

Clinical Study Protocol

A Non-Interventional, Proof of Concept Study to Collect Blood Samples from Patients with Stage 0-IV Breast Cancer and from Healthy Participants to Measure Plasma Biomarkers for Future Development of an Early-Stage Breast Cancer Detection Test

SHORT TRIAL TITLE
A Study for the Future Design of an Early-Stage Breast Cancer Test

This protocol has regard for the HRA guidance

FULL/LONG TITLE OF THE TRIAL

A Non-Interventional, Proof of Concept Study to Collect Blood Samples from Patients with Stage 0-IV Breast Cancer and from Healthy Participants to Measure Plasma Biomarkers for future development of an early-stage breast cancer detection test

SHORT TRIAL TITLE / ACRONYM

Study for the Future Design of an Early-Stage Breast Cancer Test

PROTOCOL VERSION NUMBER AND DATE

V5.0, 2026

Commented [RE1]: To be updated upon finalisation. Also update footer.

RESEARCH REFERENCE NUMBERS:

IRAS Number:	368310
ISRCTN Number / Clinical trials.gov Number:	ISRCTN18266384
Sponsor's Number:	Fast 40

PROTOCOL VERSION NUMBER AND DATE

Protocol version no.	Date issued	Author(s) of changes	Details of changes made
V1.0	02March2026	N/A	N/A
V1.1	19May2026	Rachael Evans	Updates to address REC feedback: Update to exclusion criteria; inclusion of 'Physical and Emotional Assessment' and 'Alcohol and drug screening questionnaire'
V2.0	06August2026	Rachael Evans	Age range amended from 50-71 years to 30-71 years Physical and Emotional Assessment amended to allow sub-Investigators to conduct Assessment and confirm eligibility Screening assessments expanded to include ethnicity, height, weight, BMI, breast cancer screening history, menopausal status and hormonal exposure.
V3.0	11Sep2026	Rachael Evans	Introduction of Part B to expand the study population to include a further 80

			participants: 40 with Stage 0- IV breast cancer, alongside 40 healthy volunteers.
V4.0	14Oct2026	Rachael Evans	Clarification of age matching of Part B participants The vaccination exclusion window for participants who have received an influenza vaccine has been reduced from 90 days to 21 days prior to screening.
V5.0	xxx	Rachael Evans	Removal of the requirement for mammography from the inclusion criteria; extension of the planned trial period from 6 to 12 months.

Commented [RE2]: To be updated upon finalisation.

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, Good Clinical Practice (GCP) guidelines, the Sponsor's (and any other relevant) SOPs, and other requirements as required.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the trial publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies and serious breaches of GCP from the trial as planned in this protocol will be explained.

For and on behalf of the Sponsor:

Signature: Date:

Name:

Simon Duncan

Position:

CEO and Founder

Chief Investigator:

Signature: Date:

Name:

Dr Anuj Chahal

i. LIST of CONTENTS

GENERAL INFORMATION	**Page No.**
TITLE PAGE	1
RESEARCH REFERENCE NUMBERS	2
SIGNATURE PAGE	3
i. LIST of CONTENTS	4
ii. LIST OF ABBREVIATIONS	5
iii. TRIAL SUMMARY	6
iv. FUNDING	7
v. ROLES & RESPONSIBILITIES	7
vi. KEYWORDS	7
SECTION	
1. BACKGROUND	8
2. RATIONALE	8
3. OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS	8
4. TRIAL DESIGN	9
5. TRIAL SETTING	9
6. PARTICIPANT ELIGIBILITY CRITERIA	9
7. STUDY SCHEDULE	10
8. RECORDING AND REPORTING OF EVENTS AND INCIDENTS	12
9. SAMPLE ANALYSIS	13
10. DATA MANAGEMENT	13
11. MONITORING, AUDIT & INSPECTION	14
12. ETHICAL CONSIDERATIONS	14
13. PUBLICATION AND DISSEMINATION POLICY	16
14. REFERENCES	16
15. APPENDICES	18

ii. LIST OF ABBREVIATIONS

Define all unusual or 'technical' terms related to the trial. Add or delete as appropriate to your trial. Maintain alphabetical order for ease of reference.

