ASX Announcement

3 July 2020

OncoSil presents clinical data at ESMO World Congress highlighting greater median overall survival rates vs other treatment methods

Sydney, Australia – 3 July 2020: OncoSil Medical Ltd (ASX: OSL) (**OncoSil** or the **Company**), is pleased to share poster presentations from its PanCO Study Results and Naïve indirect treatment comparison which were presented at the ESMO conference on 1 July 2020.

Key takeaways:

- The European Society of Medical Oncology (ESMO) is the leading professional organisation for medical oncology and is the pre-eminent oncology society in Europe
- OncoSil Medical presented (virtually) and shared two posters at the 2020 ESMO World Congress on Gastrointestinal Cancer, the premier event in the field attended by clinicians, researchers and healthcare industry executives globally
- Data presented in the posters includes findings from the PanCO study alongside a naïve indirect treatment comparison, whereby the median overall survival was significantly longer ($p<0.001$) in the PanCO study than other treatment regimens

OncoSil CEO, Daniel Kenny, added, "We are pleased to be able to share our compelling data with clinicians and partners at the ESMO Congress, the pre-eminent scientific event for our field. OncoSil's strong presence at the event, which included a presentation and two posters, is testament to the performance of our device and further highlights the significance of the PanCO study thus far."

The OncoSil presentation and posters are attached to this announcement.

End

Authorisation & Additional Information

This announcement was authorised by the Board of Directors of OncoSil Medical Limited.

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About OncoSil

OncoSil Medical is a medical device company seeking to advance radiation for cancer patients. OncoSil Medical's lead product, OncoSil™ is a targeted radioactive isotope (Phosphorus-32), implanted directly into a patient's pancreatic tumours via an endoscopic ultrasound.

Treatment with the OncoSil™ is intended to deliver more concentrated and localised beta radiation compared to external beam radiation. OncoSil Medical has conducted six clinical studies with positive results on tolerability, safety and efficacy. CE Marking has been granted for the OncoSil™ device which can be marketed in the European Union and the United Kingdom.

An Investigational Device Exemption (IDE) has been granted by the United States Food and Drug Administration (FDA) to conduct a clinical study of the OncoSil™ device aimed at supporting a PMA approval.

In December 2018, the FDA granted Humanitarian Use Designation (HUD) for the OncoSil™ device for the treatment of unresectable intrahepatic and distal cholangiocarcinoma. In March 2020, the FDA granted Breakthrough Device Designation for the OncoSil™ for unresectable pancreatic cancer in conjunction with systemic chemotherapy.

Pancreatic cancer is typically diagnosed at a later stage, when there is a poor prognosis for long-term survival. The World Cancer Research Fund estimated that in 2012, 338,000 people globally were diagnosed with pancreatic cancer. The prognosis for patients diagnosed with pancreatic cancer, regardless of stage, is generally poor; the relative five-year survival rate for all stages combined is approximately 5%. The estimated world-wide market opportunity for OncoSil™ in pancreatic cancer exceeds $3b.

Forward Looking Statements

This document contains certain forward-looking statements, relating to OncoSil's business, which can be identified by the use of forward-looking terminology such as "promising", "plans", "anticipated", "will", "project", "believe", "forecast", "expected", "estimated", "targeting", "aiming", "set to", "potential", "seeking to", "goal", "could provide", "intends", "is being developed", "could be", "on track", or similar expressions, or by express or implied discussions regarding potential filings or marketing approvals, or potential future sales of product candidates. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no assurance that any existing or future regulatory filings will satisfy the FDA and other authorities' requirements regarding any one or more product candidates nor can there be any assurance that such product candidates will be approved by any authorities for sale in any market or that they will reach any particular level of sales. In particular, management's expectations regarding the approval and commercialisation of the product candidates could be affected by, among other things, unexpected trial results, including additional analysis of existing data, and new data; unexpected regulatory actions or delays, or government regulation generally; our ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry, and general public pricing pressures; and additional factors that involve significant risks and uncertainties about our products, product candidates, financial results and business prospects. Should one or more of these risks or uncertainties materialise, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected. OncoSil Medical is providing this information as of the date of this document and does not assume any obligation to update any forward-looking statements contained in this document as a result of new information, future events or developments or otherwise.

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Naïve Indirect Treatment Comparison of PanCO, a Pilot Study of OncoSil P-32 Microparticles Combined with Gemcitabine + Nab-Paclitaxel or FOLFIRINOX Chemotherapy, Versus Standard-of-Care Treatment in Unresectable Locally Advanced Pancreatic Cancer

Abs. P-260

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Background

- Pancreatic cancer is a malignancy with a very poor prognosis and remains an area of high unmet medical need.
- Current standard treatment for patients with unresectable locally advanced pancreatic cancer (LAPC) is limited to chemotherapy (CT-only) or chemoradiotherapy following induction CT (ICT + CCRT).
- International guidelines (e.g. ESMO, ASCO and NCCN) recommend gemcitabine-based regimens or monotherapy as well as regimens containing fluoropyrimidines (capecitabine, 5FU) plus other agents, or ICT + CCRT, for the treatment of unresectable LAPC.[1–3]
- Brachytherapy using beta-emitting phosphorus (P-32) microparticles enables a predetermined radiation dose to be implanted into pancreatic tumours via endoscopic ultrasound (EUS) guidance.
- The results of a prospective, international, multi-centre, interventional, open-label, single-arm pilot study of P-32 microparticles (OncoSil™; OncoSil Medical) in combination with gemcitabine + nab-paclitaxel or FOLFIRINOX chemotherapy demonstrated encouraging safety and efficacy in patients with unresectable LAPC (the PanCO study: NCT03003078).[4]

Objective

- In the absence of a head-to-head randomised controlled trial, a naïve indirect treatment comparison (a universally accepted method to provide a valid categorical and statistical comparison of reported outcomes) was used to assess the results of the PanCO study against 'state-of-the-art' (SOTA) therapy obtained from a systematic literature review (SLR) of published scientific literature from prospective Phase II and III clinical studies.
- This enabled a robust determination as to whether the improvements observed in the PanCO study were due to CT alone or the combination of CT with OncoSil™.

