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SUPREMO, an MRC Phase III randomised trial to assess the role of adjuvant chest wall irradiation in 'intermediate risk' operable breast cancer following mastectomy

Submission date 23/06/2005	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 29/07/2005	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 01/02/2024	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol
http://www.cancerhelp.org.uk/trials/a-trial-looking-at-the-benefit-of-radiotherapy-after-mastectomy-for-breast-cancer

Study website
http://www.supremo-trial.com

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number
31829

ClinicalTrials.gov number
NCT00966888

Secondary identifying numbers
G0400170, IRAS 31829, BIG 2-04

Study information

Scientific Title
SUPREMO, an MRC Phase III randomised trial to assess the role of adjuvant chest wall irradiation in 'intermediate risk' operable breast cancer following mastectomy

Acronym
SUPREMO

Study objectives
To determine the effect of ipsilateral chest wall irradiation following mastectomy and axillary clearance for women with operable breast cancer at 'intermediate risk' of loco-regional recurrence.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 04/10/2005, East of Scotland Research Ethics Service (previously Fife and Forth Valley Research Ethics Committee) (East of Scotland Research Ethics Service, Tayside Academic Health Sciences Centre, Residency Block Level 3, George Pirie Way, Ninewells Hospital& Medical School, Dundee, DD1 9SY, United Kingdom; +44 (0)1382 383871; tay.eosres@nhs.scot), ref: 05/S0501 /106

Study design
Randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Patient information can be found at: http://www.supremo-trial.com/summary-of-trial.asp

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

Interventions
Chest wall irradiation versus no chest wall irradiation

Intervention Type
Other

Phase
Phase III

Primary outcome measure
Overall survival

Secondary outcome measures
Current secondary outcome measures as of 21/01/2013:
1. Chest wall recurrence
2. Regional recurrence
3. Disease free survival
4. Metastasis free survival
5. Cause of death (breast cancer, intercurrent disease [cardiovascular and non-cardiovascular])
6. Acute and late morbidity
7. Quality of life
8. Cost effectiveness

Previous secondary outcome measures until 21/01/2013:
1. Disease free survival
2. Metastasis free survival
3. Cause of death
4. Acute and late morbidity
5. Quality of Life
6. Cost effectiveness

Overall study start date
01/10/2005

Completion date
30/01/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 21/01/2013:
1.1 Stage II histologically confirmed unilateral breast cancer following mastectomy including the following pTNM stages:
pT1N1M0
pT2N1M0

pT2N0M0 if grade III histology and/or lymphovascular invasion
pT3N0M0.
If the tumour area comprises multiple small adjacent foci of invasive carcinoma then overall maximum dimension is taken to determine the size for T staging (see section 7.2.2 for a more detailed explanation). Multifocal or multicentric tumours can be included (pT1m; pT2m; pT3m). The size of the largest tumour focus determines the T stage classification. See section 7.2.1).
1.2 Stage II histologically confirmed unilateral breast cancer following neoadjuvant systemic therapy and mastectomy, if the original clinical stage was cT1-2cN0-1M0 or cT1-2pN1(sn)M0 and with the following (ypTNM) stages after neoadjuvant systemic therapy:
ypT1pN1M0
ypT2pN1M0
ypT2pN0M0 if grade III histology and/or lymphovascular invasion.
ypT0pN0 or ypT1pN0 or ypT0pN1 (pathological complete remission, or near complete remission).
ypT2N0 independent of grade or lymphovascular invasion, if the original clinical stage was cT3N0.
ypT3N0M0, if original clinical staging was cT1-3cN0 M0 or cT1-3pN0 (sn) M0.
1.3 Unilateral invasive breast cancer that conforms to the initial clinical staging of criterion 1, but has been down-staged by neoadjuvant systemic therapy to ypT0 pN0 or ypT1pN0 or ypT0pN1 (pathological complete remission, or near complete remission). If tumour stage cT3 or ypT3, then nodal status must be N0 both before and after neoadjuvant systemic therapy.
2. Undergone total mastectomy (with minimum of 1 mm clear margin of invasive cancer and DCIS) and axillary staging procedure.
3.1 If axillary node positive (1-3 positive nodes [including micrometastases >0.2mm-≤2mm]) then an axillary node clearance (minimum of 8 nodes removed) should have been performed. Isolated tumour cells do not count as micrometastases.
3.2 Axillary node negative status can be determined on the basis of either axillary clearance or axillary node sampling or sentinel node biopsy.
3.3 Sentinel nodes identified in the internal mammary chain are considered pN1b or pN1c if histologically proven. Patients can be included in the trial with microscopic metastasis in the internal mammary chain detected by sentinel node biopsy, if not more than 3 tumour positive nodes in axillary lymph nodes. If not biopsied, internal mammary chain sentinel nodes are considered tumour negative for staging.
3.4 Before neoadjuvant systemic therapy, axillary ultrasound is advised. Abnormal axillary nodes based on imaging (mammogram or ultrasound) should be sampled by guided needle sampling or core biopsy. Where axillary ultrasound is normal, negative axillary node status does not require histological confirmation before starting neoadjuvant systemic therapy. Positive, or negative, nodal status may also be determined by sentinel node biopsy before start of neoadjuvant therapy.
4. Fit for adjuvant or neoadjuvant chemotherapy (if indicated), adjuvant or neoadjuvant endocrine therapy (if indicated) and postoperative irradiation.
5. Written, informed consent.

