ISRCTN11676341 https://doi.org/10.1186/ISRCTN11676341

PROACT PLUS Registry and Echo Sub-study: Can we detect early chemotherapy-related heart damage?

Submission date 26/04/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 13/05/2018	**Overall study status** Completed	
Last Edited 14/07/2022	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Breast cancer is one of the most common cancers. In the UK 150 people per day are diagnosed. Often breast cancer is treated with anti-cancer drugs, called chemotherapy. Anthracyclines are a type of chemotherapy often used to treat breast cancer and are very effective. However, as with all drugs anthracyclines come with side effects. Heart damage is the most serious side effect. Heart damage can happen at the time of treatment, but symptoms only develop much later. Detecting heart damage relies on heart scans (called echocardiography, or echo for short). The usual measurements can only identify heart damage when it is already established. Waiting until damage is established means a reduced chance of heart recovery. Unfortunately, anthracycline heart damage can sometimes be severe and affect length and quality of life. Doctors and patients need better ways of detecting heart damage earlier. This study aims to understand if new echo measurements can be used to detect heart side effects sooner. It is not yet known whether these new measurements are better than what is currently done. Some patients are already involved in a linked study called PROACT. These patients have already given their permission for echo studies and analysis. The plan is to ask another group of patients receiving chemotherapy as part of standard care but not currently in PROACT, to participate in this study, called the PROACT PLUS registry.

Who can participate?
Patients aged 18 and over with breast cancer who are going to receive anthracycline-based treatment

What does the study involve?
There are no additional treatments involved in this study, but patients undergo additional echo scans and blood tests (called troponin). The additional echo analysis is performed on normal echo pictures and is called the PROACT echo sub-study. The plan is to follow up the registry patients for 18 months and to combine the information from both trial and registry groups to answer the study questions.

What are the possible benefits and risks of participating?
The benefit to participants is additional heart monitoring that is not routine for all breast cancer patients undergoing treatment with anthracyclines. Patients studied in the registry will be receiving anthracycline-based chemotherapy and/or Herceptin as part of their routine cancer care. The risks and burdens posed on patients from taking these drugs include: nausea, vomiting, tiredness, low white cell count, infection, diarrhoea, and abdominal or joint pains. Participation in the registry does not pose any major risks to patients due to the observational nature of the study. Furthermore no study-specific medication will be given to patients during this period. Blood sample taking could cause some discomfort and distress for patients. There is a very small risk of infection or bleeding at the site of blood taking but the risks of these are extremely small and rare. Where possible, study blood samples will be taken alongside samples taken for routine care. Echocardiography may cause some discomfort at the probe site due to some pressure used when taking the images. No radiation risk is involved in taking the scans.

Where is the study run from?
South Tees NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2018 to June 2021

Who is funding the study?
South Tees Research and Development Fund (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
Version 1.0

Study information

Scientific Title
PROACT PLUS Registry and Echocardiographic sub-study: an observational, prospective, cohort study assessing the use of novel echocardiographic tools and measurement of troponin to help detect early signs of cardiotoxicity in patients treated for breast cancer

Acronym
PROACT PLUS Registry and Echo Sub-study

Study objectives
Can we detect early signs of cardiotoxicity using novel echocardiography measurements and heart specific blood tests?

Ethics approval required
Old ethics approval format

Ethics approval(s)
HRA and Health and Care Research Wales (HCRW), 14/08/2018, REC ref: 18/EM/0177

Study design
Multicentre observational prospective cohort study

Primary study design
Observational

Study type(s)
Diagnostic

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

Interventions
PROACT PLUS registry and echo-substudy is a multicentre, observational, prospective cohort study assessing the use of novel echocardiographic tools and measurement of troponin to help detect early signs of cardiotoxicity. This registry is complimentary to the NIHR-funded PROACT clinical trial which is currently ongoing in the Northeast of England. PROACT (PRevention Of Anthracycline Cardiovascular Toxicity in patients treated for breast cancer, PB-PG-0815-20061, NCT03265574, IRAS ID 213348) is a multicentre, phase 3, randomised, open label, blinded endpoint study that aims to assess the effectiveness of enalapril in preventing cardiotoxicity in patients with newly diagnosed breast cancer requiring anthracycline based chemotherapy. One hundred and seventy patients, in whom high-dose anthracycline chemotherapy is planned will be randomised to either usual care plus enalapril or usual care. The primary end point is the presence of detectable troponin T (14ng/L or greater), measured at the end of each chemotherapy cycle and 4 weeks after chemotherapy. As part of the assessment of key secondary endpoints in the trial, transthoracic echocardiography will be performed at two time points using a standardised British Society of Echocardiography (BSE) template: prior to

