PRevention Of Anthracycline Cardiovascular Toxicity in patients treated for breast cancer: a phase 3 randomised, open label, blinded endpoint, superiority trial of enalapril to prevent anthracycline-induced cardio-toxicity (PROACT).

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Background and rationale

Many breast cancer treatment regimens include anthracyclines as they are highly effective. However, anthracyclines can cause direct, dose-related cardiotoxicity. This can reduce cardiac contractility, impair left ventricular (LV) systolic function and cause heart failure. Heart failure caused by anthracyclines carries a poor prognosis. Preventing cardiotoxicity is of particular importance for this patient group in whom 78% are alive 10-years after cancer diagnosis.

Angiotensin converting enzyme inhibitors (ACEI) are of proven benefit in heart failure, hypertension and in primary cardiovascular prevention so are widely and safely used. ACEI reduce the production of the reactive oxygen species which may be responsible for anthracycline toxicity and prevent anthracycline cardiotoxicity in animal models. ACEI have not been robustly tested as a preventative therapy for cardiotoxicity in a randomised controlled trial (RCT).

Study aim

PROACT will test the effectiveness of the ACEI enalapril in preventing cardiotoxicity in patients with breast cancer undergoing adjuvant chemotherapy.

Study design

A multi-centre, prospective, randomised, open-label, blinded end-point, superiority trial.

Trial participants and intervention

170 adult patients due to receive epirubicin-based adjuvant chemotherapy for breast cancer, will be randomised 1:1 to either enalapril or usual care. The study will include patients planned to receive standard regimens containing epirubicin >300mg/m2 (FEC75 x6 or EC90 x6).

End points and sample size

The primary end-point is cardiac troponin T release (≥14ng/L) at any time during epirubicin treatment, or one month after the last dose. With alpha 5%, the study has 90% power to detect a reduction in the presence of troponin from 47% to 20%.
Secondary endpoints include assessment of cardiac function by echocardiography and include change in global longitudinal strain and LV ejection fraction.

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