EXACT SCIENCES

Oncotype DX Breast Recurrence Score® Report

Important Update on the RxPONDER Trial Results in Node Positive Breast Cancer

The SWOG S1007 study, known as RxPONDER, is a prospective multinational phase III clinical trial in women (≥18yrs) with hormone receptor-positive, HER2-negative invasive breast cancer with 1-3 positive axillary lymph nodes. The study included 5018 eligible women with a Recurrence Score® (RS) result of 0-25 who were randomized to endocrine therapy (ET) alone versus chemotherapy (CT) followed by endocrine therapy. Women with a Recurrence Score result of 26-100 were recommended to undergo chemotherapy followed by endocrine therapy.[1]

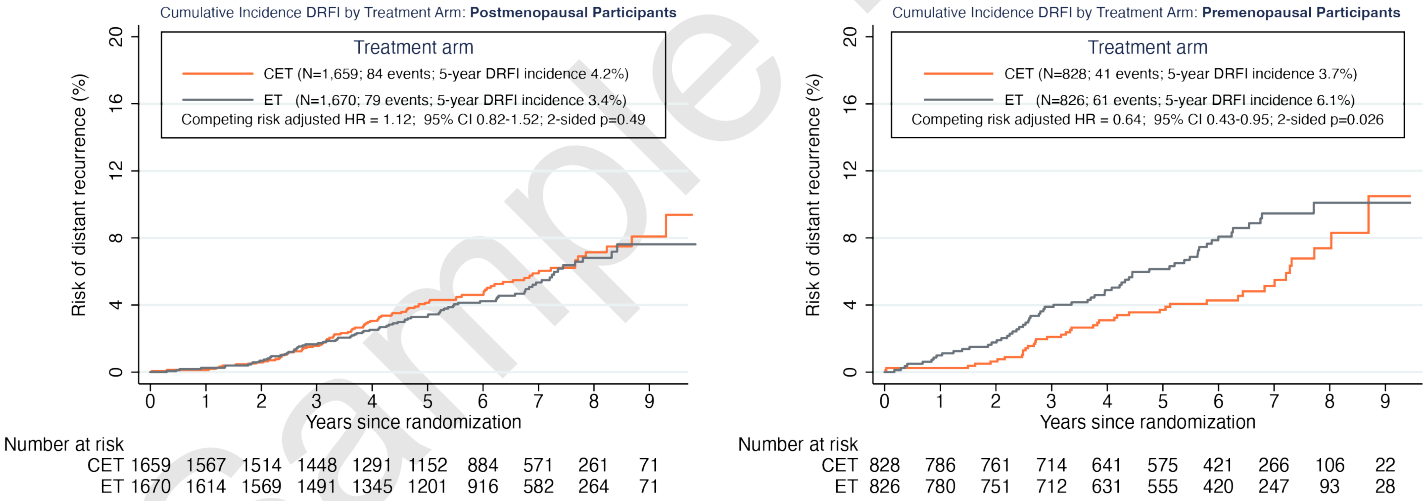
The data have been published in the New England Journal of Medicine[2] in December 2021 and were further updated at the 2021 San Antonio Breast Cancer Symposium.[3] Median follow-up of the SABCS analysis was 6.1 years.

RxPONDER Results by Menopausal Status — Effect of chemotherapy on absolute risk of distant recurrence in women with 1-3 positive axillary lymph nodes and RS result of 0-25.

Postmenopausal women with RS result of 0-25 did not show benefit of chemotherapy in addition to endocrine therapy (competing risk adjusted HR = 1.12, 95% CI 0.82-1.52, p=0.49). Consistent lack of chemotherapy benefit was observed for IDFS for subgroups of age, tumor size, grade, Recurrence Score result, and number of positive lymph nodes.

Premenopausal women with RS result of 0-25 had a significant benefit in DRFI from the addition of chemotherapy to endocrine therapy (competing risk adjusted HR 0.64, 95% CI 0.43-0.95, p=0.026). Consistent benefit of chemotherapy was observed for IDFS for subgroups of age, tumor size, Recurrence Score result, and number of positive lymph nodes. The 5-year absolute benefit of chemotherapy for distant recurrence was 2.4% (RS 0-13: 2.3%; RS 14-25: 2.8%).

