Roundtable on improving access to Precision-Panc trials: Report 7 November 2019

A Roundtable on improving access to Precision-Panc trials was held at **Alderley Park, Manchester** on **Tuesday 3 September 2019**.

ATTENDEES:

PCUK
Chris Macdonald, Head of Research
Lynne McCallum, Specialist Nurse

PCS
Fiona Brown, Development Manager
Kimberley Booth, Clinical Nurse Specialist

PCA
Ali Stunt Founder and Chief Executive
Becky Rice – Health Information Officer

PCRF
Maggie Blanks, Founder and CEO

PP Patient Advisory Group
John Lancaster

CRUK
Clare Dickinson, Nurse

University of Manchester/CRUK Manchester Institute
Professor Juan Valle, Professor & Honorary Consultant in Medical Oncology

Dr Claus Jorgensen, Group Leader

Professor Ged Brady, Genomics Team Leader and Deputy Clinical & Experimental Pharmacology

Dr Sumitra Mohan, Genomics Team

Dr Kate Vaughan, Senior Research Programme Manager

The Christie
Helen Staiger, Research Nurse

University of Glasgow/CRUK Precision-Panc
Professor Andrew Biankin, Regius Professor of Surgery, Director or Wolfson Wohl Cancer Research Centre and designer of Precision-Panc Platform
Dr David Chang, Chief Investigator of the Precision-Panc Master Protocol and Translational Lead on PRIMUS 001/002
Judith Dixon-Hughes, Precision-Panc Project Manager
Blanche Hampton, Communications Consultant

Beatson West of Scotland Cancer Centre
Dr Derek Grose, Consultant Clinical Oncologist and Honorary Senior Lecturer

Havas Lynx
Dr Vernon Bainton, Chief Medical Officer

Precision-Panc clinical trials – a treatment option for pancreatic cancer

Not all cancers are the same. Precision medicine is about tailoring treatments to an individual's cancer. Precision-Panc and it's clinical testing platform called PRIMUS (Pancreatic Cancer Individualised Multi-arm Umbrella Studies) delivers trials through the NHS and ultimately aim to match people with pancreatic cancer to the trial treatment most likely to work for them.

There is excellent evidence that participation in clinical trials is associated with better outcomes for patients, and for pancreatic cancer patients, clinical trials may be their best treatment option.

Patients are eligible to enter the programme via the Precision-Panc Master Protocol. On the basis of clinical features and, where appropriate, the molecular profile of the cancer, they are assigned to one of the PRIMUS family of clinical trials.

At the Roundtable discussion centred around:

1. **Communications and health literacy**
2. **Resource and regulatory issues as obstacles in activating and running trials**
3. **Expanded access programmes – how to extend the benefits of precision medicine to patients beyond trials**

Following a welcome by Roundtable host, the University of Manchester's Professor Juan Valle, Professor Andrew Biankin, University of Glasgow, spoke of the current state of the Precision-Panc programme and where developments might lead.

As the long term vision, Andrew referred to a 'learning healthcare system', where the data from every patient is used to inform the development of new treatments, and research is embedded within routine healthcare so that access to and testing of a novel therapeutic is a treatment option, rather than an add-on. This is especially important for pancreatic cancer patients where current options are poor, and who, when they run out of options, need access to new therapeutics.

The Glasgow Cancer Test

With genomic testing, Precision-Panc is at the leading edge of identifying treatment options. Currently, a test similar to that being used for Precision-Panc, is also being trialled across the NHS for use in other cancers, along with the cancer network in Italy. Other countries have also shown interest in taking up the test. The Glasgow Cancer Test has been licensed to Agilent Technologies on a non-exclusive basis for global distribution and was launched on 4 November 2019.

1. Communications and health literacy

The way that Precision-Panc is communicated to patients, Healthcare Professionals (HCP) and the general public also impacts trial access. This includes the staging, complexity and format of that information. Currently a patient cannot be screened or registered to Precision-Panc without reading and signing the current versions of the patient information sheets/consent forms. We can, however, influence what is said to the patient and how trials are presented. If there is sufficient evidence, there may also be a case to the ethics committees that approve the patient information and consent forms to have them modified. The concept of electronic consent was also raised.

Precision-Panc has various stakeholder groups with different engagement needs. Issues to be considered included:

- Patients' motivations – quality of life, survival, altruism. Patient stories could be very helpful in demonstrating value to a prospective trial participant, but there have been difficulties with getting PIs to ask patients if they will share their experiences. There are also time constraints in clinic, and the patient population is often too sick.

  To date reasons for declining an offered trial include: preferring standard-of-care treatment; preferring other treatments; wanting to start chemotherapy immediately; travel; declining all treatment.