Previous inclusion criteria until 21/01/2013:
1. pT1, pN1, M0 or pT2, N0-1, M0 unilateral histologically confirmed invasive breast cancer
2. Unifocal invasive breast cancer
3. Fit for adjuvant therapy, adjuvant endocrine therapy and postoperative irradiation
4. Undergone simple mastectomy and an axillary staging procedure

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
1600

Total final enrolment
1688

Key exclusion criteria
Current exclusion criteria as of 21/01/2013:
1. Any pT0pN0-1 or pT1pN0 tumours after primary surgery.
2. Any pT3pN1 or pT4 tumours. Initial stage cT3cN1 or pN1(sn) or cT4 in patients receiving neoadjuvant systemic therapy cannot be included, even if downstaging has occurred and the pathological ypT and N stage is lower.
3. Patients who have 4 or more pathologically involved axillary nodes. For the purpose of this study protocol, nodal scarring after neoadjuvant systemic therapy will be considered as evidence of previous pathological nodal involvement and count towards the total number of involved axillary nodes.
4. Past history or concurrent diagnosis of ductal carcinoma in situ (DCIS) of the contralateral breast, unless treated by mastectomy. Previous DCIS of the ipsilateral breast if treated with radiotherapy (i.e. previous DCIS treated by conservation surgery not followed by radiotherapy would be considered eligible).
5. Bilateral breast cancer. However, patients who have undergone a prophylactic contralateral mastectomy can be included, if the breast was pathologically free of invasive tumour.
6. Previous or concurrent malignancy other than non melanomatous skin cancer and carcinoma in situ of the cervix. For previous DCIS see criterion 4.
7. Male.
8. Pregnancy, at the time of radiotherapy treatment.
9. Not fit for surgery, radiotherapy or adjuvant systemic therapy.
10. Unable or unwilling to give informed consent.

Previous exclusion criteria until 21/01/2013:
1. Undergone neoadjuvant systemic therapy
2. Previous or concurrent malignancy
3. Male sex
4. Pregnancy
5. Bilateral breast cancer
6. Known BCRA1 and BCRA2 carriers

Date of first enrolment
01/10/2005

Date of final enrolment
28/11/2014

Locations

Countries of recruitment
Australia

Belgium

China

France

Germany

Ireland

Israel

Japan

Netherlands

New Zealand

Poland

Scotland

Singapore

Spain

Switzerland

Türkiye

United Kingdom

Study participating centre
Western General Hospital
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Sponsor information

Organisation
University of Edinburgh, Lothian Health Board and the Common Services Agency (UK)

Sponsor details

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/01nrxwf90

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (UK) (G0400170)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

Intention to publish date
30/04/2025

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?
Results article	results	01/11/2018		Yes	No