Methods

- A SLR was conducted, based on a previous systematic review and meta-analysis by Chang et al (2018),[5] to identify published clinical data on SOTA/'standard-of-care' treatments from prospective Phase II and III clinical studies in patients with unresectable LAPC treated with CT-only or ICT + CCRT (excluding borderline resectable LAPC; for inclusion criteria, see Table 1).
- A weighted median of medians method and meta-analysis of proportional outcomes were used to provide summary statistics for SLR outcomes.[6]
- Meta-analysis was performed in the statistical software R and R studio using the R Functions meta,[7] metaprop[8] and metamedian.[9]
- The SLR outcomes were then compared with the results of the PanCO study in a naïve indirect treatment comparison.
- A binomial test was applied to assess the strength of the PanCO results relative to the SOTA CT-only and ICT + CCRT (comparator) studies of the meta-analysis for overall survival (OS), progression-free survival (PFS), one-year survival, resection rate, disease control rate (DCR) and overall response rate (ORR).

Table 1: Inclusion Criteria for Systematic Literature Search

	Title/Abstract Screening	Full Text Screening
Population	Includes LAPC	Patients with unresectable, non-metastatic LAPC If other populations are included, outcomes are reported separately
Intervention	Any CT or CCRT Trials that include immunotherapy or other biological agents excluded if no chemotherapy control arm	Any CT or ICT and CCRT Trials that include immunotherapy or other biological agents excluded (chemotherapy control arm may be included)
Outcomes		Median OS Median PFS (and LPFS, where available) One-year survival rate DCR (and LDCR where available) ORR Resection rate
Other limits	Phase II or Phase III studies only	Phase II or Phase III studies only

Abbreviations: CCRT, consolidation chemoradiotherapy; CT, chemotherapy; DCR, disease control rate; ICT, induction chemotherapy; ITT, intention-to-treat (enrolled participants); LAPC, locally advanced pancreatic cancer; LDCR, local DCR; LPFS, local PFS; PFS, progression-free survival; ORR, overall response rate; OS, overall survival.

Results

- The SLR identified clinical outcomes including OS, PFS, one-year survival, resection rate, DCR and ORR. No studies reported LPFS or LDCR.
- In total, there were 46 included studies, comprising 58 study arms and 4,342 patients, 2,398 of whom had unresectable LAPC (see Figure 1 and Table 2).[10–55]

Figure 1. PRISMA Flowchart

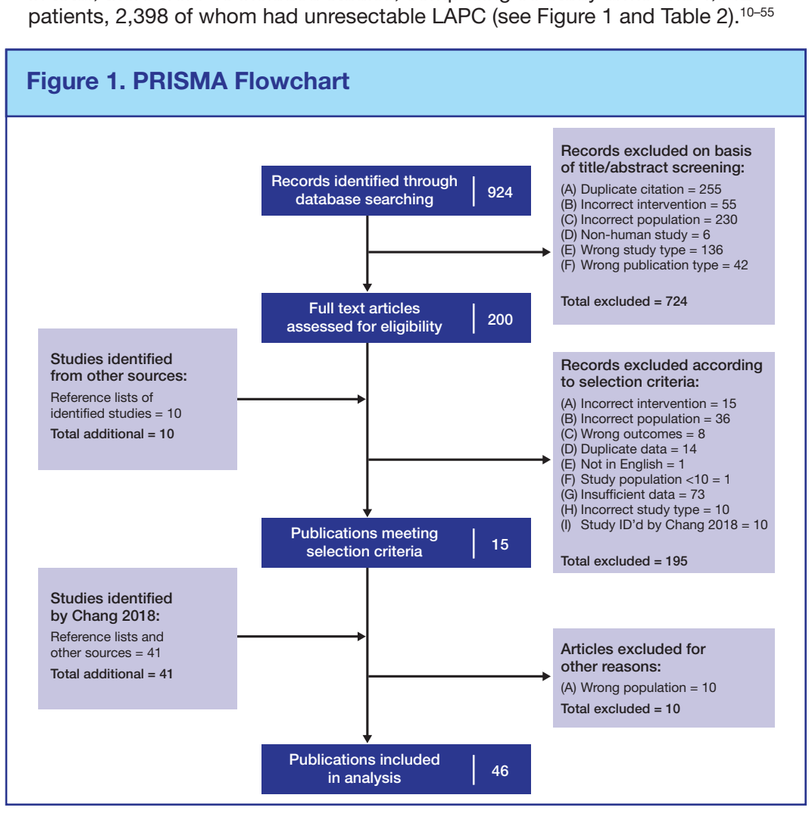

Table 2. Summary of SLR Study Numbers[10–55]

SLR Cohort	Number of Study Arms	Number of Patients	Gem-Based CT (CT or ICT)		FP-Based CT (CT or ICT)		Gem-Based CCRT		FP-Based CCRT	
			Arms	Pts	Arms	Pts	Arms	Pts	Arms	Pts
All Treatments (CT-only and ICT + CCRT)	58	2,398	46	2,034	22	694	7	199	11	371
CT-Only	38	1,690	29	1,418	15	406	na	na	na	na
CCRT-Only	20	708	17	616	7	288	7	199	11	371

Abbreviations: CCRT, consolidation chemoradiotherapy; CT, chemotherapy; ICT, induction CT; FP, fluoropyrimidine (e.g. Fluorouracil [5FU], capecitabine, S-1); Gem, gemcitabine; na, not applicable; Pts, Patients.

