PRIMUS 002
A PRECISION PANC CLINICAL STUDY

An umbrella phase II study examining two neo-adjuvant regimens (FOLFOX-A and AG) in resectable and borderline resectable Pancreatic Ductal AdenoCarcinoma (PDAC), focusing on biomarker and liquid biopsy development

Initiation Slides (Version 1: 14th December 2018)

EudraCT Ref:	2016-004156-29
ISRCTN No:	34129115
Sponsor:	NHS Greater Glasgow and Clyde
Chief Investigators:	Dr Derek Grose and Dr David Chang

Study Details

- The trial is being co-ordinated via the CRUK Clinical Trials Unit, Glasgow
- Sponsor of the trial is NHS Greater Glasgow and Clyde
- Co Chief Investigators are Dr Derek Grose, Dr David Chang and Prof Colin McKay
- Trial is being funded by a grant from Celgene and CRUK

Please note this presentation has been prepared as part of your site initiation. These slides are a compliment to the protocol. All site staff must have read and understood the protocol and the study requirements prior to signing off the initiation acknowledgement sheet.

- Study will be conducted according to ICH GCP guidelines E6
- Study conducted in accordance with the EU Directive 2001/20/EC & amendments
- Study carried out in accordance with the World Medical Association Declaration of Helsinki Ethical Principles for Medical Research involving Human Subject 1964 (as amended)

Study Team

Chief Investigators:	Dr Derek Grose (Clinical lead), Dr David Chang (Translational lead), Prof Colin McKay (Surgical lead)
Project Manager:	Sarah Bradley
Statisticians:	Jim Paul & Jamie Stobo
Pharmacovigilance:	Lindsey Connery & Pam Fergusson
Sponsor Contact:	Margaret Fegen
Sponsor Pharmacy Team:	Paula Morrison & Eliza Valentine
Clinical Trial Co-ordinator:	Hannah Weir / Craig Campbell
Clinical Trial Monitor:	Louise Dinnett

Study Design

- **PRIMUS 002** is an integrated, open label, non randomised, phase II trial of 2 neo-adjuvant regimens (FOLFOX-A and AG) assessing efficacy and toxicity with integrated translational work. The study is powered on testing a proposed DNA damage response deficient biomarker for responsiveness in patients treated with FOLFOX-A: patients being treated with AG are recruited concurrently.

- The study has a prospective safety assessment of neo-adjuvant chemotherapy and then neo-adjuvant chemotherapy followed by chemo-radiotherapy (consisting of conventional radiotherapy and Capecitabine). This safety assessment will include all patients (please see next slide)

- The study will begin with patients receiving neo-adjuvant chemotherapy (FOXFOX-A or AG) and then proceeding to surgery.

- Chemo-radiotherapy (50.4Gy in 28 fractions* along with Capecitabine) may be added if the safety assessment are met. Sites will be informed of any change to the study via email after ratification by the IDMC.

- The trial is planned to recruit 242 patients over 46 months.

*(Will be updated to 36Gy in 15 fractions in next protocol amendment)

Safety Assessments

- The Surgical Safety Assessment (SSA) is conducted in 2 stages
- In the first stage mortality following neo-adjuvant chemotherapy alone is assessed, if this proves safe the surgical mortality of neo-adjuvant chemotherapy followed by CRT prior to surgery is then assessed.
- SSA stage I – This will take place after 46 patients have had surgery (approximately 66 patients have been recruited) but may take place earlier if the number of observed surgical deaths is very low. Conversely if the surgical deaths are too high the study will stop at this time
- SSA stage 2 – If SSA stage I is completed with acceptable surgical mortality rate then chemo-radiotherapy prior to surgery will be added. The assessment of surgical mortality will be restarted and all surgical deaths will be monitored continuously with the acceptable mortality rate set at <5% and the unacceptable rate set at 15%
- Due to this continuous monitoring it is imperative that the Surgical Death Form is completed and faxed as soon as a surgical death occurs

Study Endpoints

- **Primary Endpoint:** Progression post FOLFOX-A induction treatment as defined by RECIST 1.1. The association of this with a proposed biomarker of treatment responsiveness will be examined.

