PanCO: An Open-Label, Single-Arm Pilot Study of Phosphorus-32 (P-32; OncosilTM) Microparticles in Patients with Unresectable Locally Advanced Pancreatic Adenocarcinoma (LAPC) in Combination with FOLFIRINOX or Gemcitabine + Nab-Paclitaxel (GNP) Chemotherapies

Abstract 4125

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Introduction

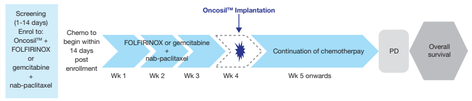
- Locally advanced pancreatic cancer (LAPC) accounts for 30% to 40% of all pancreatic cancer presentations.[1]
- Poor prognosis with a median survival of less than 12 months.[2]
- Current standard treatment is chemotherapy or chemo-radiotherapy.
- Chemo-radiotherapy has not demonstrated unequivocal overall survival advantage.
- OncosilTM is a brachytherapy device consisting of phosphorus-32 (P-32) micro-particles.
- P-32 has been investigated in combination with gemcitabine monotherapy in 23 patients with LAPC and metastatic disease in two studies.
- Demonstrated that P-32 has an acceptable tolerability and safety profile.
- Efficacy data showed potential with a target tumour response rate of 23% and a target disease control rate of 82%.
- The presented data are results from an ongoing international, multi-institutional, single-arm pilot study which is being conducted at 12 sites in Australia, the UK and Belgium.

Objective

The study objective is to further investigate the safety, efficacy, feasibility and performance of the OncoSil™ device when implanted intratumourally using EUS in a patient population undergoing standard chemotherapy for unresectable LAPC.

Study Design

Study design



Methods

- P-32 was implanted directly into the pancreatic tumour via EUS guidance, using a fine needle aspiration (FNA) needle.
- The dose of P-32 was calculated from the tumour volume to administer a predicted absorbed dose of 100 Gy.
- Diffusion pattern of the P-32 following implantation was assessed by EUS and Bremsstrahlung SPECT/CT within 4 hours and at 7 days post-implantation.
- Safety data was collected weekly with toxicity graded using the Common Terminology Criteria for Adverse Events (CTCAE v4.0).
- Response assessment was by CT scans every 8 weeks and reported weekly with toxicity graded using RECIST 1.1.
- FDG-PET scans were performed at Baseline and at Week 12.

Key eligibility criteria

- Histologically or cytologically proven adenocarcinoma of the pancreas
- Unresectable locally advanced pancreatic carcinoma
- Target tumour diameter 2-6cm
- ECOG Performance Status 0 to 1
- No distant metastases
- No prior radiotherapy or chemotherapy for pancreatic cancer

Primary endpoint:

- Safety and Tolerability

Secondary endpoints: Efficacy

- Local Disease Control Rate (LDCR) at 16 weeks
- Local Progression Free Survival (LPFS), within the pancreas
- Progression Free Survival (PFS), all sites
- Overall Survival (OS)

Statistical Assumptions for Efficacy Week 16 LDCR assessment

- Null hypothesis H0: p = 0.55
- Alternative hypothesis H1: p = 0.75
- Level of significance = 0.05 with a 2-sided test to achieve a power of 80%

Results

- 50 patients enrolled - Intent-to-Treat (ITT) population.
- 42 patients implanted with the OncoSil™ device - Per Protocol (PP) population.
- 8 participants were enrolled but withdrawn pre-implant;
  - adverse health condition prior to or at the time of scheduled implant (4)
  - finding of adverse anatomical conditions making it impractical or inadvisable to implant via EUS (2)
  - finding of metastatic disease following enrolment (2).