ABPI	Association of the British Pharmaceutical Industry
AE	Adverse Event
AJCC	American Joint Committee on Cancer
BMI	Body Mass Index
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
cTNM	Clinical Tumour, Node, Metastasis (staging system)
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HER2	Human Epidermal Growth Factor Receptor 2
HRA	Health Research Authority
HRT	Hormone Replacement Therapy
ICF	Informed Consent Form
MM	Medical Monitor
NPL	National Physical Laboratory
NSAID	Non-Steroidal Anti-Inflammatory Drug
PI	Principal Investigator
PIS	Participant Information Sheet
REC	Research Ethics Committee
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
TMF	Trial Master File
βhCG	Human chorionic gonadotropin β-subunit

iii. TRIAL SUMMARY

IRAS number	368310
Trial Title	A Non-Interventional, Proof of Concept Study to Collect Blood Samples from Patients with Stage 0-IV Breast Cancer and from Healthy Participants to Measure Plasma Biomarkers for future development of an early-stage breast cancer detection test
Internal ref. no. (or short title)	Fast 40
Clinical Phase	Observational
Health condition studied	Breast Cancer stage 0-IV
Planned Sample Size	120 participants: 60 breast cancer and 60 healthy volunteers
Planned Trial Period	12 months
Primary Objective	To obtain: Part A) 40 blood samples from healthy volunteers and from stage 0-IV breast cancer patients to be analysed in a proof of concept study for (i) metabolites in plasma by mass spectrometry, and (ii) circulating cell free-DNA by genomic testing Part B) 80 blood samples from healthy volunteers and from stage 0-IV for metabolites in plasma by mass spectrometry only.
KEY TRIAL CONTACTS	
Chief Investigator	Name: Anuj Chahal Address: Research Link, Old School Surgery, 2A Station St, Kibworth Beauchamp, Leicester LE8 0LN Tel: 0116 279 3308 Email: anuj.chahal1@nhs.net
Sponsor	Faster Diagnostics Ltd. Address: 3rd Floor, 86-90 Paul Street, London, EC2A 4NE, United Kingdom Email: sduncan@fasterdiagnostics.com Tel: 0203-9303177
Funder	Faster Diagnostics Ltd. As above
Key Protocol Contributors	Prof Charles Coombes, c.coombes@imperial.ac.uk, Tel: 0203-9303177 Prof Jacqui Shaw, js39@leicester.ac.uk Tel: 0203-9303177
Medical Monitor	Name: Charles Coombes, Chairman of Faster Diagnostic Advisory Board, Faster Diagnostics Limited Tel: 0203-9303177

	Email: c.coombes@imperial.ac.uk
Clinical Research Organisation	PHARMExcel Ltd., Albany Chambers, 26 Bridge Road East, Welwyn Garden City, Herts, AL7 1HL Tel: 0203-6426654

iv. FUNDING

The trial is funded by Faster Diagnostics Ltd.

v. ROLES AND RESPONSIBILITIES

SPONSOR: Before a trial begins the Sponsor is responsible for ensuring that arrangements are in place for the research team to access resources and support to deliver the research as proposed and allocate responsibilities for the management, monitoring and reporting of the research. The Sponsor also must be satisfied there is agreement on appropriate arrangements to record, report and review significant developments as the research proceeds and approve any modifications to the design. Further details of the trial are set out in the project plan (the Project Plan).

The Sponsor will notify the Research Ethics Committee (REC) of the end of the trial (including the reasons for premature termination, where applicable). Within one year after the end of trial, the Sponsor will submit a final report with the results, including any publications/abstracts to the REC.

FUNDER: The funder is the entity that will provide the funds (financial support) for the conduction of the trial. Funders are expected to provide assistance to any enquiry, audit or investigation related to the funded work.

CHIEF INVESTIGATOR (CI): The person who takes overall responsibility for the design, conduct and reporting of a trial. If the trial involves researchers at more than one site, the CI takes on the primary responsibility whether he/she is an investigator at any particular site.

The CI role is to complete and to ensure that all relevant approvals and confirmations of NHS Capacity and Capability (if required) are in place before the trial begins, and to ensure arrangements are in place for good trial conduct, robust monitoring and reporting, including prompt reporting of incidents, this includes putting in place adequate training for trial staff to conduct the trial as per the protocol and relevant standards.

PRINCIPAL INVESTIGATOR (PI): Individually or as leader of the researchers at a site; ensuring that the trial is conducted as per the approved trial protocol, and report/notify the relevant parties, including the CI, of any breaches or incidents related to the trial.

vi. KEY WORDS: Proof of concept; Breast cancer, non-interventional

1 BACKGROUND

Faster Diagnostics Ltd (Faster) is a health-tech company developing The Artemis Test™, a next-generation non-invasive blood test to identify cancer-informed molecular patterns in blood plasma for the early detection of breast cancer.

