Comparison of resected *vs.* non-resected patients with unresectable locally advanced pancreatic cancer (LAPC) receiving P-32 microparticles with gemcitabine/nab-paclitaxel or FOLFIRINOX chemotherapy in the PanCO study

Abstract
SO-2

PJ Ross[1]; M Nikfarjam[2]; N Nguyen[3]; M Aghmesheh[4]; D Burnett[5]; HS Wasan[6]; DM Turner[7]; D Croagh[8]

[1] Dept. Medical Oncology, Guy's & St Thomas' Hospital NHS Foundation Trust, London, UK; [2] Dept. Surgery, Austin Hospital, University of Melbourne, Victoria, Australia; [3] Dept. Gastroenterology, Royal Adelaide Hospital, Adelaide, South Australia, Australia; [4] Dept. Medical Oncology, Southern Medical Day Care Centre, Wollongong, NSW, Australia; [5] Dept. Surgery, John Hunter Hospital, Newcastle, NSW, Australia; [6] Dept. Medical Oncology, Imperial College Healthcare NHS Trust, London, UK; [7] OncoSil Medical Ltd, North Sydney, NSW, Australia; [8] Dept. Surgery, Monash Health, Clayton, Victoria, Australia.

Introduction

- Locally advanced pancreatic cancer (LAPC) accounts for 30% to 40% of pancreatic cancer cases at diagnosis.[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.
- Surgical resection has the potential to transform the prognosis of patients with borderline and LAPC by increasing median survival from ~12 months to 22–35 months. Neoadjuvant therapy can convert ≤65% of borderline-resectable cases, but resection rates in LAPC are often <10% following SoC.
- Brachytherapy using a novel device containing beta-radiation-emitting Phosphorous-32 (P-32) microparticles is implanted directly into pancreatic tumours via endoscopic-ultrasound (EUS) guidance to deliver a 100 Gy absorbed dose to the target tumour.
- The international, multi-centre, single-arm PanCO study reported an acceptable safety profile and encouraging efficacy, including a resection rate of 23.8%, in patients with unresectable LAPC treated using intra-tumoural brachytherapy comprising P-32 microparticles added to gemcitabine/nab-paclitaxel or FOLFIRINOX chemotherapy.[3]
- We report a *post-hoc* analysis of the resected *vs.* non-resected cohorts in the PanCO study.

Methods

- Key eligibility criteria: Histologically or cytologically proven adenocarcinoma of the pancreas; Unresectable locally advanced pancreatic carcinoma; Target tumour diameter 2–6cm; ECOG Performance Status 0–1; No distant metastases; No prior radiotherapy or chemotherapy for pancreatic cancer.
- Eligible patients received either gemcitabine/nab-paclitaxel or FOLFIRINOX chemotherapy by physician choice, per SoC, with P-32 microparticles (OncoSil™; OncoSil Medical) implantation planned at weeks 4–5 (see Fig. 1).
- P-32 activity was calculated from participants' tumour volume to deliver 100 Gy absorbed dose. The primary endpoint of the study was safety/tolerability graded using CTCAE v4.0.
- Response was assessed by independent central reader using RECIST 1.1 with 8-weekly CT scans and FDG-PET scans at baseline and week 12.
- Suitability for surgical resection was reviewed at multi-disciplinary team meetings/tumour boards per institutional practice.

Results

- Fifty patients were enrolled (Intention-to-Treat); 42 participants were implanted with P-32 microparticles (Per Protocol [PP] population) at a median of 31 days.
- 40 participants received gemcitabine/nab-paclitaxel and 10 FOLFIRINOX (PP: 34/8, respectively).
- Median follow-up was 31.6 months.
- 10 participants (23.8% PP; 9 received gemcitabine/nab-paclitaxel, 1 received FOLFIRINOX) underwent pancreatico-duodenectomy following repeat staging at a median of 5.8 months post-enrolment (4.4 months post-implant); 8 (80%) achieved R0 margins.
- Four further participants were sufficiently down-staged to be technically considered for surgical resection, but could not undergo surgery due to metastases, co-morbidities or patient choice.
- Baseline characteristics for resected and non-resected participants were similar for age (median 65 *vs.* 68 years), longest tumour diameter (median 4.5 *vs.* 4.5 cm) and tumour volume (median 23.2 *vs.* 24.4 cc), respectively. More resected participants were ECOG 0 (80% *vs.* 45%) and female (60.0% *vs.* 28.1%), respectively (see Table 1).
- Median relative dose intensity of chemotherapy in resected *vs.* non-resected participants was 70.6% *vs.* 54.2% for 4 cycles of gemcitabine/nab-paclitaxel and 82.9% *vs.* 71.2% for 6 cycles of FOLFIRINOX.
- Resected participants compared with non-resected patients had greater response by median decrease from baseline at week 16 in tumour longest diameter (–21.5% *vs.* –8.1%), tumour volume (–59.5% *vs.* –30.8%), CA 19-9 (–95.9% *vs.* –75.2% in those with baseline >35 U/mL) and FDG-PET at week 12 (TLG: –95.0% *vs.* –75.2%; SUV_{Max}: –80.2% *vs.* –39.8%; SUL_{Max}: –80.8% *vs.* –40.6%) (see Fig. 2).
- Median survival in the resected cohort was not reached (95% CI: 21.1 to non-calculable; median follow-up: 32.0 months) (see Fig. 3). Four resected participants survived for 18.8–22.1 months post-enrolment; 6 remained alive at study completion (5 without recurrence) 26.4–35.3 months post-enrolment.
- Treatment-emergent AEs (TEAEs) attributed to P-32 microparticles or implantation procedure were infrequent (41 *vs.* 609 attributed to chemotherapy; PP population).
- 39 TEAEs/SAEs (14 grade 3) were reported in the 30 days from and including the date of resection, in line with surgical experience.
- 5 events in 3 patients were classified as SAEs; all were Grade 3.
- No TEAEs or SAEs were attributed as possibly or probably related to the P-32 microparticle device or implantation procedure for ≤30 days following surgery.
- 0% mortality rate at 30 days, 90 days and 180 days post-resection.

