ISRCTN14337451 https://doi.org/10.1186/ISRCTN14337451

PRE-DX – the impact of earlier genomic testing in the treatment of breast cancer

Submission date 10/08/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 16/08/2022	**Overall study status** Completed	
Last Edited 18/03/2024	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Currently, the treatment of breast cancer patients follows a standard clinical care pathway where a biopsy (a small sample of tissue taken from the body, in this case of the cancer cells) is collected during surgery. The biopsy sample is tested using the Oncotype DX test which gives a Recurrence Score (RS) that clinicians can use to determine the need for adjuvant treatments (radiotherapy and/or chemotherapy) in addition to surgery.

This study aims to assess the impact on patient management if the Oncotype DX test is requested on a biopsy sample taken at the time of diagnosis as opposed to a sample obtained during surgery. The availability of the Oncotype DX RS score earlier in the clinical care pathway may streamline the pathway, reducing the time to start adjuvant cancer therapy, reducing the demand on health care services, and improving patient experience.

Who can participate?
The study will recruit adult men and women with newly diagnosed breast cancer who are preparing to undergo surgery as the first treatment.

What does the study involve?
Participants will be asked to provide permission to be contacted to discuss the study and provide consent to participate in the study. Participants will be allocated into two groups at random, with two of every three participants having the DX test performed on the core diagnostic biopsy (Intervention arm), and one of every three participants having it performed on the excision stage removed during surgery as per usual care (control arm). Following consent, the participant will be asked a few baseline questions and asked to complete the Hospital Anxiety and Depression Scale questionnaire. Participants will be asked to complete the survey along with a Health Resource Utilisation questionnaire at two further timepoints in the study, once following the post-operative clinic appointment and following the offer adjuvant treatment.

What are the possible benefits and risks of participating?
There is no specific benefit to the participants other than the potential to inform the future treatment pathway for early-stage breast cancer patients. As the intervention does not alter the

treatment received by the patient but rather just changes the time point when the DX-test is performed. It is considered to present no additional risks beyond those presented by the treatment they will receive regardless of the study arm they are in.

Where is the study run from?
The Newcastle-upon-Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
From September 2022 to July 2024

Who is funding the study?
Genomic Health Inc. (USA)

Who is the main contact?
Dr Matthew Northgraves, Matthew.northgraves@hyms.ac.uk

Contact information

Type(s)
Scientific

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Dr Matthew Northgraves

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
286636

Protocol serial number
IRAS 286636, CPMS 53118

Study information

Scientific Title
Pre-Operative Oncotype DX testing: A decision impact study

Acronym
PRE-DX

Study objectives
Primary hypothesis:
The availability of the RS® results from the core biopsy in the pre-operative setting streamlines the patient management pathway.

Secondary hypothesis:
The availability of the RS® results from the core biopsy in the pre-operative setting reduces healthcare utilisation, improves patient experience and decreases the time to the offering of adjuvant cancer therapy.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 26/07/2022, London - Surrey Research Ethics Committee (Meeting held by video-conference via Zoom, London, None available, United Kingdom; +44 (0)207 1048 088; surrey.rec@hra.nhs.uk), ref: 20/LO/0421

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Current intervention as of 02/06/2023:
As of Protocol V2.1 24/03/2023:
The Oncotype DX is a prognostic test applied to guide the treatment of breast cancer. The Recurrence Score (RS) result informs recommendations made to the patient regarding the requirement for adjuvant treatment. This is a study designed to compare the current standard patient pathway where the Oncotype DX test is performed in the post-operative setting on an excisional biopsy taken during surgery with performing the test in the pre-operative setting on the core biopsy taken at diagnosis. Patients will be randomly allocated in a 1:2 ratio into either the standard or intervention arm respectively.

Assessment Schedule:
The study visit schedule will follow routine clinical care pathways with the only additional non-routine visit being the inclusion of a telephone or video call to obtain informed consent and conduct baseline questionnaires. Clinical attendance will be scheduled by the treating clinicians according to site clinical care pathway protocols and as such, there is no visit window for any of the outlined clinical attendances.