  How do we better understand and speak to patient motivations?

- HCP, Research nurses – need to have a clear understanding of Precison-Panc trials. What do RNs need to have better conversations on Precison-Panc trials?

- GPs and oncologists – Not everyone is familiar with the complexity of pancreatic cancer and not everyone agrees on the best treatment options for patients. Often healthcare professionals have neither the time to search for, nor explain about, trials. How can healthcare professionals be supported in this?

- General public – there is a general lack of health literacy, and a lack of awareness of the role of the pharmaceutical industry, research and trials in the development of new drugs, and of pancreatic cancer and its poor prognosis.

Roundtable discussion of communications and health literacy focused on:

a) What needs to be communicated to patients regarding the Precision-Panc trials, and at what stage? Why is the programme presented as it is? Why is it complex/so hard to understand?

Chris McDonald (PCUK) asked if an "expanded access programme" (as discussed below) could just be a programme of different kind of treatments that you can enter, and within that, if we find that a patient has the inclusion criteria for PRIMUS 004, for example, and then you can slowly build their treatment narrative. 'The point of entry in this case would be really simple, "Do you want to join this programme and if you do, you'll have a suite of different options and treatments that will be tailored to you? For this you need to give a sample."' Note: if the entry point to Precision-Panc was the giving and sequencing of a sample, this would require extra funding of £750 per person as currently only a specific amount of sequencing is covered in the research grants.

Ali Stunt (PCA) asked how practical questions were being dealt with, such as 'How do I get the bus? How do I get my refund? Is it a symptom? How easy is it to do the trial? Is there parking? How often do I have to come? How's this treatment going to make me feel?' Ali spoke about the usefulness of web-based patient resources for each centre, with an interactive pop-up map. As part of their interaction, the nurses or the clinicians could use a tablet to show the patient the nearest centre, and perhaps print out a fact sheet for that particular centre that gives all the logistical information. (Note the need to bear in mind technical difficulties within the NHS). She also said the conversation about trials should be revisited over time, so that if people have symptom control, then that conversation could begin again a week or two down the line.

b) The sheer quantity of information and paperwork involved, and the need for ethics approval for patient-facing trial information. Should a one-page summary be offered first?

Juan Valle (UoManchester) spoke about the ethics committee model for up to 20 pages of information for each clinical trial and suggested a one-page summary at the front. He said that, 'We can work to fine-tune our approaches and make sure that the people who are getting engaged, stay engaged and are then are recruited into clinical trials. But there is a much bigger population who just are not eligible or are just never offered a clinical trial.'

c) **Consideration of a patient's ability to take in new complex information. Do they have a diagnosis, are they newly diagnosed? How to keep a patient involved? The need for an audit of why people do and don't participate, why they drop out.**

Chris McDonald (PCUK) said that there were too many assumptions around the patient interaction and that a piece of work was needed to understand patient motivations and their priorities. He said that, 'A patient information sheet shouldn't be an engagement tool and it is often used as that. Currently we are trying to explain a really complicated trial to people in order for them to then participate. How do we begin them on a journey, rather than just handing them a patient information sheet?'

d) **Identifying who says what to patients and when – the medium used depends on who is introducing the idea.**

Lynne McCallum (PCUK) raised the issue of the importance of personalisation at the first interaction and staging or layering the information. She said that, 'The initial conversation is critical. People can make a decision about whether they're going to have treatment or not by how they feel right now. So when we're talking about symptom control, they say "I feel crap now. This is how I'm going to feel forever. I don't want treatment." So we need to tailor the information. If they're feeling "crap", you mention this much and then you see them in two weeks and if they're feeling better, you mention this much. And you signpost them into this.'

e) **The need for stakeholder mapping to develop a strategy for each group. The need for a common lexicon.**

There was recognition of health literacy and literacy issues, with some areas have as many as 50% of patients from areas of deprivation.

f) Normalising the discussion for MDTs, HCPs, and especially research nurses.

Juan told the Roundtable that feedback is that everybody, including clinicians and scientists, find the trial information difficult and complicated. He said that, 'We're currently relying on individual research teams, and different individuals within those teams, to understand Precision-Panc and then to be able to communicate it to the patient. We have a complex programme explained to patients with varying capacities to understand, by different people who also have different levels of understanding.' The information at the clinician/researcher/HCP level needs to be consistent and clear. This is potentially where video (aimed at staff, therefore not requiring REC approval) might be useful.

Juan suggested that at the MDT level, this needs to be a "normal" conversation and he considered the best groups to target were surgeons and gastroenterologists linked to pancreatic

cancer MDTs. 'If they really understood Precision-Panc, they would want to be involved and would be helpful in getting biopsies etc.' He said that these groups were a priority, more so than oncologists, because they are, effectively, gatekeepers and the ones making the first diagnosis.

