PARTICIPANT INFORMATION SHEET

Study Name: SAFE-D

Surveillance of pAncreatic health aFtEr Diabetes diagnosis

Help us improve early pancreatic cancer detection to save lives

(**Chief Investigator**: Mr Zaed Hamady, **Sponsor Reference**: RHM GSU0292, IRAS: 326332)

You have been invited to take part in a clinical study, aimed at detecting pancreatic cancer earlier to save lives. To help you decide if you would like to take part, it is important that you understand why the research is being done and what it will involve. Clinical studies only include people who choose to take part.

Please read the information below carefully and ask questions if anything is not clear or you would like more information before you decide whether or not to take part in this research. You can also discuss your decision with your friends and family.

Figure 1. A doctor talking with a participant

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1. What is the purpose of the study?

Pancreatic cancer is often detected when it is at an advanced stage and very difficult to treat successfully. Early diagnosis is therefore key for better survival rates. Patients recently diagnosed with type II diabetes have a higher-than-normal risk of developing pancreatic cancer. In the UK, the lifetime risk of being diagnosed with pancreatic cancer is around 2%. Of these, 1 in 4 people are first diagnosed with diabetes. This is due to pancreatic cancer affecting the insulin producing cells in the pancreas.

There is currently no approved screening test for pancreatic cancer. ClearNote Health, USA, has developed a new pancreatic cancer test called Avantect. The test detects the presence or absence of pancreatic cancer in blood, but no screening test is 100% reliable. SAFE-D is a so called single-blinded, randomised study that aims to show how well the Avantect test works on early detection of pancreatic cancer in individuals newly diagnosed with type II diabetes. Blood samples, and clinical and participant reported data will be collected from individuals with new onset type II diabetes to see how well the Avantect test performs in detecting pancreatic cancer at an early, treatable stage.

2. What is a "single-blinded, randomised study" and why is this needed?

In a randomised study, participants are randomly assigned to one or more study paths, or arms, in which treatments differ. “Single-blinded” means that the participants will not know which arm they have been assigned to.

The SAFE-D study aims to find out if the new Avantect test can be used as a monitoring aid to detect and treat pancreatic cancer when it is at an earlier more curable stage. To find this out, we therefore need to compare patients who follow current standards of care with those who also will have their blood tested on the Avantect test. We will randomly assign half the study participants to the Control Arm, (following standard of care), and half to the Intervention Arm, (in which participant’s blood samples will be tested on the Avantect test as soon as possible).

If you are assigned to the Intervention Arm and a cancer signal is “detected” with the Avantect test, you and your GP will be informed, and the SAFE-D team will arrange for a follow up MRI or CT scan which would help to rule out a pancreatic cancer diagnosis.

Participants who do not receive a test result from the SAFE-D research team have either a non-actionable “not detected” Avantect test result (Intervention Arm) or have been allocated to the Control Arm where samples are not tested. Therefore, it is really important you continue to monitor your own health as normal and inform your healthcare provider of any issues.

All participant samples and related clinical data will provide us with a wealth of information that will help us establish if the Avantect test can be used as a reliable screening test for individuals with new onset of type II diabetes in the future, as well as helping us understand and treat pancreatic cancer patients better.

3. How many people will take part in the study?

In the first instance we are recruiting up to 800 people into a 6-month-long Pilot study to assess how best to engage and recruit participants. If this Pilot study proves successful,

following that, we will expand recruitment into a larger study that may involve up to 15,000 people.

4. Why have I been chosen?

You are being asked to take part in this study because you are between 50 and 84 years of age and have been diagnosed with type II diabetes in the last 6 months and are, therefore, at increased risk of having pancreatic cancer that has not yet caused symptoms.

5. Do I have to take part?

No, your participation is voluntary. It is up to you to decide whether or not to take part. If you decide not to take part, it will not affect the standard of care you receive.

6. What will happen to me if I take part?

If you decide to take part in this study, you will book an appointment through our website to attend a clinic at your local participating study site to discuss the study in more detail. Before deciding whether to take part in the study, you will have the opportunity to discuss it with your family and friends as well as your medical team. If you choose to take part, you will be asked to sign a consent form and provide a blood sample and medical information.