This trial is part of the proof of concept study, from which Faster is seeking to identify molecular changes which can be detected in plasma in early-stage breast cancer. It is envisaged that the Artemis test will be a simple non-invasive and radiation-free clinic-based blood test. The test is intended to complement existing mammography by filling the 3-year gap between screenings. The test may be offered to younger women not yet attending routine screening.

This trial will A) analyse plasma and buffy coat samples from healthy volunteers and from treatment-naïve stage 0-IV breast cancer patients for (i) metabolites in plasma by state-of-the-art mass spectrometry at The National Physical Laboratory (NPL), and (ii) circulating cell free DNA by direct third generation DNA sequencing technology at Leicester University; and B) analyse samples from healthy volunteers and stage 0-IV breast cancer patients for metabolites in plasma by state-of-the-art mass spectrometry at The National Physical Laboratory (NPL). The data from the trial will be analysed using a range of multivariate and univariate statistical methods to identify informative signatures for further development of the multi analyte test: The Artemis Test™.

2 RATIONALE

In developed countries, one in eight women (12.5%) is estimated to develop breast cancer during their lifetime[1], yet 65% of cases are diagnosed at stage II or later[2]. The UK NHS Breast Screening Programme, while effective, is limited to women aged 50–70 and misses cancers in those with dense breast tissue, and in younger women, despite 11% of cancers and 4% of deaths occurring in women aged 20-44[3]. Early screening could potentially save 700 lives annually[4]. Almost 99% of women diagnosed with breast cancer at the earliest stage live for 5 years or more, compared to approximately 32% of those diagnosed at the most advanced stage[5], highlighting the importance of early diagnosis.

Mammography infrastructure is costly, uncomfortable, and under pressure. In the UK, around 20 million women remain under-served, including approximately 800,000 women do not attend regular screening clinics[6], more than 13 million women under the age of 50, and 4 million women who fall between NHS screening rounds[7]. Each year 56,900 new cases are detected[8], and approximately 11,200 women die annually in the UK, with future projections increasing to 11,500 annually[9]. Faster aims to develop a blood-based test, that can complement a mammogram and that can be accessed through Clinics and GP services.

2.1 Assessment and management of risk

This trial is categorised as Type A = No higher than the risk of standard medical care.

See Appendix 1.

3 OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

Primary objective
To obtain blood samples from healthy volunteers and from A) stage 0-IV breast cancer patients to be analysed in a proof of concept study for (i) metabolites in plasma by mass spectrometry, and (ii) circulating cell free-DNA by genomic testing; and B) stage 0-IV breast cancer patients to be analysed for metabolites in plasma by mass spectrometry.

4 TRIAL DESIGN

In this non-interventional trial, enrolled subjects will provide one standard venous blood draw performed by a certified phlebotomist. Participants are expected to be consented and samples taken during a single visit to the trial site.

The target recruitment in Part A will be as follows:

1. 10 Participants aged 30-40 years
    - 5 breast cancer patients
    - 5 controls
2. 10 Participants aged 41-50 years
    - 5 breast cancer patients
    - 5 controls
3. 10 Participants aged 51-60 years
    - 5 breast cancer patients
    - 5 controls
4. 10 Participants aged 61-71 years
    - 5 breast cancer patients
    - 5 controls

Sites will recruit the same number of breast cancer participants and controls in each of the four groups. Each site will be assigned an anticipated recruitment target and a maximum enrolment cap.

In Part A, 20 breast cancer participants will be recruited with Stage 0-II breast cancer, and 20 controls.

In Part B, 40 breast cancer participants will be recruited with Stage 0-IV breast cancer, and 40 age-matched healthy controls.

The target recruitment of breast cancer participants in Part B will be as follows:

Stage 0: 4 breast cancer participants;

Stage I: 14 breast cancer participants;

Stage II: 12 breast cancer participants;

Stage III: 6 breast cancer participants;

Stage IV: 4 breast cancer participants.

Healthy controls will be age-matched to the breast cancer participants within the following age groups: 30–40, 41–50, 51–60, and 61–71 years.

Each site will be assigned an anticipated recruitment target and a maximum enrolment cap.

Recruitment performance will be reviewed at regular intervals (at least weekly during recruitment) to ensure alignment with projected timelines and trial objectives.

The Sponsor reserves the right to:

- Suspend enrolment at any site due to safety concerns, non-compliance, or inadequate performance

- Close the trial to enrolment earlier than anticipated if recruitment targets are achieved
- Stop the trial if there are an unacceptable rate of AEs, or for any other reason.