Breast Cancer patients referred to the Breast Cancer Symptomatic Clinic from either a GP or Mammogram Screening referral will be identified for study participation at the 'Pre-Diagnostic' MDT meeting. During the MDT meeting, the patient's breast cancer and disease staging will be confirmed and the patient management plan will be determined. The 'Pre-Diagnostic' MDT meeting is not a patient clinical attendance.

The breast cancer patient's first clinical attendance is at the 'Diagnostic Patient Clinic Visit', within which their cancer treatment will be confirmed. Potential participants will be provided with a Participant Information Sheet (PIS) at the 'Diagnostic Patient Clinic Visit' and provided the opportunity to discuss their respective study participation. With permission, potential participants will be referred to the site research team. If any results required to confirm eligibility are outstanding (e.g. HER2) at the diagnostic clinic appointment, the patient can still be approached provided it is clear that their eligibility is dependent on any outstanding test results. The potential participant will only be approached by the site research team once eligibility is confirmed. Alternatively, the information (e.g. PIS) can be posted to the patient following the appointment along with the accompanying invitation letter to introduce them to the study ahead of eligibility being confirmed.

A follow-up call with the research team will be arranged with any patients that express an interest in participation. During the call, they will be asked to provide informed consent and then complete the baseline Hospital Anxiety and Depression Scale (HADS). If the patient is due in for a routine appointment, face-to-face consenting will be permitted but the patient will not be brought in just to consent.

For participants randomly allocated into the control arm, standard practice will be followed with the Oncotype DX test requested/ordered at the 'Post-Operative MDT meeting' and performed in the post-operative setting on the excision sample obtained during surgery or if core biopsy if endocrine bridging therapy has been received). The Recurrence Score is expected to be available approximately two weeks following the 'Post Operative Results Clinic'.

For participants randomly allocated into the intervention arm, the Oncotype DX test will be performed on the core biopsy that was taken at the time of diagnosis. The results of the Oncotype DX test will be available to be discussed at the 'Post-Operative MDT meeting' following surgery. This discussion will support the decision-making on treatment options. Planned surgery will not be delayed if the Recurrence Score Results are unavailable and any change to the treatment recommendation will be recorded and discussed with the participants at an additional routine clinic appointment if required.

In the event of the Oncotype DX test failing in either group, repeat tests will be ordered on the operative biopsy as per standard practice.

Participants in both the control and intervention arm will attend a 'Post-Operative Results Clinic' following which the recommended adjuvant treatment will commence. In both arms of the study, the interpretation of the Recurrence Score result and treatment recommendation will be at the discretion of the MDT and treating clinicians following national guidelines.

The number of participant-clinician interactions between the treating team and the participant from diagnosis until being offered adjuvant treatment will be collected by the clinical research team.

The participants will complete the follow-up HADS and HRUQ one week following the Postoperative results clinic and following the offer of adjuvant treatment.

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Previous intervention:
As per Protocol V1.1 (27/06/2022):
The Oncotype DX is a prognostic test applied to guide the treatment of breast cancer. The Recurrence Score (RS) result informs recommendations made to the patient regarding the requirement for adjuvant treatment. This is a study designed to compare the current standard patient pathway where the Oncotype DX test is performed on an excisional biopsy taken during surgery with performing the test on the core biopsy taken at diagnosis. Patients will be randomly allocated in a 1:2 ratio into either the standard or intervention arm respectively.

Assessment Schedule:
The study visit schedule will follow routine clinical care pathways with the only additional non-routine visit being the inclusion of a telephone or video call to obtain informed consent and conduct baseline questionnaires. Clinical attendance will be scheduled by the treating clinicians according to site clinical care pathway protocols and as such, there is no visit window for any of the outlined clinical attendances.

