

# Adjuvant Cytotoxic chemoTherapy In Older women

<b>Submission date</b> 21/11/2005	<b>Recruitment status</b> Stopped	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 20/01/2006	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 19/03/2020	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

<http://cancerhelp.cancerresearchuk.org/trials/a-trial-comparing-adjuvant-chemotherapy-with-standard-treatment-for-older-women-with-early-stage-breast-cancer>

## Study website

<http://www.icr.ac.uk>

## Contact information

### Type(s)

Scientific

### Contact name

Prof Robert Leonard

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## Additional identifiers

### EudraCT/CTIS number

2005-005721-55

### IRAS number

### ClinicalTrials.gov number

NCT00516425

## Secondary identifying numbers

N/A

# Study information

## Scientific Title

Adjuvant Cytotoxic chemoTherapy In Older women

## Acronym

ACTION

## Study objectives

Please note that as of 22/01/2009 this record was updated to include details of an amendment to the protocol undertaken in June 2008. However, after this update to the protocol, recruitment numbers were still insufficient and the trial was closed on 24/11/2008. All changes to the initial record can be found in the relevant field under the above update date.

Amended as of 22/01/2009:

Point one of the hypothesis has been amended to the below -

1. That adjuvant chemotherapy (either Anthracycline-based chemotherapy (AC) or Epirubicin and Cyclophosphamide-based (EC) will improve disease-free survival in older women with high risk breast cancer

Initial information at time of registration:

1. That adjuvant chemotherapy (either Anthracycline-based chemotherapy (AC) or Epirubicin and Cyclophosphamide-based (EC) will improve disease-free survival in older women with high risk, ER negative/ER weakly positive breast cancer

2. That accelerated therapy with Granulocyte-Colony Stimulating Factor (G-CSF) support will not cause undue toxicity in this patient group, compared to the standard three-weekly and that both chemotherapy regimens will be acceptable and tolerated in this group of patients

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

East London and The City Research Ethics Committee gave approval prior to the trial starting recruitment (ref: 07/Q0603/1). Protocol version 1 was approved on 14/02/2007. An amendment widening the eligibility criteria to include high risk ER +ve patients (Protocol version 1.4) was approved on 16/06/2008.

## Study design

Randomised, phase III open-label clinical trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

**Study setting(s)**

Not specified

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet

**Health condition(s) or problem(s) studied**

Early stage breast cancer

**Interventions**

1. Doxorubicin 60 mg/m<sup>2</sup> or cyclophosphamide 600 mg/m<sup>2</sup> three-weekly x four cycles  
Or Epirubicin 90 mg/m<sup>2</sup> or cyclophosphamide 600 mg/m<sup>2</sup> three-weekly x four cycles

2. Accelerated - with pegylated G-CSF

Doxorubicin 60 mg/m<sup>2</sup> or cyclophosphamide 600 mg/m<sup>2</sup> two-weekly x four cycles  
Or Epirubicin 90 mg/m<sup>2</sup> or cyclophosphamide 600 mg/m<sup>2</sup> two-weekly x four cycles

**Intervention Type**

Drug

**Phase**

Phase III

**Drug/device/biological/vaccine name(s)**

Anthracycline (AC), epirubicin and cyclophosphamide

**Primary outcome measure**

Relapse free interval

**Secondary outcome measures**

Current information as of 22/01/2009:

1. Disease-free survival (DFS) (for completeness and comparison with other studies)
2. Overall survival (OS)
3. Cause-specific survival
4. Distant disease-free survival (DDFS)
5. Safety and tolerability of chemotherapy (overall and for each schedule)
6. Treatment compliance (overall and for each schedule)
7. Quality of life

Initial information at the time of registration:

1. Quality of life
2. Disease-free survival (for completeness and comparison with other studies)
3. Cause-specific survival
4. Overall survival
5. Health economic measures
6. Toxicities of chemotherapy
7. Compliance/tolerability of Computer Tomography (CT) (overall and for each schedule)

**Overall study start date**

01/02/2006

**Completion date**

01/02/2009

**Reason abandoned (if study stopped)**

Participant recruitment issues

## Eligibility

**Key inclusion criteria**

Current information as of 22/01/2009:

1. Age 70 years or over of either sex
2. Performance status 0 or 1
3. Histological diagnosis of invasive breast carcinoma
4. Primary operable breast cancer surgically treated by wide local excision or mastectomy with clear margins (greater than 1 mm apart from deep margin if full thickness resection)
5. Axillary staging performed by sentinel node biopsy, axillary sampling or clearance. All node positive patients must have had axillary clearance or radiotherapy to the axilla
6. Early stage disease with no evidence of metastases clinically or on routine staging investigations
7. High risk of relapse (approx 30%). This will include any patient with HER2 positive disease, or ER negative disease. High risk ER positive disease would typically be expected to be grade 3 with 4+ positive nodes. Other ER positive patients may be considered on an individual basis.
8. Fit to receive any of the trial chemotherapy regimens, with adequate bone marrow, hepatic, and renal function, i.e.:
  - 8.1. Haemoglobin (Hb) greater than 9 g/dL; white blood cell count (WBC) greater than  $3 \times 10^9$  /L; platelets greater than  $100 \times 10^9$  /L
  - 8.2. Bilirubin within normal range (unless known Gilberts disease)
  - 8.3. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) less than or equal to 1.5 x upper limit of normal (ULN)
  - 8.4. Albumen within normal range
  - 8.5. Creatinine less than or equal to 1.5 x ULN and calculated creatinine clearance using Cockcroft-Gault formula greater than 50 ml/min
9. No active, uncontrolled infection
10. Written informed consent given
11. No previous anthracycline chemotherapy at any time, and no other systemic anti cancer therapy within the last 5 years, unless exposure to treatment is brief, and in the context of a peri-operative trial with biological endpoints
12. No previous mantle radiotherapy
13. Randomisation as soon as reasonably possible after definitive surgery, ideally within 8 weeks
14. Patient available for routine long term hospital follow-up