- **Secondary Endpoints:**
  - Translational research assessment of clonal evolution and acquired resistance mechanisms due to treatment and the feasibility and accuracy of liquid biopsies
  - Response rate based on RECIST 1.1 post neo-adjuvant chemotherapy
  - CAP tumour regression grade post surgery
  - R0 rate post surgery
  - Overall survival
  - Disease free survival
  - Safety and tolerability of (1) study drugs (2) CRT and (3) surgical complications as assessed by NCI CTCAE v4.03
  - Neurotoxicity, quality of life and health economics

Exploratory Endpoints

- CA19.9 response
- PET-CT response (for those sites taking part in the PET sub-study)
- DWI MRI response (for those sites taking part in the MRI sub-study)*

*(Will be added to next protocol amendment)

Inclusion Criteria

Please refer to section 3.2 of the protocol for full details of the eligibility criteria for the study (Brief details of the key selection criteria only is detailed on this slide)

1	Patient has been enrolled in Precision-Panc Master Protocol and their tissue has been deemed suitable for NGS analysis
1	≥16 years old
3	Resectable or borderline resectable pancreatic cancer as defined by NCCN criteria
4	Measurable disease as per RECIST 1.1
5	Histologically or cytologically proved PDAC (and its variants)
6	Able to undergo biliary draining used a covered or partially covered self-expanding metal stent if jaundiced
7	ECOG 0-1
8	Adequate liver/bone morrow function
9	Negative pregnancy test
10	Able to comply with protocol requirements and deemed fit for surgical resection, chemotherapy and chemo-radiotherapy

Please note there will be no exception to the eligibility requirements at the time of registration. Queries in relation to the eligibility criteria should be addressed via contact with the CTU prior to registration. Patients are eligible for the trial if all the inclusion criteria are met and none of the exclusion criteria apply.

Exclusion Criteria

Please refer to section 3.3 of the protocol for full details of the eligibility criteria for the study (Brief details of the key selection criteria only is detailed on this slide)

1 Distant metastatic disease
2 Previous chemotherapy or CRT for pancreatic cancer
3 NYHA classification grade III or IV
4 BMI > 35
5 Liver cirrhosis (except for Child-Pugh A)
6 CPET results outwith appropriate level for surgical resection
7 Any patient with severe diarrhoea
8 Grade ≥2 peripheral neuropathy

Please note there will be no exception to the eligibility requirements at the time of registration. Queries in relation to the eligibility criteria should be addressed via contact with the CTU prior to registration. Patients are eligible for the trial if all the inclusion criteria are met and none of the exclusion criteria apply.

Pre-Registration Assessment Requirements

Within 28 days of registration

- Confirmation that patients has been registered to Precision-Panc Master Protocol
- Written, informed consent for PRIMUS 002 study, once the patient has signed consent a screening form should be completed and sent to CRUK CTU Glasgow
- Medical history, demographic details
- Review of concomitant medications
- Full physical exam including height, weight, BMI, BP and pulse
- ECOG PS
- ECG
- FBC – Hb, WBC, platelets, ANC, lymphocytes
- Biochem – Na, K, calcium, phosphate, Mg, CRP, urea, creatinine, protein, albumin, bili, Alk phos, AST/ALT and LDH
- Coagulation screen
- CA19.9
- Study Imaging – CT CAP, MRI liver (within 35 days of registration)
- CPET (within 35 days of registration)

Within 14 days of registration

- Pregnancy test if required

Prior to registration

- Completion of all QoL – EORTC QLQ C-30, PAN26, EQ-5D-5L and GOG-NTX4

RECIST Reporting Requirements

- All radiological investigations **MUST** be reported as per protocol / RECIST Version 1.1

- Source documentation of this must be available for review if the original report has had to be supplemented to bring it in line with protocol requirements

- CRUK CTU, Glasgow have produced a worksheet to assist with the documentation of study specific reporting and will make this available to all participating sites

PET Sub-Study

- A separate PET sub-study will take place, initially at the Beatson WoSCC only. This aims to open by February 2019.
- Patients will sign an additional PET sub-study consent at the time of signing main study consent.
- Patients will undergo a PET scan at baseline, a PET scan prior to chemo-radiotherapy commencing (if this is currently taking place) and a PET scan prior to surgery.