Breast Cancer patients referred to the Breast Cancer Symptomatic Clinic from either a GP or Mammogram Screening referral will be identified for study participation at the 'Pre-Diagnostic' MDT meeting. During the MDT meeting, the patient's breast cancer and disease staging will be confirmed and the patient management plan will be determined. The 'Pre-Diagnostic' MDT meeting is not a patient clinical attendance.

The breast cancer patient's first clinical attendance is at the 'Diagnostic Patient Clinic Visit', within which their cancer treatment will be confirmed. Potential participants will be provided with a Participant Information Sheet (PIS) at the 'Diagnostic Patient Clinic Visit' and provided the opportunity to discuss their respective study participation. With permission, potential participants will be referred to the site research team. A follow-up call with the research team will be arranged with any patients that express an interest in participation. During the call, they

will be asked to provide informed consent and then complete the baseline Hospital Anxiety and Depression Scale (HADS). If the patient is due in for a routine appointment, face-to-face consenting will be permitted but the patient will not be brought in just to consent.

For participants randomly allocated into the control arm, standard practice will be followed with the Oncotype DX test requested/ordered at the 'Post-Operative MDT meeting' and performed on the excision sample obtained during surgery (operative biopsy). The Recurrence Score will be available approximately two weeks following the 'Post Operative Results Clinic'.

For participants randomly allocated into the intervention arm, the Oncotype DX test will be performed on the core biopsy that was taken at the time of diagnosis, prior to the surgical treatment of breast cancer. The results of the Oncotype DX test will be available to be discussed at the 'Post-Operative MDT meeting' following surgery. This discussion will support the decision-making on treatment options. Planned surgery will not be delayed if the Recurrence Score Results are unavailable and any change to the treatment recommendation will be recorded and discussed with the participants at an additional routine clinic appointment if required.

In the event of the Oncotype DX test failing in either group, repeat tests will be ordered on the operative biopsy as per standard practice.

Participants in both the control and intervention arm will attend a 'Post-Operative Results Clinic' following which the recommended adjuvant treatment will commence. In both arms of the study, the interpretation of the Recurrence Score result and treatment recommendation will be at the discretion of the MDT and treating clinicians following national guidelines.

The number of participant-clinician interactions between the treating team and the participant from diagnosis until being offered adjuvant treatment will be collected by the clinical research team.

The participants will complete the follow-up HADS and HRUQ one week following the Postoperative results clinic and following the offer of adjuvant treatment.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measure as of 15/08/2023: :

As of Protocol 2.2 (04/07/2023):
Number of participant touch points from the participant diagnosis (defined as the date of attendance at diagnostic clinic) to the offer and prescription of adjuvant cancer treatment measured using patient records at the time of the offer and prescription of adjuvant cancer treatment. Participant touch points will be defined as a participant-clinician interaction (outpatient appointment or equivalent) between the treating team and the participant.
In the event of the participant declining further treatment the date of offer should be used.

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Previous primary outcome measure as of 02/06/2023:

As of Protocol 2.0 (07/02/2023):
Number of participant touch points from the initial patient approach to the offer and

prescription of adjuvant cancer treatment measured using patient records at the time of the offer and prescription of adjuvant cancer treatment. Participant touch points will be defined as a participant-clinician interaction (outpatient appointment or equivalent) between the treating team and the participant.

In the event of the participant declining further treatment the date of offer should be used.

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Previous primary outcome measure as of 28/11/2022:

Number of participant touch points from the initial patient approach to the offer of adjuvant cancer treatment measured using patient records at the time of the offer of adjuvant cancer treatment. Participant touch points will be defined as a participant-clinician interaction (outpatient appointment or equivalent) between the treating team and the participant.