Rate of Distant Recurrence by Menopausal Status



*DRFI = Time from randomization assignment to date of first invasive recurrence (distant) or death from breast cancer

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Definition of Menopausal Status:
Premenopausal: Less than 6 months since last menstrual period and not on estrogen replacement.
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Oncotype DX Breast Recurrence Score® Report

Micromets & Node Positive (1-3)

EXACT SCIENCES

PATIENT, SAMPLE

Date of Birth: **DD-MM-1950** Gender: **Female** Report Number: **OR000123456-3021** Report Date: **21-Oct-2022**

Specimen Source/ID: **Breast/SP-16_0123456**

Ordering Physician: **Dr. First-Name I. Ordering-Physician-Last-Name**

Recurrence Score® (RS) Result

Clinical factors may be considered with the RS when making individual treatment decisions.

Distant Recurrence Risk at 9 Years

With AI or TAM Alone

12%

95% CI (8%, 16%)

TransATAC

AI = Aromatase Inhibitor / TAM = Tamoxifen
CI = Confidence Intervals

Group Average Absolute Chemotherapy (CT) Benefit*

RS 0-17

No Apparent Benefit

SWOG 8814

*Refer to the cover sheet to incorporate the findings from the RxPONDER study.

Real World Evidence of SEER Registry Outcomes in Patients Treated Without CT Based on RS Results

	RS 0-10	RS 11-15	RS 16-20	RS 21-25	RS 26-100
# of Patients	1808	2196	1754	692	364
BCSS at 9 Years	98.2%	99.0%	96.7%	93.1%	84.2%

BCSS = Breast cancer-specific survival

Quantitative Single-Gene Scores[1]

10.8 ER Positive

<3.7 6.5 ≥12.5

7.3 PR Positive

<3.2 5.5 ≥10.0

10.0 HER2 Negative

<7.6 10.7 11.5 ≥13.0

1. ER Score based on quantitative ESR1 expression (estrogen receptor); PR Score based on quantitative PGR expression (progesterone receptor); HER2 Score based on quantitative ERBB2 expression.

Oncotype DX Breast Recurrence Score® Report

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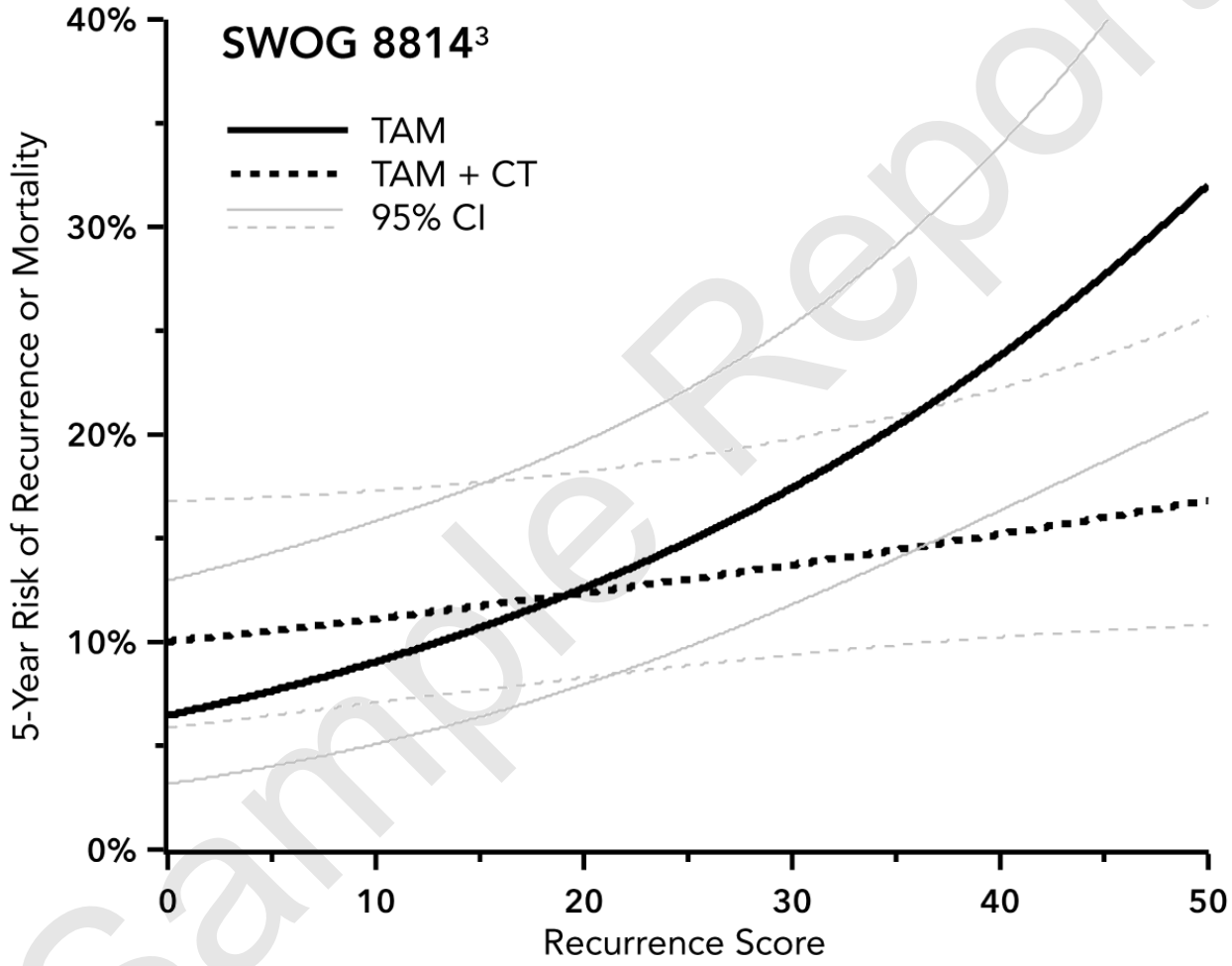
Estimated Chemotherapy Benefit for Individual Recurrence Score Results



