PanCO: An open label, single arm pilot study of OncoSil™ in subjects with unresectable locally advanced pancreatic adenocarcinoma, given in combination with standard chemotherapy

Paul Ross[1], Michelle Bradney[2], Jeremy Simpson[2]
[1]Guy's and St Thomas' NHS Foundation Trust, London, UK; [2]Oncosil Medical, Sydney, NSW, Australia
ClinicalTrials.gov Identifier: NCT03003078

PanCO

OncoSil MEDICAL Ltd

Introduction

- Locally advanced pancreatic cancer (LAPC), accounts for 30% to 40% of unresectable disease.[1] Median survival is 6-10 months.[2]
- Local tumour burden and uncontrolled progression cause significant mortality, contribute to poor quality of life, and may be the direct cause of death in this patient group. Up to 30% of pancreatic cancer patients die from consequences of locally destructive disease.[3]
- Systemic chemotherapy regimens recommended as first-line therapy for LAPC include gemcitabine alone or in combination with other agents such as nab-paclitaxel and FOLFIRINOX (5-fluoruracil/leucovorin plus oxaliplatin plus irinotecan).[4]
- Conventional radiotherapy (CRT) has been used to treat patients with advanced disease and 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.
- Brachytherapy (also known as internal radiation therapy) is a form of radiotherapy where a sealed radiation source is placed directly into (interstitial) or adjacent to the site of a cancerous tumour. Brachytherapy targets tumours more precisely and delivers higher tumouricidal doses of ionising radiation, while reducing the radiation exposure in the surrounding healthy tissues to a greater extent than CRT or stereotactic body radiation (SBRT).
- Therefore, brachytherapy may cause fewer side effects than CRT/SBRT, in addition the overall treatment time is usually shorter, and the procedure can be conducted on an outpatient basis.
- OncoSil™ is a brachytherapy device that implants a pre-determined tumouricidal dose of the beta radiation emitting isotope (Phosphorus-32), directly into cancerous tissue. The OncoSil™ device is intended for local treatment of cancerous pancreatic cells when it is implanted intra-tumourally via endoscopic ultrasound (EUS).
- OncoSil™ has been investigated in combination with gemcitabine monotherapy in 23 patients (10 with LAPC and 13 with metastatic disease) in two clinical studies. These studies demonstrated that in combination with gemcitabine chemotherapy, Brachysil™ (OncoSil™, previously known as Brachysil™) was found to have an acceptable tolerability and safety profile in patients with locally advanced or metastatic inoperable pancreatic cancer. The adverse event profile was consistent with expectations for the study population and known toxicity profile of gemcitabine. Efficacy data showed potential with evidence of a target tumour response rate of 23% (95% CI of 7% to 50%) and a high target disease control rate of 82% (95% CI of 57 to 96%). These studies establish that EUS-directed implantation of OncoSil™ is an appropriate method of delivery.
- OncoSil™ is expected to be used in combination with systemic chemotherapy in patients with LAPC in line with accepted clinical practice.

Purpose

PanCo has been designed to further investigate the safety of the active implantable (radiological) medical device, OncoSil™ when implanted intratumourally using Endoscopic Ultrasound Guidance in study participants with unresectable, locally advanced pancreatic cancer. Study participants will receive OncoSil™ with either FOLFIRINOX or gemcitabine+nab-paclitaxel chemotherapy.

Disclosures

19th World Congress on Gastrointestinal Cancer, 28 June-July 1 - Barcelona, Spain
Dr P.Ross: consulted for, conducted studies funded by, or received honoraria from OncoSil Medical Inc.;
Dr M.Bradney & Dr J.Simpson: currently full time employees of OncoSil Medical Inc

Study Design / Methods

- The screening period will be performed within a 2 week period, followed by a treatment period of investigational visits which will occur weekly from Day 0 (Visit 1) until week 12, then 4 weeks later at week 16, and then at 8-weekly intervals until study participants reach documented progression of disease (PD) criteria for both local progression free survival (LPFS) and progression free survival (PFS) which marks the end of study participation i.e. end of study (EOS) visit.
- An 8 weekly review of medical records to monitor possible device or late radiation related adverse events, and oncology treatments/procedures administered for up to 12 months post OncoSil™ implantation.
- Overall survival will be conducted via 8 weekly medical record reviews until study participant death, or until 104 weeks post the last study participant enrolled.
- Additional safety measures include Bremsstrahlung imaging, blood and urine radioactivity sampling.
- A Safety Review Committee will meet regularly during the course of the study to assess the adverse event profile.