David Chang (UoGlasgow) asked how we engage the clinicians or the researchers who are already involved in Precision-Panc and make it a continuous engagement, and also for the other HCPs. He suggested the forming of working groups for improved sharing of information and ideas.

Helen Staiger (Christie) explained that research nurses usually see the patients in a dedicated new patient clinic where everybody's been triaged for potential recruitment, so when the nurses get to meet them, they may be three or four down the line, so they're already in an overwhelmed situation. They've already seen other trials people for nutrition studies and quality of life and it has already been very challenging for them, to say the least. Explaining about trials is difficult when they're in that situation and the hardest part is not frightening them. She said that 'Anything to simplify things would be a great improvement. We're just overwhelmed ourselves about how to get this across, so we need to have a lot more input with people, not just the phone call that we normally do, or hand them some information. It's better to say that, "I can see you've had a lot of information today and we'll follow this up".'

Clare Dickinson (CRUK) said there was a need to get HCP/clinicians to recognise that trials are a treatment option, not an add-on that the patient is too unwell to take part in.

Lynne McCallum (PCUK) said that everyone should have a base knowledge, recognising that the patient isn't necessarily going to ask the right person the right questions, so they're able to talk about Precision-Panc at the beginning of people's journey. The national HPB nurses group is a key resource. Lynne indicated that the specialist HPB nurses still don't understand Precision-Panc on the whole and, as one of the primary interfaces with patients, particularly needed to be engaged.

Information needs to be consistent for HCP and researchers and working from that base, personalised for patients.

g) The need to raise the public profile of the programme and to broaden engagement around the idea that trials can be a treatment option.

What are the demographics that most urgently need to be reached, now and in the future, and what is the best medium of communication? The profile-raising work of patient organisations is critical to this.

h) The best medium for the message

There is a need for consistent messaging, possibly via video, for HCP and the public, but there is a need for a personalised message for the newly diagnosed patient; infographics of the patient journey and patient stories. The appropriateness of video/electronic media needs to be considered at different stages of the patient journey. Could the PCA patient app be utilised? Apps could be used to stay in touch and answer questions, but it was recognised that the initial conversations are critical. Ali Stunt also pointed out that not-for-profit organisations can receive a grant from Google to help with Adwords in terms of profile raising. Ged Brady (UoManchester) mentioned AstraZeneca's e trials and digital ECMT might have expertise to offer. There is also the potential in apps for misinformation and frustration in an anxious user.

Vernon Bainton (Havas Lynx) reminded Roundtable participants that community management is

extremely time consuming and that consideration should be given to resources and hiring people. He said there are opportunities to automate certain aspects of the conversation and that there are multiple solutions depending on time and cost.

PCUK, PCA, PCS and PCRF offered to disseminate Precision-Panc material. PCA has offered to put an insert into their GP resource pack.

2. Resource and regulatory issues

This topic covered the practicalities of what stops a site from activating after agreeing to open, and once open, what difficulties might exist in recruiting once a site is active.

There are now more than 200 patients on the Precision-Panc Master Protocol across 24 sites (with another nine sites in setup). While there are 24 sites open, there are still issues around activation and once active, how many patients are recruited.

Even though every trial now requires HRA approval, which is supposed to accelerate opening a site, all sites still have to review the trial at a Trust level to ensure they have the capacity and capability to undertake the project. This is normally managed by the local Research and Development Department. These teams are usually reasonably small and there can be resource issues. Another impacting factor can be Research Nurse (RN) availability and capacity. A keen Principal Investigator/ RN will ensure all the required study documents are completed to allow the study to open in a timely manner, often in liaison with local clinical trial administration teams.

Professor Juan Valle suggested having a nominated Precision-Panc "champion" within each MDT and empowering that person to be able follow through. Juan also suggested establishing a rapid setup task force at new sites where familiarity with the submission and regulatory process could both speed initial set-up (prior to handing over to the local team) and resolve difficulties.

Staffing issues can really impact site activation, and even when a site is opened, which can take some 3-12 months, if there are insufficient resources (research nurses and/or clinical trial coordinators) this in turn impacts on recruitment to trials. There is also lack of pharmacy staff and lack of space for patients in chemo units.

It was felt there was a need for more research nurses dedicated to the programme. A research nurse dividing his/her time between various trials programmes tends to be suboptimal in the case of Precision-Panc where information and issues can be complex.