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EXACT SCIENCES

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Specimen Source/ID: **Breast/SP-16_0123456**

Ordering Physician: **Dr. First-Name I. Ordering-Physician-Last-Name**

Medical Record/Patient #: **1234567-01** Client: **Community Medical Center**

Date of Collection: **06-Oct-2022**

Specimen Received: **08-Oct-2022**

Additional Recipient: **Dr. First-Name I. Recipient-Physician-Last-Name**

Pathologist: **Dr. First-Name I. Pathologist-Last-Name**

The Oncotype DX Breast Recurrence Score test uses RT-PCR to provide information on prognosis and the magnitude of chemotherapy benefit to guide chemotherapy treatment decisions in patients with early-stage, hormone receptor-positive (HR+), and lymph node-negative or lymph node-positive breast cancer. Decision on treatment should also be based on independent medical judgement of the treating physician taking into consideration all available information concerning the patient's medical condition, including other pathological tests, in accordance with your community's standard of care.

Results in this report are based on studies including both micrometastases and 1-3 positive nodes.
Advances in histopathological techniques and changes in staging criteria have resulted in an increase in the number of patients diagnosed with lymph node micrometastases (0.2 mm - 2.0 mm). Previous study results varied regarding their clinical significance. BCSS in SEER[1] for patients with RS 0-17 treated without chemotherapy are similarly favorable for patients with negative nodes, micrometastases, and 1-3 positive nodes.

The **Recurrence Score (RS) Result**, which ranges from 0-100, is calculated from the quantitative RT-PCR analysis of the 21 genes.

The **Distant Recurrence Risk** at 9 Years (Prognosis), in patients treated with tamoxifen or arimidex alone, is provided by the TransATAC[2] trial. Risk is for individual RS results. The 95% confidence intervals for distant recurrence at 9 years are ±3 to ±6% for RS 0-22, and range from ±6 to ±12% as RS increases from RS 23-50. The TransATAC trial enrolled 1,231 patients and 243 patients had 1-3 positive nodes, including micrometastases.

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Laboratory Director(s): William P. Joseph, M.D.

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Genomic Health, Inc.
301 Penobscot Drive, Redwood City, CA 94063, USA
USA/Canada +1.866.ONCOTYPE (+1.866.662.6897)
https://precisiononcology.exactsciences.com/
CLIA Number 05D1018272

