

FAST FACTS

A012301: LoTam: “A Randomized, Phase III Clinical Trial of Low-Dose Tamoxifen for Selected Patients with Molecular Low-risk Early-Stage Breast Cancer”

Eligibility Criteria

1. Unilateral invasive adenocarcinoma of the breast that is histologically confirmed. **(DCIS and/or LCIS that is identified as a component of the tumor mass is permitted).**
 - Invasive breast cancer is estrogen receptor positive in $\geq 10\%$ of cells
 - HER2 negative by current ASCO/CAP guidelines
2. The patient must have a multigene assay with a low-risk score, including any of the following (if more than one genomic assay was obtained, both are required to be low-risk):
 - Oncotype DX Recurrence Score ≤ 25
 - Mamma Print low risk
 - Prosigna Risk of Recurrence ≤ 40
 - Patients with pathologic tumor size $\leq 0.5\text{cm}$ who meet all other eligibility criteria are eligible for enrollment without multigene assay testing. The total number of enrolled patients with tumor size $\leq 0.5\text{cm}$ without genomic testing will be limited, as specified in section 13.10.3.
3. Surgical pathology requirements:
 - Tumor size must be $\leq 3\text{ cm}$ by pathologic evaluation. Multifocal tumors are permitted if the largest focus of disease is $\leq 3\text{ cm}$.
 - Adequate surgical removal of all clinically evident disease in the breast with either breast conserving surgery or mastectomy. Negative margins on final pathology are required. Additional excisions may be performed to obtain clear margins before registration.
 - No clinical (cN1, cN2, cN3) or pathologic (pN1mi, pN1, pN2, or pN3) evidence of lymph node involvement on either needle biopsy or surgical lymph node assessment. Patients with pN0(i+) or pN0 (mol+) are eligible.
 - Surgical axillary staging (sentinel lymph node biopsy \pm axillary lymph node dissection) is completed according to physician discretion.
 - For patients age <70 , clinicians may selectively choose to forego surgical axillary staging if a preoperative ipsilateral axillary ultrasound or preoperative MRI shows no lymph node involvement with no

evidence of lymphadenopathy or suspicious thickening.

- For patients age ≥ 70 without surgical axillary staging, axillary ultrasound is not required but may be obtained at the discretion of the treating investigator.
4. No tumors that are considered pT4
 5. No definitive clinical or radiologic evidence of metastatic disease
 6. No palpable or radiographically suspicious axillary, supraclavicular, infraclavicular, or internal mammary lymph nodes, unless there is histologic confirmation that these lymph nodes are negative for tumor
 7. No suspicious microcalcifications, densities, or palpable abnormalities in the ipsilateral or contralateral breast, unless biopsied and found to be benign
 8. An interval of no more than 20 weeks between the date of surgery and the date of registration.
 9. Must have had a bilateral mammogram or MRI within 9 months prior to registration.
 10. Must be intending to take endocrine therapy for 5 years duration
 11. Prior Treatment
 - No prior treatment with endocrine therapy or chemotherapy for the currently diagnosed breast cancer prior to registration. (Short course endocrine therapy of ≤ 6 weeks duration is acceptable after core biopsy and before surgery, if genomic testing is assessed on the biopsy core and meets eligibility requirements for a low-risk score.)
 - No use of oral hormone replacement therapy or transdermal estrogen replacement therapy (patch) within 7 days prior to registration.
 12. Age ≥ 18 years and female
 13. ECOG Performance Status ≤ 2
 14. Postmenopausal status confirmed as meeting one of the following:
 - No spontaneous menses ≥ 1 year or
 - No menses for < 1 year with FSH and estradiol levels within a postmenopausal range according to institutional standards or
 - Previous bilateral surgical oophorectomy
 15. None of the following conditions:
 - Abnormal or dysfunctional uterine bleeding within 1 year prior to

study enrollment or

- Any patient with known atypia or endometrial pathology that the opinion of the treating investigator would place the patient at undue risk of endometrial cancer with tamoxifen or
- Any patient with a known hypercoagulable state that in the opinion of the treating investigator would put the patient at undue risk of venous thromboembolism with tamoxifen.

16. No history of breast or thoracic radiotherapy for any previous condition. Patients may complete radiotherapy for the currently diagnosed breast cancer prior to registering for the study. In this scenario, registration must be completed within 12 weeks of completing breast radiotherapy.

17. No previous history of ipsilateral invasive breast cancer or ipsilateral DCIS, regardless of the disease-free interval.

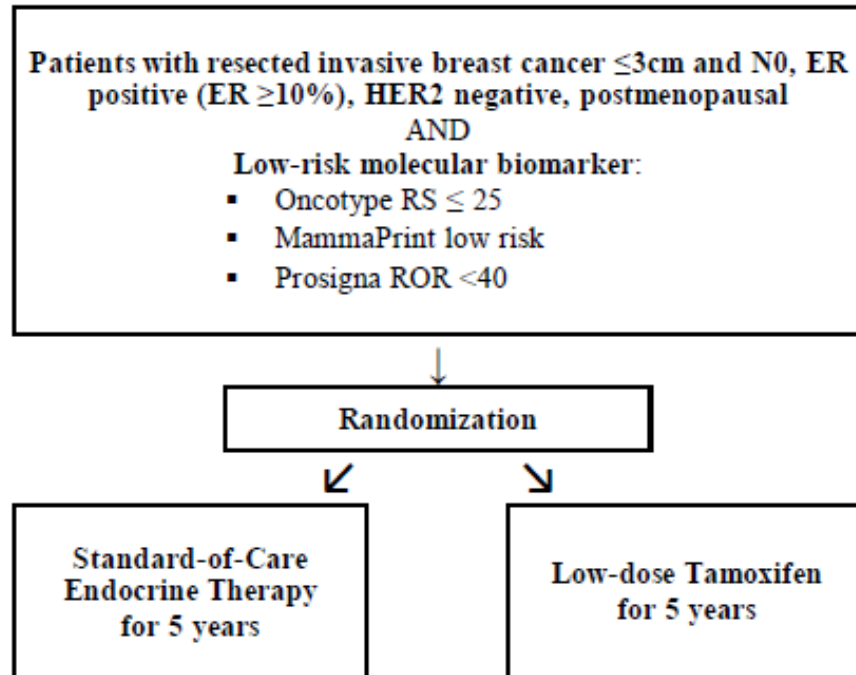
18. No synchronous or previous history of contralateral invasive breast cancer or DCIS.

19. Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

20. Concomitant Medications

- No current treatment with any endocrine therapy for breast cancer prevention or osteoporosis, including raloxifene, tamoxifen, or other selective estrogen receptor modulator.
- Patients intending to continue oral hormone replacement are not eligible.

21. HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial



Stratification factors:

- Local therapy (lumpectomy with no RT; lumpectomy + RT; mastectomy)
- Genomic test (Oncotype vs other)