- The PanCO study enrolled 50 patients (Intention-to-Treat [ITT] population) of which 42 were implanted with P-32 microparticles (Per Protocol [PP] population), with a median follow-up of 16.1 months.[4]

Overall Survival

- Median OS was significantly longer ($p<0.001$) in the PanCO study ITT and PP cohorts than CT-only and ICT + CCRT regimens (Tables 3 and 4), representing a ~20% reduction in the risk of death compared to CT-only and ICT + CCRT studies (Hazard Ratio PP: 0.79; ITT: 0.82). The PanCO median OS for ITT and PP cohorts were also significantly longer than the CT-only ($p<0.001$) and ICT + CCRT sub-groups ($p=0.0001$ or <0.0001).
- One-year survival rates in PanCO were significantly higher than SOTA ($p<0.001$ for CT-only and ICT + CCRT; see Tables 3 and 4).
- Sensitivity analyses were performed to determine the impact of patient selection and choice of therapy on the median OS. These involved:
  - Substitution of SCALOP1 data in Hurt 2017[10] with defined ITT data in Mukherjee 2013.[56]
  - Substitution of first randomisation LAP07 data with second randomisation LAP07 data from Hammel 2016.[11]
  - Removal of treatment arms containing S-1.
  - Removal of all S-1 studies.
  - Note: base case includes first randomisation LAP07 data from Hammel 2016,[11] SCALOP1 cohort data from Hurt 2017[10] and all S-1 treatment arms.
- This demonstrated that the meta-analyses of the median OS did not differ significantly for all 'state-of-the-art' CT and ICT + CCRT regimens (median OS range: 12.6–13.0 months *vs*. 12.7 months for the base case) and the subgroups (median OS range for CT-only arms: 12.3–13.0 months *vs*. 12.7 months for the base case; median OS range for ICT + CCRT arms: 12.6–13.4 months *vs*. 12.6 months for the base case) irrespective of the inclusion of studies and treatment arms that are subject to patient selection bias and confounders.

Table 3: Survival Outcomes for PanCO *vs*. Meta-Analyses of 'SOTA' Regimens

Cohort	N	Median OS (95% CI)	One-Year Survival (95% CI)
PanCO ITT PanCO PP	50 42	15.5 months (11.3, nc) 16.0 months (11.1, nc)	63.4% (47.8%, 75.4%) 64.0% (47.5%, 76.5%)
SLR: CT-only and ICT + CCRT	2,350 (54 arms) [OS]	12.7 months (12.2, 13.6)	52.5% (48.7%, 56.3%)
SLR: CT-Only	1,642 (34 arms) [OS]	12.7 months (11.9, 13.6)	50.4% (45.3%, 55.5%)
SLR: ICT + CCRT only	708 (20 arms) [OS]	12.6 months (12.2, 14.0)	55.2% (49.4%, 60.9%)

Abbreviations: CCRT, consolidation chemoradiotherapy; CI, confidence interval; CT, chemotherapy; ICT, induction CT; ITT, intention-to-treat (enrolled participants); nc, non-calculable; OS, overall survival; PP, per protocol (enrolled/implanted participants); SLR, study arms identified by Systematic Literature Review.

Table 4: PanCO OS Outcomes *vs*. 'SOTA' Regimens

Parameter	Naïve Indirect Treatment Comparator	PanCO Cohort	PanCO mOS Outcome	N Comparator Trials	n ≥ PanCO	*p*-value
mOS	CT-only and ICT + CCRT	ITT	15.5 months	54	10	<0.001
		PP	16.0 months	54	6	<0.001
	CT-only	ITT	15.5 months	34	7	<0.001
		PP	16.0 months	34	4	<0.001
	ICT + CCRT	ITT	15.5 months	20	3	0.001
		PP	16.0 months	20	2	<0.001
One-Year Survival	CT-only and ICT + CCRT	ITT	63.4%	40	8	<0.001
		PP	64.0%	40	7	<0.001
	CT-only	ITT	63.4%	21	6	0.039
		PP	64.0%	21	5	0.013
	ICT + CCRT	ITT	63.4%	19	2	<0.001
		PP	64.0%	19	2	<0.001

Abbreviations: CCRT, consolidation chemoradiotherapy; CT, chemotherapy; ICT, induction chemotherapy; ITT, intention-to-treat (enrolled participants); mOS, median overall survival; n ≥ PanCO, number of comparator trials where the result is the same as or greater than the PanCO study outcome; PP, per protocol (enrolled/implanted participants).

Surgical Resection

- The rate of surgical resection in PanCO was significantly greater than SOTA ($p<0.001$; Tables 5 and 6).

