A phase III trial evaluating De-escalation of Breast Radiation (DEBRA) following breast-conserving surgery of stage 1, HR+, HER2–, RS ≤18 breast cancer: NRG-BR007

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BACKGROUND

- Approximately 50% of newly diagnosed breast cancers are stage 1.
- The majority of these are ER/PR positive, HER2-negative.
- Local-regional recurrence (LRR) rates have steadily reduced.
- Genomic assays such as the Oncotype DX Breast Recurrence Score® (RS) have identified patients at risk of distant metastases who do not benefit from chemotherapy, sparing patients from excess toxicity.
- Multiple studies have demonstrated that genomic assays such as the RS are prognostic of LRR.
- Stage 1 hormone-sensitive (HS) breast cancer identified as "Low Risk" by a genomic assay may have little or no excess incidence of local recurrence if post-lumpectomy breast radiotherapy (RT) is omitted.
- Recently, two single-arm trials, IDEA[1] and Lumina,[2] have reported low rates of LRR at 5 years without breast radiotherapy post lumpectomy in stage 1 HS, HER2-negative breast cancer with an RS <18 or Ki67 <13%, respectively, supporting feasibility of this approach.
- De-escalation of therapy is of interest to patients, providers, and payers.

HYPOTHESIS

Breast-conserving surgery (BCS) alone is non-inferior to BCS plus radiation for ipsilateral breast recurrence (IBR) and breast preservation for women intending appropriate endocrine therapy for stage 1 breast cancer that is ER and/or PR positive, HER2-negative, and has a low Oncotype DX RS.

OBJECTIVES

Primary

- Evaluate whether BCS alone results in a non-inferior rate of non-invasive or invasive ipsilateral breast recurrence compared to BCS with RT in eligible patients.

Secondary

- Overall breast-conservation rate.
- Invasive Ipsilateral Breast Recurrence (IIBR).
- Recurrence-free Interval (RFI).
- Distant Disease-free Survival (DDFS).
- Overall Survival (OS).
- QOL (Patient-reported breast pain and worry about recurrence).
- Adherence to endocrine therapy, where applicable.

REFERENCES:
1. Jagsi R et al. *J Clinc Oncol.* 42 (4):390-98, 2024;
2. Whelan T et al. *NEJM.* 389: 612-19, 2023.

SUPPORT:
U10 CA-180868, -180822,
U24 CA196067, UG1 CA189867

STUDY DESIGN

NRG-BR007 SCHEMA

Patients ≥50 and <70 yrs with pT1N0M0, HER2-negative, ER and/or PR-positive breast cancer resected by lumpectomy and Oncotype DX RS ≤18

STRATIFICATION
- Age (<60; ≥60)
- RS (≤11; >11)
- Tumor size (≤1 cm; 1.1–2 cm)

RANDOMIZATION

ARM 1
Breast radiation therapy
+
Endocrine therapy

ARM 2
Observation
+
Endocrine therapy

Arm 1

Post-lumpectomy RT using standard methods (hypo or conventional-fractionated whole breast irradiation with or without boost or accelerated partial breast irradiation).

At least 5 yrs of endocrine therapy (tamoxifen or aromatase inhibitor).

Specific regimen of endocrine therapy is at physician's discretion.

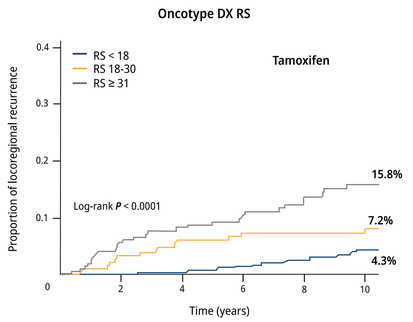
Arm 2

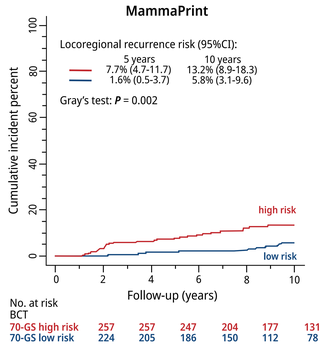
At least 5 yrs of endocrine therapy (tamoxifen or aromatase inhibitor).

Specific regimen of endocrine therapy is at physician's discretion.

NCT #: NCT04852887

"Low Risk" as Determined by Multi-gene Assay Associated with Low LRR after Lumpectomy and WBI





Can a multi-gene assay define breast cancer without RT?

OTHER CLINICAL TRIALS

Trial	CT.gov Identifier	Design	Biological selections	Eligible pt age	Target accrual
PRIMETIME	--	Prospective, biomarker-directed case cohort study	IHC4+C	>60	2,400
PRECISION	NCT02653755	Phase II, single-arm observation	PAM 50 ROR ≤40	55–65	1,380
EXPERT	NCT02889874	Phase III randomized RT *vs* observation	PAM 50 Luminal A ROR ≤60	≥50	1,167

PRO INSTRUMENTS

Outcome of Interest	Instrument	# of items
Primary Outcomes		
Breast pain	BCTOS	3
Breast cancer fear of recurrence	CanSORT Breast Cancer Worry	3
Secondary Outcomes		
Breast-related functional status	BCTOS	7
Cosmesis	BCTOS	8
General health-related QOL	PROMIS Global	10
Fatigue	PROMIS Fatigue	6
Breast cancer treatment symptoms	Treatment-related Symptom Checklist (NSABP B-39/RTOG 0413)	13
Distress related to cancer recurrence	Quality of Life After Cancer	4
Endocrine therapy adherence	Extent of Non-adherence Questionnaire (Voils)	3
Endocrine therapy symptoms	BCPT Symptom Checklist	21

ELIGIBILITY

- Stage 1: pT1 ≤2 cm, pN0 (AJCC 8th edition).
- Age ≥50 and <70 yrs.
- Status post-lumpectomy with negative margins (no ink on tumor).
- Status post-axillary nodal staging (SNB or AND) – pN0
- ER and/or PR positive by ASCO/CAP.
- HER2-negative by ASCO/CAP.
- Oncotype DX RS of ≤18 on diagnostic core biopsy or resected specimen. (Mammaprint Low is allowable if done per usual clinical care prior to screening for trial enrollment).

STATISTICAL PLAN

- Using TAILORx local-regional RFI by RS for IBR at 9 yrs adjusted to our study period of 10 yrs, we calculate the annual failure rate in the RT arm to be 0.0045.
- Assume a clinically acceptable difference in IBR at 10 yrs to judge omission of RT as non-inferior is 4% (10-yr IBR-free survival for RT group is 95.6% *vs* 91.6% for the omission-of-RT group).
- Be able to detect non-inferiority as defined with 80% power and a one-sided α=0.025 and assuming a 5-yr accrual (ramp-up for # randomly assigned: Yr 1 ~12/mos; Yr 2 ~23/mos, Yrs 3-5 ~35/mos), a total accrual of 1,670 (835 per arm) is required. This conservatively assumes loss to follow-up will be 1% per yr.
- Screening for T1a lesions requiring Oncotype DX inflates targeted registration accrual to 1,714 to randomly assign 1,670.

STUDY STATUS

- Site participation and patient enrollment continue to increase in the US, Canada, and approved international sites.
- Accrual is 1,517/1,670 (as of Nov 21, 2025).
- Interested international sites that are participating members of NCTN groups are encouraged to contact their Member Group Operations Office.

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