All decisions regarding suspension or closure will be documented and communicated in writing to the investigator and filed in the TMF.

All trial staff will have a clearly defined role, will be trained on the trial protocol, understand the activities to be undertaken and have current certifications for the roles they will perform in this trial. Documentation will be filed in the TMF.

5 TRIAL SETTING

The trial will be conducted at primary care GP and secondary care NHS sites in the UK only.

6 PARTICIPANT ELIGIBILITY CRITERIA

6.1 Inclusion criteria

An individual must fulfil all the following inclusion criteria for one of the two groups to be considered eligible for trial enrolment:

Breast Cancer Participants Group

1. Females aged ≥30 years to ≤71 years of age, inclusive at time of consent.
2. Breast cancer participants:

   Part A: diagnosed with breast cancer stage 0 to II post biopsy

   Part B: diagnosed with breast cancer stage 0 to IV post biopsy
3. Breast cancer participants: treatment naïve participants only, diagnosed by biopsy
4. Breast cancer participants: primary cancer donors only

Healthy Participant Group

1. Females aged ≥30 years to ≤71 years of age, inclusive at time of consent.
2. Healthy volunteer participants: no current or prior diagnosis of any cancer
3. Healthy volunteer participants: not currently under investigation for any suspected malignancy
4. Healthy volunteer participants: no current symptoms suggestive of breast pathology (e.g., palpable lump, nipple discharge, skin changes)

6.2 Exclusion criteria for both groups

An individual fulfilling <u>any</u> of the following exclusion criteria will not be considered eligible for trial enrolment:

1. HIV/HBV/HCV positive, as determined by rapid strip test
2. Women who are pregnant, or lactating
3. Recent receipt of a vaccine within 90 days or five half-lives, (whichever is longer) prior to screening, or receipt of an influenza vaccine within 21 days prior to screening.
4. Participants in receipt of any form of HRT within the last 90 days (including patches, pessaries, coil and tablets).

5. Participation in another clinical study investigating a vaccine, drug, medical device, or medical procedure within 90 days or five half-lives, whichever is longer, prior to consent or planned participation in such a study during the period of this clinical trial
6. Receipt of immunoglobulins, blood or blood-derived products within 90 days prior to consent
7. Chronic illness that, in the opinion of the investigator, is at a stage where it might interfere with trial conduct or trial completion.
8. Current alcohol abuse or drug addiction (reported or suspected)
9. Identified as an investigator or employee of the investigator or study centre with direct involvement in the proposed trial, or identified as an immediate family member (i.e., parent, spouse, natural or adopted child) of the investigator or employee with direct involvement in the proposed trial. (i.e., in the employment of the clinical trial sites)
10. Participants receiving any of the following medications:
    1. Thyroid Replacement Therapy: Levothyroxine sodium for the management of hypothyroidism. This medication, as well as thyroid dysfunction could alter the metabolome.
    2. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), including, but not limited to, Ibuprofen or Naproxen within 14 days.
11. Participants with a known diagnosis of Type 1 or Type 2 diabetes mellitus.

Recent receipt of a vaccine within 90 days or five half-lives, (whichever is longer) prior to Screening, or receipt of an influenza vaccine within 21 days prior to Screening.

7 TRIAL SCHEDULE

7.1 Recruitment

This trial will recruit female volunteers ≥30 years to ≤71 years of age, inclusive.
Participants will be identified using a variety of methods in line with the site's recruitment plan. These may include:

- Internal site recruitment (consent to contact) database
- Opportunistically via word of mouth or via site website.
- Text message/ phone call to potential participants
- Community engagement events
- Posters campaign across community and NHS sites
- Social media campaigns
- Newsletters/e-bulletins
- Printed media (such as newspapers)
- NIHR Be Part of Research

7.1.2 Screening

The following screening procedures will be completed during the single trial visit, as further detailed in Appendix 2.

- Informed Consent
- Collection of demographic information, including age, sex and ethnicity
- Collection of relevant medical history and baseline characteristics, including smoking history, co-morbidities, height, weight, Body Mass Index (BMI), infectious disease status (HIV/HBV/HCV), concomitant medications and treatments
- Collection of breast cancer screening and reproductive history, including screening participation status, date of last screening (if applicable), menopausal status and hormonal exposure
- Collection of breast cancer diagnostic information for participants in the breast cancer group
- Eligibility assessment against the inclusion and exclusion criteria
- Recording of the time of last nutritional and fluid intake prior to blood collection.
- Phlebotomy and sample processing procedures
- All women of childbearing potential[1] will undergo a urine human chorionic gonadotropin β-subunit (βhCG) pregnancy test.
- Alcohol and drug screening (see section 7.3)
- Physical and Emotional Assessment (see section 7.4)

*[1]An individual who has experienced menarche and who is neither surgically sterile nor post-menopausal.