Screening Process

All patients MUST have been registered on the Precision-Panc Master Protocol to take part in PRIMUS 002.

Once a patient has signed the informed consent form, site must complete a screening form and either telephone or fax this to the following numbers to received a screening ID. If the patient wishes to take part in the PET sub-study this consent form should be signed at the same time and the appropriate box ticked on the screening form to indicate this:

Telephone Number: 0141 301 7195

Fax Number: 0141 301 7946

Registration Process

All patients MUST have been registered on the Precision-Panc Master Protocol to take part in PRIMUS 002.

Registration to the trial can be performed by either telephone or fax on the following numbers:

Telephone Number: 0141 301 7195 Fax Number: 0141 301 7946

When the patient is registered CRUK CTU Glasgow will inform the site whether or not the patient should receive CRT and if the patient should receive FOLFOX-A or AG based on their performance status and age.

Informed Consent Process

Informed consent process:
•Consent Forms must be completed by a clinician (or deputy listed on delegation log)
•At least one original consent must signed and completed by the patient
•Date must be prior to registration
•Make one/two photocopies

- Original to be filed in Investigator File
- Original or photocopy to be given to patient (+PIS)
- Photocopy to be filed in hospital notes

•Consent Form must not be sent to your coordinating trials office

CONSENT WITHDRAWAL

This is when the patient **specifically** asks to withdraw their consent at any point in the study. If this occurs:

- Document clearly in the patient notes that the patient has withdrawn consent, the level of consent withdrawal and the reason (if the patient has given any)
- Contact CRUK CTU with full details of withdrawal
- Where applicable the CTU will request site completes a Consent Withdrawal Form
- No further follow-up should be collected on the patient from the date of consent withdrawal onwards.

Please remember that stopping treatment is NOT the same as withdrawing consent!

Study Treatment Details

Patients will receive either:

Nab-Paclitaxel + gemcitabine (AG) arm (28-day cycle) – Patients will have 3 cycles of treatment

- *nab*-paclitaxel: 125 mg/m^2 IV over 30 minutes, day 1,8, and 15 (administered first)
- Gemcitabine 1000 mg/m^2 IV over 30 mins on days 1, 8, and 15 (immediately following *nab*-paclitaxel)

Or

FOLFOX A arm (14-day cycle) – Patients will have 6 cycles of treatment

- *nab*-paclitaxel: 150mg/m^2 IV over 30 minutes, day 1 (administered first)
- Oxaliplatin: 85mg/m^2, IV over 2 hours, day 1
- Folinic acid: 350 mg flat dose, IV over 2 hours, day 1
- 5-FU infusion:1200mg/m^2/day, as a continuous IV infusion over 2 days, day 1 and day 2 (for a total dose of 2400mg/m^2 over 46 hours (or 48 hours as per standard practice))
- Patients in the FOLFOX-A arm will also receive daily G-CSF as primary prophylaxis against neutropenic events for all cycles. This should be given as per local policy for 14 days chemotherapy regimens i.e. it may be started on day 4 for 7 days (preparation and dose should be given as per local policy).

****Please refer to study protocol for detailed information on study treatments, including administration of treatment, prohibited therapies and potential drug interactions.****

Study Treatment Details Continued

If SSA Stage I is met and chemo-radiotherapy is introduced Capecitabine will be administered as per institutional standard of care.

Patients will take oral Capecitabine 830 mg/m^2 twice a day, on the days that radiotherapy is administered. Patients may receive a combination of tablet strengths to achieve the prescribed dose.

Capecitabine will be taken from usual pharmacy stock.