Other resource issues included the need for extra funds if there was to be the possibility of testing all biopsies, as the current research grants don't cover this. There is also the question of assisting with transport/accommodation costs for patients. Patient expenses are not included in the grant. However, as this becomes part of the normal standard of care, this will be less of an issue.

Ali Stunt (PCA) spoke of the need for a UK-wide audit of pancreatic cancer services as a baseline from which to judge improvement; where they're diagnosed, who diagnosed them, where they're referred to, how many have surgery followed by chemotherapy, how many having chemotherapy, how many going on clinical trials. She said this had been done for lung cancer with Public Health England. Fiona Brown (PCS) indicated that there is some audit work being done in Scotland and that PCS would share the results. There were difficulties, however, in how different hospitals record the information and a lack of consistency.

3. Expanded access programmes

Andrew Biankin (UoGlasgow) told the Roundtable that we can never test for every cancer therapeutic the way we do clinical trials now, particularly for early drug development, and especially not for pancreatic cancer.

One of the major obstacles in preventing people with pancreatic cancer having access to trials is the stringency of inclusion and exclusion criteria. So perhaps another way of accessing new therapeutics, beginning with less-common and high-mortality cancers, such as pancreatic cancer, is to allow patients to safely access novel therapeutics and collect robust data as part of routine healthcare (as opposed to simply giving people off-label treatments and learning nothing collectively from the experience). This would allow testing of multiple novel therapeutics and combinations to identify signals of efficacy and define a "line-of-sight" for a randomised study.

In this discussion "expanded access" encompasses many mechanisms of accessing novel therapeutics including "Name-Patient Access", "Compassionate Use" or "Early Access to Medicines"), importantly, with the acquisition of data on safety and efficacy and may be:

- A licensed drug (eg for thyroid cancer) used for an unlicensed indication (eg pancreatic cancer);
- An unlicensed drug used in an unlicensed indication. These are highly regulated by regulatory authorities and have a high level of safety reporting; or
- A drug being tested in pancreatic cancer, but being used in a wider population than the tight inclusion/exclusion criteria set out in a study protocol.

This type of expanded access concept is essentially accessing the benefits of a clinical trial, without running a clinical trial for both patient and drug developer. This kind of expanded access doesn't require the same EMA or FDA regulatory approval, but it allows us to acquire data in a reliable way that generates value to the patient by offering them novel therapies, and to pharma through robust data, which could be used to support regulatory submissions.

Drug developers have tight inclusion/exclusion criteria so as to only have the best performers as trial patients, but in pancreatic cancer we don't have many patients that are "athletes". An expanded access programme allows the inclusion/exclusion criteria to be substantially relaxed because there is reduced risk for the drug developer as an expanded access programme is not a trial. However, if the drug developer is running a trial with the same drug and sees the same signal or the same efficacy in the expanded access programme, they can also include that data for regulatory filing, expanding the label, and also benefitting patients who may not receive the drug in practice.

Precision-Panc could incorporate an **expanded access programme**, or maybe just include off-label therapies where we record important information and data, which is essential for therapeutics developers as well as research. Formal clinical trials aren't essential to capture good information for drugs in early development.

For Precision-Panc we need to consider if we just want trials, or if we want access for treatments for our patients?

'We want to be able to make this work for everybody who has cancer and Precision-Panc is the first step in doing this. We're just signing with a company called MyTomorrows which is helping us access therapeutics for Precision-Panc, whether it be expanded access, a clinical trial, or off-label therapeutics. They are also offering to help find patients, not just in the UK but also across Europe.

'This is a new model of healthcare, cancer care and delivery and is something that we can do as Precision-Panc within the next five to ten years. Somebody's got to do it and we have the opportunity and the urgency. Just to motivate us, **one person dies every hour in the UK of pancreatic cancer.'**

Next steps:

- In conjunction with PCUK, PCS, the national HPB nurse group, and the PPAG, the Precision-Panc team is working on the first stage of a communications/health literacy project to analyse and improve the critical first interaction between research nurses and patients. To support this, a single sheet explainer is being developed as a basis for discussion. This exercise will serve to establish areas where research nurses need more information and how that is best communicated to patients. Further materials, including short summaries, will be developed with this basis in mind. More to come.
- Identify a Precision-Panc champion within each HPB MDT.
- Look at resource of setting up a Rapid Task Force for study set-up
- Where resourcing of research nurses or clinical trials coordinators is an issue, would it be possible for sites to seek funding for additional resource from the patient organisations?
- If patient accommodation or transport is an issue, would the patient organisations consider funding for the patients on an individual basis?
- Investigation of the expanded access concept with MyTomorrows. More to come.
- PCUK, PCS, PCA, PCRF to signpost patients to Precision-Panc as appropriate.