Genomics in Breast Cancer:

Learning Objectives

- Provide background on breast cancer, its staging and current adjuvant treatments
- Distinguish between role of Genomics and Genetics in clinical practice
- Understand the clinical utility of new genomic tests, such as the Onco*type* DX® Breast Cancer Assay
- Explain the Onco*type* DX Recurrence Score ® result and its association with risk of recurrence and prediction of chemotherapy benefit
- Identify the patients for whom the Onco*type* DX assay has been clinically validated
- Describe the mechanism to obtain assistance regarding ordering and reimbursement of the Onco*type* DX assay

Breast Cancer Figures

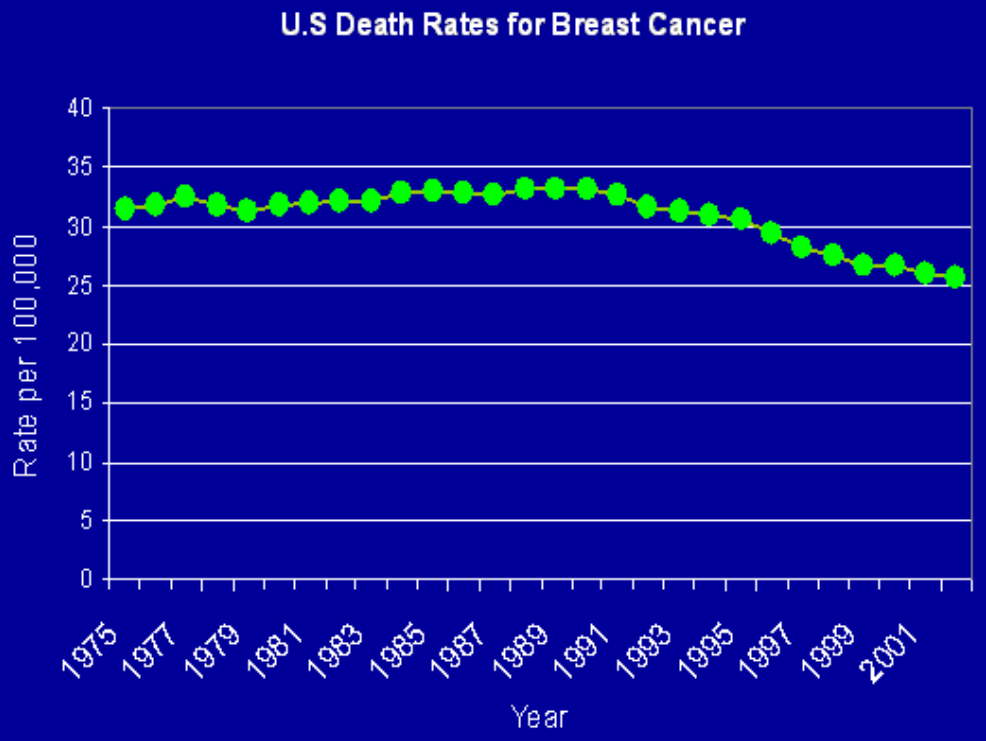
- **1 in 8** women in the United States will develop breast cancer, most occurring by age 70
- Incidence: **180,000** people in the United States will be diagnosed in 2007 with invasive breast cancer including 2,000 men
- **Over 40,000** women and men will die from the disease in 2007
- **Over 77%** of breast cancer cases are diagnosed in people **over the age of 50**

Source: American Cancer Society and National Cancer Institute

Breast Cancer Progress Report

- Breast Cancer mortality rates have decreased by 2.3% annually since 1990

- The decline in mortality is primarily due to *early detection* and *new treatment* methods



Source: *Breast Cancer Facts and Figures 2005-2006*

National Center for Health Statistics data as analyzed by NCI

The Stages of Breast Cancer

Breast Cancer is diagnosed according to stages (stages 0 through IV) under the TNM classification.

Factors used in staging of Breast Cancer:

- Tumor Size

Size of primary tumor

- Nodal status

Indicates presence or absence of cancer cells in lymph nodes

- Metastasis

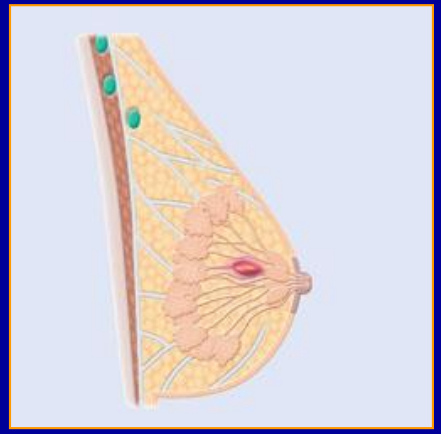
Indicates if cancer cells have spread from the affected breast to other areas of the body (i.e. skin, liver, lungs, bone)

Source: National Cancer Institute

Early Stage Breast Cancer

Stage 0
Ductal carcinoma in situ (DCIS) is very early breast cancer that has not spread beyond the duct.

Stage I
Tumor is < 2 cm and has not spread outside the breast.



Stage IIA
No tumor is found in the breast, but cancer is found in the axillary lymph nodes, or tumor is ≤ 2 cm and has spread to the axillary lymph nodes, or tumor is 2-5 cm but has not spread to the axillary lymph nodes.

Stage IIB
Tumor is 2-5 cm and has spread to the axillary lymph nodes or is > 5 cm but still confined to the breast.

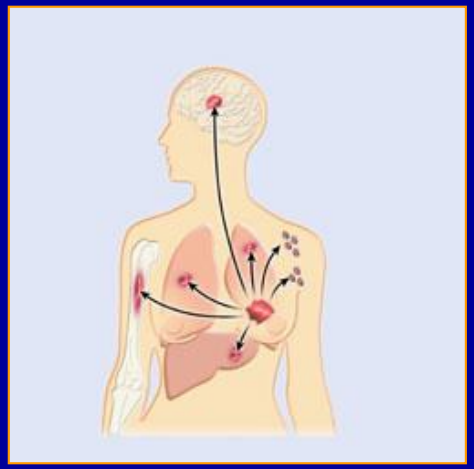
Source: National Cancer Institute

Advanced Breast Cancer

Stage IIIA
The tumor in the breast is smaller than 5 centimeters and the cancer has spread to underarm lymph nodes that are attached to each other or to other structures, OR the tumor is more than 5 centimeters across and the cancer has spread to the underarm lymph nodes.

Stage IIIB
Tumor has spread to tissue near the breast (i.e. the skin or chest wall) and may have spread to lymph nodes within the breast area or under the arm.

Stage IIIC
Tumor has spread to the lymph nodes beneath the collarbone and near the neck, and may have spread to the lymph nodes within the breast area or under the arm and to the tissues near the breast.



Stage IV
Tumor has spread to other organs of the body (i.e. lungs, liver, or brain).

Source: National Cancer Institute

Genetics and Genomics

Genetics Help us Identify Patients at High Risk of Developing Breast Cancer

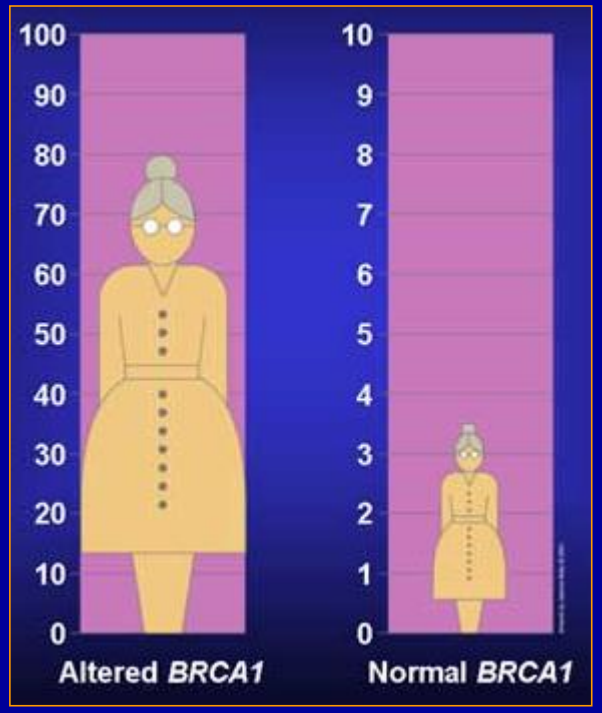
Genetics

– Genetics is the study of heredity

- While genetics influence genomics, genetics is responsible for only *5-10%* of breast cancer

- Genetics focuses primarily on the *likelihood of developing cancer*

- Genetic tests find *mutations, not disease*



Source: *Understanding Cancer Series: Gene Testing,* National Cancer Institute

Genomics Help us Look at the Patients Individual Tumor Biology

Genomics

- Genomics is the study of how genes interact and are expressed as a whole
- Genomics and gene expression profiling tools focus on the *cancer itself* and can help determine
  - How aggressive is the cancer (prognosis)
  - What is the likely benefit from treatment (prediction)

Examples of Genetic and Genomic Tests

Genetic Test

- BRCA1 and BRCA2
  - The genetic make up of patients is tested for BRCA1 and BRCA2 mutations. Patients with those mutations have higher chances of *developing* breast cancer.

