PanCO: An Open Label, Single Arm Pilot Study of Oncosil™, Administered to Study Participants with Unresectable Locally Advanced Pancreatic Adenocarcinoma, Given in Combination with Folfirinox or Gemcitabine+Nab-Paclitaxel Chemotherapies

Poster Mo1304

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Introduction

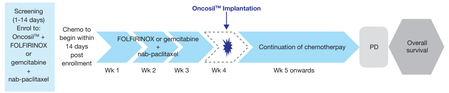
Locally advanced pancreatic cancer (LAPC) accounts for 30% to 40% of unresectable disease[1] and is associated with a poor prognosis. Median survival is 6-10 months.[2] Current standard treatment is limited to chemotherapy or chemo-radiotherapy. Conventional radiotherapy (CRT) has been used to treat patients with advanced disease and is usually given with gemcitabine or fluoropyrimidine-based chemotherapy. However, conventional radiotherapy is limited by the amount of radiation that can be delivered to the gastrointestinal tract due to side effects. Novel treatment approaches are crucial in attempting to combat this unmet medical need. Phosphorus-32 (P-32) Microparticles is a brachytherapy device that implants a pre-determined tumouricidal dose of the beta radiation emitting isotope (Phosphorus-32) directly into cancerous tissue. The (P-32) Microparticles device is intended for local treatment of cancerous pancreatic cells when it is implanted intra-tumourally via endoscopic ultrasound (EUS). P-32 has been investigated in combination with gemcitabine monotherapy in 23 patients with LAPC and metastatic disease in two clinical studies. These studies demonstrated that, in combination with gemcitabine chemotherapy, P-32 was found to have an acceptable tolerability and safety profile. Efficacy data showed potential with evidence of a target tumour response rate of 23% and a target disease control rate of 82%. These studies established that EUS-directed implantation of P-32 is an appropriate method of delivery. The presented data are early 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. The purpose of this interim analysis is to report on the early observations and experience from the first 20 enrolled and implanted patients up to Week 16 of follow up.

Study design

Figure 1. Study design



Methods

Eligible patients received either gemcitabine + nab-paclitaxel or FOLFIRINOX chemotherapy by physician choice. P-32 implantation took place during the 4th or 5th week following the initiation of chemotherapy. P-32 was implanted directly into the pancreatic tumour via EUS guidance, using a fine needle aspiration (FNA) needle. Each patient's dose was calculated from the tumour volume where the absorbed dose of P-32 to the tumour was calculated to equal 100 Gy. Diffusion pattern of the P-32 suspension following implantation was assessed by EUS and by Bremsstrahlung SPECT/CT imaging within 4 hours and 7 days post implantation. Chemotherapy was continued after the implantation. Safety data was collected weekly and toxicity was graded using the Common Terminology Criteria for Adverse Events (CTCAE). Centrally-read CT scans were conducted every 8 weeks to assess response defined as complete response [CR], partial response [PR], and stable disease [SD]) according to RECIST 1.1 criteria. FDG-PET scans were performed at Baseline and at Week 12. Overall survival (OS) was determined at 8-weekly intervals until subject death or 104 weeks after last subject enrolment.

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

Results

Baseline patient demographics and characteristics are shown in Table 1 for the first 20 patients implanted with the OncoSil™ device up to the 9th of January 2018.

Table 1: Patient Demographics and Baseline Characteristics (N=20)

Characteristic	
Age, years Median Range	 65 54-84
Male, n (%) Female, n (%)	12 (60) 8 (40)
ECOG PS, n (%) 0 1	 9 (45) 11 (55)
Tumour location within the pancreas, n (%) Head Body	 17 (85) 3 (15)
Longest diameter of target lesion, mm Median Range	 50 32-71
Tumour volume, cc Median Range	 31.3 7.9-52.5

Safety and Tolerability

A total of 319 AEs were reported by Week 16 of which 50 were ≥ Grade 3 in severity and 18 were reported as SAEs. All SAEs were considered to be causally related to the chemotherapy, underlying disease or comorbidities and not considered to be related to the device or to the implant procedure. Table 2 lists the most commonly reported AEs. The majority of the AEs of ≥ Grade 3 were AEs of the gastrointestinal and blood System Organ Class (SOC). Twenty four (24) AEs were considered as possibly or probably related to the device or to the implant procedure, 20 of which also had a possible or probable relationship to the chemotherapy.