EXACT SCIENCES

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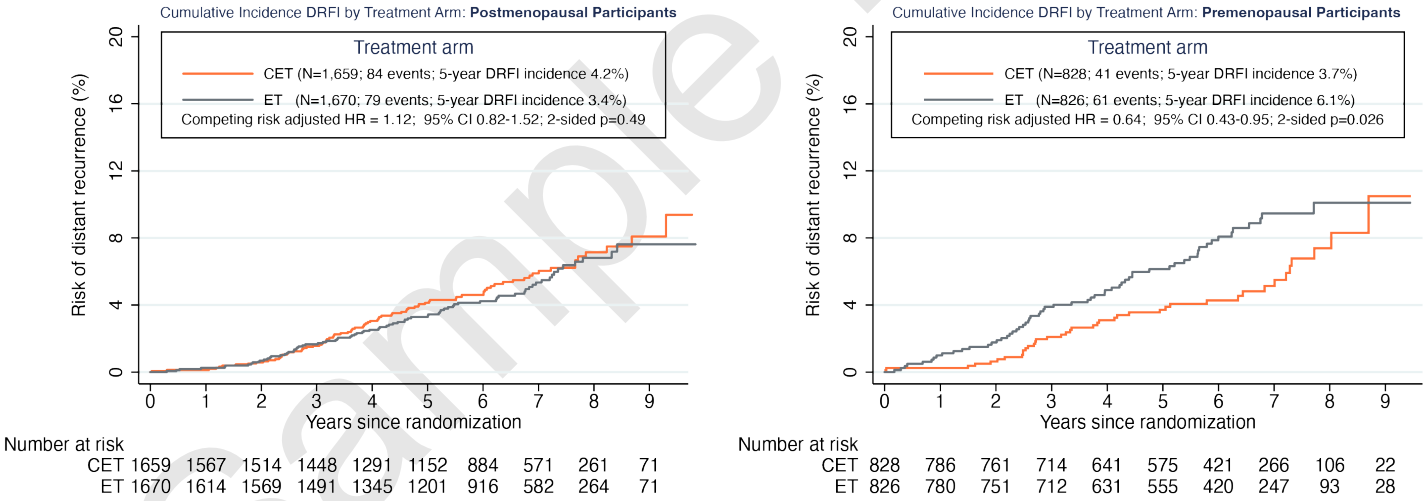

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EXACT SCIENCES

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Specimen Source/ID: **Breast/SP-16_0123456**

Ordering Physician: **Dr. First-Name I. Ordering-Physician-Last-Name**

Recurrence Score® (RS) Result

Clinical factors may be considered with the RS when making individual treatment decisions.

Distant Recurrence Risk at 9 Years

With AI or TAM Alone

18%

95% CI (13%, 23%)

TransATAC

AI = Aromatase Inhibitor / TAM = Tamoxifen
CI = Confidence Intervals

Group Average Absolute Chemotherapy (CT) Benefit*

RS 18-30

CT Benefit for this group cannot be excluded.

95% CI (-5%, 7%)

SWOG 8814

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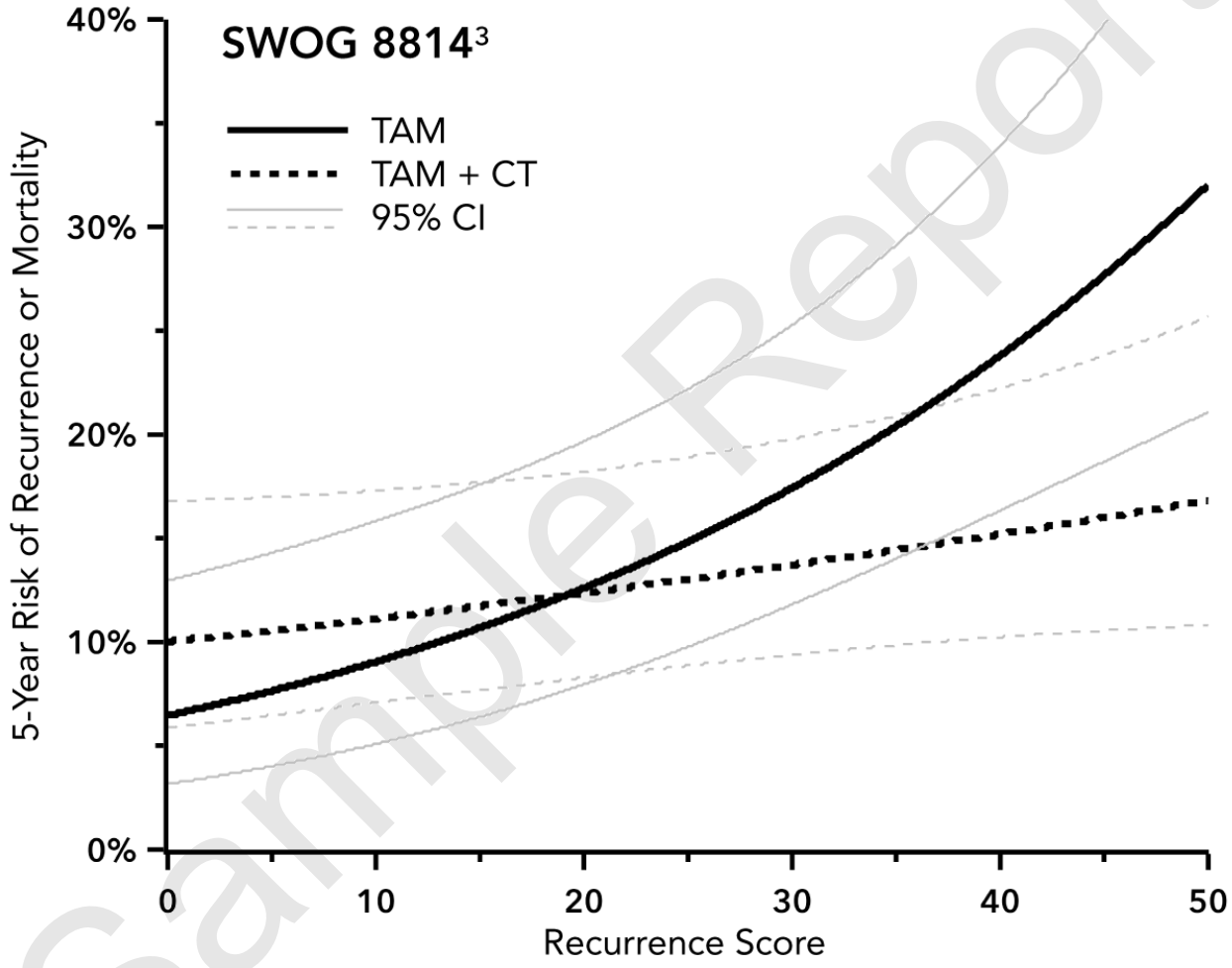

