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Neoadjuvant Chemotherapy in Palpable Breast Cancer: Evaluation of Physiologic, Radiologic, and Molecular Markers in Predicting Response

Submission date
24/03/2010

Recruitment status
No longer recruiting

Registration date
14/04/2010

Overall study status
Completed

Last Edited
14/04/2010

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Alphonse Taghian

Contact details
Department of Radiation Oncology, Massachusetts General Hospital
100 Blossom Street
Cox Building 302
Boston
United States of America
02114

Additional identifiers

ClinicalTrials.gov (NCT)
NCT00096291

Protocol serial number
CDR0000382123, DFCI-99278

Study information

Scientific Title
A Multicentre, Phase II, Neoadjuvant Chemotherapy in Palpable Breast Cancer: Evaluation of Physiologic, Radiologic, and Molecular Markers in Predicting Response

Study objectives
This randomized phase II trial is comparing two different regimens of doxorubicin and paclitaxel to see how well they work in treating women who are undergoing surgery for breast cancer.

Rationale:
Drugs used in chemotherapy, such as doxorubicin and paclitaxel, work in different ways to stop tumor cells from dividing so they stop growing or die. Giving chemotherapy before and after surgery may shrink the tumor so it can be removed and may kill any tumor cells remaining after surgery.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Massachusetts General Hospital - Dana-Farber Cancer Institute (MGH-DFCI) Institutional Review Board (IRB) approved on the 15th of May 2000 (ref: 1999P010935)

Study design
Multicentre phase II randomized active controlled parallel group comparative trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
This is a randomized, multicenter study. Patients are stratified according to tumor size (> 5 cm vs ≥ 3-5 cm) and presence of palpable regional lymph nodes (yes vs no). Patients are randomized to 1 of 2 treatment arms.

All patients undergo biopsy, bilateral mammogram, magnetic resonance imaging (MRI), ultrasound, blood marker, molecular (gene microarrays and functional p53 status), and physiologic studies before initiation of neoadjuvant chemotherapy. Some of these studies are repeated after completion of treatment with the first chemotherapeutic agent and after completion of treatment with the second chemotherapeutic agent as outlined below.

1. Arm I: Patients receive doxorubicin intravenously (IV) on days 1, 15, 29, and 43.
1.1. Patients with no residual tumor (indicated by clinical evaluation and radiologic studies) after completion of doxorubicin undergo definitive surgery. After surgery, patients receive paclitaxel IV over 1 hour on days 1, 8, 15, 22, 29, 36, 43, 50, and 57.
1.2. Patients with residual tumor > 2 cm after completion of doxorubicin undergo 8-12 core

needle biopsies.
1.3. Patients with residual tumor < 2 cm after completion of doxorubicin undergo 4-6 core needle biopsies. After core needle biopsies, patients receive paclitaxel as above.

2. Arm II: Patients receive paclitaxel IV over 1 hour on days 1, 8, 15, 22, 29, 36, 43, 50, and 57.
2.1. Patients with no residual tumor (indicated by clinical evaluation and radiologic studies) after completion of paclitaxel undergo definitive surgery. After surgery, patients receive doxorubicin IV on days 1, 15, 29, and 43.
2.2. Patients with residual tumor > 2 cm after completion of paclitaxel undergo 8-12 core needle biopsies.
2.3. Patients with residual tumor < 2 cm after completion of paclitaxel undergo 4-6 core needle biopsies. After core needle biopsies, patients receive doxorubicin as above.

In both arms, treatment continues in the absence of disease progression or unacceptable toxicity.

Samples from core needle biopsies are analyzed by microarray analysis for gene expression profiles.

Patients are followed every 6 months for 5 years.

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
1. Determine whether tumors in women with palpable invasive breast cancer with wild type p53 are more sensitive to doxorubicin than to paclitaxel when given as sequential single-agent neoadjuvant chemotherapy.
2. Determine whether tumors with inactivated p53 are more sensitive to paclitaxel than to doxorubicin when given as sequential single-agent neoadjuvant chemotherapy in these patients.

Key secondary outcome(s))
1. Correlate other biological markers (physiological and molecular) with tumor response in patients treated with these regimens.
2. Determine changes in these biological markers during and after neoadjuvant chemotherapy in these patients.
3. Compare breast MRI, in terms of assessing tumor response, with physical exam, mammogram, and ultrasound in patients treated with these regimens.
4. Determine whether there are MRI indicators (e.g., tumor morphology or lesion enhancement) that are predictive of response in patients treated with these regimens.

Completion date
30/05/2004

Eligibility

Key inclusion criteria

1. Women, aged ≥ 18
2. Diagnosis of invasive breast cancer
3. Tumor more than 3 cm and palpable
4. Multiple masses are allowed provided at least 1 mass is more than 3 cm
5. Clinically positive axillary or supraclavicular lymph nodes allowed
6. Fine needle aspiration or core needle biopsy positive for invasive breast cancer AND/OR fine needle aspiration of lymph nodes positive
7. Estrogen receptor (ER)-positive OR ER-negative
8. ER2/neu-positive OR negative
9. Premenopausal or postmenopausal
10. Performance status: Karnofsky 60-100%
11. Granulocyte count more than 1,000/mm^3
12. Platelet count more than 100,000/cmm
13. Bilirubin more than 2 times upper limit of normal (ULN)
14. Serum glutamic oxaloacetic transaminase (SGOT) more than 2 times ULN
15. Left Ventricular Ejection Fraction (LVEF) not less than 50%

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Inflammatory breast cancer
2. Distant metastases
3. Congestive heart failure or other significant cardiovascular disease
4. Pregnancy or nursing
5. Severe medical or psychiatric condition that would preclude study compliance
6. HIV positivity
7. Patients with other prior or concurrent malignancies if they have received prior chemotherapy or are not cured from the prior malignancy

Date of first enrolment
01/06/2000

Date of final enrolment
30/05/2004

Locations

Countries of recruitment
United States of America

Study participating centre
Department of Radiation Oncology, Massachusetts General Hospital
Boston
United States of America
02114

Sponsor information

Organisation
National Cancer Institute (NCI) (USA)

ROR
https://ror.org/040gcmg81

Funder(s)

Funder type
Research organisation

Funder Name
National Cancer Institute (NCI) (USA) - Avon-NCI Progress for Patients Award on the Dana-Farber /Harvard Cancer Center Specialized Programs of Research Excellence (SPORE) in Breast Cancer (ref: CA089393)

Results and Publications

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?
Results article	results on comparison of mammography, sonography, and MRI	01/03/2005		Yes	No

Results article	results	20/03/2005		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes