# Tomosynthesis (TS) Versus Ultrasonography (US) in Women With Dense Breast (ASTOUND)

This study is currently recruiting participants. (see Contacts and Locations)

*Verified November 2015 by University of Genova*

**Sponsor:**
University of Genova

**Collaborator:**
University of Sydney

**Information provided by (Responsible Party):**
Alberto Tagliafico, University of Genova

**ClinicalTrials.gov Identifier:**
NCT02066142

First received: February 10, 2014
Last updated: November 30, 2015
Last verified: November 2015
History of Changes



## Purpose

Hypothesis The study aims to demonstrate at least equivalence, or non-significant difference between TS and US in women with dense breast screened negative at 2D Mammography.

If the equivalence between TS and US will be demonstrated, US may be substituted by TS with great benefits for the patients and for the healthcare resources.

Aims

1. Assess if TS may detect additional cancers in dense breast that approximate US detection capability but with less false positive findings than US.
2. If TS detects new cancers in dense breast similarly to US (approximate rate or marginally lower rate), evaluate the the true positive/false positive ratio.
3. Cost-analysis. In case of less false positives detected by TS, the true-positive / false positive trade-off might be strongly in favour of TS with a great potential of costs reduction.

| Condition | Intervention |
|---|---|
| Breast Cancer | Device: 3D mammography (Tomosynthesis)<br>Device: Ultrasound |

Study Type: Interventional
Study Design: Allocation: Non-Randomized
Endpoint Classification: Efficacy Study
Intervention Model: Parallel Assignment
Masking: Single Blind (Investigator)
Primary Purpose: Diagnostic

Official Title: Tomosynthesis (TS) Versus Ultrasonography (US) in Screening Women With Dense Breast

**Resource links provided by NLM:**

Genetics Home Reference related topics: breast cancer

MedlinePlus related topics: Mammography Ultrasound

U.S. FDA Resources

**Further study details as provided by University of Genova:**

Primary Outcome Measures:

- 1) Sensitivity of TS [ Time Frame: up to 36 months ] [ Designated as safety issue: No ]

  We want to verify if TS may detect additional cancers in dense breast that approximate US detection capability but with less false positive findings than US.

Secondary Outcome Measures:

- 2) Specificity of TS [ Time Frame: up to 36 months ] [ Designated as safety issue: No ]

  If TS detects new cancers in dense breast similarly to US (approximate rate or marginally lower rate), evaluate the the true positive/false positive ratio.

Estimated Enrollment: 4000
Study Start Date: December 2012
Estimated Study Completion Date: July 2018
Estimated Primary Completion Date: July 2018 (Final data collection date for primary outcome measure)

| Arms | Assigned Interventions |
|---|---|
| Active Comparator: Tomosynthesis<br>Tomosynthesis will be compared to Ultrasound | Device: 3D mammography (Tomosynthesis)<br>Tomosynthesis will be used as normally employed in clinical practice |
| Ultrasound<br>Ultrasound (sensitivity and specificity) will be compared to Tomosynthesis | Device: Ultrasound |

## Eligibility

Ages Eligible for Study: 18 Years to 90 Years
Genders Eligible for Study: Female
Accepts Healthy Volunteers: No

**Criteria**

Inclusion Criteria:

- Asymptomatic subjects <50 years of age presenting for mammography, with the exception of those that, on previous mammograms are found to have breast density 1-2 according to the Breast Imaging Reporting and Data System (BIRADS D1-2). - Asymptomatic subjects ≥ 50 years of age who request mammography and have breast density BIRADS 3-4.
- No history of breast cancer - Written informed consent

Exclusion Criteria:

- Pregnant and breast feeding women

- No history of breast cancer - Written informed consent

Exclusion Criteria:

- Pregnant and breast feeding women
- Unable to tolerate breast compression
- Breast implants
- Unable to understand or execute written informed consent
- Unable or unwilling to agree to follow-up during observation period

## Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02066142

**Locations**

**Italy**

UNIGE **Recruiting**
Genova, Italy, 16132
Contact: Alberto S Tagliafico, MD +390103637873 alberto.tagliafico@unige.it
Principal Investigator: Alberto S Tagliafico, MD

**Sponsors and Collaborators**

University of Genova

University of Sydney

**Investigators**

Principal Investigator: Alberto S Tagliafico, MD UNIGE

## More Information

No publications provided

| | |
|---|---|
| Responsible Party: | Alberto Tagliafico, Assistant Professor, University of Genova |
| ClinicalTrials.gov Identifier: | NCT02066142 History of Changes |
| Other Study ID Numbers: | PRA20132014 |
| Study First Received: | February 10, 2014 |
| Last Updated: | November 30, 2015 |
| Health Authority: | Italy: Ethics Committee<br>Italy: Ministry of Health |

ClinicalTrials.gov processed this record on March 09, 2016

TO TOP

For Patients and Families | For Researchers | For Study Record Managers

# Trial of Low Dose Tamoxifen in Women With Breast Intraepithelial Neoplasia (TAM-01)

This study is ongoing, but not recruiting participants.