Genomic Test

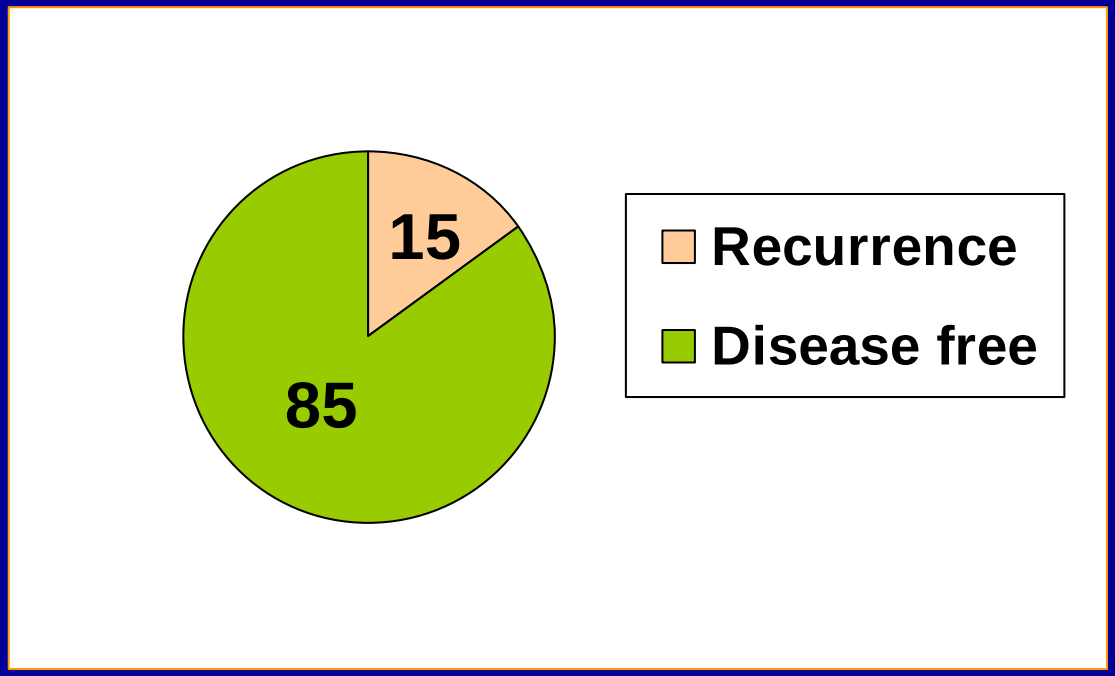
- Onco*type* DX® Breast Cancer Assay
  - The expression level of 21 genes is measured in *tumor tissue* from patients that have already been diagnosed with breast cancer. This assay evaluates if a patient is going to *recur* (prognostic) and *predicts benefit* from chemotherapy and hormonal therapy (predictive).

Adjuvant Treatment for Early Stage Breast Cancer Today

Hormonal Therapy

- Based on the Landmark NSABP B-14 Study using Tamoxifen

If 100 women with ER+, N- disease are treated with hormonal therapy how many will recur within 10 years?

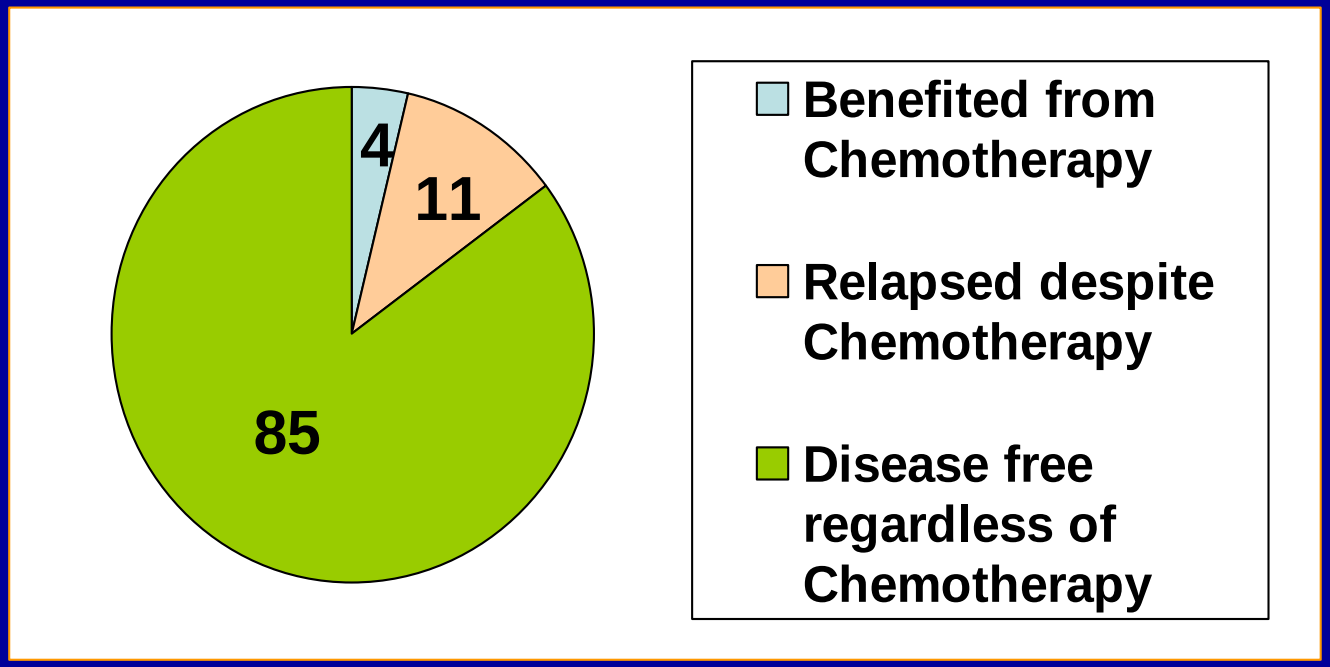


Fisher et al. *N Engl J Med* 1989;320(8):479-84

Chemotherapy and Hormonal Therapy

- Based on the Landmark NSABP B-20 Study using Tamoxifen + Chemotherapy

If all 100 women with ER+, N- disease are treated with chemotherapy and hormonal therapy, how many will benefit from the addition of chemotherapy?



Fisher et al. *J Natl Cancer Inst* 1997;89:1673-82

Your Patient Needs Better Tests to Assess Her Risk of Recurrence and Optimize Her Treatment

- Will her cancer spread?
- Does she need chemotherapy after surgery for her cancer type?
- What are the benefits and side effects of chemotherapy for her?
- Are there any new drugs for her cancer?
- Will she survive?

How Do We Assess Risk in Breast Cancer Patients?