Following the initial research appointment, you will be asked to attend two further follow up research appointments at 6 and 12 months at your local participating study site. The purpose of these visits is to increase the chances of detecting pancreatic cancer if present.

The study visits will be additional to the medical appointments you attend for review and management of your diabetes. If you are in the Interventional Arm and if a cancer signal is detected in your blood sample, both you and your GP will be notified. A clinical pancreatic imaging scan will be arranged at a local hospital to determine if you have pancreatic cancer. This will be arranged by the SAFE-D team at the location you have attended for the study visits.

7. How long will the Research Appointments take?

Your initial research appointment will take **up to 1 hour**.

At this initial appointment you will sign the consent form and details about your health and medical conditions will be collected before up to 30 mL (about 2 tablespoons) of your blood will be taken from your vein by a trained professional. You will also be asked to complete a short health questionnaire in relation to your medical history and quality of life which will help us better understand the study impact.

The follow-up visits will take approximately **30 minutes each**.

Over the next 12 months you will have another two follow up appointments, at around 6 and 12 months after your first appointment, where the research team will review your medical history and up to 30 mL blood (around 2 tablespoons) will be collected. You will be asked to complete the same questionnaire that you completed at your initial visit. It is important that you tell the research team about any changes to your health since your last visit.

A schedule of what will happen at each research visit is below:

	Initial Research Visit	***6 months Research Visit***	***12 months Research Visit***
Completion of consent Form	✓		
Blood collection	✓	✓	✓
Completion of Questionnaires	✓	✓	✓
Collection of Medical Information	✓		

On up to 3 occasions, over the duration of the study, we will collect your data from the cancer and mortality registries to see if you have been diagnosed with any cancers, details of any treatments for those cancers, and confirmation that you are still alive. You will not need to attend an appointment, and we will not need to contact you for this. However, with your permission we would like to contact some of our participants to gather more information relating to the health questionnaire.

8. What will happen to my blood sample?

Your blood samples will be transferred to the University Hospital Southampton Wessex Investigational Sciences Hub (WISH) for processing and storage. From there, a portion of the blood samples collected from each patient randomised to the Intervention Arm will then be sent to ClearNote Health laboratory (San Diego, USA) for Avantect testing as soon as possible. With your permission, all other samples will remain at the WISH lab for potential future testing or research. All samples will be with be labelled with a participant specific ID number to protect confidentiality.

We will take great care looking after your blood sample, however, should unforeseen issues happen during for example transport, processing, or analysis, we may contact you to ask for a repeat blood sample to be collected.

9. What are the possible disadvantages and risks of taking part?

Risks related to blood being taken: this is very rare. There may be some minor but short-term discomfort/bruising when providing a blood sample; you may experience a scratching sensation as the needle goes in.

Risk related to Avantect: similar to other screening tests, with Avantect testing there are risks related to false positive and false negative results. False negative results would not detect pancreatic cancer and could cause false reassurance, thereby delaying diagnosis and treatment. Therefore, regardless of your participation in this study it is important you continue to monitor your own health as normal and inform your healthcare provider of any issues. False positive results may lead to imaging of your pancreas when in fact, no pancreatic cancer is present. We only expect a small percentage of false positives. If we happen to find something unexpected when your pancreas is scanned, like cancer in another organ or a serious but non-cancerous condition, we will let you and your GP know, and your GP will arrange for any further investigations or treatments if needed. In such situations, it is possible that you may be referred for further scans.

Risk related to MRI: subjects assigned to the interventional arm with an Avantect "detected" result, will be asked to undergo an imaging scan, such as an MRI scan, which similar to an x-ray takes a detailed picture of your pancreas to check for abnormalities. You may experience some discomfort during the process. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel "closed in" and become anxious while in the scanner. The magnetic field used in MRI scanning may harm people who have metal in their bodies (pacemakers, neurostimulators, certain clips, or staples from surgery).

MRI uses a contrast dye called gadolinium that may cause skin irritation, bleeding, and/or infection. The dye may increase the risk of a rare kidney disease for people with pre-existing kidney failure. In rare cases, an allergic reaction to the contrast agent might occur. If you are medically unable to undergo an MRI, we may be able to offer you a CT scan instead.