7.1.3 Payment

Participants will receive reasonable compensation for completion of their trial visit. The amount will be detailed in the Participant Information Sheet (PIS). Details regarding reimbursement procedures will be provided to the participant during the informed consent process.

7.2 Consent

Wherever possible a copy of the PIS and Consent Forms will be provided to potential participants in advance (by post, email or website link). If willing to participate, the trial staff will provide a patient information sheet (PIS), provide sufficient time to answer all questions participants may have, and then obtain a signed Consent Form.

7.2.1 Additional consent provisions for collection and use of participant biological specimens in ancillary studies

Surplus plasma will not be used for any purpose other than for Faster's follow-up clinical trials. These studies will be for the same research purposes as this trial. Samples not utilised will be destroyed according to site procedure 2 years after the end of this trial. Destruction will be recorded after written consent from the Sponsor, and a certificate of destruction will be sent to the Sponsor to be filed in the Trial Master File.

The use of samples for future research is optional, and participants will be asked to consent specifically for this and will be free to withdraw this consent at any point.

7.3 Alcohol and drug screening questionnaire

Participants will undergo assessment for alcohol and drug use by trial staff using the Alcohol and Drug Screening Questionnaire. The PI will review the results to confirm the participant's eligibility to continue with study procedures, including phlebotomy.

7.4 Physical and Emotional Assessment

Following completion of informed consent, pregnancy testing (if required), HIV/HBV/HCV screening, and assessment of alcohol and drug use by trial staff, the Principal Investigator (PI) or sub-Investigator will review all screening results and conduct a Physical and Emotional Assessment.

The PI or sub-Investigator will offer appropriate support, review and discuss the screening results (pregnancy and HIV/HBV/HCV tests) with the participant, and confirm that the participant remains eligible to proceed with the remaining study procedures, including phlebotomy. Participants will not proceed with study procedures if, in the opinion of the PI or sub-Investigator, the screening results raise concerns regarding participant safety or trial conduct.

7.5 Blood sample handling

A total of 30 mL will be collected from each participant in part A, and 10 mL in Part B. Plasma and buffy coat to be processed and stored at site at -80ºC within two hours of collection. In part A plasma and buffy coat to be sent to Leicester University; plasma only will be sent to NPL or stored at the site for up to 2 years after the end of this trial at -80ºC. In Part B plasma only will be sent to NPL or stored at the site for up to 2 years after the end of this trial at -80ºC

Detailed guidance will be provided in the Blood Processing Manuals.

7.6 Storage conditions

Plasma and buffy coat: short term storage\long term storage: -80ºC

It is the responsibility of the trial site to ensure that samples are appropriately labelled in accordance with the trial procedures to comply with the 2018 Data Protection Act. Biological samples collected from participants as part of this trial will be transported, stored, accessed and processed in accordance with national legislation relating to the use and storage of human tissue for research purposes and such activities shall at least meet the requirements as set out in the 2004 Human Tissue Act and the 2006 Human Tissue (Scotland) Act.

7.7 Withdrawal criteria

Participants can withdraw at any time during or after the trial. At this point all samples can be requested to be destroyed and data not used. After closure of the trial, a request can be made, but it may not be possible after sample analysis.

7.8 End of trial

This trial will complete when the total target number of participants has been reached and all sample analyses and data cleaning have been completed, or at a date determined by the Sponsor, whichever occurs last.

8 RECORDING AND REPORTING OF EVENTS AND INCIDENTS

8.1 Definitions

Trial related events and incidents can encompass incidents that involve participants, staff or a carer/visitor during the trial. All events and incidents (and near misses) that occur to participants and/ or staff that are unexpected and directly related to the trial will be reported to the Sponsor and NHS Trust reporting systems and documented in the Trial Master File/Investigator Site File via trial-specific incident logs (and related correspondence if required). This will be completed by the CI or PI. The Sponsor will be responsible for investigating, reviewing, or escalating to a serious breach if required.