Classic Pathological Criteria

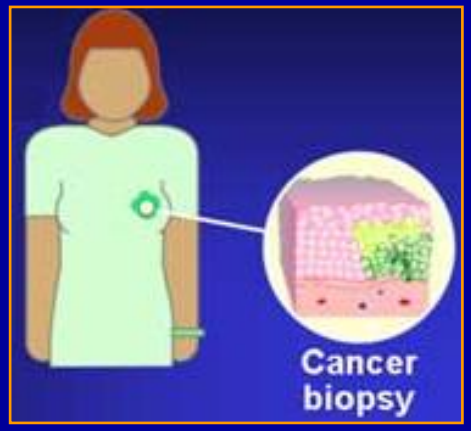
Tumor Size

Lymph Node Status

Age

Tumor Grade

ER/PR HER2



New tools in the Genomic Era…

Oncotype DX®

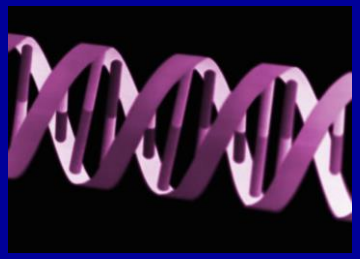
Adjuvant!
Computer-based model

With Genomic Tools We Can Now Analyze Cancer at the Molecular Level

1. Patient's tumor

2. Onco*type* DX® Assay

3. Analyze expression of tumor's genes



4. Onco*type* DX® Report

5. Shared Decision Making

Onco*type* DX®: A Genomic Assay

Oncotype DX® 21-Gene Recurrence Score® (RS) Assay

16 Cancer and 5 Reference Genes From 3 Studies

PROLIFERATION
Ki-67
STK15
Survivin
Cyclin B1
MYBL2

INVASION
Stromelysin 3
Cathepsin L2

ESTROGEN
ER
PR
Bcl2
SCUBE2

GSTM1

BAG1

CD68

HER2
GRB7
HER2

REFERENCE
Beta-actin
GAPDH
RPLPO
GUS
TFRC

Paik et al. *N Engl J Med.* 2004;351: 2817-2826

Oncotype DX® 21-Gene Recurrence Score® (RS) Assay

Calculation of the Recurrence Score Result

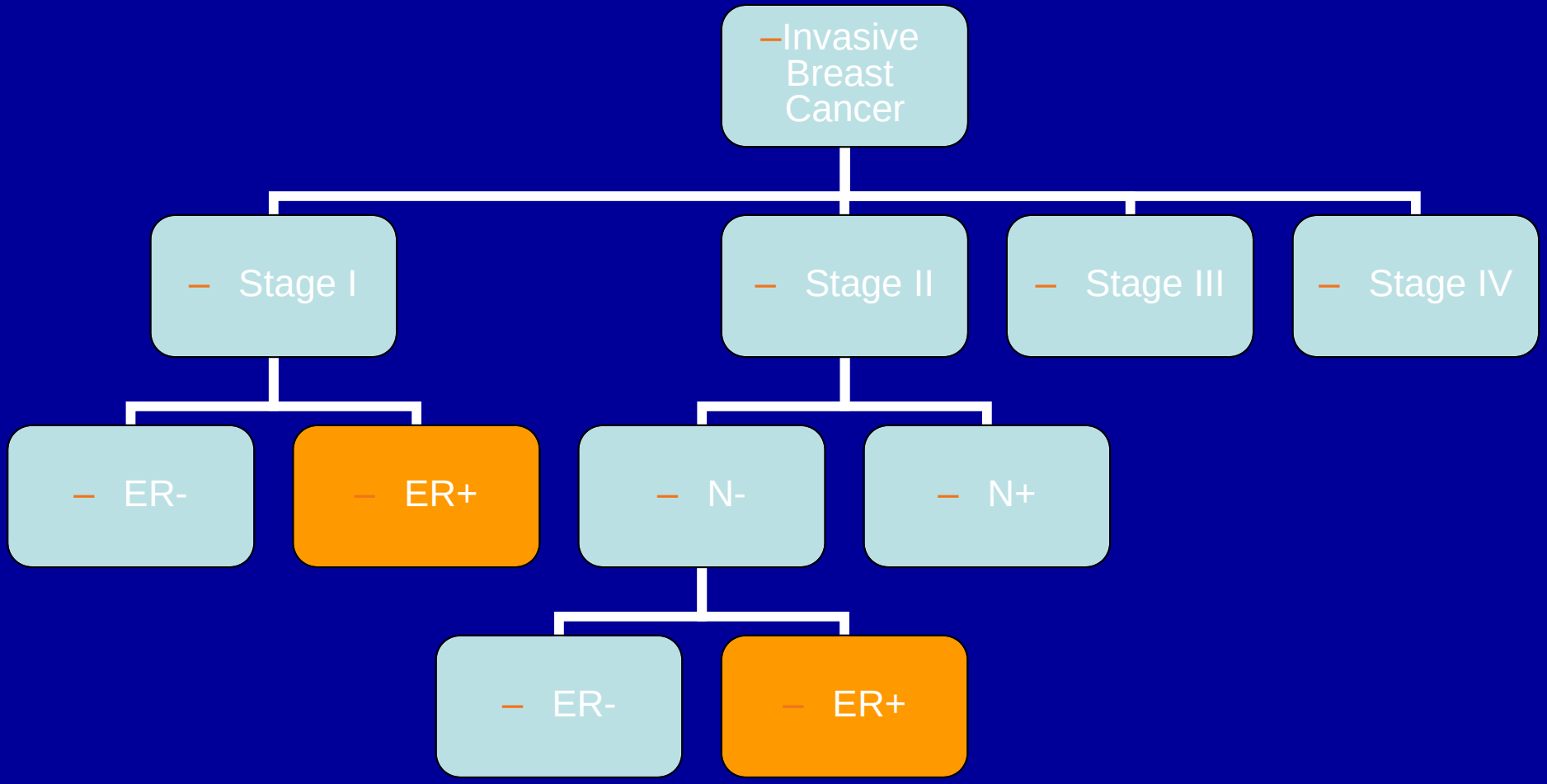
Coefficient x Expression Level

RS = + 0.47 x HER2 Group Score
- 0.34 x ER Group Score
+ 1.04 x Proliferation Group Score
+ 0.10 x Invasion Group Score
+ 0.05 x CD68
- 0.08 x GSTM1
- 0.07 x BAG1

Category	RS (0-100)
Low risk	RS <18
Int risk	RS ≥18 and <31
High risk	RS ≥31

Paik et al. *N Engl J Med.* 2004;351: 2817-2826

The Oncotype DX® Assay is for N-, ER+ Breast Cancer Patients



The Oncotype DX® Assay Has Been Extensively Studied in 3,300+ Patients

Study	Type	No. Pts	References
Providence	Exploratory	136	Proc Am Soc Clin Oncol 21: 2002 Abstract 3017
Rush	Exploratory	78	Clin Cancer Res 2005; 11: 8623-31
NSABP B-20	Exploratory	233	SABCS 2003; Abstract 16
NSABP B-14	Prospective	668	NEJM 2004; 351:2817-26
MD Anderson	Prospective	149	Clin Cancer Res 2005; 11: 3315-19
Kaiser Permanente	Prospective Case-Control	790 Cases/ Controls	Breast Cancer Res 2006; 8: R25
NSABP B-14	Prospective Placebo vs Tam	645	JCO 2005; 23 (16S): Abstract 510
Instituto Nazionale Tumori, Milan	Exploratory Pathologic CR	89	JCO 2005; 23: 7265-77
NSABP B-20	Prospective Tam vs Tam+Chemo	651	JCO 2006; 24: 3726-34
ECOG 2197	Exploratory and Prospective	776	JCO 2007; 25 (18S): Abstract 526

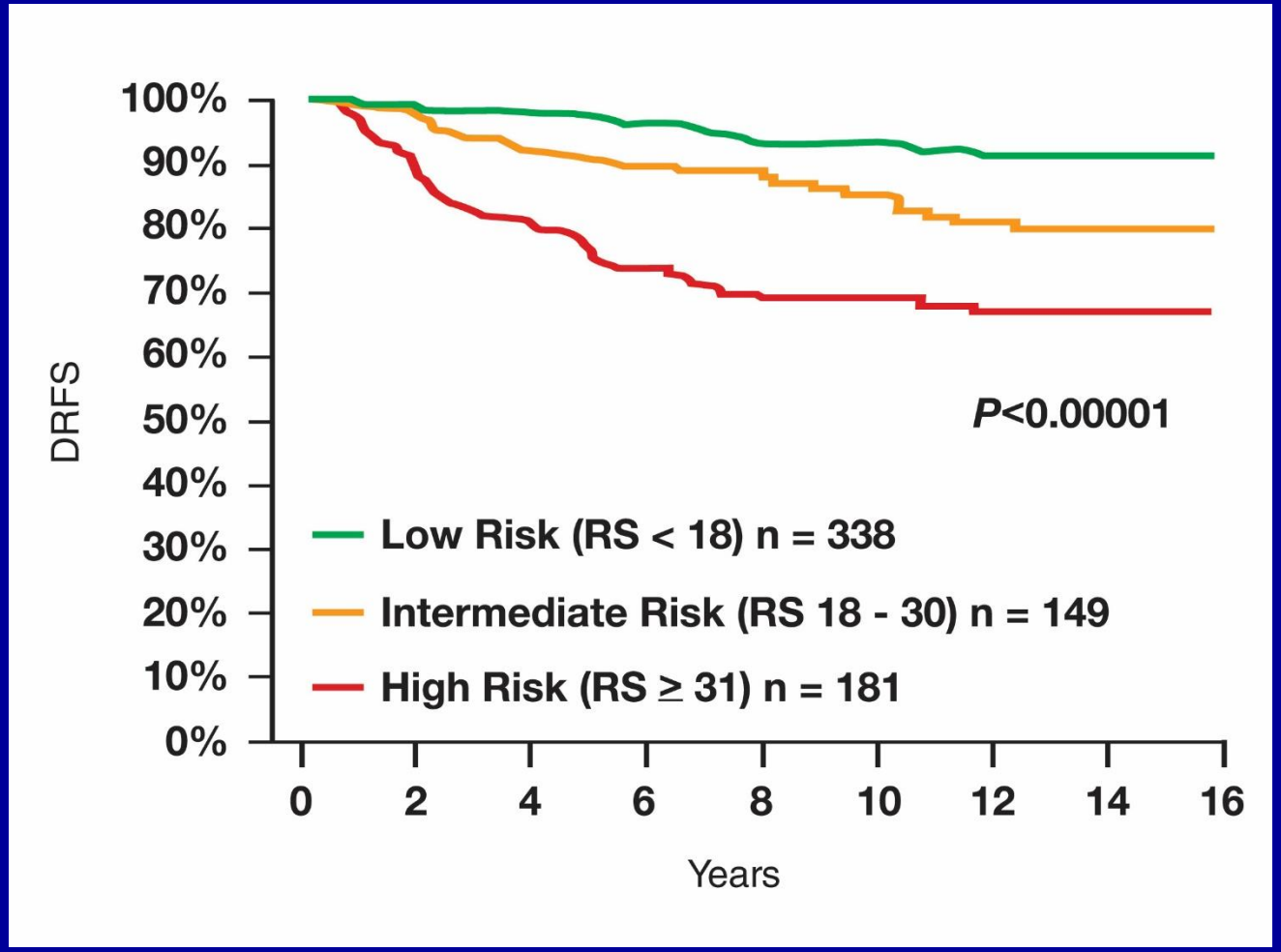
39,000+ Commercial Assays as of September 30, 2007

NASBP B-14 Validation Trial for the Oncotype DX® Assay

- Purpose: To evaluate the Oncotype DX 21-gene panel and its Recurrence Score® (RS) result as predictors of the likelihood of distant recurrence
- Population: Tumor tissue from 668 N-, ER+, tamoxifen-treated patients enrolled in the NASBP B-14 study
- Design:
  - Multi-center study using a pre-defined panel of 21 genes with prospectively-defined endpoints, analysis plan and algorithm for calculation of the RS result
  - Blinded, triplicate analysis by RT-PCR of 10 µm fixed tumor block sections

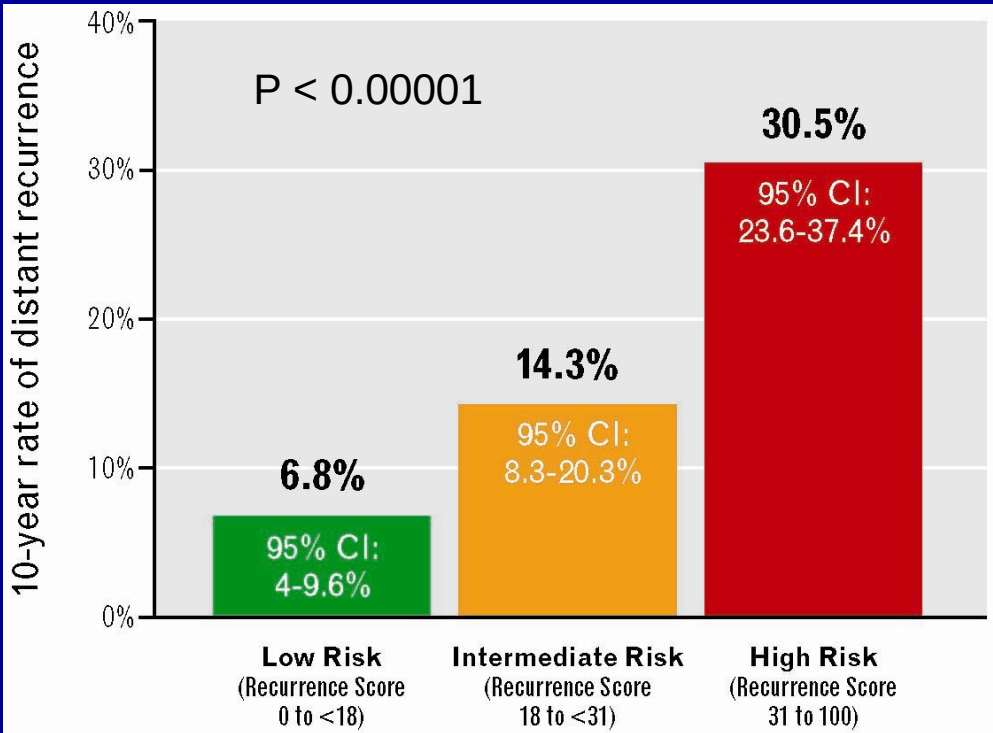
Paik et al. *N Engl J Med.* 2004;351: 2817-2826