Table 5: Resection Rate Outcomes for PanCO *vs*. Meta-Analyses of 'SOTA' Regimens

Cohort	N	Resection Rate (95% CI)
PanCO ITT PanCO PP	50 42	20.0% (10.0%, 33.7%) 23.8% (12.1%, 39.5%)
SLR: CT-only and ICT + CCRT	391 (16 arms)	9.9% (6.7%, 13.5%)
SLR: CT-Only	149 (7 arms)	7.7% (3.1%, 13.5%)
SLR: ICT + CCRT only	242 (9 arms)	11.5% (7.4%, 16.2%)

Abbreviations: CCRT, consolidation chemoradiotherapy; C.I., confidence interval; CT, chemotherapy; ICT, induction chemotherapy; ITT, intention-to-treat (enrolled participants); PP, per protocol (enrolled/implanted participants); SLR, study arms identified by Systematic Literature Review.

Table 6: PanCO Resection Rate Outcomes *vs*. 'SOTA' Regimens

Parameter	Naïve Indirect Treatment Comparator	PanCO Cohort	PanCO Outcome	N Comparator Trials	n ≥ PanCO	*p*-value
Resection Rate	CT-only and ICT + CCRT	ITT	20.0%	16	1	<0.001
		PP	23.8%	16	0	<0.001
	CT-only	ITT	20.0%	7	1	0.063
		PP	23.8%	7	0	0.008
	ICT + CCRT	ITT	20.0%	9	0	0.002
		PP	23.8%	9	0	0.002

Abbreviations: CCRT, consolidation chemoradiotherapy; CT, chemotherapy; ICT, induction chemotherapy; ITT, intention-to-treat (enrolled participants); n ≥ PanCO, number of comparator trials where the result is the same as or greater than the PanCO study outcome; PP, per protocol (enrolled/implanted participants).

Progression-Free Survival

- Median PFS was significantly longer ($p<0.001$) than the combined CT-only and ICT + CCRT or CT-only regimens (Tables 7 and 8).

Table 7: PFS Outcomes for PanCO *vs*. Meta-Analyses of 'SOTA' Regimens

Cohort	N	Median PFS (95% CI)
PanCO ITT PanCO PP	50 42	9.3 months (5.9, 12.2) 9.3 months (7.2, 12.2)
SLR: CT-only and ICT + CCRT	1,936 (43 arms)	7.6 months (6.6, 7.8)
SLR: CT-Only	1,355 (27 arms)	6.6 months (6.2, 7.8)
SLR: ICT + CCRT only	581 (16 arms)	9.1 months (7.6, 9.3)

Abbreviations: CCRT, consolidation chemoradiotherapy; C.I., confidence interval; CT, chemotherapy; ICT, induction chemotherapy; ITT, intention-to-treat (enrolled participants); PP, per protocol (enrolled/implanted participants); SLR, study arms identified by Systematic Literature Review.

Table 8: PanCO PFS Outcomes *vs*. 'SOTA' Regimens

Parameter	Naïve Indirect Treatment Comparator	PanCO Cohort	PanCO mPFS Outcome	N Comparator Trials	n ≥ PanCO	*p*-value
mPFS	CT-only and ICT + CCRT	ITT	9.3 months	43	11	<0.001
		PP	9.3 months	43	11	<0.001
	CT-only	ITT	9.3 months	27	5	<0.001
		PP	9.3 months	27	7	0.010
	ICT + CCRT	ITT	9.3 months	16	6	0.227
		PP	9.3 months	16	6	0.227

Abbreviations: CCRT, consolidation chemoradiotherapy; CT, chemotherapy; ICT, induction chemotherapy; ITT, intention-to-treat (enrolled participants); mPFS, median progression-free survival; n ≥ PanCO, number of comparator trials where the result is the same as or greater than the PanCO study outcome; PP, per protocol (enrolled/implanted participants).

Disease Control and Overall Response Rates

- DCR and ORR were significantly higher than the combined CT-only and ICT + CCRT or CT-only regimens (Tables 9 and 10).

Table 9: DCR and ORR Outcomes for PanCO *vs*. Meta-Analyses of 'SOTA' Regimens

Cohort	N (DCR/ORR)	DCR (95% CI)	ORR (95% CI)
PanCO ITT PanCO PP	47/47 42/42	95.7% (85.5%, 99.5%) 100.0% (91.6%, 100.0%)	29.8% (17.3%, 44.9%) 31.0% (17.6%, 47.1%)
SLR: CT-only and ICT + CCRT	751 (19 arms)/ 962 (26 arms)	70.1% (72.9%, 86.4%)	18.2% (13.3%, 23.7%)
SLR: CT-Only	440 (10 arms)/ 640 (16 arms)	71.3% (61.4%, 80.3%)	14.7% (9.0%, 21.3%)
SLR: ICT + CCRT only	311 (9 arms)/ 322 (10 arms)	88.5% (80.4%, 94.9%)	24.2% (15.8%, 33.7%)

Abbreviations: C.I., confidence interval; ITT, intention-to-treat (enrolled participants); DCR, disease control rate (stable disease, partial response or complete response by RECIST v1.1 for best response on imaging); ORR, overall response rate; PP, per protocol (enrolled/implanted participants); SLR, study arms identified by Systematic Literature Review.