Table 2. Most commonly reported AEs (N=20)

Adverse Event	Patients, n (%)	Number of AEs	Number of AEs ≥ Grade 3
Total	20 (100)	319	50
Neutropenia	9 (45)	15	10
Thrombocytopenia	5 (25)	11	1
Abdominal pain	9 (45)	11	0
Constipation	8 (40)	9	3
Diarrhoea	11 (55)	19	2
Nausea	10 (50)	20	1
Vomiting	6 (30)	10	3
Fatigue	16 (80)	33	3
Decreased appetite	7 (35)	12	0

Efficacy

Radiological Response

Table 3 reports the Local Disease Control Rate (LDCR) and Best Response as assessed by central reader review per RECIST 1.1

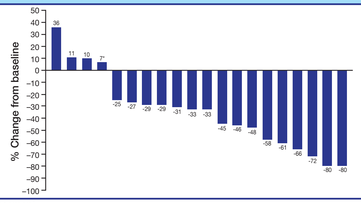
- At Week 8, LDCR was 100%
- At Week 16, LDCR was 85%
- Response Rate (either CR or PR) by Week 16 was 20%

Table 3. Local Disease Control Rate and Best Response Rate

Local Disease Control Rate, n (%)	N = 20
Week 8 PR SD LDCR at Week 8	 3 17 20 (100%)
Week 16 PR SD PD LDCR at Week 16	 3 14 3 17 (85%)
Best Response by Week 16 per RECIST 1.1 CR PR Overall Response Rate	 0 4 20%

Tumour Volume measurement by CT scan assessments reported a median change in tumour volume from Baseline to Week 16 of -33% (36% to -80%). Figure 2 shows the volumetric change per patient from Baseline to Week 16.

Figure 2. Percentage change in tumour volume from Baseline to Week 16 (N=20)



*Week 8 assessment

PET scan assessment

PET scans were reported on by a central reader.

17 of 20 patients had evaluable PET scan assessments at Baseline and at Week 12.

Total Lesion Glycolysis (TLG) as measured by PET scan showed a median reduction from Baseline to Week 12 of 54% (range +45% to -100%).

Metabolic resolution and absence of defined viable neoplastic disease was reported for two patients at the Week 12 PET scan assessment.

OncoSil™ Implantation and Intra-tumoural Localisation

Implantation experience was satisfactory with the device considered relatively straightforward to implant by operators. Table 4 outlines the endoscopists assessment of the implantation procedure as captured by questionnaires completed by the endoscopist following the procedure. No significant or serious procedural complications were reported. Figure 3 shows EUS views of an implantation procedure where tumour access is difficult due to proximity to the duodenum, mesenteric vessels and the bile duct with metallic biliary stent in-situ. This case demonstrates the utility of EUS in accessing tumours even in a difficult location where access is a challenge. Radioactive contamination of the endoscope was eliminated safely and swiftly immediately following the procedure in all cases.

Device localisation as demonstrated by SPECT-CT Bremsstrahlung imaging was acceptable. Table 5 captures this assessment as reported on by the site. Figure 4 is an example of the imaging technique at the two timepoints of assessment.

Table 4. Endoscopist Assessment of Implantation Procedure (N=20)

Ease of tumour access	Very Easy Easy Difficult	7 (35%) 8 (40%) 5 (25%)
Implantation method used	Single Deposit Tracking Unknown	13 (65%) 6 (30%) 1 (5%)
Number of deposits implanted	1 2	17 (85%) 3 (15%)
Stent in-situ	Yes No	10 (50%) 10 (50%)

Figure 3.

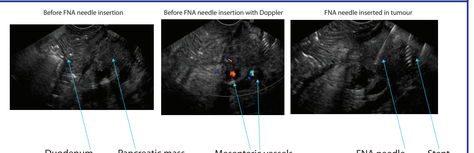
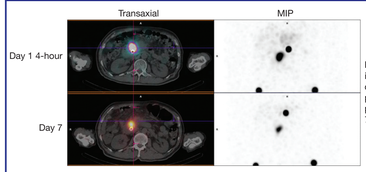


Figure 4.



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

MIP = Maximum Intensity Projection

Table 5. Device performance according to SPECT-CT Bremstrahlung imaging reports (N=20)

	4-Hour Observation Period Post-Implantation	7 Days Post-Implantation
Radiation Localised to the Implant Site	18	17
Radiation Uptake in the Gastrointestinal Tract	9	2
No Radiation Detected	0	1*

*Patient with no detectable radioactivity at Day 7 was reported as having detectable localisation of radioactivity at implantation site at Day 1

Conclusions

Preliminary findings from the first 20 implanted patients in the PanCO study indicate that the OncoSil™ device has an acceptable safety profile and in combination with chemotherapy showed evidence of target tumour regression and of local disease control. The implantation experience was satisfactory and considered relatively straightforward. There have been no significant safety concerns or toxicities associated with the Oncosil™ device or with the procedure. Local disease control rate at 16 Weeks was 85% with notable tumour volumetric reductions. Twenty per cent of patients benefited from a Partial Response by this timepoint. The feasibility and tolerability of EUS-guided implantation of Oncosil™ was demonstrated as was the utility of SPECT-CT Bremsstrahlung imaging in confirming the satisfactory localisation of the implanted device. The clinical trial is ongoing and additional safety and efficacy data will be presented.

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Disclosures

D Croagh, M Harris, M Aghmesheh, D William & P Ross are participating investigators in the study.
M Bradney & A Kraszewski are past and current employees, respectively, of Oncosil Medical Ltd.

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