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Evaluation of a novel blood test (Avantect) detecting signals of the presence of pancreatic cancer early in patients recently diagnosed with type 2 diabetes

Submission date
27/01/2025

Recruitment status
Recruiting

Registration date
28/01/2025

Overall study status
Ongoing

Last Edited
19/03/2025

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Pancreatic cancer is often detected when it is at an advanced stage and very difficult to treat successfully. Early diagnosis is key for better survival rates. People with newly diagnosed type 2 diabetes have a higher-than-normal risk of being diagnosed with 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 cells in the pancreas. The aim of the study is to find out if the new experimental blood test called Avantect can be used as a monitoring aid to detect and treat pancreatic cancer at an early more curable stage.

Who can participate?
Males and females 50-84 years old who have been diagnosed with type 2 diabetes within the last 6 months

What does the study involve?
Participants will be allocated at random into the intervention group or the control group (following the standard of care). The participant will not know their allocation in the study. Participants in the intervention group will have their blood samples tested on the Avantect test as soon as possible, where “detected” results will be shared with participants and their General Practitioner to allow for further diagnostic investigation (MRI or CT scan). Participants in the control group will receive the current standard of care for diabetes management, and their blood samples will be used for potential future Avantect testing and/or future research. Participants will attend three study visits during a 12-month period, and provide a blood sample (30 ml) at each visit.

What are the possible benefits and risks of participating?
Benefits:
Improving care for people with a new diagnosis of type 2 diabetes by detecting pancreatic

cancer early when it is still curable. If allocated to the intervention group participants will learn if the Avantect test has returned a “detected” result suggesting the possible presence of pancreatic cancer, and will have the opportunity to undergo further assessment or treatment at an earlier stage when more treatable. Data collected from the study will help doctors better understand how the Avantect test can help identify people at risk of pancreatic cancer in the future.
Risks:
Related to blood being taken – very rare, minor and short-term bruising/ discomfort or scratching sensation when the needle goes in.
related to the Avantect test – possible false positive or false negative results. False-negative results would not detect pancreatic cancer and could cause false reassurance, delaying diagnosis and treatment. False positive results may lead to imaging of pancreas when no pancreatic cancer is present. Only a small percentage of false positives is expected. In the event of incidental findings, the participant would be informed of such findings and any follow-up recommendations.
Related to MRI – Participants may experience some discomfort. 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 the MRI is contraindicated, participants would receive a CT pancreas scan instead.
Related to CT scan – ionising radiation may cause cancer many years or decades after the exposure. 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 which could cause rare allergic reactions. Scans may also detect other incidental findings, such as cysts that are not cancer and may require attention.

Where is the study run from?
Primary Care – GP practices and Specialist Diabetes Service Centres (UK)

When is the study starting and how long is it expected to run for?
February 2023 to February 2032

Who is funding the study?
ClearNote Health (USA)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
326332

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 56822

Study information

Scientific Title
SAFE-D: Surveillance of pAncreatic health aFter diabEtes Diagnosis: a randomised trial to evaluate the cfDNA pancreatic cancer test (Avantect) in the early detection of pancreatic cancer in patients with newly diagnosed diabetes mellitus

Acronym
SAFE-D

Study objectives
A new diagnostic blood test (Avantect) is able to detect pancreatic cancer early in patients diagnosed with type 2 diabetes in the last 6 months.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/02/2025, East Midlands - Leicester South Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8193/+44 (0)207 104 8079; Leicestersouth.rec@hra.nhs.uk), ref: 25/EM/0016

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Diabetes

Interventions
This is a prospective, single-blinded interventional randomised multicentre study. Blood samples will be collected at three separate timepoints over 12 months to evaluate the Avantect pancreatic cancer test. State-Trait Anxiety Inventory (STAI) questionnaires and routine clinical data will also be used for the study. The study will initiate with a 6-month pilot phase recruiting up to 800 participants to assess recruitment feasibility and strategies, followed by Stage 1 (recruiting an additional 5,600 participants) and Stage 2 (recruiting an additional 8,600 participants).

Aims:
To determine:
1. Whether it is feasible to recruit individuals diagnosed with type II diabetes within the last 6 months to a clinical trial investigating a novel diagnostic blood test for pancreatic cancer at a

fast enough rate (Pilot)
2. Whether the sensitivity and specificity of the Avantect test are sufficient, and that its use results in an acceptable improvement in the proportion of diagnosed pancreatic cancers that are considered resectable (stage I/II)

Where the research will take place:
In Primary Care setting: Up to 3,000 GP practices and up to 200 Specialist Diabetes Service Centres (SDSC).

Identification and approach:
Participants will be identified at Patient Identification Centres (PICs). These will be GP practices or SDSCs where newly diagnosed diabetic patients are referred to for support and education sessions. Staff at GP practices will search patient electronic health records (EHC) and SDSCs staff will screen available SDSC medical records for eligible patients. Participants will also be identified by the commercial platform (EMIS) that will search EHCs at their connected GP practices. Suitable potential participants will be invited to the study by text message, email or letter with a link to the study website where they can access more study information, the Patient Information Sheet, contact details for the research team and the booking system for selecting a convenient location for the first study visit. The study will be advertised at participating GP practices and SDSCs, and promoted within diabetes and pancreatic cancer communities.