8.2 Adverse Events and Serious Adverse Events

Adverse events are any untoward medical occurrence in a trial participant, which does not necessarily have a causal relationship with the procedure involved. This trial is not expected to result in any significant AEs or SAEs (Serious Adverse Events) as non-invasive beyond the blood sampling. All AEs will be recorded, and any SAEs will be reported to the CI and Sponsor within 24 hours of the site becoming aware. The severity, causality and expectedness will be recorded in the participant's medical records, CRF and AE log, with a description of clinical symptoms and the event, including dates as appropriate.

Any concerns with the trial and an AE/SAE of concern will be raised directly with the CI.

8.3 Incidental Findings in Research

No significant incidental findings are expected for participants.

8.4 Protocol deviations

Protocol deviations are usually an unintended departure from the expected conduct of the trial protocol/ Standard Operating Procedure (SOPs). Should protocol deviations occur, they must be adequately documented on the relevant forms and reported to the Sponsor/ Contract Research Organisation (CRO).

8.5 Early Termination of Trial

The Sponsor has the right to terminate the trial at any time and will notify the REC that originally approved the trial within 15 days using the End of Study Notification Form found on the Health Research Authority (HRA) website. This will be followed by a final report within 12 months.

9 SAMPLE ANALYSIS

The aim of this proof of concept study is to analyse (i) metabolites in plasma by mass spectrometry, and (ii) circulating cell free-DNA by genomic testing.

Sample size calculation

This trial is designed to provide initial review of the expected variability within and difference between the populations being compared and the variability (standard deviation) within the data, e.g. relative uncertainty of the method. As such, this proof of concept trial is designed to enable robust sample size calculations for the next phase of research. There is not a formal sample size calculation as this trial is for feasibility to provide information for future studies.

10 DATA MANAGEMENT

10.1 Data collection tools and source document identification

The Sponsor/CRO will set up a password-protected excel spreadsheet for data inputting at each site, which will be validated prior to use and a validation plan filed in the Trial Master File (TMF). The CRO will perform a QC of the spreadsheet against the protocol, ensuring all data entry points are captured in both. The CRO will produce a guideline document for data entry.

Only authorized staff will have access to the spreadsheet for purposes of data entry and will input data from the source notes. Once recruitment has been completed and all monitoring queries resolved, the spreadsheet will be locked by the PI and a copy sent to the Sponsor. Each site will retain the original locked spreadsheet.

The investigator must maintain records and data during the trial in compliance with all applicable legal requirements. Each data point must be supported by a source document at the trial site. Records or documents used as the source of information are to be retained for review by authorized representatives of the Sponsor.

All completed databases from the trial are the exclusive property of the Sponsor.

10.2 Access to Data

Direct access will be granted to authorised representatives from the Sponsor and CRO to permit trial-related monitoring, audits and inspections, in line with participant consent.

10.3 Archiving

Records and documents, including signed Informed Consent Forms (ICFs), pertaining to the conduct of this trial must be retained by the investigator for a minimum of 10 years after trial completion. Archiving will be authorised by the Sponsor following submission of the end of trial report.

No records may be destroyed during the retention period without the written approval of the Sponsor.

No records may be transferred to another location or party without written notification to the Sponsor.

11 MONITORING, AUDIT & INSPECTION

Details of the monitoring procedures will be available in the Project Plan, which includes the monitoring plan.

The Sponsor or designee is responsible for the data management of this trial, including quality checking of the data.

The Sponsor assumes accountability for actions delegated to other individuals (e.g., CRO).

Monitoring will be conducted by the CRO following the CRO's SOPs. Written reports will be provided to the Sponsor following on-site monitoring visits, and regular updates provided in terms of recruitment, data capture and any other trial-related issues. Any reportable protocol deviations or violations as defined in the Project Plan, will be discussed with the CI and notified to the Sponsor, and reporting of serious breaches will occur if such events are identified.

Auditing activities will be the responsibility of the Sponsor.

12 ETHICAL CONSIDERATIONS

12.1 Research Ethics Committee (REC) review & reports

The trial was deemed to require approval from the following bodies: REC Favourable Opinion and HRA Approval. Before any site can enrol participants into the trial, the Chief Investigator (CI) / Principal Investigator (PI) or designee will ensure that the appropriate approvals have been issued, and NHS Confirmation of Capacity and Capability (if required) and Sponsor's green light is in place.

All correspondence with the Sponsor, REC and HRA will be retained in the Trial Master File. The Chief Investigator will notify the Sponsor and REC of the end of the trial.