**Sponsor:**
Andrea DeCensi

**Collaborators:**
Associazione Italiana per la Ricerca sul Cancro
European Institute of Oncology

**Information provided by (Responsible Party):**
Andrea DeCensi, Ente Ospedaliero Ospedali Galliera

**ClinicalTrials.gov Identifier:**
NCT01357772

First received: May 17, 2011
Last updated: August 3, 2015
Last verified: August 2015
History of Changes



## Purpose

The long-lasting phase of precursors of invasive cancer, i.e. dysplasia or intraepithelial neoplasia (IEN), is particularly relevant among risk determinants. At present, about 15-20% of all breast cancers are diagnosed in a non-invasive phase. Despite their good prognosis, women with breast IEN (lobular and ductal intraepithelial neoplasia, LIN and DIN) have a 10-15/1000 annual risk of invasive disease (8-10 times the same age general population), and thus represent an important target for chemoprevention. In the National Surgical Adjuvant Breast and Bowel Project (NSABP-P1 trial), tamoxifen use at 20 mg/day was associated with a 86% reduction of invasive breast cancer in women with previous atypical ductal hyperplasia (ADH) (RR=0.14, 95% IC, 0.03-0.47) and with a 56% risk reduction in women with previous Lobular Carcinoma in situ (LCIS) (RR=0.44, 95% IC, 0.16-1.06). However, tamoxifen use in this setting is hampered by serious adverse events attributable to its partial estrogenic activity, such as increased risk of endometrial cancer and of venous thromboembolism, which have significantly limited its broad use in chemoprevention.

To improve the risk-benefit ratio, the use of lower doses of the drug has been proposed. Recent trials from our group have shown that the dose can be reduced up to 1 mg/day with no loss of tamoxifen antiproliferative activity on breast cancer. By contrast, a dose of 5 mg/day does not increase endometrial proliferation and is associated with a decrease of the estrogenic activity of tamoxifen on insulin like growth factor (IGF-I), sex hormone-binding globulin (SHBG) and antithrombin-III, with a potential decrease of venous thromboembolic events. Moreover, tamoxifen exhibits a high tissue distribution, so that a dose of 5 mg/day attains at the breast tissue level a concentration 10 times higher than that needed to inhibit cell growth in vitro. The promising clinical activity of 5 mg/day of tamoxifen is supported by an ongoing 2x2 phase IIb trial of low-dose tamoxifen and fenretinide in premenopausal women, where tamoxifen lowers breast cancer events compared with placebo. The cytochromeP450 2D6 (CYP2D6) enzyme mediates oxidation of N-desmethyl tamoxifen to endoxifen, the most active metabolite of tamoxifen. The single nucleotide polymorphism (SNP) CYP2D6*4 (1846G>A) allele accounts for 75% of CYP2D6 poor metabolizer phenotype and poor metabolizers showed a trend to a higher risk to develop a breast event compared to wildtype.

| Condition | Intervention | Phase |
|---|---|---|
| Intraepithelial Carcinoma | Drug: Tamoxifen<br>Drug: placebo | Phase 3 |

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Caregiver, Investigator)
Primary Purpose: Prevention

Official Title: Randomized Placebo-controlled Phase III Trial of Low Dose Tamoxifen in Women With Breast Intraepithelial Neoplasia

**Resource links provided by NLM:**

Drug Information available for: Tamoxifen Tamoxifen citrate

U.S. FDA Resources

**Further study details as provided by Ente Ospedaliero Ospedali Galliera:**

Primary Outcome Measures:

- Incidence of invasive breast cancer [ Time Frame: 36 months ] [ Designated as safety issue: No ]

  The Primary endpoint of the proposed trial is to assess if tamoxifen at a low dose, 5mg/d reduces the incidence of invasive breast cancer and ductal carcinoma in situ (DIN 1c, 2, 3) of the breast, in woman operated for lobular intraepithelial neoplasia (LIN1, 2 and 3) or ER-positive ductal intraepithelial neoplasia (DIN 1b, DIN2, DIN3, 1a excluded) of the breast.

Secondary Outcome Measures:

- Incidence of other non-invasive breast disorders [ Time Frame: 36 months ] [ Designated as safety issue: No ]

  The secondary endpoint will evaluate the incidence of other non-invasive breast disorders (i.e., LIN, ductal atypical hyperplasia), endometrial cancer, clinical bone fractures, cardiovascular events, venous thromboembolic events, and clinically manifest cataract and overall mortality.

- To determine CYP2D6 genotype [ Time Frame: 36 months ] [ Designated as safety issue: Yes ]

  To determine whether CYP2D6 genotype and blood concentrations of drug and metabolites can explain tamoxifen modulation of surrogate biomarkers tamoxifen efficacy and safety, including circulating IGF-I, hormones, mammographic density, endometrial thickness and hot flashes, tamoxifen efficacy and toxicity on clinical events.