Table 10: PanCO Response Outcomes *vs*. 'SOTA' Regimens

Parameter	Naïve Indirect Treatment Comparator	PanCO Cohort	PanCO Outcome	N Comparator Trials	n ≥ PanCO	*p*-value
DCR	CT-only and ICT + CCRT	ITT	95.7%	19	3	0.002
		PP	100.0%	19	2	<0.001
	CT-only	ITT	95.7%	10	0	<0.001
		PP	100.0%	10	0	<0.001
	ICT + CCRT	ITT	95.7%	9	3	0.254
		PP	100.0%	9	2	0.090
ORR	CT-only and ICT + CCRT	ITT	29.8%	26	6	0.005
		PP	31.0%	26	6	0.005
	CT-only	ITT	29.8%	16	2	0.002
		PP	31.0%	16	2	0.002
	ICT + CCRT	ITT	29.8%	10	4	0.377
		PP	31.0%	10	4	0.377

Abbreviations: CCRT, consolidation chemoradiotherapy; CT, chemotherapy; DCR, disease control rate; ICT, induction chemotherapy; ITT, intention-to-treat (enrolled participants); n ≥ PanCO, number of comparator trials where the result is the same as or greater than the PanCO study outcome; ORR, overall response rate; PP, per protocol (enrolled/implanted participants).

Conclusions

- **The results from the PanCO study provide a broad and consistently positive outcomes compared to standard-of-care CT-only and ICT + CCRT regimens.**
- **The naïve indirect treatment comparison to state-of-the-art therapy indicated that P-32 microparticles combined with standard-of-care chemotherapy may provide significant and clinically relevant benefits for patients with unresectable LAPC and a valuable treatment option in an area of high unmet medical need.**

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Disclosures

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PanCO: Updated Results of an Open-Label, Single-Arm Pilot Study of OncoSil P-32 Microparticles in Unresectable Locally Advanced Pancreatic Adenocarcinoma (LAPC) with Gemcitabine + Nab-Paclitaxel or FOLFIRINOX Chemotherapy

Abstract 0-1

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Introduction

- Locally advanced pancreatic cancer (LAPC) accounts for 30% to 40% of all pancreatic cancer presentations.[1] Unresectable LAPC has a poor prognosis with a median survival of <12 months.[2] Current Standard-of-Care (SoC) remains limited to chemotherapy or chemo-radiotherapy.
- Phosphorous-32 (^{32}P) Microparticles (OncoSil™; OncoSil Medical) is a brachytherapy device that implants a predetermined 100 Gy dose of beta-radiation-emitting ^{32}P into pancreatic tumours via endoscopic ultrasound (EUS) guidance.
  - ^{32}P Microparticles investigated in combination with gemcitabine monotherapy in 23 patients with LAPC and metastatic disease in 2 studies, demonstrating acceptable tolerability and safety.
  - CE Marking approval for EU and US FDA 'Breakthrough' Designation have recently been granted for OncoSil™.
- This analysis reports updated results of the 'PanCO' pilot study of ^{32}P Microparticles in combination with SoC chemotherapy in patients with unresectable LAPC

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.

Methods

- International, multicentre, single-arm pilot study (Fig. 1); with 10 sites in 3 countries: Australia, Belgium and the UK. Recruitment period: March 2017 to June 2018.
- Chemotherapy: gemcitabine + nab-paclitaxel or FOLFIRINOX, by physician choice, per SoC.
- ^{32}P Microparticles was implanted directly into the pancreatic tumour via EUS guidance, using fine needle aspiration; ^{32}P activity was calculated from the tumour volume to administer a predicted absorbed dose of 100 Gy; ^{32}P diffusion pattern 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 CTCAE v4.0.
- Independent central reader analysis of 8-weekly CT scans for response assessment by RECIST 1.1 and tumour volume (using Voxels of Interest and eMass software [ERT; Brussels]) and FDG-PET scans (Baseline *vs*. 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

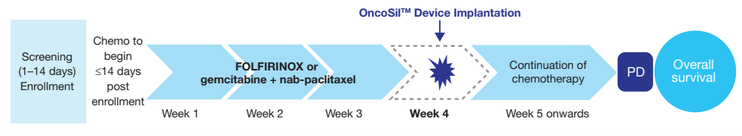
Primary Performance Outcome: Local Disease Control Rate at 16 weeks ($LDCR_{16\ weeks}$)

Statistical Assumptions for $LDCR_{16\ weeks}$ Efficacy 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%.

Study Design

Figure 1. Study Design



Results

- 50 study participants were enrolled – Intent-to-Treat (ITT) population; 42 were implanted with the OncoSil™ device – Per Protocol (PP) population (Table 1).

Table 1: Participant Demographics & Baseline Characteristics (ITT)

Demographic/Characteristic, n (%) unless stated		N = 50
Age, years	Median (Range)	65 (42–84)
Sex	Male : Female	28 (56%) : 22 (44%)
Race	White/Caucasian Black/African American Asian Other	40 (80%) 2 (4%) 7 (14%) 1 (2%)
ECOG Performance Status	0 : 1	26 (58%) : 24 (42%)
CA 19-9, (U/mL) [N = 49]	Median (Range)	163 (1–6576)
Pancreatic tumour location	Head : Body	41 (82%) : 9 (18%)
Target lesion longest diameter, cm	Median (Range)	4.5 (2.6–7.1)
Tumour volume, cc	Median (Range)	24.35 (7.9–68.7)
Study Days to OncoSil Implantation [N = 42]	Median (Range)	31 (21–77)
Chemotherapy	gemcitabine + nab-paclitaxel FOLFIRINOX	40 (80%) 10 (20%)

Chemotherapy Intensity

- Relatively low chemo intensity (dose delays ≥1 week, dose reductions and/or early termination), which was seen prior to OncoSil™ implantation (median 1 cycle) and in a similar proportion of study participants who did not receive OncoSil™ (Table 2).