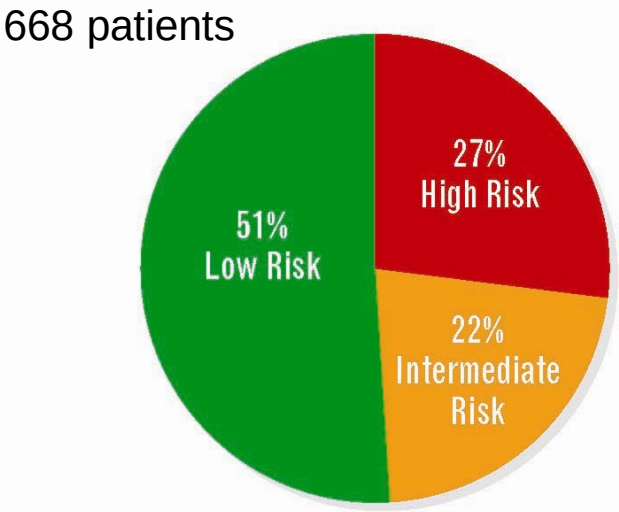
The Recurrence Score® Result Stratifies Patients by their 10-Year Distant Recurrence-Free Survival



Paik et al. *N Engl J Med.* 2004;351:2817-2826

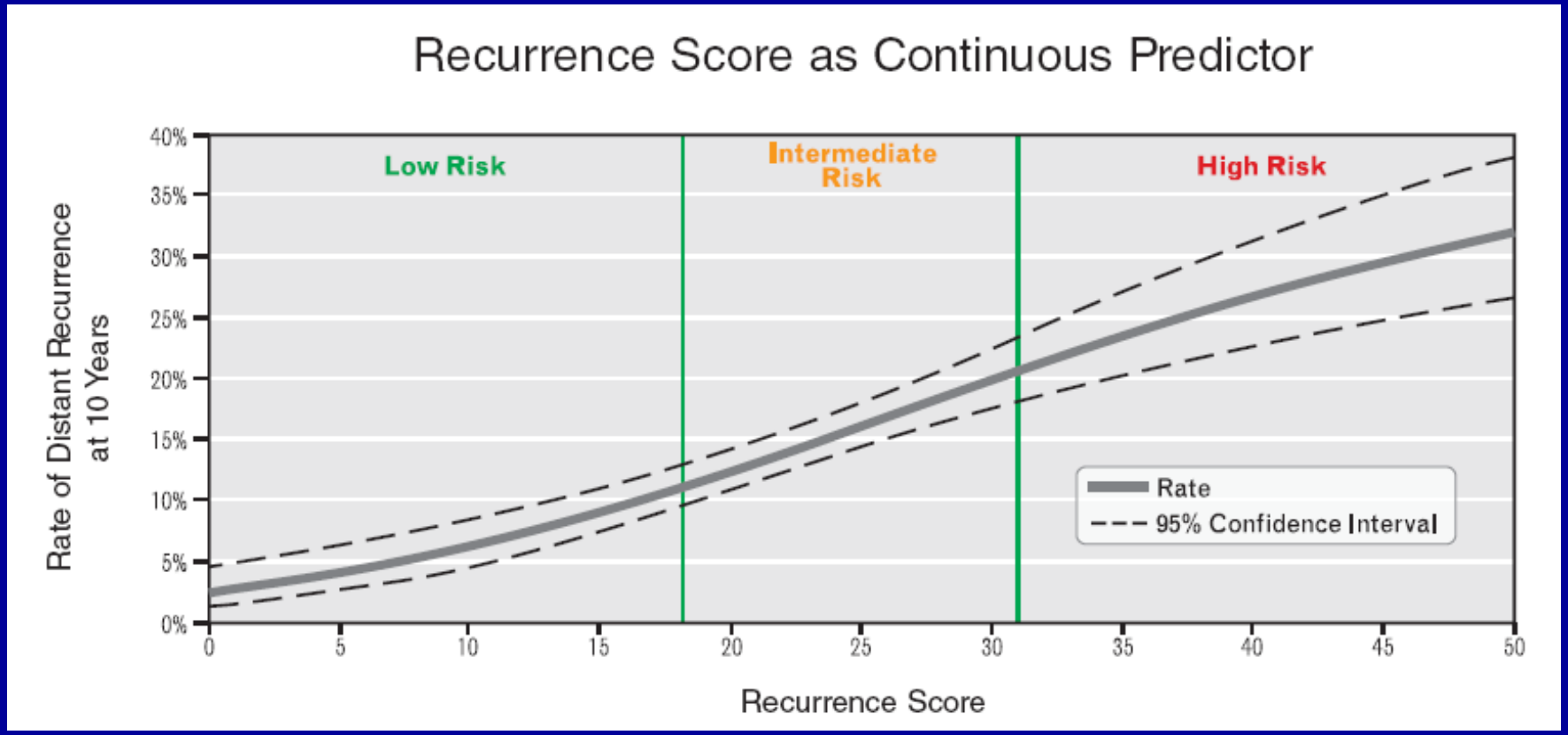
The Recurrence Score® Result Quantifies the Risk of Distant Recurrence (Prognosis)





Paik et al. *N Engl J Med.* 2004;351:2817-2826

The Recurrence Score® is a Continuous Predictor of the Risk of Distant Recurrence



Paik et al. *N Engl J Med.* 2004;351:2817-2826

Summary of the NASBP B-14 Trial

- Clinical validation study for the Onco*type* DX® assay showing that the Recurrence Score® result quantifies the likelihood of distant recurrence in N- ER+, tamoxifen-treated breast cancer patients (prognosis)
- The Recurrence Score result identified a large subset of patients with low risk of recurrence
- The Recurrence Score result was a consistent predictor of distant recurrence independent of patient age, tumor size and tumor grade

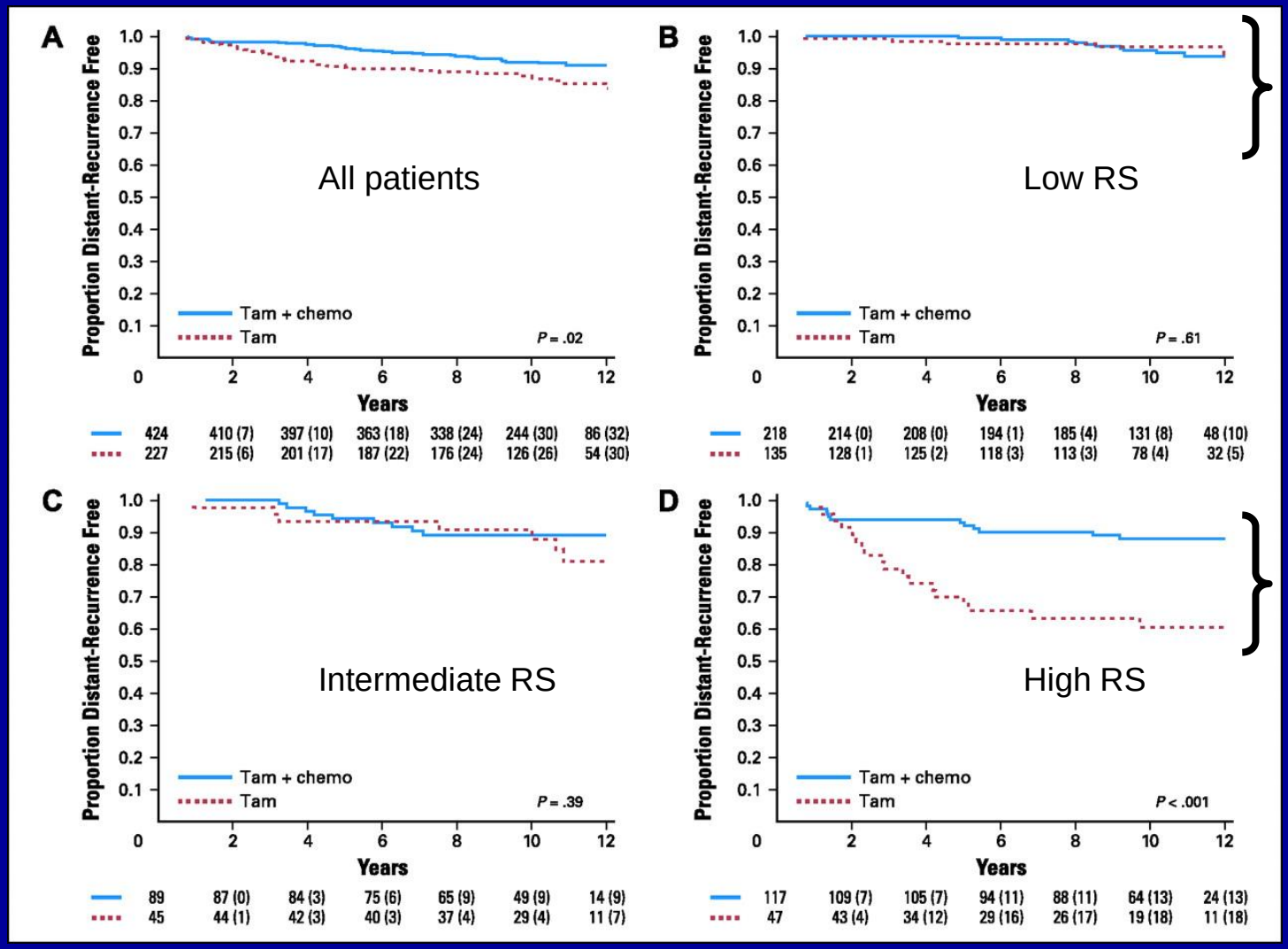
Paik et al. *N Engl J Med.* 2004;351:2817-2826

NASBP B-20 Chemotherapy Benefit Trial for the Onco*type* DX® Assay

- Purpose: To determine whether the Onco*type* DX assay and its Recurrence Score® result could predict magnitude of chemotherapy benefit
- Population: Tumor tissue from 651 N-, ER+ patients from the NASBP B-20 study treated with either tamoxifen alone (n=227) or with tamoxifen plus CMF or MF chemotherapy (n=424)
- Design:
  - *Multi-center, randomized trial* using a pre-defined panel of 21 genes with prospectively-defined endpoints, analysis plan and algorithm for calculation of the RS result
  - Blinded, triplicate analysis by RT-PCR of 10 µm fixed tumor block sections