Estimated Enrollment: 1400
Study Start Date: November 2008
Estimated Study Completion Date: December 2023
Estimated Primary Completion Date: December 2019 (Final data collection date for primary outcome measure)

| Arms | Assigned Interventions |
|---|---|
| Experimental: Tamoxifen<br>tamoxifen at daily dose of 5 mg for a total treatment time of 3 years | Drug: Tamoxifen<br>at daily dose of 5 mg for a total treatment time of 3 years |
| Placebo Comparator: placebo<br>placebo at daily dose of 5 mg for a total treatment time of 3 years | Drug: placebo<br>placebo at daily dose of 5 mg for a total treatment time of 3 years |

**Detailed Description:**
The time interval between Study Start Date (November 2008) and Study First Release (May 17, 2011) was related to bureaucratic problems.

## Eligibility

Ages Eligible for Study: 18 Years to 75 Years
Genders Eligible for Study: Female
Accepts Healthy Volunteers: No

**Criteria**

Inclusion Criteria:

- Women of age < 75 years
- Women operated on for lobular (LIN 2 and 3) or ER positive or unknown ductal (DIN 1-3, excluded DIN 1a) intraepithelial neoplasia. Both incident (diagnosis within 12 months) and prevalent cases (diagnosis between previous 12 and 60 months) will be included, upon stratification.
- Written informed consent

Exclusion Criteria:

- Any type of malignancy, with the exclusion of non-melanoma skin cancer;
- Active proliferative disorders of the endometrium such as atypical hyperplasia, history of active endometriosis, unresected polyps;
- Alterations of metabolic, liver, renal and cardiac grade 2 function (NCI criteria grade 2 or higher);
- Any type of retinal disorders or severe cataract;
- Presence of significant risk factors for venous events, including immobilization within the last 3 months for longer than 2 weeks following surgery or trauma, deep venous thrombophlebitis or other significant venous thrombotic event (VTE) (pulmonary embolism, stroke, etc.);
- Use of tamoxifen, raloxifene or other selective estrogen receptor modulator (SERMs) within the last 4 weeks;
- Anticoagulant therapy in progress (heparin or dicoumarol);
- Active infections;
- Severe psychiatric disorders or inability to comply to the protocol procedures.

## Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT01357772

**Locations**

**Italy**

Istituto Scientifico Romagnolo per lo studio e la cura dei tumori
Meldola, Forlì-Cesena, Italy, 47521

Ospedale di Carpi "Bernardino Ramazzini"
Carpi, Modena, Italy, 41012

IRCCS Ospedale Oncologico di Bari - Istituto tumori "G. Paolo II"
Bari, Italy, 70124

Fondazione per la ricerca e la Cura dei Tumori "T. Campanella"
Catanzaro, Italy, 88100

E.O. Ospedali Galliera
Genoa, Italy, 16128

AOU IRCSS San Martino - IST
Genova, Italy, 16100

A. O. Universitaria Policlinico di Modena
Modena, Italy, 41100

Istituto nazionale per lo studio e la cura dei tumori, IRCCS "Fondazione Pascale"
Napoli, Italy, 80131

Fondazione Salvatore Maugeri
Pavia, Italy, 27100

Ospedale Santa Maria delle Croci
Ravenna, Italy, 48018

A.O. Universitaria S. Giovanni Battista - "Le Molinette"
Torino, Italy, 10123

Presidio Ospedaliero "SS. Antonio e Margherita"
Tortona, Italy, 15057

Ospedale di Circolo e Fondazione Macchi
Varese, Italy, 21100

A.O. Vicenza
Vicenza, Italy, 36100

**Sponsors and Collaborators**

Andrea DeCensi

Associazione Italiana per la Ricerca sul Cancro

European Institute of Oncology

**Investigators**

Principal Investigator: Andrea De Censi, MD E.O.Ospedali Galliera

## More Information

No publications provided

| | |
|---|---|
| Responsible Party: | Andrea DeCensi, Medical Oncology Director, Ente Ospedaliero Ospedali Galliera |
| ClinicalTrials.gov Identifier: | NCT01357772 History of Changes |
| Other Study ID Numbers: | GAL 01 |
| Study First Received: | May 17, 2011 |
| Last Updated: | August 3, 2015 |
| Health Authority: | Italy: The Italian Medicines Agency |

Additional relevant MeSH terms:

Carcinoma in Situ
Carcinoma
Neoplasms
Neoplasms by Histologic Type
Neoplasms, Glandular and Epithelial
Tamoxifen
Antineoplastic Agents
Antineoplastic Agents, Hormonal
Bone Density Conservation Agents
Estrogen Antagonists
Estrogen Receptor Modulators
Hormone Antagonists
Hormones, Hormone Substitutes, and Hormone Antagonists
Pharmacologic Actions
Physiological Effects of Drugs
Selective Estrogen Receptor Modulators
Therapeutic Uses

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