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Clinical Trials (PDQ®)

Diagnostic Study of Contrast-Enhanced Magnetic Resonance Imaging and Correlative Molecular Studies in Women With Locally Advanced Breast Cancer Who Are Receiving Neoadjuvant Chemotherapy

Last Modified: 1/1/2011 **First Published:** 4/1/2002

Alternate Title

Diagnostic Procedures in Women With Locally Advanced Breast Cancer Who Are Receiving Chemotherapy Before Breast Cancer Surgery

Basic Trial Information

Phase	Type	Status	Age	Sponsor	Protocol IDs
No phase specified	Diagnostic	Closed	18 and over	NCI	**CALGB-150007** NCT00033397

Objectives

Primary

I. Support accrual to the ACRIN-6657/CALGB-150012 magnetic resonance imaging (MRI) correlative science study.
II. Determine whether molecular markers, alone or in combination with MRI, at the time of diagnosis or early in the course of therapy, predict 3-year disease-free survival (DFS) in women with locally advanced breast cancer who are receiving neoadjuvant chemotherapy.
III. Identify two groups of participants who have statistically different 3-year DFS, based on 1 or more biomarkers, including MRI.
IV. Determine whether biomarkers, in combination with MRI, early in the course of chemotherapy, improve the prediction of 3-year DFS and are at least as good of a predictor of DFS as residual disease at the time of surgery in these patients.
V. Determine whether molecular markers are associated with specific imaging patterns seen on MRI of these patients.
VI. Predict response with MRI results and marker data from cell cycle check points, proliferation, angiogenesis, hormone receptors, and molecular profiles in these patients.

Secondary

I. Determine the molecular predictors of lack of radiologic complete response (CR) in HER-2/neu negative patients (immunohistochemistry [IHC] score of 0, 1+, 2 and fluorescence in situ hybridization [FISH] not amplified) after a neoadjuvant anthracycline-based regimen.

II. Determine the molecular predictors of lack of radiologic CR in HER-2/neu positive patients (IHC 3+ or FISH amplified > 2.0) after a neoadjuvant anthracycline-based regime followed by a taxane alone regimen or in combination with trastuzumab.
III. Determine the molecular predictors of complete magnetic resonance imaging radiologic response to a neoadjuvant anthracycline-based regimen when gene expression profiling is performed in a sequential, real-time fashion.

Entry Criteria

Disease Characteristics:

Histologically confirmed newly diagnosed adenocarcinoma of the breast by core needle biopsy, incisional biopsy, or fine needle aspiration (FNA)

Incisional biopsy must result in < 10% removal of gross residual disease

Measurable disease

At least 1 unidimensionally measurable lesion ≥ 20 mm by conventional techniques OR ≥ 10 mm by spiral CT scan

OR

Nonmeasurable disease

Meets one of the following staging criteria:

Stage II or III disease

T4, any N, M0, including clinical or pathologic inflammatory disease

Regional stage IV disease where supraclavicular/infraclavicular lymph nodes are only site of metastasis

No clinical or imaging evidence of distant metastasis

Metaplastic carcinomas allowed

Synchronous bilateral primaries allowed if the more advanced tumor meets staging criteria

Patients for whom FNA was used to confirm initial diagnosis must have histologically confirmed invasive carcinoma by the start of chemotherapy

Her-2/neu status known

Currently receiving neoadjuvant chemotherapy consisting of a taxane-based regimen alone or followed by an anthracycline-based regimen

Concurrent enrollment in the ACRIN-6657/CALGB-150012 imaging protocol required

Hormone receptor status:

Any estrogen receptor or progesterone receptor status

Prior/Concurrent Therapy:

Biologic therapy

Not specified

Chemotherapy

See Disease Characteristics

No prior chemotherapy to the ipsilateral breast for this malignancy

Endocrine therapy

At least 4 weeks since prior tamoxifen or raloxifene

Radiotherapy

No prior radiotherapy to the ipsilateral breast for this malignancy

Surgery

Not specified

Other

No other prior cytotoxic regimens

Patient Characteristics:

Age

18 and over

Sex

Female

Menopausal status

Not specified

Performance status

Not specified

Life expectancy

Not specified

Hematopoietic

Not specified

Hepatic

Not specified

Renal

Not specified

Cardiovascular

No uncontrolled or severe cardiovascular disease

Other

Not pregnant or nursing
Negative pregnancy test
No ferromagnetic prostheses including the following:

Metallic implants not compatible with a magnetic resonance imaging machine
Heart valves
Aneurysm clips
Orthopedic prosthesis
Any metallic fragments anywhere in the body

Expected Enrollment

384

A total of 384 patients will be accrued for this study within 3 years.

Outline

This is a diagnostic, multicenter study conducted concurrently with CALGB-150012/ACRIN-6657 imaging protocol and concurrently with neoadjuvant anthracycline-based chemotherapy.

Patients receive an injection of gadopentetate dimeglumine and undergo magnetic resonance imaging (MRI) of the breast before initiation, 1-3 days after initiation, and then after completion of neoadjuvant anthracycline-based chemotherapy and prior to surgery. Patients who previously received a taxane also undergo an additional contrast-enhanced MRI scan.

Patients undergo biopsies before initiation and at the time of surgery. Patients also undergo blood draws at the time of the first biopsy and prior to surgery. Serum and tissue samples are used to assess biomarkers of genetic instability, cell cycle progression and cellular proliferation as predictors for anthracycline responsiveness, markers of apoptotic potential as predictors for taxane responsiveness in vivo, angiogenesis, hormone receptors, and molecular profiles using immunohistochemical methods.

Mammograms and possibly ultrasounds are performed prior to and after chemotherapy (before surgery).

Patients are followed every 6 months for 5 years and then annually for up to 10 years.

