SUPREMO (Selective Use of Postoperative Radiotherapy AftEr MastectOmy). A phase III randomised trial to assess the role of adjuvant chest wall irradiation in *intermediate risk* operable breast cancer following mastectomy.

Published: 21-11-2006
Last updated: 19-08-2024

Primary objective: To determine whether there is an overall survival benefit for patients with an intermediate risk breast cancer from chest wall irradiation following mastectomy, in addition to treatment with optimal modern systemic therapy....

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON55797

Source
ToetsingOnline

Brief title
SUPREMO

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer, mammary carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: EORTC European Organisation for Research and Treatment of Cancer
Source(s) of monetary or material Support: EORTC en KWF

Intervention

Keyword: breast cancer, mastectomy, overall survival, radiotherapy

Outcome measures

Primary outcome

The primary objective is overall survival

Secondary outcome

Evaluation of the effects of chest wall irradiation on: chest wall recurrences,

regional recurrrences, disease free survival, metastasis free survival,

cause-specific survival (breast cancer, cardiac and non-cardiac), and early and

late morbidity. Molecular radiobiological differences between patients with or

without a local recurrence.

Study description

Background summary

Loco-regional radiotherapy following mastectomy for breast cancer is standaard treatment for patients with high risk tumours (stage T3 and/ or N2 disease with more than 3 lymph node metastases). Analysis of trials of postmastectomy radiotherapy (PMRT) and overviews of these trials suggests that there is also a clinically significant survival advantage from PMRT for patients with intermediate risk disease (stages T1N1-T2N1) with a 17% reduction in the odds of death and an absolute survival advantage of 9% - 7% after 14 and 20 years respectively (Danish and Canadian trials). Because most locoregional recurrences occur on the chest wall, most of the survival advantage is thought (but not proven) to be due to the chest wall irradiation, rather than the nodal

irradiation.

Study objective

Primary objective: To determine whether there is an overall survival benefit for patients with an intermediate risk breast cancer from chest wall irradiation following mastectomy, in addition to treatment with optimal modern systemic therapy.
Secondary objective: evaluation of the effects of chest wall irradiation on: chest wall recurrences, regional recurrences, disease free survival, metastasis free survival, cause-specific survival, and early and late morbidity. Futher to carry out translational research with tumour and blood material to identify molecular biological factors that are related for example to local recurrence risk and radiation resistance (TRANS-SUPREMO substudy)

Study design

A phase III randomised trial with randomisation between chest wall irradiation following mastectomy (and, if indicated, chemotherapy), versus no chest wall irradiation.

Intervention

One randomisation group recieves chest wall irradiation, 40-50 Gy in 15-25 fractions over 3-5 weeks, and the controle group does not have radiotherapy.

Study burden and risks

Patients taking part in the TRANS-SUPREMO substudy (translational research) will be asked to give 30 ml of blood. For patients taking part in the main trial, with randomisation to no chest wall irradiation (the control group), there is no additional burden. For patients in the intervention group with chest wall irradiation, there is the following additional burden: before the start of the irradiation simulation of the treatment set-up with a simulator of CT scan (15-30 minutes) and marks are made on the skin. The radiation is given in 15-25 sessions during 3-5 weeks. The time per session is 10-15 minutes, plus travelling time to the hospital. Weekly on treatment check-ups by the radiotherapist (external physical examination). Side effects of the radiation are: skin redening with an itchy burning sensation, this goes away after the end of the treatment. Late side effects are: a tight feeling in the skin of the chest wall (fibrosis), radiation pneumonitis (1%), ribfractures (1-2%) and possible heart problems at 10 years or more. After the radiotherapy there is standard clinical follow-up, as for the control group.
This study is justified because with this trial we want to obtain a survival advantage of chest wall irradiation for breast cancer patients. The risks of

chest wall irradiation are generally limited and not life-threatening.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. 1 Stage II histologically confirmed unilateral breast cancer following mastectomy including the following pTNM stages:
-pT1, pN1, M0
-pT2, pN1, M0
-pT2, pN0 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 taken to determine the T staging. Multifocal or multicentric tumours can be included. The size of the largest tumour determines the T stage classification.

1.2 Stage II histologically confirmed unilateral breast cancer following neoadjuvant systemic therapy and mastectomy, if the original clinical stage was cT1-2cN0-1 or cT1-2pN1(sn)M0 and with the following (ypTNM) stages after neoadjuvant systemic therapy:
- ypT1N1M0
- ypT2pN1M0
- ypT2pN0M0 if grade III histology and/or lyphovascular invasion
- ypT0pN0 or ypT1pN0 or ypT0pN1 9pathological complete remission or near complete remission)
-ypT2N0, independant of grade or lymphovascular invasion, if the priginal stage was cT3N0
also:
-ypT3N0M0, if the original clinical staging was cT1-3cN0M0 or cT1-3pN0 (sn) M0,
1.3 Unilateral invasive breast cancer that conforms to the initial clinical staging of criterion 1, but has been downstaged by neoadjuvant systemic therapy to ypT0N0 or ypT1pN0 or ypT0N1 (pathological complete remission or near complete remission). If the tumour stage cT3 or ypT3, then nodal status must be N0 both before ans 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 axillarynode positive (1-3 positive nodes[including micrometastases >0.2 mm->= 2mm]) then an axillary node clearance (minimum 8 nodes removed) should have been performed. Isolated tumour cells do not count as micrometastases., 3.2 Axillary node 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 axillaey lymph nodes. If not biopsied, internal mammary chain sentinel nodes are considered tumour negative for staging., 3.5 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 chemotherapy (if indicated), adjuvant endocrine therapy (if indicated) and postoperative irradiation.
axillary node sampling or sentinel node biopsy.
5. Written, informed consent.
NB Patients undergoing immediate breast reconstruction are eligible for inclusion.

Exclusion criteria

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 occured 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 scaring 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 current 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. Unwilling or unable to give informed consent.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-11-2006
Enrollment:	275
Type:	Actual

Ethics review

Approved WMO Date:	21-11-2006
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	17-10-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-05-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-09-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-10-2021
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL13909.031.06