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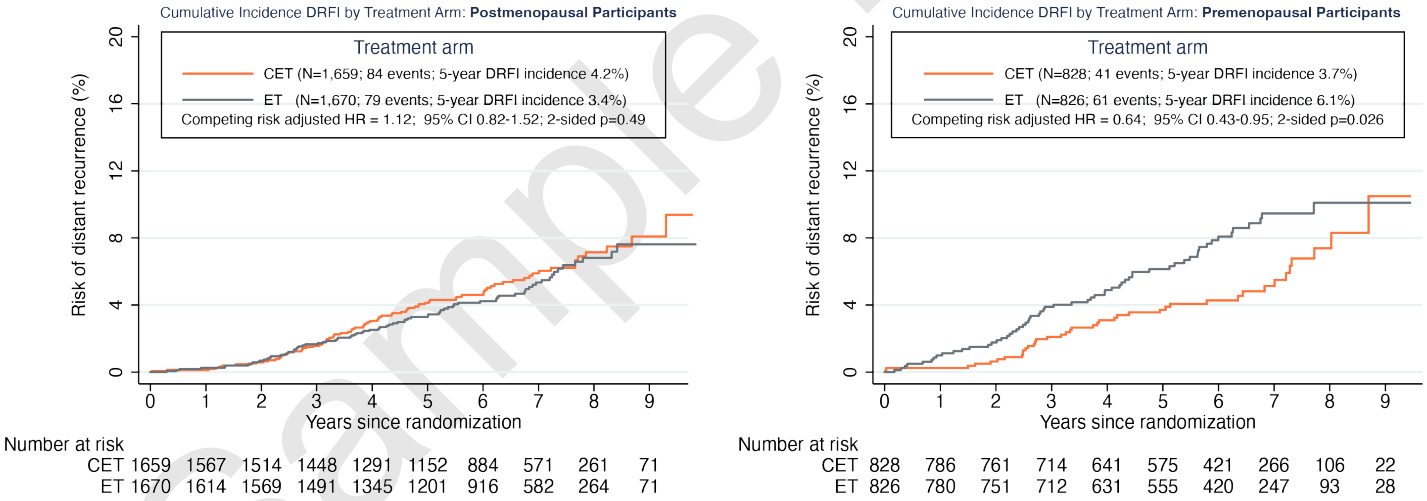

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Micromets & Node Positive (1-3)

EXACT SCIENCES

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Specimen Source/ID: **Breast/SP-16_0123456**

Ordering Physician: **Dr. First-Name I. Ordering-Physician-Last-Name**

Recurrence Score® (RS) Result

Clinical factors may be considered with the RS when making individual treatment decisions.