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Previous primary outcome measures:

1. Number of participant touch points from the initial patient approach to the offer of adjuvant cancer treatment measured using patient records at the time of the offer of adjuvant cancer treatment. Participant touch points will be defined as a participant-clinician interaction (outpatient appointment or equivalent) between the treating team and the participant.
2. Anxiety and depression symptoms measured using the Hospital Anxiety and Depression Score (HADS) at baseline, following the post-surgery clinic appointment, and following the offer of adjuvant treatment
3. Healthcare resource use measured using the patient-reported Health Resource Utilisation Questionnaire (HRUQ) completed following the post-surgery clinic appointment and following the offer of adjuvant treatment

Key secondary outcome(s))

Current secondary outcome measures as of 15/08/2023:

As of Protocol 2.2 (04/07/2023):
1. Time in days between the participant diagnosis (defined as the date of attendance at diagnostic clinic) and the offer and prescription of adjuvant cancer treatment (chemotherapy, radiotherapy or endocrine therapy)
2. Time in days between the participant diagnosis (defined as the date of attendance at diagnostic clinic) and the start of the first adjuvant cancer treatment (chemotherapy, radiotherapy or endocrine therapy)
3. Alteration in the recommended treatment sequence. This is measured when a participant in the intervention arm receives neo-adjuvant treatment as the result of the Recurrence Score (RS) results from the core biopsy rather than proceeding directly to surgery.
4. Anxiety and depression symptoms measured using the Hospital Anxiety and Depression Score (HADS) at baseline, following the post-surgery clinic appointment, and following the offer of adjuvant treatment
5. Healthcare resource use measured using the patient-reported Health Resource Utilisation Questionnaire (HRUQ) completed following the post-surgery clinic appointment and following the offer of adjuvant treatment
6. Rate of failure of the Oncotype DX® assay (RS result cannot be issued) on diagnostic core biopsy specimen. This will be measured when a test on the diagnostic core biopsy specimen fails.

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Previous secondary outcome measures as of 02/06/2023:

As of Protocol 2.0 (07/02/2023):
1. Time in days between the participant diagnosis (defined as the date of attendance at diagnostic clinic) and the offer and prescription of adjuvant cancer treatment (chemotherapy, radiotherapy or endocrine therapy)
2. Alteration in the recommended treatment sequence. This is measured when a participant in the intervention arm receives neo-adjuvant treatment as the result of the Recurrence Score (RS) results from the core biopsy rather than proceeding directly to surgery.
3. Anxiety and depression symptoms measured using the Hospital Anxiety and Depression Score (HADS) at baseline, following the post-surgery clinic appointment, and following the offer of adjuvant treatment
4. Healthcare resource use measured using the patient-reported Health Resource Utilisation Questionnaire (HRUQ) completed following the post-surgery clinic appointment and following the offer of adjuvant treatment
5. Rate of failure of the Oncotype DX® assay (RS result cannot be issued) on diagnostic core biopsy specimen. This will be measured when a test on the diagnostic core biopsy specimen fails.

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Previous secondary outcome measures as of 28/11/2022:

1. Time in days between the participant diagnosis (defined as the date of attendance at diagnostic clinic) and the start of adjuvant cancer treatment (chemotherapy, radiotherapy or endocrine therapy)
2. Alteration in the recommended treatment sequence. This is measured when a participant in the intervention arm receives neo-adjuvant treatment as the result of the Recurrence Score (RS) results from the core biopsy rather than proceeding directly to surgery.
3. Anxiety and depression symptoms measured using the Hospital Anxiety and Depression Score (HADS) at baseline, following the post-surgery clinic appointment, and following the offer of adjuvant treatment
4. Healthcare resource use measured using the patient-reported Health Resource Utilisation Questionnaire (HRUQ) completed following the post-surgery clinic appointment and following the offer of adjuvant treatment
5. Rate of failure of the Oncotype DX® assay (RS result cannot be issued) on diagnostic core biopsy specimen. This will be measured when a test on the diagnostic core biopsy specimen fails.