Participant Demographics & Baseline Characteristics (ITT population)

Demographic/Characteristic	N=50
Age, years Median (Range)	65 (42-84)
Sex Male, n (%) Female, n (%)	28 (56%) 22 (44%)
Race, n (%) White/Caucasian Black/African American Asian Other	40 (80%) 2 (4%) 7 (14%) 1 (2%)
ECOG PS, n (%) 0 1	26 (58%) 24 (42%)
Cancer Antigen 19-9 (CA 19-9), (U/mL) Median (Range)	N=49/50 163 (1-6576)
Tumour location within the pancreas, n (%) Head Body	41 (82%) 9 (18%)
Longest diameter of target lesion, cm Median (Range)	4.5 (2.6-7.1)
Tumour volume, cc Median (Range)	24.35 (7.9-68.7)
Study Days to Implantation Median (Range)	N=42 31 (21-77)
Chemotherapy, n (%) Gemcitabine + nab-paclitaxel FOLFIRINOX	40 (80%) 10 (20%)

Safety and Tolerability

- One hundred Serious Adverse Events (SAEs) were reported.
- Two AEs were reported as Serious Adverse Device Events (SADE):
  - abdominal pain
  - venous intravasation.

Most commonly reported AEs considered as possibly or probably related to the study device and/or to the implant procedure – (Per Protocol/Implanted Population, N=42)

Adverse Events (AEs), n (%)	Gemcitabine + nab-Paclitaxel (GNP) or FOLFIRINOX (FFX) (N=42) Total AEs All-Grade	Grade ≥ 3
Patients with ≥ 1 Adverse Event	19 (45.2%)	2 (4.8%)
Abdominal pain	3 (7.1%)	1 (2.4%)
Nausea	5 (11.9%)	0
Fatigue	7 (16.7%)	1 (2.4%)
Weight decreased	3 (7.1%)	0

Most commonly reported AEs
All Grade AEs in ≥ 20 % of Study Participants - (ITT population)

Adverse Events (AEs), n (%)	Total AEs (n=50: GNP=40; FFX=10) All-Grade	Grade ≥ 3
Participants with ≥ 1 adverse event	50 (100)	41 (82)
Anaemia	15 (30)	7 (14)
Neutropenia	23 (46)	18 (36)
Thrombocytopenia	13 (26)	3 (6)
Abdominal Pain	27 (54)	7 (14)
Constipation	24 (48)	1 (2)
Diarrhoea	30 (60)	1 (2)
Nausea	30 (60)	5 (10)
Vomiting	17 (34)	4 (8)
Fatigue	39 (78)	7 (14)
Peripheral Oedema	10 (20)	1 (2)
Pyrexia	17 (34)	4 (8)
Weight Decreased	14 (28)	1 (2)
Decreased Appetite	19 (38)	1 (2)
Hypokalaemia	10 (20)	4 (8)
Peripheral Neuropathy	18 (36)	1 (2)
Alopecia	21 (42)	0
Rash	13 (26)	0

Efficacy

Radiological response

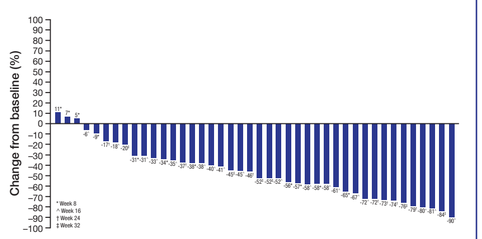
Local Disease Control Rate at 16 Weeks & 24 Weeks Response Rate

	ITT (N=50)	PP (N=42)
Number of subjects with local disease control at Week 16 (%)	41 (82%)	38 (90.5%)
Proportion of subjects with local disease control at Week 16 (95% CI)	0.82 (0.69,0.91)	0.90 (0.77,0.97)
p-value	0.0001	<0.0001
Number of subjects with local disease control at Week 24 (%)	31 (62%)	30 (71.4%)
Proportion of subjects with local disease control at Week 24 (95% CI)	0.62 (0.47,0.75)	0.71 (0.55,0.84)
Response Rate	28%	31%

Tumour Volume

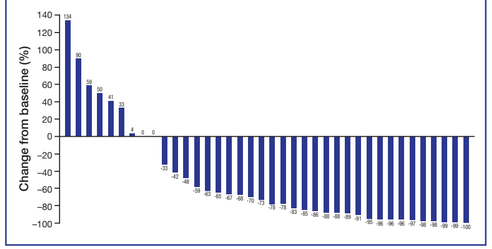
- Tumour volume assessment was a pre-specified exploratory analysis.