Paik et al. *J Clin Oncol.* 2006;24:3726-3734

The Oncotype DX® Assay: Patients Do Not Benefit Equally from Chemotherapy

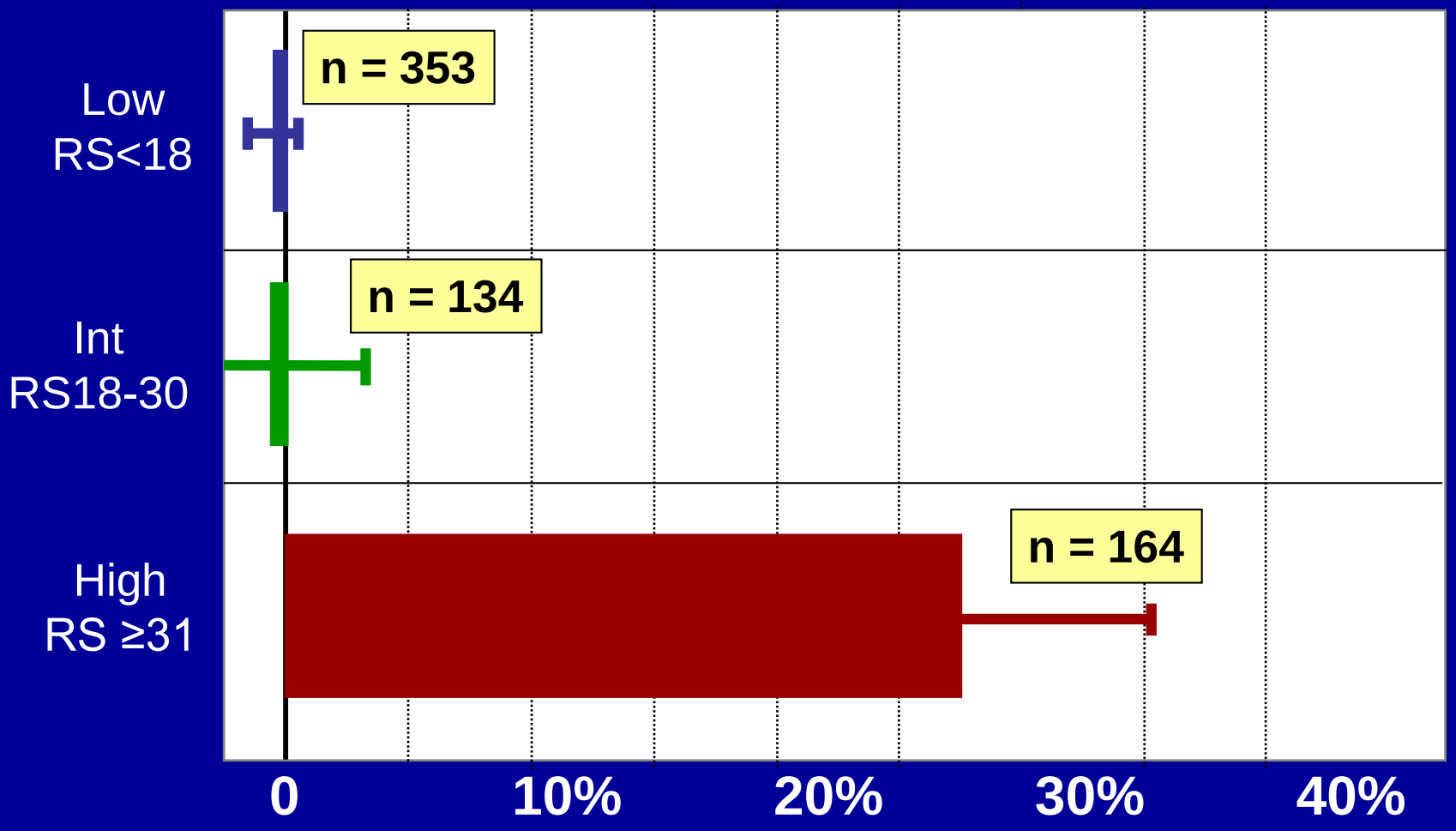


Little, if any, benefit

28% Absolute Benefit

Paik et al. *J Clin Oncol.* 2006;24:3726-3734

Patients with High RS Derive Significant Benefit from Chemotherapy (Prediction)



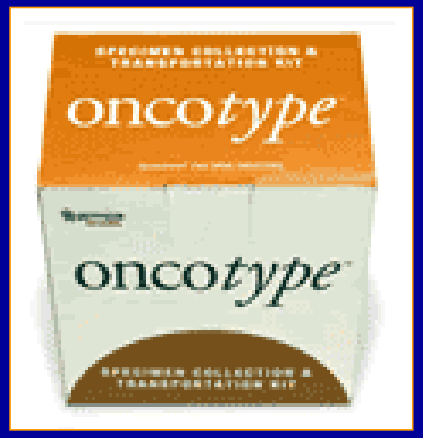
Paik et al. *J Clin Oncol.* 2006;24:3726-3734

Summary of the NASBP B-20 Trial

- The Recurrence Score® (RS) result not only quantifies the risk of recurrence in women with N-, ER+ breast cancer, but also predicts the magnitude of chemotherapy benefit (predictive)

- Patients with a low RS have *minimal*, if any benefit, from chemotherapy while patients with a high RS have a *significant* benefit from chemotherapy

Paik et al. *J Clin Oncol.* 2006;24:3726-3734



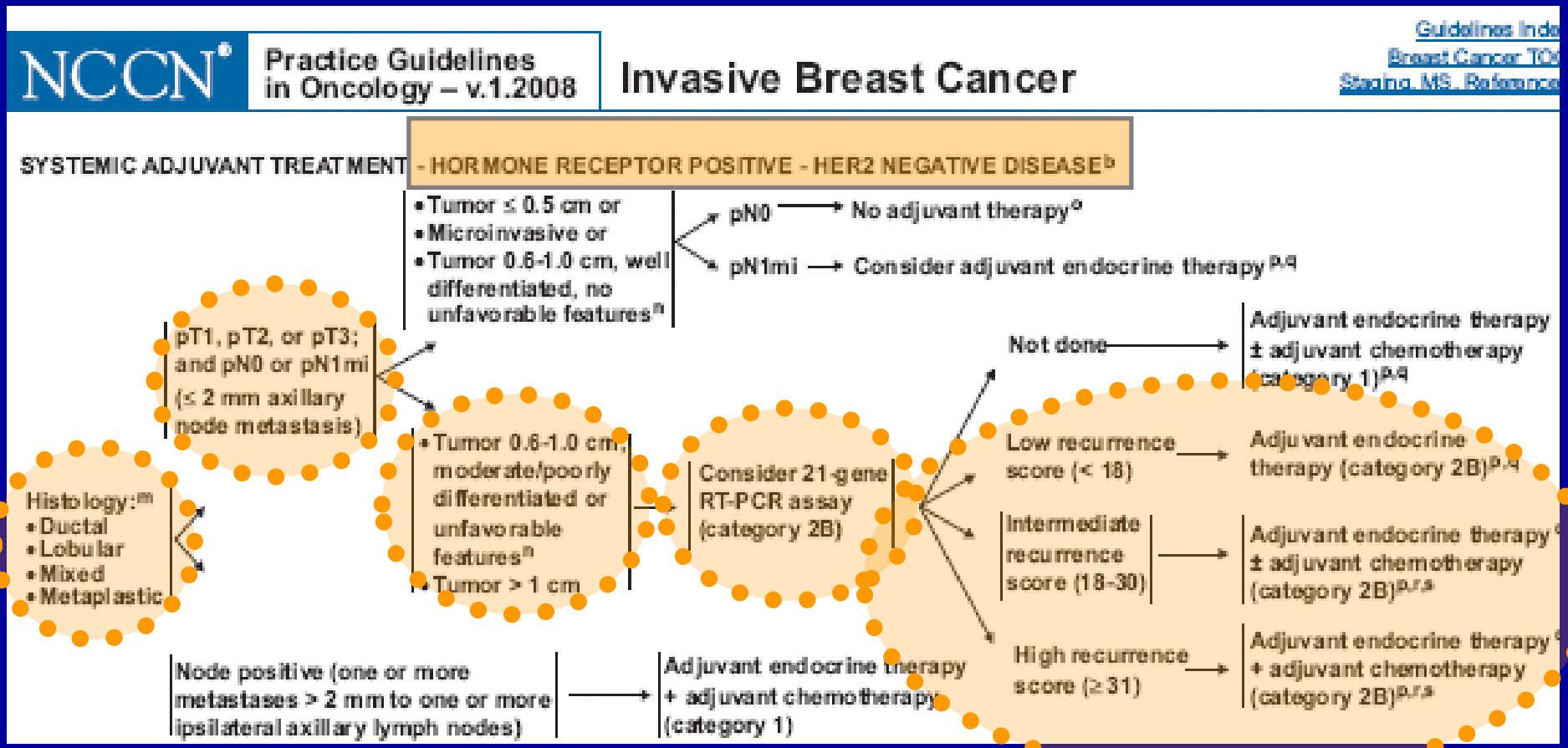
The Oncotype DX® Assay in Clinical Practice

The Onco*type* DX® Assay Recommended in ASCO Clinical Practice Guidelines

- The Onco*type* DX assay is recommended on the ASCO Clinical Practice Guidelines for use in newly diagnosed patients with N-, ER+ breast cancer to:
  - *Predict risk of recurrence*
  - Identify patients who are predicted to obtain the *most therapeutic benefit from tamoxifen* and *may not require chemotherapy*
  - Identify patients with high RS scores who appear to *derive greater benefit from chemotherapy* (specifically CMF) than from tamoxifen
- Conclusions may not be generalizable to hormonal therapies other than tamoxifen, or to other chemotherapy regimens
- The Onco*type* DX assay is the only multi-parameter gene expression assay found to show clinical utility in breast cancer

Harris et al. *J Clin Oncol.* 2007; published online ahead of print

The Oncotype DX® Assay Recommended for Consideration in NCCN Clinical Practice Guidelines



The Oncotype DX® Assay in Clinical Practice

- The Onco*type* DX assay has been offered by Genomic Health, Inc., since January 2004
  - Genomic Health has a CLIA-certified and CAP-accredited reference lab
  - Send tumor block or 6 fixed, paraffin-embedded sections (10 µm each) to Genomic Health using the Onco*type*® Specimen Kit
  - Turnaround time: 10-14 days
  - Customer Service: 1-866-ONCOTYPE
    1-866-662-6897