Published Results

Esserman LJ, Perou C, Cheang M, et al.: Breast cancer molecular profiles and tumor response of neoadjuvant doxorubicin and paclitaxel: The I-SPY TRIAL (CALGB 150007/150012, ACRIN 6657). [Abstract] J Clin Oncol 27 (Suppl 15): A-LBA515, 2009.

Hylton N, Blume J, Gatsonis C, et al.: MRI tumor volume for predicting response to neoadjuvant chemotherapy in locally advanced breast cancer: findings from ACRIN 6657/CALGB 150007. [Abstract] J Clin Oncol 27 (Suppl 15): A-529, 2009.

Lin C, Moore D, DeMichele A, et al.: Detection of locally advanced breast cancer in the I-SPY TRIAL (CALGB 150007/150012, ACRIN 6657) in the interval between routine screening. [Abstract] J Clin Oncol 27 (Suppl 15): A-1503, 2009.

Pradhan SM, Carey L, Edmiston S, et al.: P53 mutation and differential response to neoadjuvant chemotherapy in women with locally advanced breast cancer: results from the I-SPY trial (CALGB 150007/1500012 and ACRIN 6657). [Abstract] J Clin Oncol 27 (Suppl 15): A-11099, 2009.

Gomez RE, Zakhireh J, Moore D, et al.: Sentinel node biopsy performed in the neoadjuvant setting for breast cancer: results from the I-SPY TRIAL (CALGB 150007/150012 & ACRIN 6657). [Abstract] 31st Annual San Antonio Breast Cancer Symposium, December 10-14, 2008, San Antonio, Texas. A-202, 2008.

Livasy C, Carey L, DeMichele A, et al.: Influence of anthracycline- and taxane-based neoadjuvant chemotherapy on tumor HER2 protein expression in locally advanced breast cancers: results from the I-SPY TRIAL (CALGB 150007/150012 & ACRIN 6657). [Abstract] 31st Annual San Antonio Breast Cancer Symposium, December 10-14, 2008, San Antonio, Texas. A-703, 2008.

Livasy C, Carey L, DeMichele A, et al.: Biomarkers associated with pathologic complete response to neoadjuvant chemotherapy in women with locally advanced breast cancer: results from the I-SPY TRIAL (CALGB 150007/150012 & ACRIN 6657). [Abstract] 31st Annual San Antonio Breast Cancer Symposium, December 10-14, 2008, San Antonio, Texas. A-5102, 2008.

Conway K, Edmiston SN, Tolbert D, et al.: Preliminary evaluation of p53 mutation type, tumor characteristics and clinical response among neoadjuvantly treated breast cancer patients in I-SPY1 (CALGB 150007/ACRIN 6657). [Abstract] Breast Cancer Res Treat 100 (Suppl 1): A-3029, S134, 2006.

Related Publications

Van 't Veer LJ, Das D, DeMichele A, et al.: Neoadjuvant response in the context of a biologically defined low or high risk tumor has a different clinical consequence, the I-SPY trial (CALGB 150007/150012, ACRIN 6657). [Abstract] 32nd Annual San Antonio Breast Cancer Symposium, December 9-13, 2009, San Antonio, Texas. A-2003, 2009.

Wolf DM, Das D, Lenburg ME, et al.: From the lab to the clinic: gene-expression profiles that are associated with Mek-inhibitor sensitivity in vitro are coordinately co-expressed in breast cancer biopsy samples from the I-SPY Trial (CALGB 150007/150012, ACRIN 6657). [Abstract] 32nd Annual San Antonio Breast Cancer Symposium, December 9-13, 2009, San Antonio, Texas. A-2042, 2009.

Esserman LJ, van't Veer LJ, Perou C, et al.: Biology of breast cancers that present as interval cancers and at young age should inform how we approach early detection and prevention. [Abstract] 31st Annual San Antonio Breast Cancer Symposium, December 10-14, 2008, San Antonio, Texas. A-6034, 2008.

Carey LA, Oh D, Sawyer L, et al.: Gene expression subtype and p53 mutational status are correlated among neoadjuvantly treated breast cancers in UNC LCCC9819 and I-SPY1 (CALGB 150007/ACRIN 6657). [Abstract] J Clin Oncol 24 (Suppl 18): A-10048, 552s, 2006.

Trial Contact Information

Trial Lead Organizations

Cancer and Leukemia Group B

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Related Information

PDQ® clinical trial CLB-49808 [1]
PDQ® clinical trial ACRIN-6657 [2]

Registry Information

Official Title	Contrast-Enhanced Breast MRI, MRS, And Correlative Science Studies To Characterize Tumor Response In Patients Undergoing Neoadjuvant Treatment For Locally Advanced Breast Cancer
Trial Start Date	2002-02-01
Trial Completion Date	2005-06-05 (estimated)
Registered in ClinicalTrials.gov	NCT00033397 [3]
Date Submitted to PDQ	2002-02-28
Information Last Verified	2011-01-01
NCI Grant/Contract Number	CA31946

Note: The purpose of most clinical trials listed in this database is to test new cancer treatments, or new methods of diagnosing, screening, or preventing cancer. Because all potentially harmful side effects are not known before a trial is conducted, dose and schedule modifications may be required for participants if they develop side effects from the treatment or test. The therapy or test described in this clinical trial is intended for use by clinical oncologists in carefully structured settings, and may not prove to be more effective than standard treatment. A responsible investigator associated with this clinical trial should be consulted before using this protocol.

Table of Links

1 http://www.cancer.gov/search/ViewClinicalTrials.aspx?cdrid=68617&version=healthprofessional
2 http://www.cancer.gov/search/ViewClinicalTrials.aspx?cdrid=69496&version=healthprofessional
3 http://clinicaltrials.gov/ct/show/NCT00033397