evaluate the surgical feasibility of delivering PTM-101 via laparoscopy. Prior to insertion of PTM-101 into the peritoneal cavity, the surgeons prepared each product by suturing a 3-0 Vicryl SH (Ethicon) at four evenly spaced locations around the edge of the flat circular product (Figure 3). A periumbilical 10mm Hasson port was placed to insufflate the abdomen, followed by placement of 3 additional working ports (5mm) (Figure 4). The liver capsule was carefully surveyed to mimic the surgical process utilized in the clinical settings to exclude metastatic disease. The surgeons opened a window into the lesser sac through the greater omentum, lifting the stomach up from the transverse colon to expose the pancreas. PTM-101 (a 6cm diameter film) was rolled into a tubular shape, inserted through the cannula, and affixed to the peri-pancreatic fat with existing sutures.

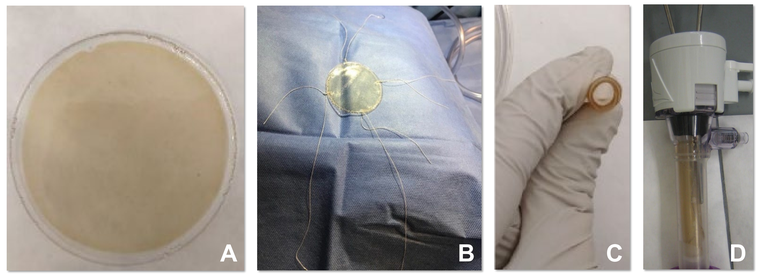

Figure 3: PTM-101 is an absorbable drug product designed as a film (A) with sutures attached (B) to be rolled up (C) and administered through a port (D) for ease of laparoscopic implantation directly on a pancreatic tumor

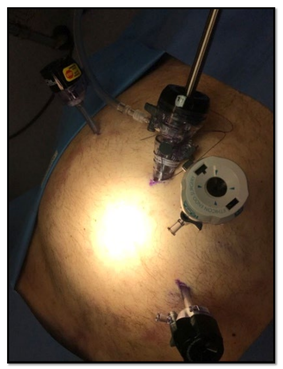

Figure 4: Layout of the four ports inserted in the inflated abdomen for laparoscopic administration

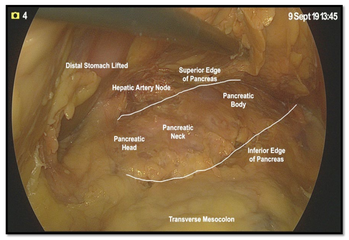

Figure 5: Pancreas and surrounding relevant area visualized through the laparoscopic camera

Results

The total operative time from placement of the first trocar to removal of all equipment, for each of the three procedures, was 45 minutes. The operations included 25 minutes for entry, port placement, and exposure of a likely pancreatic tumor. The time required to place and suture PTM-101 was only 20 minutes.

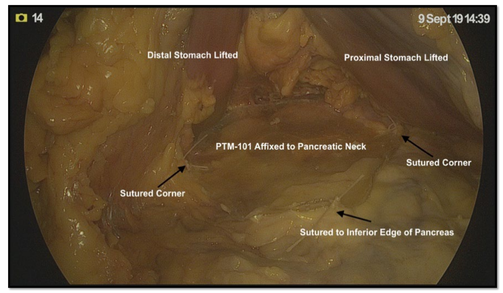

Figure 6: PTM-101 placed on the head of the pancreas and sutured into place

PTM-101 was rolled to fit through the port and was sutured to peri-pancreatic fat that surrounds the capsule of the pancreas. To simulate a tumor with hepatic artery involvement, the implant was sutured towards the hepatoduodenal ligament in one specimen, near the area of the gastroduodenal artery takeoff, proper hepatic artery, and proximal portal vein (Figure 6). PTM-101 covered the entire head/neck area of the simulated tumor locations without disruption of the tumor area or dissection of the tunnel under the pancreatic neck (Figures 7-8).

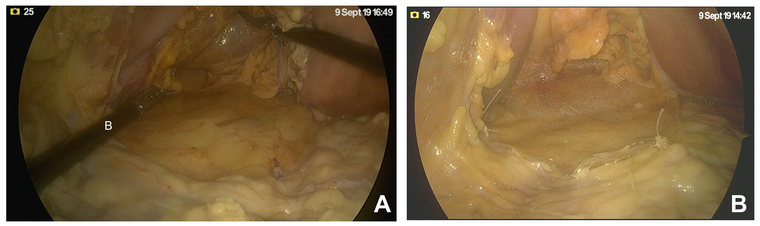

Figure 7: PTM-101 is flexible and conforms easily to the underlying topography, both in A) a concave (i.e., with the tumor intact) and B) convex (i.e., after resection) scenario

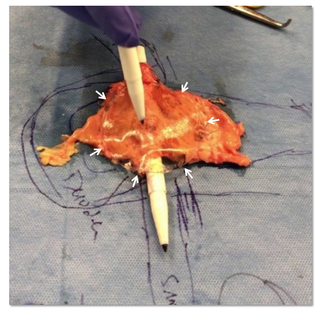

Figure 8: Pancreas excised from the body after implant shows that PTM-101 covers the entire area on top of the vessels (pen is placed through the SMV/portal vein, white arrows indicate edges of PTM-101)

Conclusion

The overall PTM-101 surgical experience in human anatomy was favorable and the product was successfully deployed to cover targeted region of the pancreas using minimally invasive techniques. Main study's findings were:

- PTM-101 can be consistently and effectively placed laparoscopically in proximity to relevant tumors and associated vasculature
- PTM-101 conforms to pancreatic tissue, allowing for close contact with the tissue and optimal drug delivery
- The size and flexibility of the product enables it to cover areas near relevant vasculature. This pliable features allows the product to be used in both neoadjuvant as well as adjuvant treatment settings.
- The ability to provide continuous, highly concentrated doses of powerful chemotherapy drugs exclusively near the tumor has the potential to drastically improve tumor responses, potentially translating to impactful clinical benefits.
- Downsizing of pancreatic tumors could reduce involvement with critical veins and arteries around the pancreas, potentially improving the probability of tumor resection.
- **PTM-101 has now been successfully evaluated in a Phase 1 clinical trial in treatment naïve, localized, non-metastatic pancreatic cancer patients**, which demonstrated an excellent safety profile and favorable anti-tumor responses (see poster # 9505).

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