Risk related to CT: If you take part in this study you may have CT pancreas scans. All of these will be extra to those that you would have if you did not take part in the trial. These procedures use ionising radiation to form images of your body. Ionising radiation may cause cancer many years or decades after the exposure.

We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study will increase the chances of this happening to you by about 0.4%."

CT scans also use the contrast dye gadolinium and could cause rare allergic reactions. This scan may also detect other incidental findings, such as cysts that are not cancer, and may require attention. A CT scan is not designed to rule out other cancer beyond the pancreas.

10. What are the possible benefits of taking part?

Participating in this study may help improve care for people with new diagnosis of type II diabetes by detecting pancreatic cancer early when it is still curable. If you are randomly assigned to the Intervention arm, you could learn if you are identified to have an abnormal signal that has been associated with pancreatic cancer which will help you to undergo further assessment or treatment after the study. The data we get from you will help future patients and may also help doctors to know how Avantect could help other patients at risk of pancreatic cancer.

11. How will you use information about me?

We will need to use information from your medical records, your GP and the cancer and mortality registries (currently managed by NHS England but this may change over time) for this research project. This information will include

- your name
- address
- sex at birth
- NHS number
- contact details (phone number, email)
- date of birth

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be

able to see or use your personal information, including name or contact details. Your data will have a code number instead.

University Hospital Southampton NHS Foundation Trust is the sponsor of this research, and is responsible for looking after your information. We will keep all information about you safe and secure by: -

- We will protect your identity by using a study specific code number instead of any identifiable information.
- We will keep all information about you in an access restricted database for the duration of the study.
- Only delegated and trained research staff will have access to your information.

International transfers:

We will need to share your coded data and limited personal data (age at blood draw and sex) outside the UK for research related purposes to: -

- enable ClearNote Health to run their Avantect pancreatic cancer tests
- store study data safely and securely in the access restricted database hosted by Medidata Solutions on US servers
- to verify how well the Avantect test is performing

As in the UK, we only share the data that is needed. We will also make sure that you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

- Data storage organisations such as Medidata Solutions
- ClearNote Health, based in San Diego, US
- IRB/IEC (Institutional Review Board/Independent Ethics Committee), a US agency responsible for reviewing and approving clinical studies and ensuring the research projects are ethical and protect their participants ethical approvals
- The US Food and Drug Administration (FDA), responsible for keeping research safe

Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is protected and safe outside the UK by doing the following:-

- We use specific contracts approved for use in the UK which give personal data the same level of protection it has in the UK. For further details visit the Information Commissioner's Office (ICO) website
- We do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says
- We need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing

The blood samples you have provided at study visit will be shipped outside the UK.

Once we have finished the study, we will keep the collected data for up to 15 years so we can check the results and publish our findings. We will write our reports in a way that no-one can work out who took part in the study. The study data will then be securely archived or destroyed.

12. How will you store information about me?

University Hospital Southampton NHS Foundation Trust is the sponsor of this research and is responsible for looking after your information. We will keep all information about you safe and secure by:-

- Storing it in an access restricted database (Rave) or access restricted folders on the University of Southampton server.
- All collaborators, as data processors, both in the UK and abroad, must strictly adhere to UK GDPR laws which ensures that your coded and personal information is stored securely.

13. Can I access the information about me?

You will not be able to access, change or move your information, as we need to manage your information in specific ways in order for the research to be reliable and accurate. To safeguard your data, we will use the minimum personally identifiable information possible.

You can find out more about how we use your information:

- by visiting the study website [www.ctu.soton.ac.uk]
- by asking one of the local SAFE-D research team (contact details for your local SAFE-D team can be found via links on the study website)
- by sending an email to dataprotection@uhs.nhs.uk or
- by ringing us on 023 8120 5079
- by visiting https://clinicalresearch.uhs.nhs.uk/for-researchers/data-protection
- by visiting the HRA link: www.hra.nhs.uk/patientdataandresearch

14. What will happen if I don't want to carry on with the study?

You can decide to stop participating in the study at any time, without giving a reason. If you no longer want to remain in the study, please inform the research team. This will not affect the standard of care you receive. If you withdraw from the study, you will no longer attend study-related visits.

You will be asked if you will be specifically withdrawing from the following:

- All further participation in the study including any further follow up.
- Withdrawal of consent for further visits and follow up and the use of any remaining samples obtained in the study.