Conclusions

- EUS-guided P-32 microparticle implantation appears safe, with encouraging clinical outcomes and may convert unresectable LAPC to surgical resection.
- Nearly one-in-four PP participants (23.8%) underwent surgical resection with curative intent and one-in-three (33.3%) were technically resectable
- Baseline characteristics of study participants who underwent surgical resection were similar to those who were not resected.
- Complications in the 30 days' post-resection were in line with surgical experience.
- Resected participants had a substantial response to treatment compared to non-resected participants, particularly decrease in tumour volume, and encouraging survival.
- Further clinical studies adding P-32 microparticles to SoC chemotherapy are planned.

Fig. 1: Study Schema

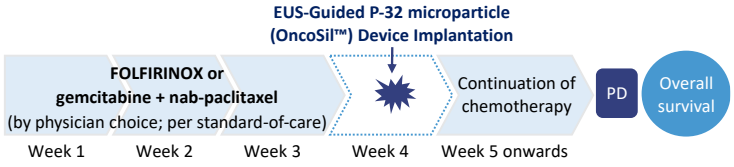
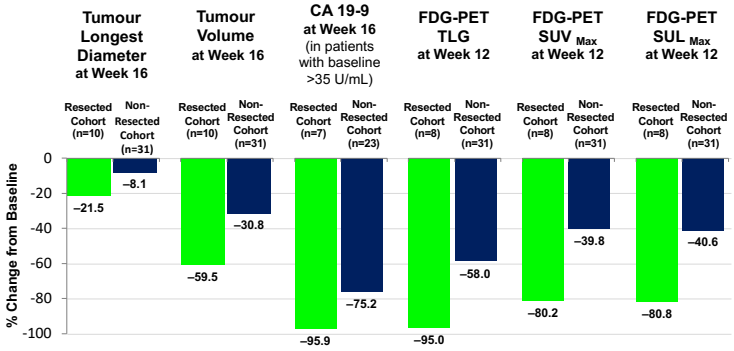


Table. 1: Baseline Characteristics for Resected *vs.* Non-Resected Patients

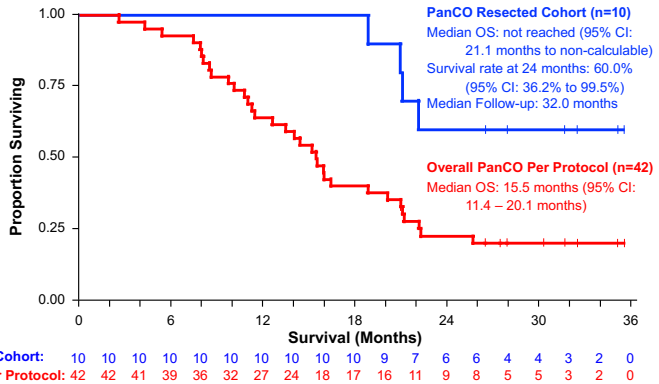
Characteristic, n (%) unless stated		Resected Patients (n = 10)	Non-Resected Patients (n = 32)
Age, years	Median (Range)	65 (56–78)	68 (49–84)
Sex	Male : Female	4 (40%) : 6 (60%)	23 (71.9%) : 9 (28.1%)
Race	White/Caucasian Black/African American Asian	8 (80%) 0 2 (20%)	26 (81.3%) 3 (9.4%) 3 (9.4%)
ECOG Performance Status	0 : 1	8 (80%) : 2 (20%)	16 (50.0%) : 16 (50.0%)
CA 19-9, (U/mL) in participants with baseline >35 U/mL [n=33]	Median (Range) Mean	191.5 (1–1479) 397.5	290.5 (38–6576) 941
Pancreatic tumour location	Head : Body	9 (90%) : 1 (10%)	25 (78.1%) : 7 (21.9%)
Target lesion longest diameter*, cm	Median (Range)	4.5 (3.0–6.6)	4.5 (3.0–7.1)
Tumour volume*, cc	Median (Range)	23.2 (9.9–50)	24.4 (7.9–68.7)
Study Days to P-32 Implant, days	Median (Range)	39 (26–76)	31 (21–77)
Chemotherapy	gemcitabine/nab-paclitaxel FOLFIRINOX	9 (90%) 1 (10%)	25 (78.1%) 7 (21.9%)

Fig. 2: Median Change in Tumour Response Outcomes at Weeks 12 or 16



Abbreviations: SUL_{Max}, maximum standardized uptake value corrected for lean body mass; SUV_{Max}, maximum standardized uptake value; TLG, total lesion glycolysis. All assessments exclude post-resection imaging. Tumour longest diameters and volumes calculated by independent central reader at each imaging assessment; volumes calculated using Voxels of Interest and eMass software (ERT, Brussels). Implanted participants with evaluable PET scan assessments at Baseline and at Week 12.

Fig. 3: Overall Survival in the Resected Cohorts and Per Protocol Population



References

1. Ariake K et al. *Surg Case Rep* 2017; 3: 15.
2. Ducreux M et al. *Ann Oncol* 2015; 26 (Suppl 5): v56-v68.
3. Ross PJ et al. *ESMO Open* 2022; 7 (1): 100356.