Patients should be instructed to take their Capecitabine within 30 minutes of a meal and as close to 12 hours apart as possible.

If the patient is unable to swallow their tablet whole they can dissolve the tablets in approximately 200ml of water.

Treatment/Dose Modifications

All dose adjustments to be made based upon the worst or most clinically significant preceding toxicity.

For FOLFOX-A and AG two dose reductions only are permitted.

If the patient's treatment is delayed for more than 3 weeks the patient should stop treatment (apart from hepatic toxicity related to biliary obstruction or for reasons of peripheral neurotoxicity).

Day 1 treatment may be delayed or brought forward for up to 48 hours for administrative reasons, day 8 or day 15 treatment may be delayed or brought forward by up to 24 hours.

**Please refer to section 5.10.1 and 5.10.2 of the study protocol for full details of treatment modifications/dose reductions/delays (brief details in relation to treatment modifications are provided on these slides). **

Process for notification of protocol deviations by sites

- All participating sites must notify the Sponsor (via CRUK CTU) of all deviations from the protocol or GCP immediately.

- The Sponsor requires a report on the incident(s) and a protocol deviation form will be provided during site initiation which should be used for informing of protocol deviations.

- If site staff are unsure whether a certain occurrence constitutes a deviation from the protocol or GCP, the CRUK CTU trial team and Sponsor can be contacted immediately to discuss. The Sponsor will assess all incidents with respect to the criteria of a “serious breach”.

Management of Serious Breaches

- The PI and site staff will be notified of any potential issues that have been identified which are considered to require escalation to the sponsor.
- The CRUK CTU will act as the liaison between the PI and Sponsor to clarify any details or request any further information in relation to the issues.
- Once agreed by the Sponsor that the issues are a potential serious breach or are a serious breach they will prepare the report to the MHRA.
- It is important that sites respond to requests for further information in a timely manner as serious breaches are required to be reported within 7 days of the sponsor becoming aware of issue.
- Sponsor will onwardly report as required.
- The MHRA respond to Sponsor and further investigation is carried out as appropriate with same staff as outlined above.

Monitoring plan and visits

Monitoring Visits/Schedule:

Sites will receive a monitoring call on a yearly basis by the CRUK CTU monitoring team. Each site will be visited once during the study. For cause monitoring will be arranged on an ad hoc basis

Telephone & Remote Monitoring:

- The time & date will be agreed with a member of the Site Study Team.
- A site file checklist will be sent to sites for completion prior to the call.
- Please set aside 30 minutes for this call.

On Site Monitoring:

- All patient source documentation should be made available to enable Source Document Verification by the Clinical Trial Monitor.
- A full working day is required for on-site visits & arrangements should be in place to facilitate the monitor access on the agreed date.
- If sites are able to provide printed results/reports these must be filed in the source documents.
- If a site is using electronic data reporting systems or electronic records & hard copies are not available – the clinical trial monitor must be permitted access to the system either by being issued with a temporary login or a member of staff available for the duration of the visit to facilitate electronic access to authorised reports/results.
- Pharmacy visits will include review of Pharmacy Site File – Temperature Logs – Drug Returns – Drug Accountability Logs.
- All findings will be discussed at an end of visit meeting and any unresolved issues raised as Action Points.
- Action Points will be followed up by the monitor until resolved.

Data Management

The trial uses the electronic data capture system MACRO and paper randomisation and quality of life forms.

MACRO log ins will be required for members of staff entering data and the PI, who will be required to sign off certain form, and can be requested from the CTC/PM.

Data Escalation Process:

- CRUK CTU will regularly chase outstanding data from participating sites. Routine requests for outstanding data and outstanding data queries will be performed quarterly or more regularly if required for a specific study.
- Sites will be routinely requested to return outstanding data and data queries within 6 weeks of queries being raised on the MACRO system or the CRF being due for completion.
- Sites consistently not returning data or answering queries could be temporarily suspended from study recruitment pending agreement by the TMG.

Site Set Up

CRUK CTU GLASGOW will provide

REC approval - MHRA approval – HRA Document Package - Site Initiation Slides - Investigator Site File - Pharmacy Site File

↓

SITE to submit

Delegation and Study Specific Training Log – SSI (if required) – R&D Approval/ confirmation – Clinical Trial Agreement – Principle Investigator and Lead Pharmacist CVs - GCP Certificate for PI and Lead Pharmacist – PIS/CF, GP Letter etc. on Trust headed paper - Lab normal ranges and accreditation certificates (haem and biochem) – Pharmacy Site Assessment Form

↓

INITIATION PROCESS

↓

DRUG SUPPLY

↓

SITE ACTIVATED

Confidentiality

- All information collected during the course of the study will be kept strictly confidential. Information will be held securely on paper and/or electronically at the CRUK CTU. The CRUK CTU will comply with all aspects of the 2018 Data Protection Act and National Health Service Guidelines for storage, transmittal and disclosure of patient information.

- Data on patients treated on the study will be held in study electronic case report forms (eCRFs), these files will be identified by a trial number and patient initials only.

- Patient identifiable data (such as full name/or initials with date of birth) should not be sent on email correspondence. If you need to refer to a patient use trial and patient number.

- Where central monitoring of source documents by CRUK CTU (or copies of source documents) are required (e.g. scan results of blood results) the personal data of the patients must anonymised on the report e.g. black out the patient's name and any other identifiable information.

- Where anonymisation of documentation is required, sites are responsible for ensuring no patient identifiable data is present before sending to CRUK CTU.

Record Retention and Archiving Arrangements for study

- Archiving of the trial essential documents should be performed by both the participating trial site and Sponsor/CRUK CTU.

- Participating sites are responsible for archiving their trial related documentation and should follow the requirements of their R&D Office in conjunction with advice from the CRUK CTU and Sponsor regarding the duration of document retention.

- Sites should not archive their trial documentation until they have been instructed by the CRUK CTU or Sponsor that they are able to do so. Where possible, at the time of archiving, sites will be notified of the archiving retention period. If this is not confirmed at the time of archiving, sites should not destroy archived documentation until authorisation is given from the Sponsor.

- The Sponsor and CRUK CTU will be responsible for archiving the Trial Master File (TMF) and all other essential trial documentation that is not held at participating trial sites as per their applicable SOPs.

Pharmacovigilance

Clinical Trial Regulations require:

- Investigators document Adverse Events (AEs) in patient notes and the eCRF as required
- Investigators report Serious Adverse Events (SAEs) immediately to the CRUK Clinical Trials Unit Glasgow
- The CTU (on behalf of the Sponsor) will make expedited reports of SAEs that meet the criteria for SUSARs to the Regulatory Authority (MHRA),REC & Investigators (additionally for PRIMUS 002 the Sponsor + AstraZeneca (AZ) will receive the reports).
- The CTU will produce Development Safety Update Reports in conjunction with the Chief Investigator and submit these reports to the Regulatory Authority and REC within 60 days of the anniversary of the Clinical Trial Authorisation (the Sponsor, AZ and Investigators will also receive a copy of the report).

PHARMACOVIGILANCE DOCUMENTATION

The Pharmacovigilance section of the site file must be maintained and contain the following documentation:

- Copy of all SUSAR and DSUR reports
- All SAE reports that have been submitted by the site Copies of the current and previous Reference Safety Information (RSI) with other related documentation such as the front sheet document
- All other correspondence from Pharmacovigilance

CRUK CTU PHARMACOVIGILANCE TEAM

If you have any queries about safety reporting please contact the CRUK CTU Pharmacovigilance team who will be happy to provide assistance:

Email: mvls-ctu-pv@glasgow.ac.uk Telephone: 0141 211 3567/ 0203/ 0352/ 3968

Safety Reporting Requirements(1)

ADVERSE EVENTS (AEs)

- All AEs must be followed;
  - until resolution,
  - or if the AE was present at pre-treatment, until the event returns to the CTCAE grade observed at pre-treatment
  - or until AE is confirmed as unlikely ever to resolve

