Abstract # 9505

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 peritumoral 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 peritumoral placement and deliver drug directly onto the tumor for up to 6 weeks.

Preclinical 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 toward the tumor in the anterior/posterior direction.

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 adenocarcinoma. Subjects were monitored closely for local and systemic toxicities, as well as for signals of efficacy (e.g., tumor response by RECIST). An independent central imaging lab reviewed CT scans to determine the tumor volume and anterior/posterior dimension.

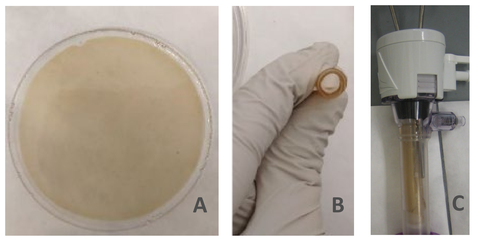


Figure 1: PTM-101 is a film (A) that was designed to be rolled up (B) for ease of laparoscopic implantation (C) directly on a pancreatic tumor. It delivers chemotherapy directly to the site of the tumor.

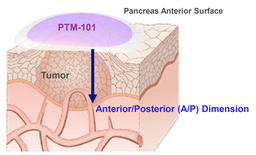


Figure 2: Schematic illustrating placement of PTM-101 overlaying a tumor and visualization of anterior/posterior dimension

Results

PTM-101 was successfully implanted at the tumor site in all three subjects with no complications. All surgical procedures were successful, with PTM-101 deployment lasting between 18 and 32 minutes. Subjects were followed for at least 6 months after implantation of PTM-101 to monitor adverse events and assess response to treatment. No product related serious adverse events (SAEs), defined as events related to either the PTM-101 implantation procedure or PTM-101 treatment over 3 months post implantation, were reported. Overall, PTM-101 was well tolerated with a total of five Grade 1 adverse events judged to be at least possibly related to the procedure or the product (Table 1).
No deaths occurred. Paclitaxel was undetectable in the circulation at all time points. Best overall response rate according to RECIST was stable disease (2 subjects) and partial response (1 subject) (Table 2).

	N (3)
Subjects with at least 1 event	3
Fatigue	1
Procedural Pain	1
Alanine Aminotransferase Increased	2
Aspartate Aminotransferase Increased	1

[1] Adverse Events are those which have a possible, probable, or definite relationship to the device and/or procedure.

Table 1: Product and/or Procedure Related Adverse Events

	Borderline Resectable (N=1)	Locally Advanced (N=2)	Overall (N=3)
Partial Response (PR)	0	1	1
Stable Disease (SD)	1	1	2
Overall Response Rate	0%	50%	33.3%

Table 2: Best overall response per RECIST 1.1

The local delivery of paclitaxel via PTM-101 resulted in reductions in anterior/posterior tumor dimensions in all three subjects, which is consistent with unidirectional, sustained release of paclitaxel to the tumor microenvironment.

Figure 3: PTM-101 placed over tumor bulge visualized from the camera of the laparoscopic tower

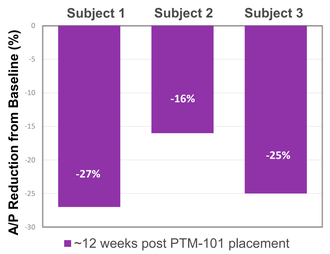


Figure 4: Tumor size change from baseline in the Anterior/Posterior direction

Two out of three subjects treated with PTM-101, in addition to FOLFIRINOX, had substantial volume reduction of 40% or more. Median overall volume reductions of ~20% associated with FOLFIRINOX treatment of similar patient populations have been reported [2].

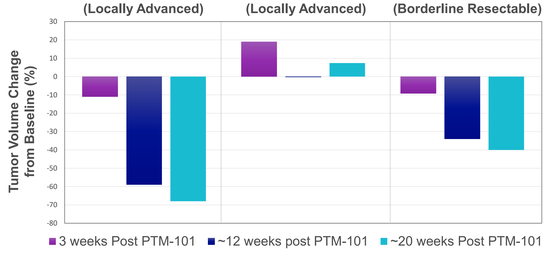


Figure 5: Change in tumor volume over 6 months

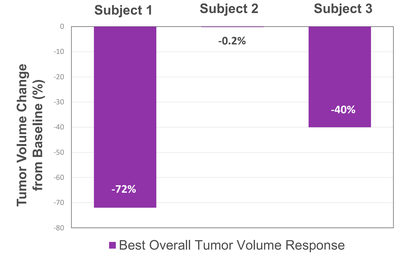
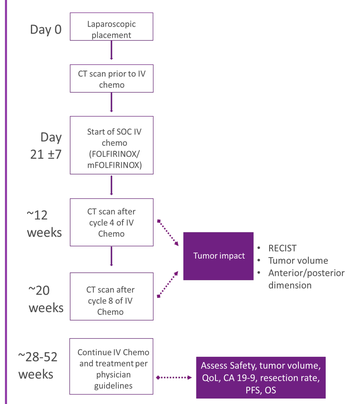


Figure 6: Best overall tumor volume response

Demographics

	Borderline Resectable (N=1) 33.3%	Locally Advanced (N=2) 66.7%	Overall (N=3) 100.0%
Age			
N	1	2	3
Mean (Standard Deviation)	61	51.5 (2.1)	54.7 (5.7)
Median (Min, Max)	61 (61, 61)	51.5 (50, 53)	53 (50, 61)
Sex			
Female	100% (1/1)	0.0% (0/2)	33.3% (1/3)
Male	0.0% (0/1)	100% (2/2)	66.7% (2/3)
Race			
Asian	100% (1/1)	50% (1/2)	66.7% (2/3)
White	0.0% (0/1)	50% (1/2)	33.3% (1/3)
Height(cm)			
N	1	2	3
Mean (Standard Deviation)	156	171 (5.7)	166 (9.5)
Median (Min, Max)	156 (156, 156)	171 (167, 175)	167 (156, 175)
Weight(kg)			
N	1	2	3
Mean (Standard Deviation)	57.7	78.5 (30.3)	71.5 (24.6)
Median (Min, Max)	57.7 (57.7, 57.7)	78.5 (57, 99.9)	57.7 (57, 99.9)
BMI(kg/m^2)			
N	1	2	3
Mean (Standard Deviation)	23.7	26.5 (8.6)	25.6 (6.3)
Median (Min, Max)	23.7 (23.7, 23.7)	26.5 (20.4, 32.6)	23.7 (20.4, 32.6)

Study Schema



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 SAEs or deaths reported during 6 months of follow up
- 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 naïve, borderline resectable or locally advanced pancreatic cancer.

References

[1] Indolfi L, Ligorio M. et al, "A tunable delivery platform to provide local chemotherapy for pancreatic ductal adenocarcinoma," Biomaterials, Volume 93, 2016, Pages 71-82, ISSN 0142-9612
[2] Hester C, Perri G, et al.,"Radiographic and Serologic Response to First-Line Chemotherapy in Unresected Localized Pancreatic Cancer", J Natl Compr Canc Netw 2022,20(8):887-897

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