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Cancer detection by analysing non-invasively collected colorectal mucus

Submission date 07/11/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 15/11/2016	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 01/12/2022	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Colorectal cancer (CRC), also known as bowel cancer, is the third most common cancer. It is a global healthcare problem, causing almost 700,000 deaths worldwide every year. This disease usually affects people over the age of 50 and does not produce symptoms at its early stages. Very often CRC is detected too late to be successfully treated. Early detection of this cancer, especially through population screening, saves lives, but the existing tests used for this purpose are not sensitive enough or too expensive. DiagNodus Ltd has recently developed a new technique for collecting samples of colorectal mucus which can be used to measure the levels of chemicals called biomarkers and detect inflammatory bowel disease (IBD). As it is well known that CRC also produces dramatic changes in colorectal mucus, it is highly likely that CRC biomarkers can be found in this material as well. The aim of this study is to examine if the new approach devised by DiagNodus Ltd is suitable for detecting CRC.

Who can participate?
Patients aged over 45 with confirmed colorectal cancer, and tumour-free patients for comparison

What does the study involve?
Participants have their diagnoses confirmed by colonoscopy, a test where the doctor looks at the inner lining of the colon using a thin, flexible tube. Participants are then provided with a kit for sample collection and are instructed to collect two samples of colorectal mucus 3-5 days after colonoscopy (CRC patients usually have surgery at least two weeks after colonoscopy). Sample collection is performed by the participants at home. Once samples are collected, they are sent to the laboratory of DiagNodus Ltd, where all planned laboratory tests are carried out. The results of the tests are matched to diagnostic information (colonoscopy) at the end of the study.

What are the possible benefits and risks of participating?
Although patients are unlikely to benefit from participating, the results of the study are likely to provide significant benefits for patients and medical professionals in terms of developing a new approach to CRC early detection and screening. The eventual goal is to provide a simple, highly sensitive and affordable test for CRC screening. Providing samples does not interfere with

routine treatment. Sample collection is safe and very well accepted by patients. For these reasons no potential risks of participating in the study can be identified.

Where is the study run from?
1. DiagNodus Ltd (UK)
2. St George's Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2017 to December 2019

Who is funding the study?
DiagNodus Ltd (UK)

Who is the main contact?
Dr Alexandre Loktionov

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Screen2C-012017-Pilot 3

Study information

Scientific Title

Colorectal cancer detection by quantifying biomarkers in non-invasively collected colorectal mucus: an observational case-control study

Study objectives
The main hypothesis is that colorectal mucus excreted during bowel opening constitutes a highly informative material that can be successfully analysed for non-invasively detecting biomarkers of colorectal cancer presence. Performance of a range of candidate biomarkers is going to be tested in order to select the best diagnostic marker(s).

Ethics approval required
Old ethics approval format

Ethics approval(s)
London – South East Research Ethics Committee, 30/12/2016, REC ref: 16/LO/2273

Study design
Observational case-control study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Colorectal cancer

Interventions
At the initial (pilot) stage of this observational case-control study it is planned to recruit at least 50 patients with colorectal cancer (between diagnostic colonoscopy and surgery) and 50 neoplasia-free (endoscopically confirmed) patients. All recruited patients are asked to collect samples of colorectal mucus. The collected samples are used for quantitative biomarker determination (ELISA for protein biomarkers; possibly PCR-based techniques for DNA and RNA) and cytological examination. All analytical procedures are blinded with regard to patient identity and diagnosis. At the end of the study the results of sample analysis are compared with the corresponding diagnostic information (reference standard: colonoscopy) (unblinding). Conclusions on individual biomarker performance are made, and larger scale further study is planned if the pilot phase is successful. The pilot phase is planned to be completed by 31/12 /2017, and the decision to extend the study beyond this date depends on its outcome.

Intervention Type

Other

Primary outcome measure
All results will be obtained at a single time point.

Protein biomarkers:
1. Calprotectin measured using ELISA
2. EDN measured using ELISA
3. MUC2 measured using ELISA
4. MMP9 measured using ELISA
5. VEGF measured using ELISA
6. Soluble Cytokeratin 18 measured using ELISA
7. M2-PK measured using ELISA
8. Haemoglobin measured using ELISA
9. Measurement of additional protein biomarkers may be introduced at later stages of the project

Nucleic acid markers:
1. Total DNA measured by spectrophotometry
2. Total DNA measured by real time PCR (beta-globin gene fragment amplification)
3. Measurement of additional DNA & RNA markers may be introduced at later stages of the project

Cytology and immunocytochemistry:
1. Qualitative cytological examination of collected samples using microscopy
2. Immunocytochemical visualisation of protein biomarkers and qualitative assessment of their distribution using microscopy

Secondary outcome measures
Performance of each of the biomarkers/assays listed above as a diagnostic test comparing CRC presence versus CRC absence, measured by ROC (receiver operating characteristic) curve analysis (area under the curve, sensitivity, specificity) and calculation of test negative and positive predictive values as well as positive and negative likelihood ratios

Overall study start date
01/01/2017

Completion date
31/12/2019

Eligibility

Key inclusion criteria
1. Colorectal cancer (case) group: the presence of endoscopically confirmed colorectal cancer
2. Control group: absence of neoplasia confirmed by endoscopy
3. Aged over 45

Participant type(s)
Patient

Age group

Adult

Sex
Both

Target number of participants
100-150 (pilot phase)

Total final enrolment
137

Key exclusion criteria
1. Age below 45
2. The presence of active gastrointestinal diseases or major gastrointestinal surgery in the past
3. Ongoing treatment with hormonal, immunosuppresive or cytostatic drugs

Date of first enrolment
15/01/2017

Date of final enrolment
30/09/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
DiagNodus Ltd
Bldg 280
Babraham Research Campus
Cambridge
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Study participating centre
St George's Hospital
Blackshaw Rd
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Sponsor information

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Sponsor type
Industry

Website
http://www.diagnodus.com

ROR
https://ror.org/04r796168

Funder(s)

Funder type
Industry

Funder Name
DiagNodus Ltd

Results and Publications

Publication and dissemination plan
It is planned to publish the future results of this study in peer-reviewed biomedical journals. Study outcome will also be presented at international scientific conferences.

Intention to publish date
31/12/2019

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are available from Dr Andrew Poullis (apoullis@sgul.ac.uk; Andrew.Poullis@stgeorges.nhs.uk) on reasonable request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		13/05/2020	01/12/2022	Yes	No
HRA research summary			28/06/2023	No	No