Reimbursement Support for Your Practice for the Oncotype DX® Assay

- Genomic Health helps your patient and practice by taking assignment of benefits and managing the billing and claims process
- The Genomic Access Program (GAP) performs comprehensive benefits investigations and informs patients of their coverage and potential financial responsibility within 2 business days

The Oncotype DX® Assay Is Widely Covered in the United States

- Onco*type* DX is covered by several insurance plans representing 165+ million lives in the US[1]
  - Plans include: Medicare[2], Aetna, United Healthcare, Kaiser Permanente, Cigna, WellPoint, Highmark BC, Harvard Pilgrim, BC/BS of Michigan, BC/BS FEP, CareFirst BC/BS, BC/BS of Minnesota, BC/BS of Alabama, BC/BS of New Jersey and others
- GAP also provides a generous financial assistance to qualifying patients

[1] As of September 2007

[2] Through a local coverage decision developed by the National Heritage Insurance Company which applies to all testing billed by Genomic Health's California facility

Procedure for Ordering the Oncotype DX® Assay

1. **Patient Education and Reimbursement Information**

– Ensure that each patient that is considering the Oncotype DX assay has a copy "A Patient's Guide to Oncotype DX"

2. **Requisition Form**

– Fill out form completely, have an authorized Healthcare Provider sign form

– If the authorized Healthcare Provider would like a Benefits Investigation done, complete the Benefits Investigation section by selecting service options and adding a Statement of Medical Necessity

– Select Specimen Retrieval service option

– FAX completed form to Genomic Health Customer Service (650-556-1073)

3. **Acknowledgement of Referral Form**

– You will receive a FAX from GAP confirming the receipt of your Benefits Investigation

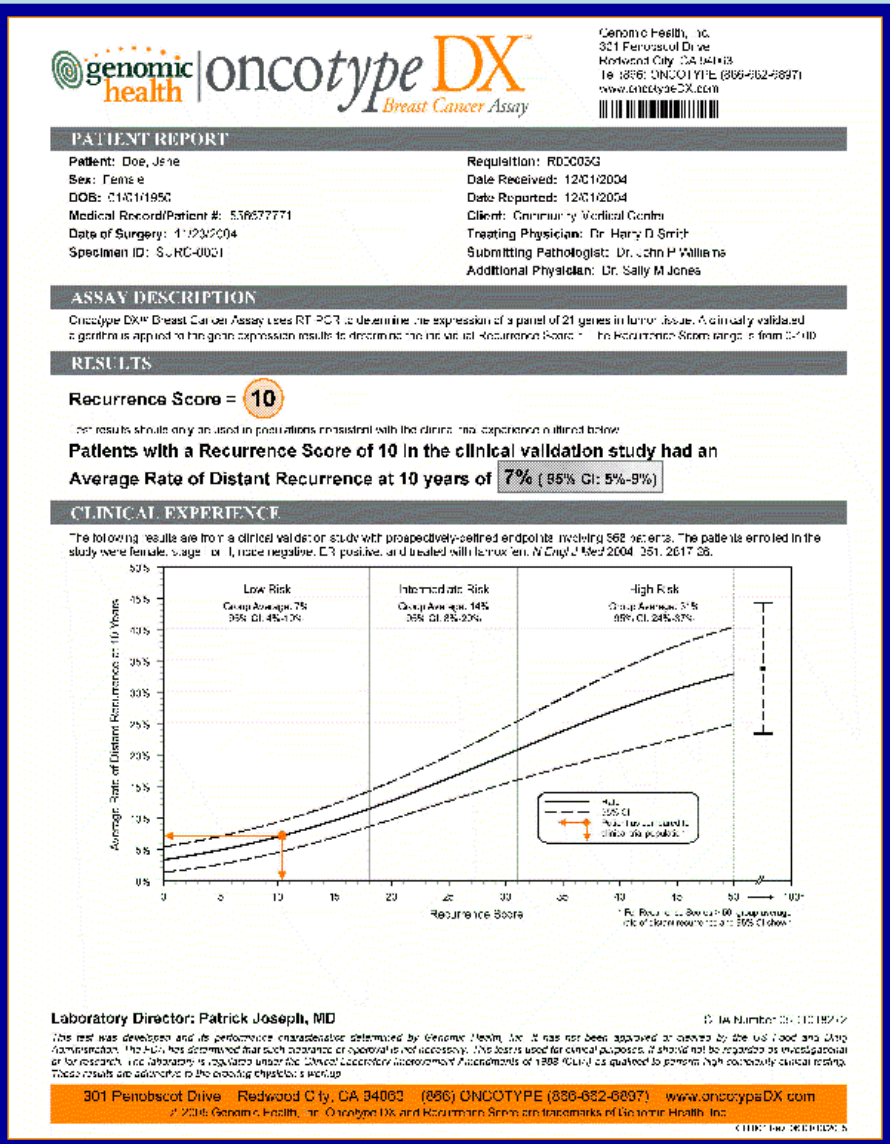
4. **Benefits Summary**

– If you have selected a Benefits Investigation, within 2 business days you will receive a FAX entitled "Benefits Summary" and a GAP representative will call your patient to explain their laboratory benefits and any financial responsibility resulting from performing the assay

– If you selected, "YES Investigate – Proceed pending patient confirmation", Genomic Health Customer Service will be contacting you on how the test should proceed

Oncotype DX® Patient Report

- The patient report includes:
  - Recurrence Score® (RS)
  - Average 10-year distant recurrence rate for that RS
  - Graph of 10-year recurrence risk as a function of RS in tamoxifen-treated patients
- The report is sent to:
  - Treating physician
  - Submitting pathologist



genomic health | oncotype DX Breast Cancer Assay

Genomic Health, Inc.
301 Penobscot Drive
Redwood City, CA 94063
Tel (866) ONCOTYPE (866-662-6897)
www.oncotypeDX.com

PATIENT REPORT

Patient: Doe, Jane
Sex: Female
DOB: 01/01/1950
Medical Record/Patient #: 536677771
Date of Surgery: 11/23/2004
Specimen ID: SURG-0001

Requisition: RDC0053
Date Received: 12/01/2004
Date Reported: 12/01/2004
Client: Community Medical Center
Treating Physician: Dr. Harry D Smith
Submitting Pathologist: Dr. John P Williams
Additional Physician: Dr. Sally M Jones

ASSAY DESCRIPTION

Oncotype DX™ Breast Cancer Assay uses RT-PCR to determine the expression of a panel of 21 genes in tumor tissue. A clinically validated algorithm is applied to the gene expression results to determine the individual Recurrence Score® result. The Recurrence Score result ranges from 0-100.

RESULTS

Recurrence Score = 10

These results should only be used in populations consistent with the clinical trial experience outlined below.

Patients with a Recurrence Score of 10 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of 7% (95% CI: 5%-9%)

CLINICAL EXPERIENCE

The following results are from a clinical validation study with prospectively-defined endpoints involving 668 patients. The patients enrolled in the study were female, stage I or II, node negative, ER positive, and treated with tamoxifen. *N Engl J Med* 2004; 351: 2817-26.

Laboratory Director: Patrick Joseph, MD

This test was developed and its performance characteristics determined by Genomic Health, Inc. It has not been cleared or approved by the US Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical testing. These results are adjunctive to the existing physician's workup.

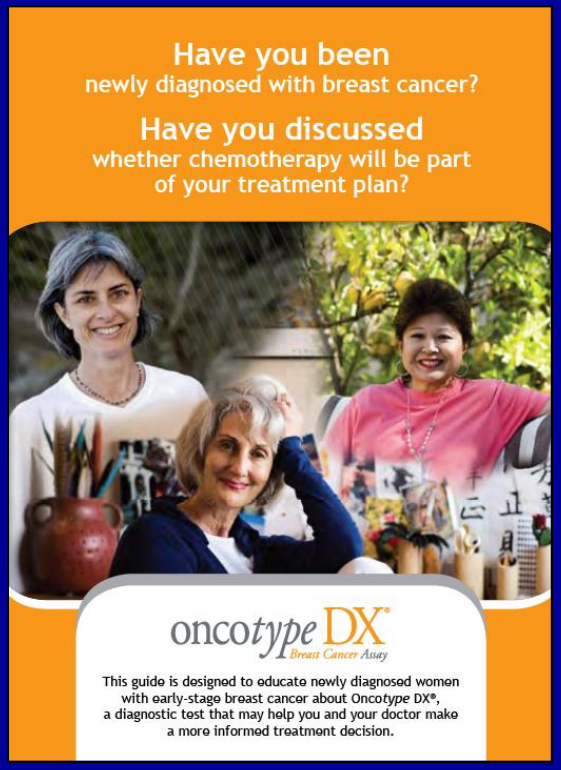
301 Penobscot Drive Redwood City, CA 94063 (866) ONCOTYPE (866-662-6897) www.oncotypeDX.com

How Can Nurses be Involved with the Onco*type* DX® Assay?

- Identify appropriate patients
  - Stage I/II, lymph node negative, ER positive, who need to make decisions regarding adjuvant chemotherapy
    - Not for DCIS patients
    - Not for lymph node positive patients
- Educate patients on the Onco*type* DX assay
- Help inform and assist with enrollment of eligible patients on the TAILORx trial

Oncotype DX® Resources for Nurses

- Patient Education Brochure
  - English and Spanish
- *My Breast Cancer Coach*
  - Interactive online program developed with the Breast Cancer Network of Strength. This program enables newly diagnosed women to personalize their online search for breast cancer information by answering a series of eight questions about their diagnosis, based on the information contained in their pathology reports
- www.MyTreatmentDecision.com
  - Patient website providing an overview of invasive breast cancer and the tools used to determine recurrence risk and help make treatment decisions



Genomic Health's Commitment to Nursing

- Offer educational programs and activities on Genomics at both local and national levels
- Provide accurate medical and clinical information in a timely manner, including one on one assistance from our medical team
- Provide valuable assay results that are reliable, sensitive and reproducible
- Deliver actionable insights that can improve decision making for breast cancer patients
- Address reimbursement concerns
- Provide patient education and support
- Partner with advocacy groups to support breast cancer efforts

Patient Cases

Patient 3: 39-year-old with 1.5 cm tumor

- **Age: 39**
- **Tumor Type: Infiltrating Ductal Carcinoma (IDC)**
- **Tumor Size: 1.5 cm**
- **ER: 90% (Strong +)**
- **PR: 90% (Strong +)**
- **HER2/neu: Negative**
- **Grade: 2**

The patient is a professional, recently engaged and concerned about fertility.

