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Biomarker improvement and development in non-endoscopic samples

Submission date 20/12/2022	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 31/01/2023	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 31/01/2023	**Condition category** Digestive System	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
In the past two years, Cyted Ltd (UK) has provided more than 10,000 non-endoscopic based tests for Barrett's oesophagus and Oesophageal adenocarcinoma. These tests have enabled NHS Trusts to address the endoscopic backlog created during COVID. Cyted's current test relies on a pathologist reading a standard haematoxylin and eosin (H&E) stained slide alongside a slide-based antibody stain (TFF3) to diagnose Barrett's, and a separate slide-based antibody stain (P53) to identify patients at who are at a high risk of cancer. We aim to improve these tests, ensuring that patients continue to be provided with the best information available regarding their personal disease risk. This includes expanding our ability to test for oesophageal squamous cell carcinoma (OSCC) and other oesophageal diseases such as eosinophilic oesophagitis (EoE).

Who can participate?
Samples collected from patients with Barrett's oesophagus and Oesophageal adenocarcinoma during a routine diagnostic procedure

What does the study involve?
This study intends to:
1. Improve the accuracy of our existing artificial intelligence platform with the inclusion of additional slide images from our diagnostic archive
2. Develop additional biomarkers to supplement the existing slide-based stains (i.e. TFF3, P53) for diagnosis and risk stratification in Barrett's screening and surveillance samples - Identify diagnostic biomarkers for OSCC and EoE

Improvements to these diagnostic tests will also enable improvements in our pathology reporting to NHS Trusts through increased accuracy for cancer risk, and screening for other diseases (i.e. EoE) that are currently only available through endoscopic sampling.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
Cyted Ltd (UK)

When is the study starting and how long is it expected to run for?
November 2022 to December 2025

Who is funding the study?
Cyted Ltd (UK)

Who is the main contact?
Dr Sarah Killcoyne (Principal investigator), sarah.killcoyne@cyted.ai (UK)
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Contact information

Type(s)
Principal investigator

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
322308

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 322308

Study information

Scientific Title
Biomarker improvement and development in non-endoscopic samples within the Cyted diagnostic pathway

Study objectives
This study's primary objective is to improve our available biomarker tests to ensure continued high-quality diagnostic information is provided to patients. This will be achieved by identifying additional biomarkers that can be used in addition to, or as an alternative to the current TFF3 /P53/atypia slide-based stains.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/12/2022, South Central - Berkshire B Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +442071048276; berkshireb.rec@hra.nhs.uk), ref: 22/SC/0470

Study design
Single-centre retrospective cohort study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Diagnosis of oesophageal conditions in patients with reflux including Barrett's oesophagus, Oesophageal cancer, and Eosinophilic oesophagitis.

Interventions
This study is a single-centre retrospective cohort study using diagnostic samples collected during a routine diagnostic procedure and reported a minimum of 3 months prior to inclusion.

A targeted set of molecular tests will be run to assess sufficiency for the existence of specific cell types relating to disease, sensitivity/specificity analysis in comparison to existing methods and assess what the normal/healthy range is in patients without cancer. Image-based machine learning methods will include analysis of cellular mixtures and ratios of cell types in different cohorts and an accuracy assessment for our internal quality control procedures.

Intervention Type
Other

Primary outcome(s)
1. Sensitivity/specificity for any new biomarker for the given endpoint (1) diagnosis of Barrett's by endoscopy OR (2) risk of cancer) at the end of the study
2. Accuracy as measured against the pathologist's diagnosis for Barrett's diagnosis at the end of the study

Key secondary outcome(s))
1. General improvements to our internal laboratory processes for sample testing and reporting to pathologists. Improvements are measured against the current internal standard for sample processing. Each improvement will be evaluated against an appropriate internal sample set, sample size calculations will be performed based on the specific process we address. The final timepoint for all improvement studies will be the end of the study.
2. Identification of biomarkers for other oesophageal conditions including EoE or OSCC measured using a combination of IHC biomarkers, the gold standard for any new biomarker is our pathologist's diagnosis and non-inferiority with our current IHC biomarker tests. Timepoint is at the end of the study.

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Patient aged 18 and over
2. Male or female
3. Final pathology report submitted a minimum of 3 months prior to search

Participant type(s)
All

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Samples submitted less than 3 months prior search
2. Samples that have not yet resulted in a pathology report

Date of first enrolment

01/01/2023

Date of final enrolment
01/12/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cyted Ltd
22 Station Road
Cambridge
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Sponsor information

Organisation
Cyted Ltd

Funder(s)

Funder type
Industry

Funder Name
Cyted Ltd

Results and Publications

Individual participant data (IPD) sharing plan
Summary datasets generated during and/or analysed during the current study will be published as a supplement to the results publication. Individual results will not be made available to ensure anonymisation is preserved.

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet version 1.0	11/11/2025	11/11/2025	No	Yes
Protocol file		11/11/2022	22/12/2022	No	No