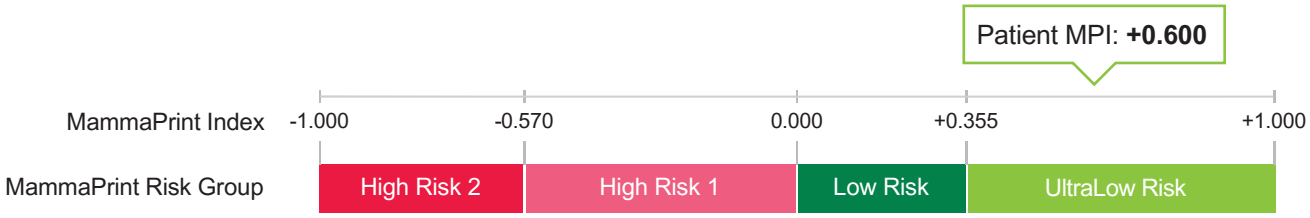
MammaPrint® and BluePrint® Explanation of Results

Specimen File ID: NGS23-000332I1P1C1S1_S19_L00041_15Jan2025-NGS23-000332I1P1C1S1_S19_L00041_15Jan2025

AGENDIA MAMMAPRINT+BLUEPRINT

GENOMIC TESTING RESULTS

MammaPrint Risk Group	MammaPrint Index	BluePrint Molecular Subtype
UltraLow Risk	**+0.600**	**Luminal A**



CLINICAL IMPLICATIONS

This explanation of results assumes the patient's tumor is hormone receptor-positive. Clinical implications are based on observed outcomes from clinical research studies depicted below and further referenced on page 3. Results should be taken in the context of all other relevant clinico-pathological factors and standard practice of medicine.

Neoadjuvant Chemotherapy Planning

Probability of pCR with Neoadjuvant Chemotherapy

2%

NBRST[A]

Adjuvant Chemotherapy Planning

Absolute Chemotherapy Benefit

No CT Benefit

MINDACT[D]

8-Year Distant Metastasis Free Interval with ET alone

97.4%

MINDACT[D]

Adjuvant Endocrine Therapy Planning

Standard Endocrine Therapy Duration

Applies only to LN0 patients

Premenopausal	Postmenopausal
5 years	**Consider < 5 years in event of intolerance**

STO-3[C]

Absolute Benefit from Extended Endocrine Therapy

Applies only to postmenopausal patients

No

NSABP B-42[E]

CT: Chemotherapy | **ET:** Endocrine Therapy | **LN0:** Lymph Node Negative | **MPI:** MammaPrint Index | **pCR:** Pathologic Complete Response

Note: This summary is provided for general informational purposes. It is not part of any official diagnostic report. Please refer to the MammaPrint and BluePrint Technical Report and Instructions for Use for comments, assay information, and references.

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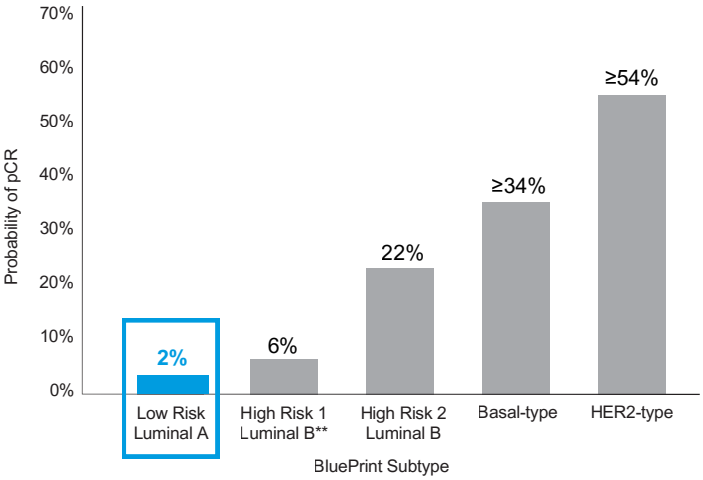
AGENDIA MAMMAPRINT+BLUEPRINT