General Health: Perfect

Lymph Nodes: 0

Patient Cases

- Patient was identified as low risk by Onco*type* DX® with a Recurrence Score ® result of 4
- Patient received hormonal therapy since she was in a group in which chemotherapy does not provide benefit

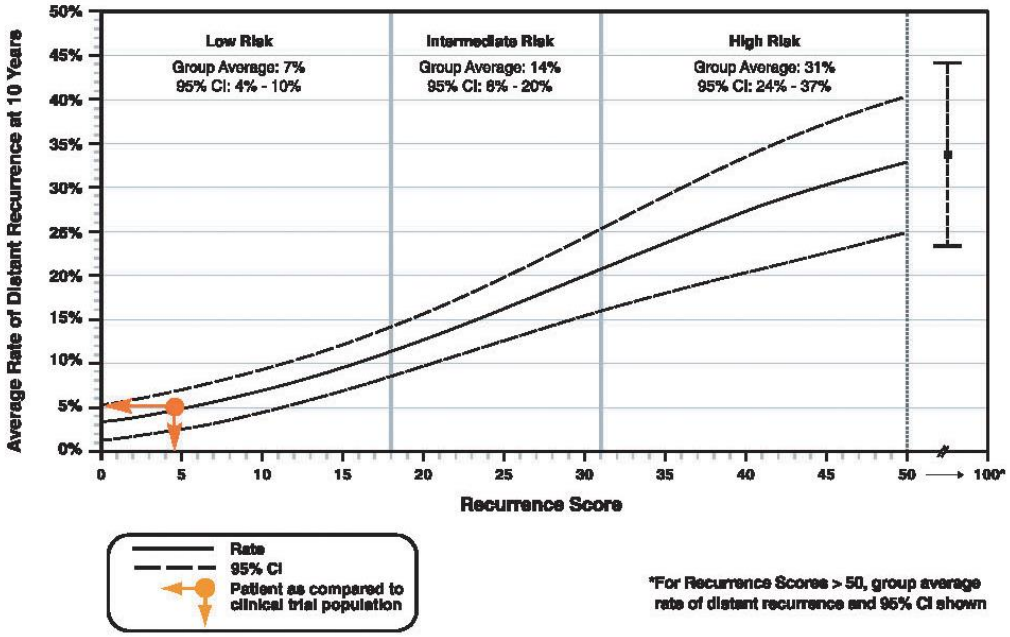
RESULTS

Recurrence Score = 4 Test results should be interpreted using the information in the Clinical Experience section below, which applies only to patients consistent with this clinical experience.

CLINICAL EXPERIENCE

Patients with a Recurrence Score of 4 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of **5%** (95% CI: 2%-7%)

The following results are from a clinical validation study with prospectively-defined endpoints involving 668 patients. The patients enrolled in the study were female, stage I or II, node negative, ER-positive, and treated with tamoxifen. *N Engl J Med* 2004; 351: 2817-26.



Patient Cases

Patient 4: 58-year-old with 1.3 cm tumor

- **Age: 58**
- **Tumor Type: Infiltrating Ductal Carcinoma (IDC)**
- **Tumor Size: 1.3 cm**
- **ER: 100% 3+ IHC**
- **PR: Negative**
- **HER2/neu: Negative (FISH)**
- **Grade: 3 (Nottingham 8/9)**

The patient is a 58-year-old postmenopausal woman, eager not to have chemotherapy for a newly diagnosed T1c N0 ER-positive IDC.

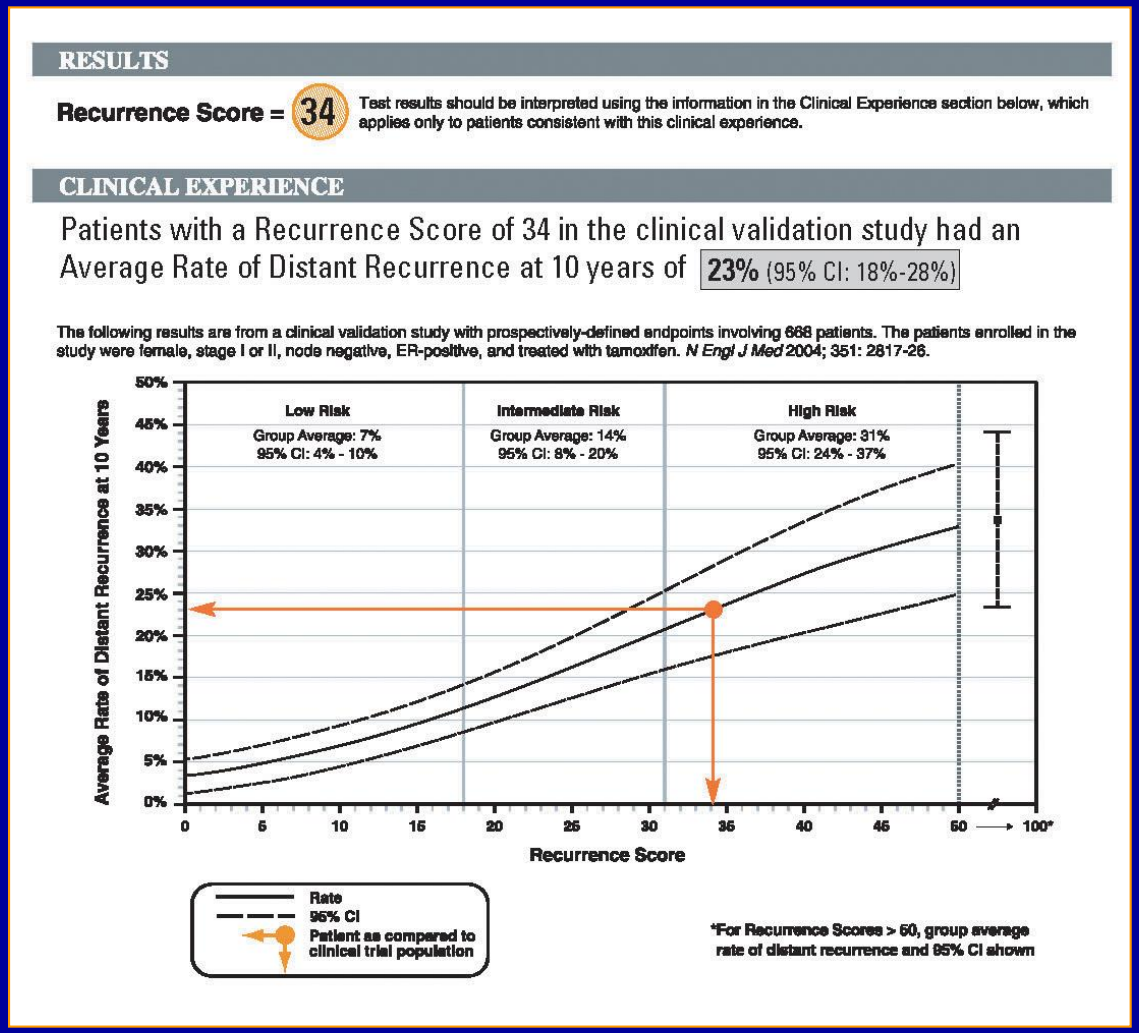
DCIS: Nuclear grade 2, 5%

Margins: Negative

Lymph Nodes: 0/3 (negative)

Patient Cases

- Patient was identified as high risk by Onco*type* DX® with a Recurrence Score® result of 34
- The Recurrence Score helped convince the patient on the likely benefits of taking chemotherapy given the biology of her disease
- Patient received chemotherapy and hormonal therapy



Patient Cases

Patient 7: 68-year-old with 2.3 cm tumor

- **Age: 68**
- **Tumor Type: Infiltrating Ductal Carcinoma (IDC)**
- **Tumor Size: 2.3 cm**
- **ER: 30%**
- **PR: 50%**
- **HER2/neu: Negative**
- **Grade: 2**

The patient is a 68-year-old, healthy, postmenopausal woman.

General Health: Perfect

Lymph Nodes: 0

Patient Cases

- Patient was identified as intermediate risk by Onco*type* DX® with a Recurrence Score® result of 25
- Is there benefit from chemotherapy for this patient? The TAILORx trial evaluates the utility of chemotherapy in the mid-range risk group

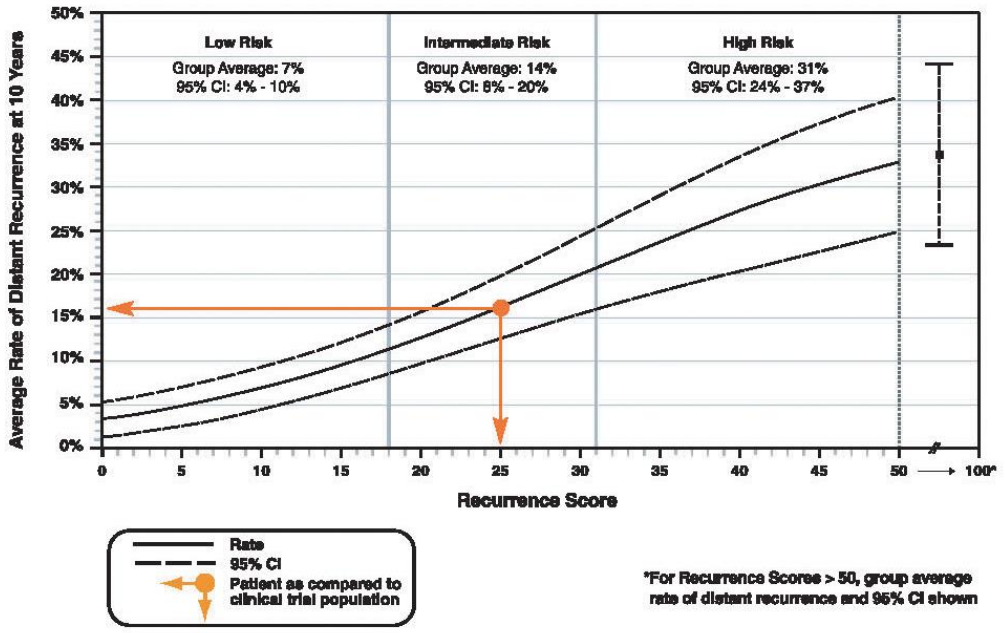
RESULTS

Recurrence Score = 25 Test results should be interpreted using the information in the Clinical Experience section below, which applies only to patients consistent with this clinical experience.

CLINICAL EXPERIENCE

Patients with a Recurrence Score of 25 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of **16%** (95% CI: 13%-20%)

The following results are from a clinical validation study with prospectively-defined endpoints involving 668 patients. The patients enrolled in the study were female, stage I or II, node negative, ER-positive, and treated with tamoxifen. *N Engl J Med* 2004; 351: 2817-26.



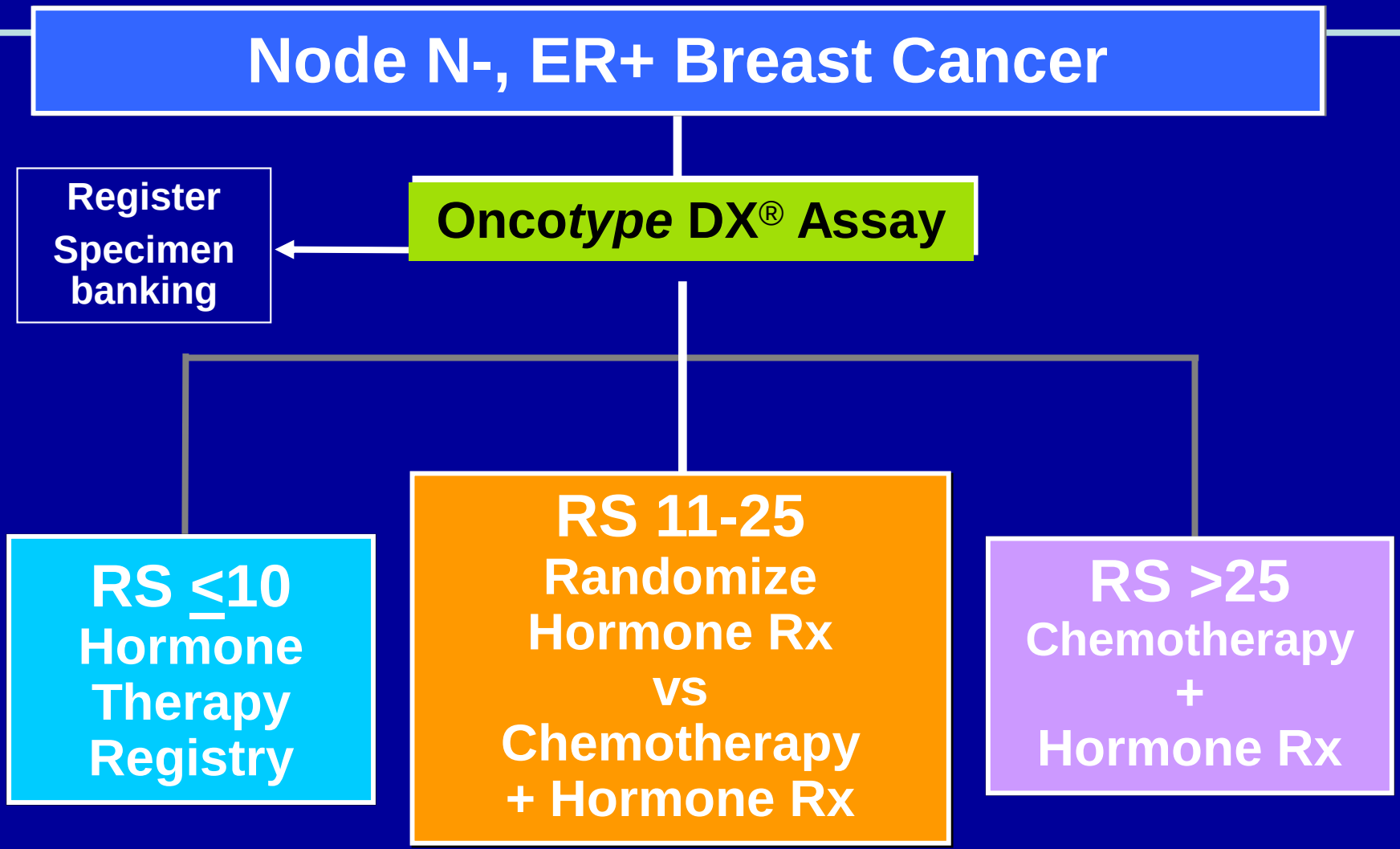
Integration of New Tests in Clinical Decision-Making: TAILORx

*T*rial *A*ssigning *I*ndividua*L*ized *O*ptions for Treatment (*R*x) (TAILORx)

- Premise
  - Integration of a new cancer test, the Onco*type* DX® assay, into the clinical decision-making process
- Implications
  - Reduce chemotherapy *over-treatment* in those likely to be optimally treated with hormonal therapy alone
  - Reduce *inadequate treatment* by identifying individuals who likely will derive great benefit from chemotherapy
  - Evaluate benefit of chemotherapy where uncertainty still exists about its utility

Trial sponsored by NCI. Participating cooperative groups include ECOG, SWOG, NCCTG, CALGB, NCIC, ACOSOG, and NSABP

TAILORx Schema



Primary study group

Primary Objectives TAILORx

- To determine whether adjuvant hormonal therapy (i.e. experimental arm) is *not inferior* to adjuvant chemohormonal (standard arm) for patients in the "primary study group" (Onco*type* DX® RS 11-25)

- To create a tissue and specimen bank for patients enrolled in this trial to learn more about breast cancer

TAILORx: Key Points

- Participating groups
  - Major North American cooperative groups, including ECOG, SWOG, NCCTG, CALGB, NCIC, ACOSOG, and NSABP
- Adjuvant therapy
  - Choice of hormonal and/or chemotherapy regimen is at discretion of treating physician
  - Permissible options are outlined in protocol, and are generally consistent with NCCN guidelines
- Other trials
  - May enroll on other CTSU or other cooperative group studies if treatment assignment on other trial is consistent with PACCT-assigned treatment
- Cost
  - Genomic Health will assist in securing reimbursement for patients who have health insurance
  - By agreement with NCI to avoid bias in enrollment in the trial, patients who are uninsured or who have co-payments or deductibles will not be responsible for the cost of the Onco*type* DX® assay

TAILORx Information Resources

Protocol and General Information

- **Clinical Trials Support Unit**
  - 1-888-823-5923
  - CTSUcontact@westat.com
  - www.ctsu.org

Eligibility Questions

- **Eastern Cooperative Oncology Group**
  - ecog.tailorx@jimmy.harvard.edu
  - www.ecog.org

TAILORx Patient Education Materials

- **Eastern Cooperative Oncology Group**
  - http://www.ecog.org/general/tailorx.html

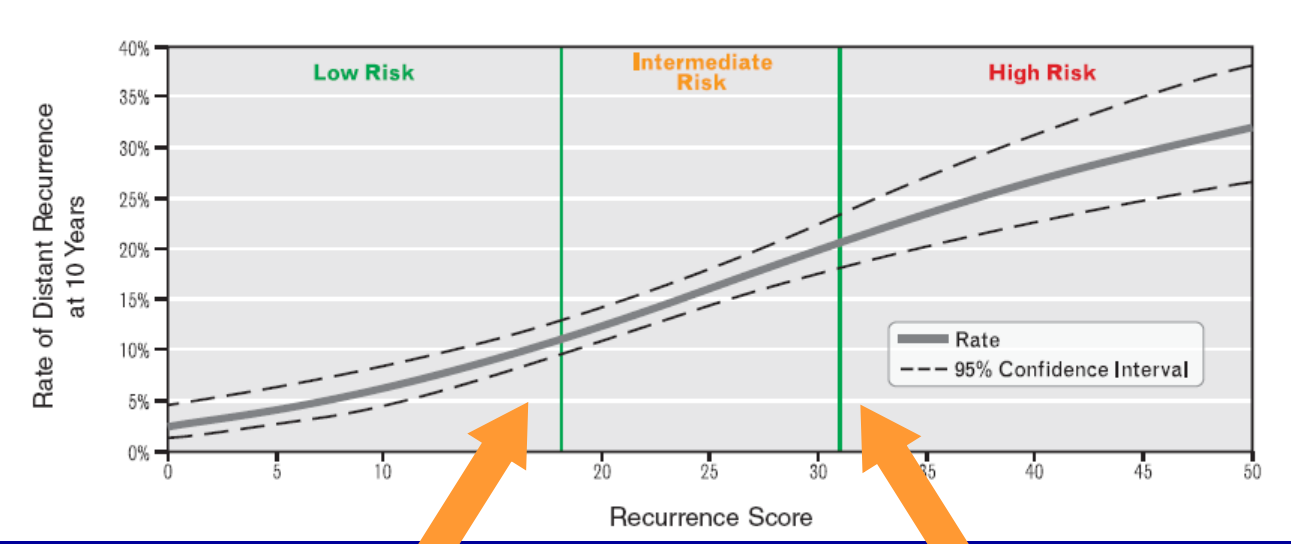
Onco*type* DX® Information

- **Genomic Health Customer Service**
  - 1-866-ONCOTYPE (1-866-662-6897)
  - www.oncotypedx.com

Conclusions

Oncotype DX® is a Standardized and Quantitative Assay

Recurrence Score® in N-, ER+ patients



Lower RS's

- **Lower likelihood of recurrence**
- **Minimal, if any, chemotherapy benefit**

Higher RS's

- **Greater likelihood of recurrence**
- **Clear chemotherapy benefit**

1) Paik et al. *NEJM* 2004, 2) Habel et al. *Breast Cancer Research* 2006
3) Paik et al. *JCO* 2006, 4) Gianni et al. *JCO* 2005

Oncotype DX® Summary

- The Oncotype DX Recurrence Score® assay predicts likelihood of recurrence (prognostic) and magnitude of adjuvant treatment benefit for chemotherapy (predictive)
- The Oncotype DX Recurrence Score assay shows consistent results across multiple independent studies