Table 2: Chemotherapy Delivered

N, (%) unless stated	ITT Cohort (N=50)	PP Cohort (N=42)
gemcitabine + nab-paclitaxel (28-day Cycle, N)	40	34
Cycles, median (range)	4 (1–22)	5 (1–22)
Median Relative Dose Intensity (1st 6 Cycles)	47.9%	48.5%
Any dose reduction/delay(s) ≥1 week	45 (90.0%)	31 (91.2%)
Pre-implantation dose reduction/delay(s) ≥1 week	na	76.5%
FOLFIRINOX (14-day Cycle, N)	10	8
Cycles, median (range)	6 (2–13)	6 (3–13)
Median Relative Dose Intensity (1st 12 Cycles)	42.5%	46.0%
Any dose reduction/delay(s) ≥1 week	10 (100%)	8 (100%)
Pre-implantation dose reduction/delay(s) ≥1 week	na	87.5%

Safety and Tolerability (PP Cohort)

- 988 AEs reported; 148 were Grade ≥3 (see Table 3). No serious device- or radiation-related toxicities were reported.
- 330 AEs (33%) occurred pre-OncoSil™ implantation (35 Grade ≥3) *vs*. 658 AEs (67%) post-implant (113 Grade ≥3) [median follow-up: 1 *vs*. 15.1 months, respectively], with 41 *vs*. 609 attributed to the OncoSil™ device and/or implantation procedure *vs*. chemotherapy, respectively (see Figure. 2).
- No increased incidence of AEs pre-implantation *vs*. per cycle, overall and by key categories, post-implantation (see Table 4).

Table 3: Most Commonly Reported AEs (≥20% Incidence in PP Cohort)

AE Category, n (%)	PP Cohort (N=42)		Incidence by Causality† (N=42)			
			OncoSil™ device/implant.		Chemotherapy	
	All-Grade	Grade ≥3	All-Grade	Grade ≥3	All-Grade	Grade ≥3
Pts with ≥1 AE/SAE	**42 (100%)**	**34 (81.0%)**	**16 (38.1%)**	**3 (7.1%)**	**42 (100%)**	**28 (66.7%)**
Diarrhoea	27 (64.3%)	2 (4.8%)	-	-	22 (52.4%)	1 (2.4%)
Nausea	26 (61.9%)	3 (7.1%)	3 (7.1%)	-	23 (54.8%)	2 (4.8%)
Abdominal pain*	21 (50.0%)	5 (11.9%)	3 (7.1%)	1 (2.4%)	5 (11.9%)	1 (2.4%)
Constipation	20 (47.6%)	1 (2.4%)	-	-	10 (23.8%)	-
Vomiting	14 (33.3%)	4 (9.5%)	-	-	10 (23.8%)	1 (2.4%)
Fatigue	35 (83.3%)	6 (14.3%)	5 (11.9%)	1 (2.4%)	34 (81.0%)	5 (11.9%)
Pyrexia	16 (38.1%)	3 (7.1%)	-	-	10 (23.8%)	2 (4.8%)
Peripheral oedema*	10 (23.8%)	-	-	-	8 (19.0%)	-
Neutropenia*	23 (54.8%)	18 (42.9%)	2 (4.8%)	1 (2.4%)	21 (50.0%)	16 (38.1%)
Thrombocytopenia*	13 (31.0%)	4 (9.5%)	1 (2.4%)	1 (2.4%)	12 (28.6%)	3 (7.1%)
Anaemia*	14 (33.3%)	7 (16.7%)	1 (2.4%)	-	12 (28.6%)	5 (11.9%)
Alopecia	16 (38.1%)	-	-	-	16 (38.1%)	-
Rash	13 (31.0%)	-	-	-	13 (31.0%)	-
Decreased appetite	19 (45.2%)	1 (2.4%)	-	-	16 (38.1%)	-
Peripheral neuropathy*	15 (35.7%)	1 (2.4%)	-	-	15 (35.7%)	1 (2.4%)
Weight decreased	12 (28.6%)	1 (2.4%)	1 (2.4%)	0 (0.0%)	10 (23.8%)	1 (2.4%)

Abbreviations: implant., implantation; PP, per protocol (enrolled and implanted pts); Pts, Participants. Notes: Multiple records from same subject only counted once within same category. *, Combined records: Neutropenia includes neutropenia, febrile neutropenia, neutropenic sepsis and/or neutrophil count decreased; †, Causality = Possible or Probable; Abdominal pain includes abdominal pain irrespective of abdominal site of pain (lower, upper or not otherwise specified); Thrombocytopenia includes thrombocytopenia and/or platelet count decreased; Peripheral neuropathy includes peripheral neuropathy and/or peripheral sensory neuropathy; Anaemia includes AEs reported as anaemia and/or haemoglobin decreased; Peripheral oedema includes AEs reported as oedema peripheral and/or peripheral swelling.