If the trial is ended prematurely, the Chief Investigator will notify the Sponsor and REC, including the reasons for the premature termination.

The Sponsor will notify the REC of the end of the trial (including the reasons for premature termination, where applicable). Within one year after the end of trial, the Sponsor will submit a final report with the results, including any publications/abstracts to the REC.

12.2 Peer review

This trial part A has been reviewed externally by:

Professor Jacqui Shaw, Professor of Translational Cancer Genetics, Leicester University, UK.

This trial part B has been reviewed by:

Professor Charles Coombes, Imperial College London, South Kensington Campus, London SW7 2AZ.

12.3 Protocol compliance

The PI/CI agree to comply with the requirements of the Protocol and Good Clinical Practice.

Prospective, planned deviations or waivers to the protocol are not allowed and must not be used e.g. it is not acceptable to enrol a participant if they do not meet the eligibility criteria or restrictions specified in the trial protocol.

Accidental protocol deviations can happen at any time. They must be adequately documented on the relevant forms, reported to the CRO and then to the sponsor immediately.

Deviations from the protocol which are found to frequently recur are not acceptable, will require immediate action and could potentially be classified as a serious breach.

12.4 Notification of Serious Breaches to GCP and/or the protocol

A "serious breach" is a breach which is likely to effect to a significant degree –

(a) the safety or physical or mental integrity of the participants of the trial; or
(b) the scientific value of the trial

The sponsor should be notified of any case where the above definition applies during the trial conduct phase. The sponsor (or designee) will notify the REC in writing of any serious breach.

12.5 Data protection and participant confidentiality

The trial is compliant with the requirements of the General Data Protection Regulations (GDPR) and the UK Data Protection Act (2018). Faster Diagnostics will act as the data controller for this trial, with overall responsibility for the collection, management, and lawful processing of trial data in accordance with UK GDPR. The data processors are the CRO, Leicester University and NPL.

The lawful basis for processing personal data under Article 6(1) of UK GDPR is that processing is necessary for the performance of a task carried out in the public interest (Article 6(1)(e)). The condition for processing special category health data under Article 9(2) is that processing is necessary for scientific research purposes (Article 9(2)(j)), subject to appropriate safeguards as required under UK law.

All investigators and trial site staff are required to comply with the requirements of the Data Protection Act 2018 with regards to the collection, storage, processing and disclosure of personal information, and will uphold the Act's core principles.

All personal information that is collected, will be kept securely, and maintained. In general, this involves:

- The creation of coded, depersonalised data where the participant's identifying information is replaced by an unrelated sequence of characters.
- Secure maintenance of the data and the linking code in separate locations using encrypted digital files within password protected folders and storage media.
- Limiting access to the minimum number of individuals necessary for quality control, audit, and analysis
- Confidentiality of data will be preserved when the data are transmitted to the Sponsor by ensuring all data is anonymised.

12.6 Financial and other competing interests for the Chief Investigator and Principal Investigator at each site

The CI and PI are receiving no personal remuneration and have no conflict of interest in relation to the trial.

12.7 Indemnity/Insurance

Insurance for the trial will be obtained by the Sponsor.

The sponsor will abide by ABPI guidelines set out in the form of indemnity for non-interventional clinical studies. The NHS indemnity scheme will apply.

12.8 Amendments

For any amendments to the trial, the Sponsor/designee, will submit information to the appropriate body for them to issue approval for the amendment. The Sponsor or designee will work with sites (R&D departments (if required) as well as the trial delivery team) to confirm ongoing capacity and capability for the trial.

Version control will be maintained for any amendments made. Substantial Amendments (SAs) will be identified by a whole number change (i.e. v1.0, v2.0) and non-substantial amendments (NSAs) identified by a decimal change (i.e. v1.1, v1.2). All amendments will be logged at each site and a central copy maintained in the TMF.

12.9 Access to the final trial dataset

The Sponsor will have jurisdiction over the release of the final trial dataset. Site investigators will not be able to access the full dataset.

13 PUBLICATION AND DISSEMINATION POLICY

Information regarding the protocol will be posted on clinicaltrials.gov. All data generated or collected during this trial are the sole property of the Sponsor. The PI/CI and the institution(s) hold the data in confidence and will not use it for any purpose other than the trial, without prior written consent from the Sponsor.