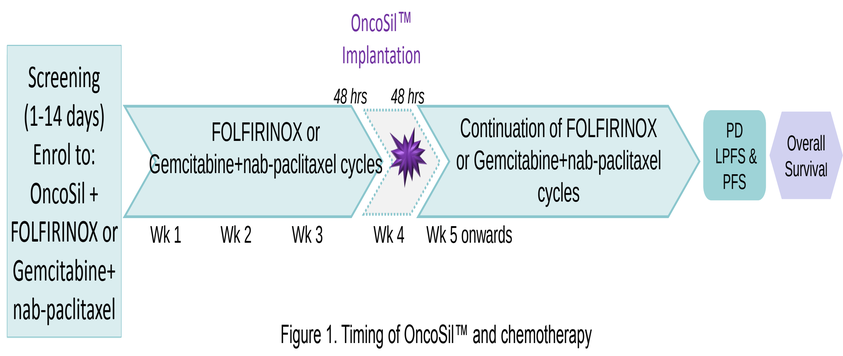

Figure 1. Timing of OncoSil™ and chemotherapy

Primary Endpoint

- Safety and tolerability will be assessed by adverse events evaluated according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE).

Secondary Endpoints

Efficacy will be determined by Target Tumour Response (per RECIST 1.1), Duration of Response (LPFS and PFS)

- Local Progression Free Survival (LPFS), within the pancreas
- Progression Free Survival (PFS), all sites
- Overall Survival (OS)
- Change in body weight
- Impaired function utilising Karnofsky Performance Status
- Pain Scores utilising the Numerical Rating Scale and The European Organization for Research and Treatment in Cancer (EORTC) Pancreatic Cancer module (EORTC QLQ-PAN26)

Exploratory Endpoint

- Target tumour volumetric change as measured by a central reading centre
- Target tumour FDG-PET parameters as measured by a central reading centre
- EORTC quality of life core cancer questionnaire (EORTC QLQ-C30) will be used to assess quality of life

Statistical Methods

- No formal hypothesis is being tested and therefore no formal sample size calculation has been performed.
- The aim of the study is to establish the safety profile of the OncoSil™ device in study participants with locally advanced pancreatic cancer. It is considered a sample size of 20 study participants is the minimum that will allow reasonable description of the safety profile on which to base a formal sample size calculation for a larger, future study of efficacy.

Treatment

- OncoSil™ is implanted using endoscopic-guided ultrasound following FOLFIRINOX or gemcitabine+nab-paclitaxel chemotherapy per local prescribing standards.
- The intended average absorbed radiation dose per treated tumour is 100 Gy ± 20%.

Participants

- Prospective, interventional, open-label, single arm 20 participant pilot safety study
- Participants enrolled in at least 10 Australian and European sites (UK and Belgium)

Key Inclusion Criteria

- Histologically or cytologically proven adenocarcinoma of the pancreas
- Unresectable LAPC
- Pancreatic target tumour diameter of ≥ 2.0 cm (shortest axis) to ≤ 6.0 cm (longest axis) and a minimum tumour volume of 14.0 ml
- An ECOG Performance Status of 0 to 1 and Karnofsky Performance Status of 80 to 100
- Study participants ≥ 18 years of age at screening
- To commence first-line standard FOLFIRINOX or nab-paclitaxel and gemcitabine chemotherapy (per standard of care according to the approved prescribing schedule), with OncoSil™ implantation to occur during the fourth (4th) week of the first chemotherapy cycle
- Adequate renal, liver and bone marrow function
- Prothrombin Time (PT) or Partial Thromboplastin Time (PTT) within normal range
- Life expectancy of at least 3 months at the time of screening as judged by the investigator
- Treated with or eligible to commence prophylactic treatment with a proton-pump inhibitor prior to implantation, and to continue to receive treatment for at least 6 months post implantation

Key Exclusion Criteria

- Evidence of distant metastases as determined by the central reading committee
- More than one primary lesion
- Any prior radiotherapy or chemotherapy for pancreatic cancer
- In the opinion of the investigator, EUS directed implantation posing undue study participant risk e.g. previous EUS Fine Needle Aspiration (FNA) was considered technically too difficult to perform, or imaging demonstrates multiple collateral vessels surrounding or adjacent to the target tumour within the pancreas
- History of malignancy, treated or untreated, within the past five years

Conclusion

This study will help determine the safety and shed further light on the efficacy of OncoSil™ in patients with locally advanced, unresectable pancreatic cancer treated with contemporary chemotherapy regimens.

References

1. Ariake K, et al. Surg Case Rep 2017;3:15, 2. Keane MG, et al. World J Gastroenterol 2014;20:2267-78, 3. Iacobuzio-Donahue CA, et al. J Clin Oncol 2009;27:1806-13, 4.Balaban EP, et al. J Clin Oncol 2016;34:2654-68.

19WCGIC
229--P
Clinical Pancreatic Cancer
Paul J Ross
DOI: 10.3252/pso.eu.19wcgic.2017
Poster presented at: 19th World Congress on Gastrointestinal Cancer
PosterSessionOnline.com