commencing chemotherapy, and 1 month after the completion of anthracycline chemotherapy. Trial echocardiographic secondary endpoints include the established measures of LVEF and global longitudinal strain (GLS).

The PROACT PLUS registry includes adult patients with newly diagnosed breast cancer who are planned to receive anthracyclines either in an adjuvant or neo-adjuvant setting for their treatment. Patients will not be eligible for inclusion in the registry if they meet the inclusion criteria for the PROACT clinical trial or have metastatic breast cancer. Therefore, the PROACT PLUS registry is complementary to the PROACT clinical trial and eligibility for trial or registry is mutually exclusive. The aim is to include 85 patients, which will be the same number as a single arm in the PROACT trial. A patient information sheet will be provided and any uncertainties about the registry raised by the patient will be addressed. After all questions are answered, the patient will be asked to sign the consent form to confirm participation.

Once patient has agreed to participate they will undergo a series of assessments during their treatment as described below:
1. Review of medical history
2. Height and weight measurement
3. Blood pressure and heart rate
4. Blood samples for troponin measurement (prior to each chemotherapy cycle, 4 weeks and 12 months after the last dose of anthracyclines)
5. Blood samples for future research (prior to cycle 1, 3 and 5 and 4 weeks and at least 12 months after the last dose of anthracyclines)
6. Heart scan (echocardiogram) at baseline, 4 weeks and 12 months after anthracyclines
7. Cheek swab for DNA analysis (optional): will be done once only during the registry period

No study specific drugs will be given to patients in the registry. The assessments in the registry will mirror the assessments in the PROACT clinical trial to allow a direct comparison of patients within and in both groups. The combined PROACT trial and PROACT PLUS registry data obtained from this cohort of patients with breast cancer will help inform the future of cardiovascular care in patients treated with anthracyclines and can lead to further useful research in the field of cardio-oncology.

Intervention Type
Other

Primary outcome(s)
The presence (≥14ng/L) or absence of cardiac troponin T (<14ng/L) release at any time during anthracycline treatment, 1 month and 12 months after the last dose of anthracycline:
1. Cardiac troponin I release during, 1 month and 12 months after the last dose of anthracyclines
2. Cardiac function assessed by echocardiogram, including GLS, measurement of LVEF, and measurement of novel echocardiographic strain parameters (namely: Global Radial Strain (GRS), Global Circumferential Strain (GCS), torsion and twist, Right Ventricular Free Wall (RVFW), left and right atrial strain), at baseline, 4 weeks following completion of chemotherapy and at 12 months

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
01/06/2021

Eligibility

Key inclusion criteria
1. Adult patients with a new diagnosis of histopathologically confirmed breast carcinoma
2. Age ≥ 18
3. Planned to receive anthracycline based treatment (adjuvant or neoadjuvant) – any dose
4. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Meets eligibility criteria for the PROACT trial*
2. Known metastatic breast cancer
*Patients who are otherwise eligible for the PROACT trial will not be eligible to participate in the PROACT registry

Date of first enrolment
01/06/2018

Date of final enrolment
17/02/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
South Tees NHS Foundation Trust
The James Cook University Hospital
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Sponsor information

Organisation
South Tees NHS Foundation Trust

ROR
https://ror.org/02js17r36

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
South Tees Research and Development Fund

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication. There are no plans to disseminate any results that include identifiable personal data. Data will be fully anonymised prior to publication, with all identifiable data removed. Results will be presented in aggregated form in publications.

IPD sharing plan summary
Other

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	11/11/2025	11/11/2025	No	Yes