Where possible, we will destroy the samples you have provided if that is your wish. If not possible, we will tell you why we cannot do this. We will not be able to remove data about you that we have already collected as this is required to protect the validity of the study.

In the unlikely event that you lose the capacity to consent to remain in the study, you will be withdrawn from it. Data and samples you have provided prior to that point would be retained and used confidentially for the purposes for which consent had been originally provided.

15. Future Research

With your permission we would also like to keep any samples left over from this study and use these in other future research studies or diagnostic test development to increase our understanding of diseases and how to treat patients better. We thereby maximise what we can learn from your donated blood samples. For this we may send scientists at other organisations, including private companies located within the UK or abroad, part of your donated sample for analysis at collaborator's laboratories, which may include genetic analysis. At present we cannot know what these future studies specifically may look at. What we do know is that the use of your blood sample in these future studies will only be carried out following independent ethical review and approval.

For the same reason, with your permission we would also like to keep your coded medical data, including MRI or CT scans (if applicable). The use of your coded data in these future research studies will only be carried out for the duration of those new studies and only following independent ethical review and approval. For these future, approved research studies we may grant scientists at other organisations, including private companies located within the UK or abroad, access to your coded collected data. All future collaborators, in the UK and abroad, must adhere to UK GDPR and keep your coded and personal information safe.

16. Involvement of your GP

With your permission, your Family Doctor, General Practitioner (GP), will be informed of your involvement in the study. Should any unexpected medical findings be identified as a result of taking part in this study these will be shared with you and your GP.

17. What happens when the research study ends?

After the research study ends you will continue being managed for your diabetes as usual by your own clinicians. If you have any ongoing concerns following the completion of this research study, please discuss these with your doctor.

18. What will happen to the results of the research study?

Once the study is complete a formal report will be written, and the results will be published to make them available to the public. Throughout the study, we will post regular study updates and progress on the SAFE-D website [www.ctu.soton.ac.uk] and at the end of the study we will also post a plain English summary report on the SAFE-D website as well as the Southampton CTU website. You will also be able to request a plain English summary report at the end of the study by emailing the SAFE-D CI and study team on SAFEDCI@soton.ac.uk. You will not be named or identified in any publications or study updates.

19. What rights do I have to the results of the research?

Any information derived directly or indirectly from this research, as well as any patents, diagnostic tests, drugs, or biological products developed directly or indirectly as a result of this research may be used for commercial purposes. We can't give you any rights to this property or to any share of the profits that may be earned directly or indirectly as a result of this research.

20. Who is organising and funding the research?

University Hospital Southampton NHS Foundation Trust is the sponsor of this study and is partnering with ClearNote Health, a private company that markets the AVANTECT test and who will be the main funder. The study will be run by Southampton Clinical Trials Unit.

The study has also been reviewed by patient and public involvement (PPI) representatives and the East Midlands – Leicester South Research Ethics Committee has given a favourable opinion of the study.

21. What if there is a problem?

If you have a concern about any aspect of this study, please contact;

- your local SAFE-D research team (contact details for your local SAFE-D team can be found via links on the study website [www.ctu.soton.ac.uk])
- the Chief Investigator on SAFEDCI@soton.ac.uk.

If you remain unhappy and wish to complain formally, you can do this through NHS Complaints Procedure, via the Patients Advice and Liaison Service (PALS). PALS can provide confidential, impartial advice regarding concerns and complaints. PALS helps to improve the NHS by listening to your concerns and suggestions.

Please be aware that if you are harmed as a result of taking part in the Safe-D trial, there are no special compensation arrangements. University Hospital Southampton NHS Foundation Trust provides clinical trials indemnity insurance for negligence in its management or design of the trial. If you are harmed because of someone's negligence, you may be able to take legal action, but you may have to pay your own legal costs.

The contact details for University Hospital Southampton NHS foundation Trust PALS Office are as follows:

Patient Support Services C Level Centre Block Mailpoint 81
Southampton General Hospital Tremona Road
Southampton SO16 6YD
Tel: 023 8120 6325 or Email: patientsupportservices@uhs.nhs.uk

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Thank you for taking the time to read and consider this information sheet. Should you decide to take part in the study, you will be given a copy of the information sheet and a signed consent form to keep.