Figure. 2: Incidence of AEs over Time by Causality (PP Cohort)

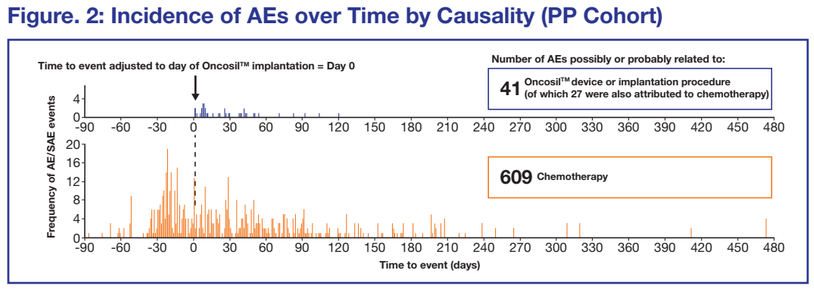


Table 4: Grade ≥3 AE Incidence per Cycle, of Specific Categories

Grade ≥3 AEs, as % of PP Participants Alive	Pre-Implant	Chemo Cycle, Adjusted to OncoSil™ Implant = Day 0					
		Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6
Number at Risk	42	42	42	41	40	39	37
All AEs, Grade ≥3	50.0%	28.6%	33.3%	17.1%	15.0%	10.3%	18.9%
Haematological AEs	21.4%	14.3%	19.0%	12.2%	5.0%	0%	0%
Neutropenia	19.0%	7.1%	16.7%	4.9%	0%	0%	0%
Non-Haematological AEs	33.3%	21.4%	19.0%	12.2%	12.5%	10.3%	18.9%
Gastrointestinal AEs	9.5%	9.5%	9.5%	4.9%	2.5%	5.1%	2.7%

Efficacy

Local Disease Control Rate (see Table 5)

Table 5: Local Disease Control

	ITT Cohort (N=50)	PP Cohort (N=42)
Local Disease Control at 16 weeks, n (%)	41 (82.0%)	38 (90.5%)
$LDCR_{16\ weeks}$ (95% CI)	**0.82** (0.68–0.91)	**0.90** (0.77–0.97)
p-value for $LDCR_{16\ weeks}$	0.0001	<0.0001
Local Disease Control at 24 weeks, n (%)	31 (62.0%)	30 (71.4%)
$LDCR_{24\ weeks}$ (95% CI)	**0.62** (0.47–0.75)	**0.71** (0.55–0.84)

p-values for Fisher's Exact test, comparing the binomial proportion to the null hypothesis proportion of 0.55

Tumour Response

Best Response (by Central Imaging Analysis) (see Table 6)

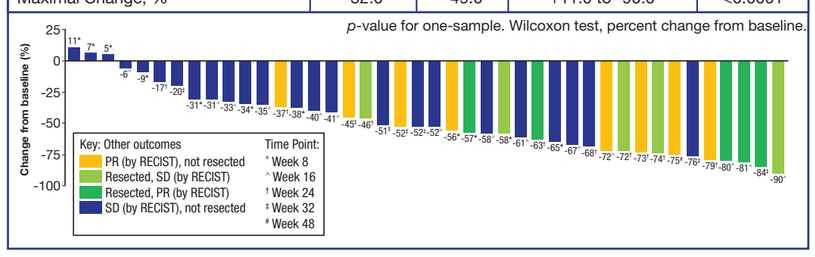
Table 6: Best Response in Evaluable Participants

Best Response	ITT Cohort, n (%) (N=47/50)	PP Cohort, n (%) (N=42/42)
Complete Response [CR]	0 (0%)	0 (0%)
Partial Response [PR]	14 (29.8%)	13 (31.0%)
Stable Disease [SD]	31 (65.6%)	29 (69.0%)
Progressive Disease [PD]	2 (4.0%)	0 (0%)
Overall Response Rate [ORR]	14 (**29.8%**)	13 (**31.0%**)
Disease Control Rate [DCR]	45 (**95.7%**; 95% CI: 85.5–99.5%)	42 (**100%**; 95% CI: 91.6–100%)

Tumour Volume (by Central Imaging Analysis) (see Table 7/Figure 3)

Table 7/Figure 3: Maximum Change in Tumour Volume from Baseline by Outcome (PP Cohort Prior to Surgical Resection)

Tumour Volume, PP Cohort (N=42)	Median	Mean	Range of Change	*p*-value
Maximal Change, %	-52.0	-49.0	+11.0 to -90.0	<0.0001



CA 19-9 Response (PP Cohort; in Participants with Baseline ≥35 U/mL Prior to Resection)

- ≥50% reduction in CA 19-9 was reported in 81.3% of patients; ≥70% reduction in 65.6%; and ≥90% reduction in 37.5% (see Table 8/Figure 4).

FDG-PET Response (PP Cohort; Baseline *vs*. Week 12 Prior to Resection)

- Metabolic resolution (100% reduction in TLG and SUV Max) and absence of defined viable neoplastic disease for 5 study participants at Week 12 (see Table 9/Figure 5).

Surgical Resection with Curative Intent

- Ten implanted patients underwent surgical resection by Whipple procedure (see Table 10), 9 received gemcitabine + nab-paclitaxel; 1 received FOLFIRINOX. Resections took place from 70 to 267 days post-implantation.
- At least 4 further patients were sufficiently downstaged to be technically considered for surgical resection but could not undergo surgery due to concomitant co-morbidities and/or other considerations (advanced age, patient choice).
- HPB surgeons noted reduction in the fibrosis of the tumours along blood vessels and favourable tissue planes.

Table 8/Figure 4: Maximum Change in CA 19-9 from Baseline by Outcome (PP Cohort in Participants with Baseline ≥35 U/mL Prior to Resection)

CA 19-9, PP Cohort	N	Median	Range	*p*-value
Maximal Change, %	32/34	-80.8	+50.0 to -90.9	<0.0001

p-value for one-sample. Wilcoxon test, percent change from baseline.