NEOADJUVANT CHEMOTHERAPY PLANNING DATA*

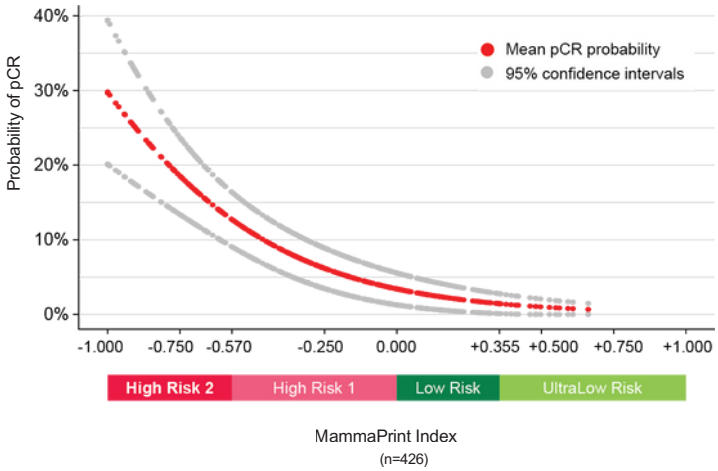
Probability of pCR Based on BluePrint Subtype and MP Risk Group

NBRST/FLEX[A,B]



Probability of pCR Based on MPI and MP Risk Group

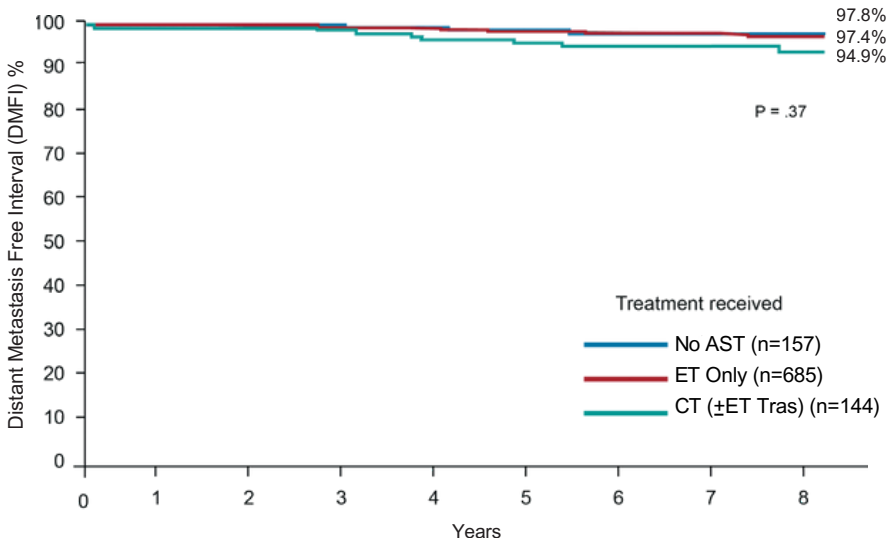
NBRST[A]



ADJUVANT CHEMOTHERAPY PLANNING DATA*

8-Year DMFI in MP UltraLow Risk Patients by Treatment

MINDACT[D]



***Clinical implications are based on observed outcomes from clinical research studies depicted above and further referenced on page 3. Results should be taken in the context of all other relevant clinico-pathological factors and standard practice of medicine.**

**A pathologically ER+/HER2+ patient with a Luminal B-Type result has a 16% probability of pCR with neoadjuvant chemotherapy.

AST: Adjuvant Systemic Treatment | **ET:** Endocrine Therapy | **MP:** MammaPrint | **MPI**: MammaPrint Index | **pCR:** Pathologic Complete Response
Tras: Trastuzumab

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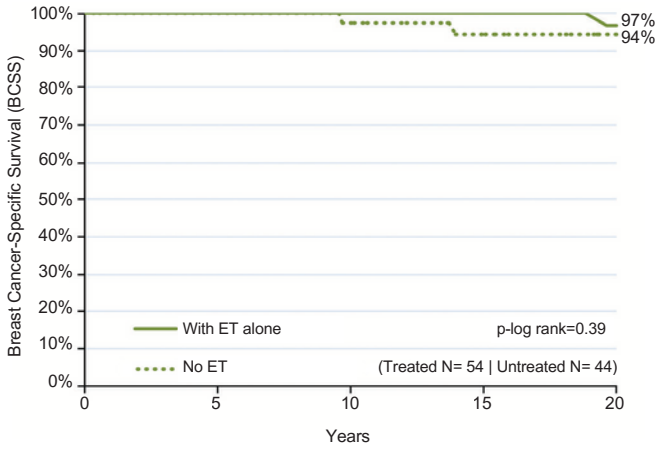
AGENDIA MAMMAPRINT+BLUEPRINT

ADJUVANT ENDOCRINE THERAPY PLANNING DATA*

20-Year BCSS in UltraLow Risk Patients with 5 Years or Less of ET

STO-3[C]



***Clinical implications are based on observed outcomes from clinical research studies depicted above and further referenced below. Results should be taken in the context of other relevant clinico-pathological factors and standard practice of medicine. The standard endocrine data only apply to post-menopausal women with clinically and/or pathologically confirmed negative lymph nodes. Data are limited in the setting of positive lymph nodes. Clinical implications of MammaPrint UltraLow Risk on pre-operative core needle biopsy samples in clinically node-negative breast cancer will apply if lymph nodes are found to be pathologically negative at surgical resection.**