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Previous secondary outcome measure:

There are no secondary outcome measures

Completion date
23/11/2023

Eligibility

Key inclusion criteria

Current inclusion criteria as of 02/06/2023:
As of Protocol 2.1 (24/03/2023):
1. Aged ≥18 years
2. Oestrogen receptor positive HER2-negative invasive early-stage breast cancer confirmed on diagnostic core biopsy, as per definition of hormone receptor status in NICE DG34 guidance
3. Pre-operative staging of grade 2 cancer ≥ 20 mm on all imaging modalities or grade 3 cancer of any size and N0 on axillary staging or any size or grade which is N1 on preoperative axillary ultrasound scan +/- FNA or core biopsy (If local reimbursement available for N1 patients oncotype)
3. Surgery planned as first definitive treatment
4. Fit for adjuvant chemotherapy
5. Able to provide written or remote (eConsent or postal) informed consent
6. Able to complete questionnaires and study assessments

Participants receiving endocrine bridging therapy are eligible for the study provided the reason is due to a delay in planned surgery rather than for the purpose of downstaging the tumour.

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Previous inclusion criteria:
As per Protocol V1.1 (27/06/2022):
1. Aged ≥18 years
2. Oestrogen receptor positive HER2 negative invasive early stage breast cancer confirmed on diagnostic core biopsy, as per definition of hormone receptor status in NICE DG34 guidance
3. Pre-operative staging of grade 2 cancer >20 mm, or any grade 3 cancer >10 mm on all imaging modalities. N0 on axillary staging, or any size or grade which is N1 on preoperative axillary ultrasound scan +/- FNA or core biopsy (If local reimbursement available for N1 patients oncotype).
3. Surgery planned as first definitive treatment
4. Fit for adjuvant chemotherapy
5. Able to provide written or remote (eConsent or postal) informed consent
6. Able to complete questionnaires and study assessments

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Total final enrolment

341

Key exclusion criteria
1. ER negative or HER2 positive breast cancer
2. Grade 4 or N2 disease on pre-operative staging
3. Planned for neo-adjuvant systemic therapy
4. Unfit for surgical treatment or systemic chemotherapy
5. Are unable to provide informed consent
6. Have co-existing malignant disease only if this would affect the study in the investigator's opinion
7. Are unable to complete study questionnaires even with the assistance of the study nurse
8. Are already participating in another clinical trial

Date of first enrolment
10/10/2022

Date of final enrolment
01/12/2023

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Royal Liverpool University Hospital NHS Trust
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Gateshead Health NHS Foundation Trust
Queen Elizabeth Hospital
Sheriff Hill
Gateshead
United Kingdom
NE9 6SX

Study participating centre
Aneurin Bevan University Lhb
Headquarters - St Cadoc's Hospital
Lodge Road
Caerleon
Newport
United Kingdom
NP18 3XQ

Study participating centre
The Shrewsbury and Telford Hospital NHS Trust
Mytton Oak Road
Shrewsbury
United Kingdom
SY3 8XQ

Study participating centre
Hywel Dda University Lhb
Corporate Offices, Ystwyth Building
Hafan Derwen
St Davids Park, Jobswell Road
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United Kingdom
SA31 3BB

Study participating centre
NHS Grampian
Summerfield House
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AB15 6RE

Study participating centre
Hull University Teaching Hospitals NHS Trust
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HU3 2JZ

Study participating centre
Chesterfield Royal Hospital NHS Foundation Trust
Chesterfield Road
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S44 5BL

Study participating centre
Wirral University Teaching Hospital NHS Foundation Trust
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CH49 5PE

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SS0 0RY

Study participating centre
Nottingham University Hospitals NHS Trust - City Campus
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Study participating centre
Mid Yorkshire Teaching NHS Trust
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WF1 4DG

Study participating centre
North Tees and Hartlepool Ft
Hardwick Road
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United Kingdom
TS19 8PE

Study participating centre
Airedale NHS Trust
Airedale General Hospital
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United Kingdom
BD20 6TD

Study participating centre
North Cumbria University Hospitals NHS Trust
Cumberland Infirmary
Newtown Road
Carlisle
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CA2 7HY

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Industry

Funder Name
Genomic Health

Alternative Name(s)
Genomic Health Inc.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		15/03/2024	18/03/2024	Yes	No