14 REFERENCES

1. https://www.annlabmed.org/journal/view.html?uid=3612&vmd=Full
2. https://crukcancerintelligence.shinyapps.io/EarlyDiagnosis/_w_6c6e5cac19d346a2bee3633e925f78c4/?Tab=incByStageRCRD
3. European commission JCR breast cancer 2022 https://ecis.jrc.ec.europa.eu/sites/default/files/2024 01/jrc_Breast_cancer_2022_Oct_2023.pdf
4. https://www.cam.ac.uk/research/news/enhanced-breast-cancer-screening-in-the-uk-could-detect-an-extra-3500-cancers-per-year-trial-shows
5. https://www.cdc.gov/nccdphp/priorities/breast-cancer.html
6. https://digital.nhs.uk/data-and-information/publications/statistical/breast-screening-programme/england---2022-23#:~:text=2,45
7. https://digital.nhs.uk/data-and-information/publications/statistical/breast-screening-programme/england---2023-24#:~:text=1.95%20million%20women%20screened%20(aged%2045%2B)
8. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer?
9. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/mortality

15. APPENDICES

15.1 Appendix 1 - Risk

Risks associated with trial procedures

☒ A ≡ Comparable to the risk of standard medical care

☐ B ≡ Somewhat higher than the risk of standard medical care

☐ C ≡ Markedly higher than the risk of standard medical care

Justification: Briefly justify the risk category selected and your conclusions below (where the table is completed in detail the detail need not be repeated, however a summary should be given):

There are not any expected significant risks or disadvantages for participants taking part in this trial.

The blood sample being taken specifically for research carries the same risk as routine blood samples, that is, bruising around the needle puncture site, pain and redness.

There is a potential risk of loss of privacy and breach of confidentiality.

What are the key risks related to the trial procedures?		**How will these risks be minimised?**		
Procedure	**Body system/Hazard**	**Activity**	**Frequency**	**Comments**
Blood sample	Bruising around the needle puncture site, pain and redness.	A single sample will be taken by adequately trained staff. Participants will be consented before trial procedures begin	N/A	N/A
Data breach	N/A	An anonymised participant identification code that allows identification of all the data reported for each participant will be used.	N/A	N/A

Outline any other processes that have been put in place to mitigate risks to participant safety (e.g. DMC, independent data review, etc.)

Procedures will be carried out by adequately trained staff

Outline any processes (e.g. IMP labelling +/- accountability +/- trial specific temperature monitoring) that have been simplified based on the risk adapted approach.

Only one blood sample will be taken from participants.

Staff training and qualifications will be documented.

15.2 Appendix 2 – Schedule of Procedures

Procedure	Visit 1
Eligibility assessment	X
Consent	X
Demographics: • Age (at time of consent) • Sex • Ethnicity	X
Clinical history: • Smoking History • Co-morbidities • Infectious disease status (HIV/HBV/HCV[1])	X
Breast Cancer Screening and Reproductive History: • Screening participation status (NHS invited or self-referral) • Last screening date, if applicable • Menopausal status (pre-, peri- or post-menopausal[2]) • Hormonal exposure (HRT or oral contraceptive pill) • Family history of breast and ovarian cancer • Age at first birth • Age at menarche • Prior benign breast biopsy	X

Cancer diagnosis. Collect the following information for breast cancer participants, if available:
• Biopsy Pathology:
  ○ histological type
  ○ grade
  ○ vascular invasion (if present: yes/no)
  ○ oestrogen and progesterone receptor status
  ○ HER2 status
• Imaging: summary of findings from Mammogram report:
  ○ Date of mammogram
  ○ Breast density (BI-RADS density A–D)
  ○ BI-RADS assessment category
• Staging: Breast cancer clinical stage defined by cTNM (Clinical Tumor, Node, Metastasis) and overall cStage (0-IV) according to AJCC 8th Edition
	X

Concomitant medication: All current medications and treatments taken within 90 days of trial entry.	X

Physical Measurements • Height (cm) • Weight (kg) • Body Mass Index (BMI, kg/m²)	X
βhCG testing[3]	X
Time of last nutritional and fluid intake 3 hours prior to the time of blood draw	X
Adverse event assessments	X
Alcohol and drug screening questionnaire	X
Physical and Emotional Assessment by principal investigator or sub-Investigator[4]	X
Phlebotomy	X
Blood sample processing	X

1. Rapid strip finger prick test. The result must be negative prior to enrolment.
2. ≥12 months amenorrhoea without another medical cause
3. All individuals of childbearing potential will undergo a urine pregnancy test as per section 7.1.2. The result must be negative prior to enrolment.
4. The PI or sub-Investigator will discuss the screening results and confirm if participant eligible for phlebotomy as per section 7.4.