CLINICAL STUDY AND TRIAL REFERENCES

A. NBRST: A prospective study that included 1,069 patients with histologically proven early stage breast cancer (ESBC), aged 18–90 years, who were scheduled to receive neoadjuvant therapy. Patients were enrolled from 40 US institutions and received both MammaPrint and BluePrint genomic testing. Treatment was at the discretion of the physician adhering to NCCN-approved or other peer-reviewed, established regimens. Intrinsic preoperative chemosensitivity and long-term outcomes were precisely determined by MammaPrint and BluePrint regardless of patient age, supporting the utility of these assays to inform treatment and surgical decisions in ESBC.[1-4]

B. FLEX (NCT03053193): An ongoing prospective, observational trial that has enrolled >17,000 patients with ESBC who were tested with MammaPrint as standard of care, with or without BluePrint, and consented to clinically annotated full transcriptome data collection (data locked August 2024).[5-7]

C. STO-3: The Stockholm tamoxifen trial included 1,780 lymph node-negative, hormone receptor-positive, postmenopausal patients with tumors smaller than or equal to 3 cm in diameter, randomized to 2 (65%) to 5 (35%) years of adjuvant tamoxifen vs no adjuvant treatment. MammaPrint was retrospectively assessed on a translational cohort of 652 patients; 313 had received tamoxifen (2–5 years) and 339 had not received adjuvant systemic therapy.[8,9]

D. MINDACT: A phase 3, prospective, randomized clinical trial that enrolled 6,693 patients at 112 academic and community hospitals in 9 European countries. Patients were eligible to enroll if they were women aged 18–70 years with histologically confirmed unilateral primary non-metastatic (M0) invasive breast cancer (clinical stage T1 or T2 or operable T3) with 0–3 positive axillary lymph nodes. For hormone-positive women ≤ 50 years, there was a 2.6% benefit in 5-year distant metastasis free survival for women who received chemotherapy (CT) vs those that received endocrine therapy (ET) alone. Although this difference is possibly due to CT-induced ovarian function suppression, it should be part of informed, shared decision making.[10,11]

E. NSABP B-42: An adjuvant extended endocrine therapy (EET) trial which included 3,966 postmenopausal women with stage I–IIIA hormone receptor-positive breast cancer, who were disease-free after 5 years of ET. Patients were randomized to receive either an additional 5 years of letrozole (EET) or placebo. MammaPrint was retrospectively analyzed on a translational cohort of 1,866 patients; 916 patients received EET and 950 patients received placebo.[12]

F. IDEAL: A phase 3 randomized, prospective, EET clinical trial that enrolled 1,824 postmenopausal patients with stage I–III HR+ breast cancer who had completed 5 years of adjuvant endocrine therapy and were randomized to receive either 2.5 or 5 additional years of letrozole (EET). MammaPrint was performed retrospectively on 515 available tumor specimens with 10-year follow-up data, where 265 were from the 2.5-year treatment arm and 250 from the 5-year treatment arm. IDEAL and NSABP-B42 are complementary Level 1 trials that together meet 1B evidence criteria.[13]

References:

1. Whitworth P et al. *Ann Surg Oncol*. 2017 Mar;24(3):669-675. | **2.** Whitworth P et al. *JCO Precis Oncol*. 2022 Apr;6(1):e2100463. | **3.** Whitworth P et al. *Ann Surg Oncol*. 2022 Apr 4;29(7):4141-4152. | **4.** Whitworth P et al. *JCO Precis Oncol*. 2022 Sep:6:e2200197. | **5.** O'Shaughnessy J et al. JCO 2021 May; 39(15_suppl), 563–563. | **6.** O'Shaughnessy J et al. Cancer Res 2024 May; 84(9_suppl), PO5-15–04. | **7.** Brufsky A et al. JNCI Cancer Spectr. 2025;9(5):pkaf079. | **8.** van 't Veer L et al. Breast Cancer Res Treat. 2017;166(2):593-601. | **9.** Esserman LJ et al. JAMA Oncol. 2017;3(11):1503-1510. | **10.** Piccart M et al. Lancet Oncol. 2021;22(4):476-488. | **11.** Lopes-Cardozo J et al. J Clin Oncol. 2022;40(12):1335-1345. | **12.** Rastogi P et al. J Clin Oncol. 2024;00:1-9. | **13.** van 't Veer LJ, et al. JAMA Netw Open. 2024;7(11):e2447530.

ET: Endocrine Therapy