- All AEs and toxicities must be graded according to the NCI-CTCAE Version 4.03
- An exacerbation of a pre-existing condition is an AE
- AEs occurring between signing pre-screening consent and drug subgroup consent should only be recorded on the eCRF if they are a result of a study related procedure
- All AEs occurring after drug subgroup consent prior to the start of study IMP require to be recorded on the eCRF

SERIOUS ADVERSE EVENTS (SAEs)

- Serious Adverse Events (SAEs) must be reported immediately (within 24 hours of knowledge of the event) using the current version of the PRIMUS 002 SAE report form. If the patient experiences a SAE relating to the PET sub-study this must also be reporting within 24 hours on the PET Sub-study SAE Report Form

- Sites must complete and fax the report to CRUK CTU Glasgow Pharmacovigilance (PV) on fax number **0141 232 2157. SAE report forms may also be emailed to mvls-ctu-pv@glasgow.ac.uk**

- The CRUK CTU PV will create a SAE reference number and will send an acknowledgement email to confirm receipt of the initial report. Please contact PV if you do not receive an acknowledgement.

- The CRUK CTU PV will request additional information if the event is unexpected and will raise queries for any inconsistent or missing information. Completed queries must be returned within 5 working days.

- SAEs are required to be reported from consent for up to 30 days post-surgery (or day of last study treatment). Additionally once the trial has closed, the obligation to report continues, so if the Investigator becomes aware of a SAE suspected to be related to the IMPs, radiotherapy or surgery (or PET scanning if applicable) it also requires reporting

Safety Reporting Requirements(2)

EXPEDITED REPORTING

The assessment of expectedness for SAEs and regulatory reporting will be undertaken by the CRUK CTU PV and CI. SAEs that meet the criteria for SUSARs will be reported to the MHRA, REC, Sponsor, Sites and AZ.

Additionally expedited reporting of all serious, related and unexpected events thought to be related to radiotherapy and/or surgery or participation in the PET sub-study will be made to the REC, Sponsor, PIs and trial sites.

- Fatal or life threatening SUSARs will be reported within 7 days of the CRUK CTU PV receiving the first notification of the unexpected event. Any additional information will be reported within eight days of sending the initial report.

- All other SUSARs will be reported within 15 days of the CRUK CTU PV receiving the first notification of the unexpected reaction.

- If the SAE is a suspected SUSAR then follow up information must be provided as quickly as possible and in the timeframe requested by the CRUK CTU and CI. All follow-up information is required to be reported promptly and follow up reports are required to be submitted until all AEs listed on the initial SAE report resolve whether the event is a SUSAR or not.
- SAEs will be reported to the REC where, in the opinion of the CI, the event was:
  - Related – that is, it resulted from administration of any of the research procedures and is
  - Unexpected – that is, the type of event is not listed in the protocol as an expected event

- Reports of related and unexpected SAEs will be submitted within 15 days of the CRUK CTU becoming aware of the event.

Safety Reporting Requirements(3)

PREGNANCY REPORTING

Pregnancy occurring in a clinical trial participant, or the partner of a participant, while not considered an AE or a SAE, requires monitoring and follow-up.

- Any pregnancy occurring in a patient or a patient's partner during IMP treatment or occurring within 6 months of last administration of IMP must be reported to Pharmacovigilance within 24 hours of the site staff becoming aware of it by completing the Pregnancy Notification eCRF and also submitting a completed Pregnancy Notification Form (PNF) to Pharmacovigilance either by fax 0141 232 2157 or email to mvls-ctu-pv@glasgow.ac.uk
- It is the Investigator's responsibility to obtain approval from the patient or patient's partner for following-up the pregnancy until outcome. Investigators must also submit an updated PNF with the pregnancy outcome at delivery or if there is a change in condition during pregnancy such as miscarriage or planned termination.
- Any pregnancies that result in a congenital anomaly or birth defect will require to be reported by the Investigator as a SAE.