Research visits:
Baseline (T0) – within 6 months from type II diabetes diagnosis
Participants will attend the first research visit at a location of their choice (GP recruitment hub, NIHR Research Delivery Network recruitment hub or SDSC hub) where they can discuss the study further with a member of the research team before consenting to take part. Blood samples (up to 30mL) will be collected from the participant, medical history and short State-Trait Anxiety Inventory (STAI) questionnaire completed, and height, weight and waist measurements taken. The next study visit (T1) will be booked with the participant via the online booking system on the SAFE-D study website. After the visit, blood samples will be shipped to the WISH Laboratory in Southampton, where patients will be randomised to the intervention or control arm of the study and the sample processed and stored.

T1 – 6 months from T0
Participants will attend the T1 research visit, where blood samples (up to 30 ml) will be collected, medical history and short STAI questionnaire completed, and weight and waist measurements taken. Eligibility will be re-confirmed, and in case participants have been diagnosed with any cancer since the last visit, they will be withdrawn from the study. The next study visit (T2) will be booked with the participant via the online booking system on the SAFE-D study website. After the visit, blood samples will be shipped to the WISH Laboratory in Southampton for processing and storage.

T2 – 12 months from T0
Participants will attend the T2 research visit, where blood samples (up to 30 ml) will be collected, medical history and short STAI questionnaire completed, and weight and waist measurements taken. Eligibility will be re-confirmed, and in case participants have been diagnosed with any cancer since the last visit, they will be withdrawn from the study. After the visit, blood samples will be shipped to the WISH Laboratory in Southampton as above.

T3-Follow up (36 months from T0)
On 3 occasions during the study, the study team will remotely collect data from the cancer

registry and mortality registry to see if participants have been diagnosed with any cancers, record details of and treatments for those cancers, and confirm whether participants are still alive. On these three occasions, only registries for patients within the 36-month follow-up period will be searched. Patient will therefore have up to 3 registry searches during their study participation. With permission, we will also contact some of our participants to gather more information relating to the health questionnaire.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
1. The sensitivity of the Avantect test in detecting PC is measured as the percentage of participants with PC diagnosed who have an Avantect “detected” result (within the intervention arm) at 6 months after T1, and after 3-year follow-up data has been collected for all participants.
2. Specificity of the Avantect test in ruling out PC is measured as the percentage of participants without PC diagnosed who have one or more Avantect “not detected” results and no Avantect “detected” results (within the intervention arm) at 6 months after T1, and after 3-year follow-up data has been collected for all participants.
3. The resectability rate of PC is measured as the percentage of PCs deemed resectable by the study MDT (compared between arms) at 6 months after T1, and after 3-year follow-up data has been collected for all participants.

Secondary outcome measures
1. Pancreatic cancer stage shift is measured as the percentage of PCs diagnosed at stage I/II (compared between arms) at 6 months after T1, and after 3-year follow-up data has been collected for all participants.
2. Positive Predictive Value (PPV) of the Avantect test for detecting PC is measured as the percentage of individuals with an Avantect “detected” result who have PC diagnosed (within the intervention arm) at 6 months after T1, and after 3-year follow-up data has been collected for all participants.
3. Negative Predictive Value (NPV) of the Avantect test for ruling out PC is measured as the percentage of individuals with no Avantect “detected” test results who have no diagnosis of PC (within the intervention arm) at 6 months after T1, and after 3-year follow-up data has been collected for all participants.
4. Resection of PC is measured as the percentage of individuals with PC who underwent resection (compared between arms) at 6 months after T1, and after 3-year follow-up data has been collected for all participants.

Overall study start date
28/02/2023

Completion date
29/02/2032

Eligibility

Key inclusion criteria

1. 50 – 84 years of age at the time of enrolment (within a year of birth, not month of birth)
2. Haemoglobin A1c (HbA1c) >=48 or 6.5% and/or confirmed type II DM diagnosed within the last 180 days (+20 days flexibility allowance)
3. Willing to provide up to 30 mL of blood for each study visit
4. Willing and eligible to undergo MRI scan (or CT scan if MRI is contraindicated)
5. Understands the study process and is willing to take part in the study and sign the informed consent form

Participant type(s)
Patient

Age group
Mixed

Lower age limit
50 Years

Upper age limit
84 Years

Sex
Both

Target number of participants
Planned Sample Size: 15000; UK Sample Size: 15000

Key exclusion criteria
1. Prior type I or type II DM diagnosis >6 months
2. A history of pancreatic cancer, pancreatic neuroendocrine tumour (pNET) or Pancreatitis
3. Under investigation for pancreatic cancer/ pancreatic cyst
4. Any known pancreatic surgery (not including ERCP), or other major surgery requiring anaesthesia within 3 months
5. Any invasive solid or haematological cancer in the past 3 years, including cancer recurrence after treatment in the last 3 years
6. Current chronic or acute oral or systemic steroid use within 3 months of initial HbA1c or diabetes diagnosis (estimate rather than accurate)
7. Blood transfusion within 1 month
8. Solid organ transplant recipient
9. Currently pregnant
10. Needing dialysis

Date of first enrolment
03/03/2025

Date of final enrolment
29/02/2028

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

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+44 (0)2381205213
sharon.davies-dear@uhs.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.uhs.nhs.uk/home.aspx

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Industry

Funder Name

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
28/02/2033

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from the Southampton Clinical Trials Unit Data Sharing Release Committee (sctu@soton.ac.uk).
SCTU is committed to the responsible sharing of clinical study data and samples with the wider research community. Data access is administered through the SCTU Data Release Committee, which will consider requests once the final analysis has been published.

IPD sharing plan summary
Available on request