Distant Recurrence Risk at 9 Years

With AI or TAM Alone

24%

95% CI (18%, 30%)

TransATAC

AI = Aromatase Inhibitor / TAM = Tamoxifen
CI = Confidence Intervals

Group Average Absolute Chemotherapy (CT) Benefit*

RS 31-100

~15%

95% CI (3%, 28%)

SWOG 8814

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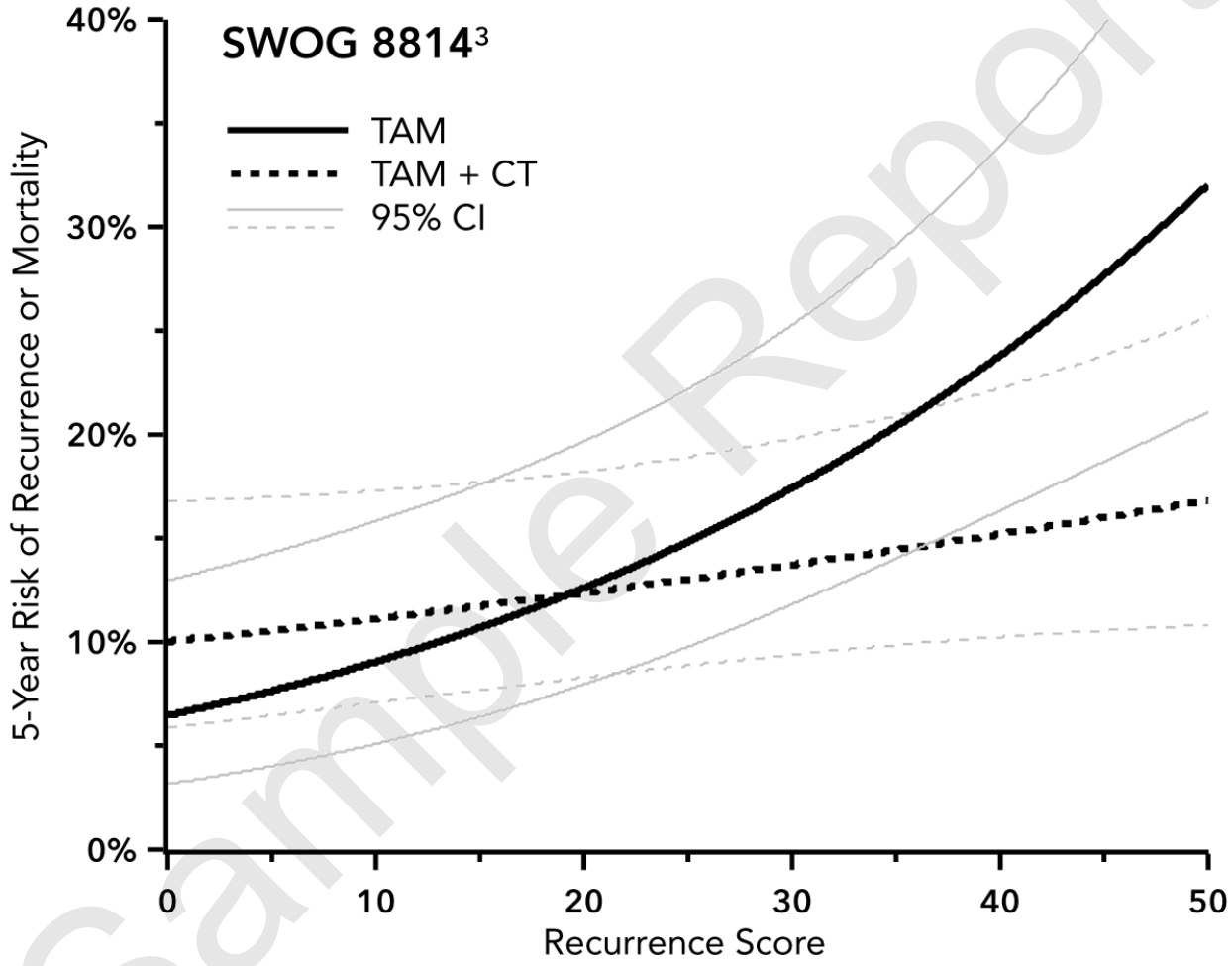
Estimated Chemotherapy Benefit for Individual Recurrence Score Results



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References:

1. Roberts et al. *Breast Cancer Res Treat.* 2017.; Genomic Health (data on file). 2. Dowsett et al. *J Clin Oncol.* 2010. 3. Albain et al. *Lancet Oncol.* 2010.; Genomic Health (data on file).
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This test was developed and its performance characteristics determined by Genomic Health, Inc. It has not been cleared or approved by the FDA, nor is it currently required to be. The laboratory is regulated under CLIA and qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research.

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