Maximum Percentage Change in Tumour Volume from Baseline (Per Protocol population)



CA 19-9 tumour marker

% change in CA 19-9 Tumour Marker from Baseline to Week 16 (Per Protocol population)



- 11/38 patients (29%) demonstrated a decrease in CA 19-9 of > 90%.

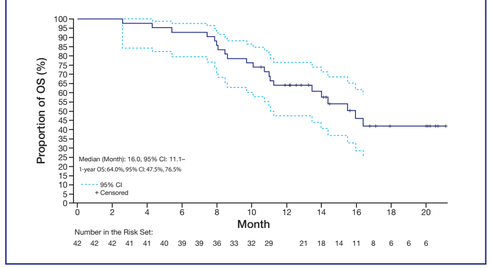
PET scan assessments

- 39 of 42 patients had evaluable PET scan assessments at Baseline and at Week 12.
- Metabolic resolution (100% reduction in TLG and SUV Max) and absence of defined viable neoplastic disease was reported for 5 participants at Week 12.
  - 4 have undergone surgical resection with curative intent.

Overall Survival

- 21 patient deaths at time of analysis.
- Median OS = 16 months.
- 12 month survival rate = 64%.

Overall Survival (Per Protocol population)



Chemotherapy utilisation (Per Protocol population)

	GNP (N=34)	FFX (N=8)
Total Number of Cycles Median (Range)	5 (1-14)	6 (3-13)
Duration of Exposure (Days)* Median (Range)	147 (7-420)	89.5 (37-316)

*Duration of exposure (days): Date of first treatment to date of treatment discontinuation

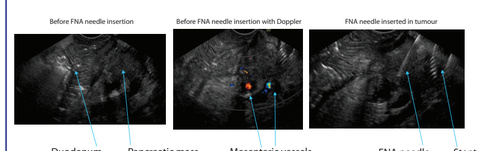
Surgical Resection with curative intent

- Ten implanted patients underwent surgical resection by Whipple procedure.
  - 20% resection rate in the ITT population.
  - 23.8% resection rate in the PP population.
- 9 patients received concomitant GNP and 1 patient received FFX.
- Resections took place from 70 to 267 days post-implantation.
- Histopathological assessment confirmed R0 surgical margin status in 8 patients and R1 status in 2 patients.

OncoSilTM Implantation and Intra-tumoural Localisation

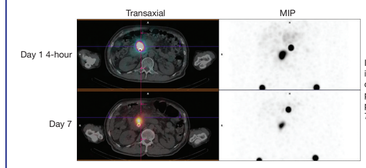
- Device considered straightforward to implant by endoscopists.
- No significant or serious procedural complications.
- EUS views shown below demonstrate the utility of EUS in accessing tumours.

EUS imaging



- Device localisation by Bremsstrahlung SPECT/CT was acceptable.

Bremsstrahlung SPECT/CT



Images show excellent intra-tumoural retention of activity within the pancreatic head at 2 hours post-implantation and at 7 days post-implantation.

Conclusions

The PanCO study demonstrates:

- Evidence of acceptable local tumour control (RECIST; tumour volume, PET) with OncoSil™ and chemotherapy, with potential for downstaging to resectability;
- Promising preliminary survival estimate – median OS = 16 months;
- A satisfactory safety profile when OncoSil™ is combined with contemporary chemotherapy;
- Confirmation of the feasibility of EUS-directed implantation.

The PanCO study results justify future studies to further develop the use of the OncoSil™ device in PDAC.

References

1. Ariake K, et al. Surg Case Rep 2017;3:15.
2. Ducreux M, et al. Annals of Oncology 26 (Supplement 5):v56-v68, 2015.

Acknowledgements

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Disclosures

P Ross, D Croagh, M Aghmesheh, A Nagrial, N Nguyen, M Nikfarjam, H Wasan, T Ajithkumar, C Iwuji, A Hendlisz & M Harris are participating investigators in the study. T Maher & A Kraszewski are employees of Oncosil Medical Ltd.

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