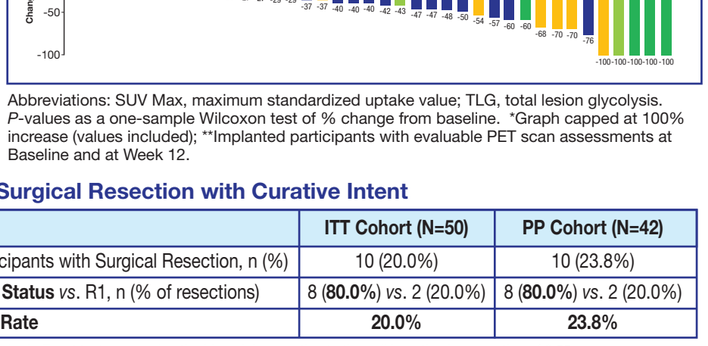
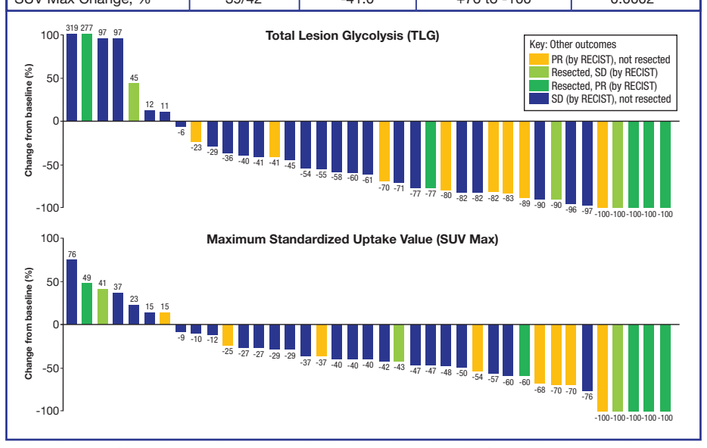


Table 9/Figure 5: % change in FDG-PET from Baseline to Week 12* by Outcome (PP Cohort Prior to Resection)

FDG-PET, PP Cohort	N**	Median	Range	*p*-value
TLG Change, %	39/42	-65.2	+319 to -100	0.0010
SUV Max Change, %	39/42	-41.0	+76 to -100	0.0002



Abbreviations: SUV Max, maximum standardized uptake value; TLG, total lesion glycolysis. *P*-values as a one-sample Wilcoxon test of % change from baseline. *Graph capped at 100% increase (values included); **Implanted participants with evaluable PET scan assessments at Baseline and at Week 12.

Table 10: Surgical Resection with Curative Intent

	ITT Cohort (N=50)	PP Cohort (N=42)
Study Participants with Surgical Resection, n (%)	10 (20.0%)	10 (23.8%)
R0 Margin Status *vs*. R1, n (% of resections)	8 (**80.0%**) *vs*. 2 (20.0%)	8 (**80.0%**) *vs*. 2 (20.0%)
Resection Rate	**20.0%**	**23.8%**

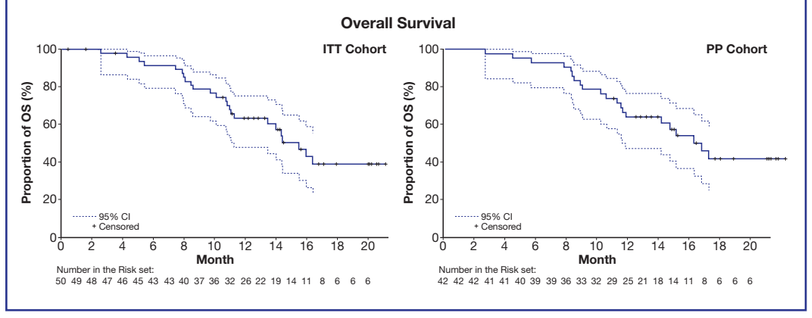
p-values for Fisher's Exact test, comparing the binomial proportion to the null hypothesis proportion of 0.55

Survival

(see Table 11/Figure 6)

Table 11/Figure 6: Kaplan-Meier Analysis of Survival

At median follow-up: 16.1 months	ITT Cohort (N=50)	PP Cohort (N=42)
Median Progression-Free Survival (95% CI)	9.3 months (5.9, 12.2)	9.3 months (7.2, 12.2)
One-year PFS Rate, % (95% CI)	32.8% (21.3%, 50.6%)	32.3% (20.4%, 51.3%)
Median Overall Survival (95% CI)	**15.5 months** (11.3, nc)	**16.0 months** (11.1, nc)
One-year Survival Rate, % (95% CI)	63.4% (47.8%, 75.4%)	64.0% (47.5%, 76.5%)



Abbreviations: ITT, intention-to-treat; nc, not calculable; PP, per protocol (enrolled and implanted participants); 95% CI, 95% confidence interval.

Conclusions

- Use of EUS-guided ^{32}P implantation is feasible, with an acceptable safety profile in combination with first-line SoC chemotherapy for LAPC over a prolonged study timeframe
  - Relatively few AEs were attributed to the OncoSil™ device and/or implantation procedure compared to chemotherapy
- At a relatively mature follow-up (median 16.1 months), the PanCO study results provide a consistent set of outcomes that suggest clinically relevant benefits for patients with unresectable LAPC treated using the OncoSil™ device in combination with systemic chemotherapy
- Encouraging clinical efficacy outcomes were observed, particularly tumour response (LDCR, ORR, Tumour Volume, CA19-9 and FDG-PET), surgical resection with curative intent (including a high proportion with R0 margins), PFS and overall survival
- Further clinical studies on OncoSil™ are in development

References

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Disclosures

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- N Wilson & D Kenny are employees of and D Turner is a consultant to Oncosil Medical Ltd.
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