PHARMACOVIGILANCE DATA ESCALATION PROCESS

- CRUK CTU Pharmacovigilance team will regularly chase outstanding data from participating sites in relation to SAE report forms with request for data/ queries to be returned within 5 working days.
- If, following requests, a response is not received from site staff an escalation process will begin.
- Please ensure all queries for further SAE information are responded to promptly to enable the gathering of required safety data for the Sponsor to make decisions regards patient safety for this trial.

General Pharmacy Information

For the purposes of this trial, the following are considered IMP: *nab*-paclitaxel, oxaliplatin, fluorouracil, gemcitabine, folinic acid and capecitabine.

Patients who are eligible for this trial will be allocated to receive either:

- ***Nab*-Paclitaxel + gemcitabine (AG) arm (28-day cycle)**

Or

- **FOLFOX A arm (14-day cycle)**

Treatment will continue for approximately 3 months.

BSA capping is not recommended but is permitted as per standard practice

Dose banding is permitted for all drugs (apart from nab-paclitaxel) where it is local practice

Nab-paclitaxel will be provided FOC from Celgene and distributed by Fisher Clinical Services

For details on dose modifications for toxicities, supportive therapy, prohibited therapy and potential drug interactions please refer to the protocol.

Full instructions regarding management, labelling and accountability of the IMPs are given in a separate IMP Management Document, provided to participating sites in the Pharmacy Site File.

Please also see the Pharmacy Initiation slides for further training for Pharmacy staff.

Translational Research Requirements

- Patients will undergo a biopsy and paired blood sample under the Precision-Panc Master Protocol prior to registering on the PRIMUS-002 study
- If chemo-radiotherapy is being given as part of the study a biopsy and paired blood sample will be taken at the time of placing the fiducial markers
- If the patient proceeds to surgery, tissue from the surgical sample will be taken for research along with a paired blood sample
- If the patient cannot proceed to surgery for any reason they will be referred back to Precision-Panc Master Protocol to assess if there is further trial options. If so, the patients should be referred to Precision-Panc Master Protocol for further biopsy.
- All samples will be transferred to the Biorepository at the Queen Elizabeth University Hospital, Glasgow via Royal Mail Safeboxes
- **Please see the PRIMUS 002 lab manual for full details of translational sampling**

Other Staff

The Principal Investigator has overall responsibility for the conduct of the clinical trial at the trial site.

BUT

- All staff must comply with GCP
- Staff should only perform tasks delegated to them
- Staff should ensure that their details are available to the Investigator
- Staff should maintain appropriate confidentiality at all times

Protocol Amendment 1

An amendment will be submitted to update:

- Pregnancy test at screening to be completed up to 14 days prior to randomisation rather than treatment start date.

N.B. Please follow randomisation form and not protocol until amendment. Complete pregnancy test up to 14 days prior to randomisation.

- Addition of an MRI DWI sub-study.
- Stipulate that the MRI Liver and PET are not mandatory at baseline but as per local practice.
- Update radiotherapy regimen to 36Gy in 15 fractions.
- Update schedule of assessment to clarify that if not proceeding to surgery EUS biopsy & paired blood sample done under Precision Panc protocol.

Contact Details for CRUK CTU, Glasgow

Project Manager

Sarah Bradley
Tel: 0141 301 7540
Fax: 0141 301 724
E-mail: sarah.bradley@glasgow.ac.uk

Trial Coordinator

Craig Campbell
Tel: 0141 301 7195
Fax: 0141 301 7946
E-mail: craig.campbell@glasgow.ac.uk

Clinical Trial Monitor

Louise Dinnett
Tel: 0141 211 3801
E-mail: louise.dinnett@glasgow.ac.uk

Sponsor Pharmacy Rep

Paula Morrison
Tel: 0141 232 1797
E-mail: paula.morrison@ggc.scot.nhs.uk

CRUK CTU, Glasgow
Cancer Research UK Clinical Trials Office
Level 0, Beatson West of Scotland Cancer Centre
1053 Great Western Road, Glasgow, G12 0YN