Initial information at the time of registration:

1. Age 70 years or over
2. Histological diagnosis of invasive breast carcinoma
3. Primary operable breast cancer surgically treated by wide local excision with clear margins (equal to or more than 1 mm) or mastectomy
4. Axillary staging for node negative cases and axillary clearance or radiotherapy for axillary

node positive disease

5. ER negative or ER weakly positive e.g. Allred/Quick score less than three or Histo score less than 100

6. Early stage disease with no evidence of metastases clinically or on routine staging investigations

7. Risk factors for relapse suggest risk more than 30% in five years e.g. any of the following:

a. Grade three

b. Node positive

c. More than 2 cm tumours with unknown grade

d. Neuropsychiatric Inventory (NPI) score 4.4 or higher

7. Fit to receive any of the trial chemotherapy regimens, with adequate bone marrow, hepatic and renal function i.e.

a. Hb more than 9 g/dL, White blood cell (WBC) count more than  $3 \times 10^9/l$ , platelets more than  $100 \times 10^9/l$

8. Bilirubin within normal range (unless known Gilberts disease)

9. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) AST/ALT less than or equal to 1.5 x Upper Limit of Normal (ULN)

10. Albumen within normal range

11. Creatinine less than or equal to 1.5 x ULN and calculated creatinine clearance using Cockcroft-Gault formula more than or equal to 50 ml/min

12. No active, uncontrolled infection

13. Written informed consent given

14. No previous chemotherapy, hormonal therapy or radiotherapy for the treatment of pre-invasive or invasive cancer

15. Previous radiotherapy for basal cell carcinoma is permitted

16. Randomisation no later than eight weeks after definitive surgery)

17. No previous malignancy except Ductal Carcinoma in Situ (DCIS), basal cell carcinoma or cervical carcinoma in situ, unless disease-free for ten years, after surgical treatment only

18. Patients with previous non-invasive breast cancer are eligible provided they have only received surgery

19. No concomitant medical, psychiatric or geographic problems that might prevent completion of treatment or follow-up

## **Participant type(s)**

Patient

## **Age group**

Senior

## **Sex**

Both

## **Target number of participants**

1000

## **Key exclusion criteria**

Current information as of 22/01/2009:

1. Previous invasive breast cancer within the last 5 years

2. Previous ductal carcinoma in situ (DCIS) within the last 5 years if treated systemically

3. Any previous haematological malignancy or melanoma

4. Primary inoperable breast cancer (T4 and/or N3 disease)

5. Patients who have had breast-conserving surgery in whom there is a contra-indication for, or decline of, post-operative radiotherapy
6. Patients with significant cardiac disease as determined by multiple-gated acquisition scan (MUGA) or ECHO (left ventricular ejection fraction [LVEF] less than 55% excluded)
7. Patients not able or willing to give informed consent

Initial information at the time of registration:

1. Previous invasive breast cancer or bilateral breast cancer (DCIS or lobular carcinoma in situ [LCIS]. LCIS is allowed)
2. Locally advanced breast cancer (T4 and/or N3 disease)
3. Patients who have had breast conserving surgery in whom there is a contra-indication for, or refusal of post-operative radiotherapy
4. Patients not able or willing to give informed consent
5. Patients not available for a minimum of five years follow-up
6. Patients with known serious viral infection such as active Hepatitis B, Hepatitis C or Human Immunodeficiency Virus (HIV)
7. Patients with significant cardiac disease, such as impaired left ventricular function or active angina (requiring regular anti-anginal medication and/or resulting in restricted physical activity)
8. Patients with a history of significant renal impairment or disease

**Date of first enrolment**

01/02/2006

**Date of final enrolment**

01/02/2009

## Locations

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

Charing Cross Hospital

London

United Kingdom

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## Sponsor information

**Organisation**

The Institute of Cancer Research and Imperial College Healthcare NHS Trust (UK)

**Sponsor details**

c/o Peter Rigby (Chief Executive of ICR)  
Institute of Cancer Research  
123 Old Brompton Road  
London  
United Kingdom  
SW7 3RP

**Sponsor type**

Charity

**Website**

<http://www.icr.ac.uk>

**ROR**

<https://ror.org/056ffv270>

## **Funder(s)**

**Funder type**

Charity

**Funder Name**

Cancer Research UK (CRUK) (UK) (ref: C4831/A4782)

**Alternative Name(s)**

CR\_UK, Cancer Research UK - London, CRUK

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Other non-profit organizations

**Location**

United Kingdom

**Funder Name**

Amgen

**Alternative Name(s)**

Amgen Inc., Applied Molecular Genetics Inc.

**Funding Body Type**

Government organisation

**Funding Body Subtype**  
For-profit companies (industry)

**Location**  
United States of America

## Results and Publications

**Publication and dissemination plan**  
Not provided at time of registration

**Intention to publish date**

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**  
Not provided at time of registration

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Basic results</a>				No	No