

The Oncotype DX[®] Assay in the Contemporary Management of Invasive Early-stage Breast Cancer

The Recurrence Score[®] Result Uses Key Genes Linked to Critical Molecular Pathways

16 BREAST CANCER RELATED GENES

Estrogen	Proliferation	HER2	Invasion	Others
ER PR Bcl2 SCUBE2	Ki-67 STK15 Survivin Cyclin B1 MYBL2	GRB7 HER2	Stromelysin 3 Cathepsin L2	CD68 GSTM1 BAG1

5 REFERENCE GENES

Beta-actin	GAPDH	RPLPO	GUS	TFRC
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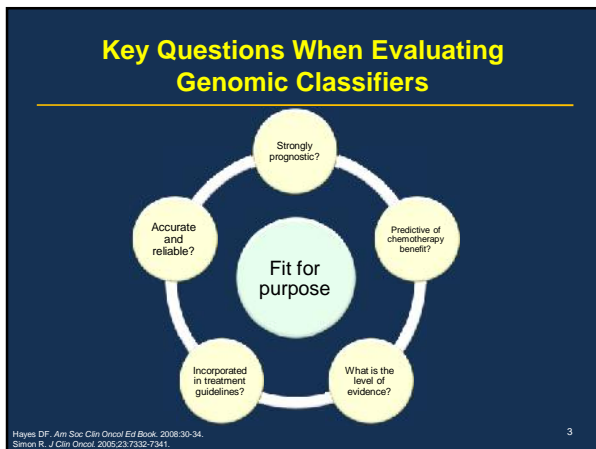
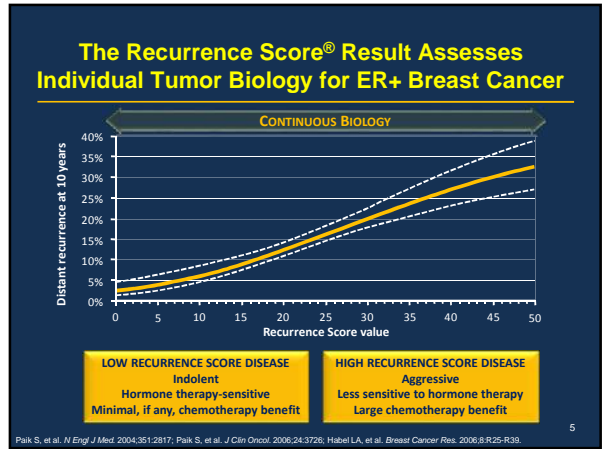
Paik S, et al. N Engl J Med. 2004;351:2817-2826.

Cancer – The Biology Century

- Understanding and treating the underlying tumor biology
 - Cancer genetic studies demonstrate the transition of basic research to clinical application (i.e. BRCA testing)
 - Targeted cancer therapies developed based on the unique tumor genetic characteristics (i.e. tamoxifen and trastuzumab)
 - Sequencing of the human genome
 - Gene expression profiling shown to predict clinical outcome

Scientific breakthroughs making personalized medicine in cancer a reality

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Clinical Validation of the Oncotype DX[®] Breast Cancer Assay in Node-Negative Disease

Oncotype DX® Clinical Validation: NSABP B-14

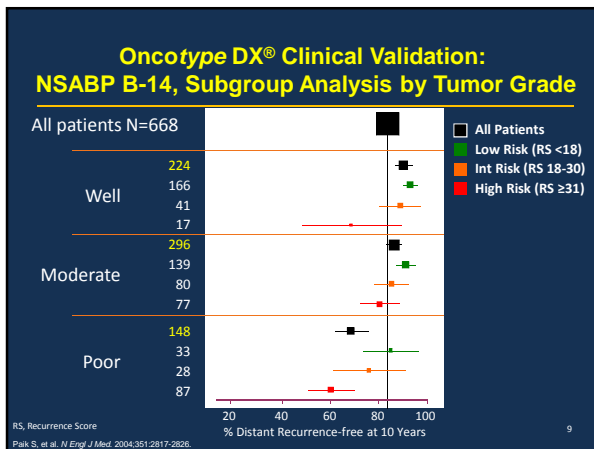
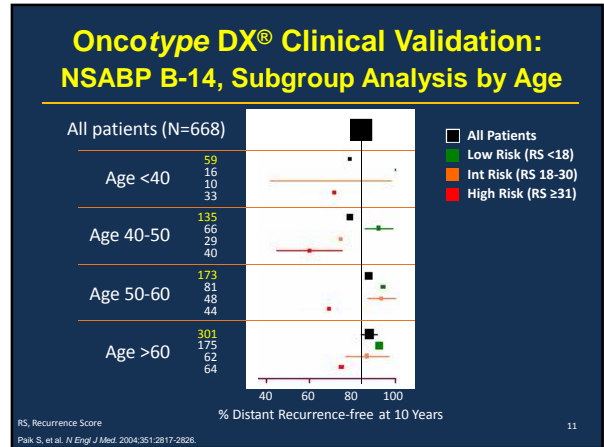
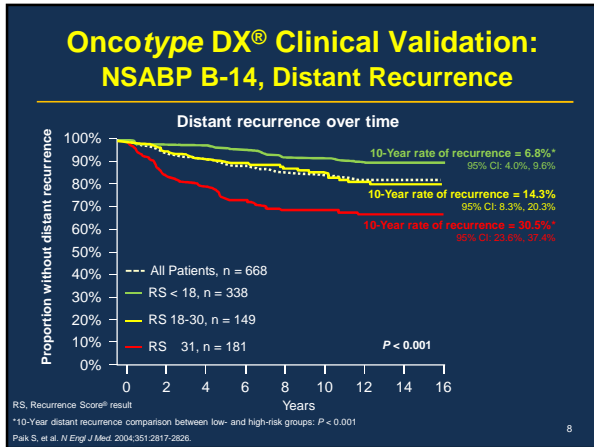
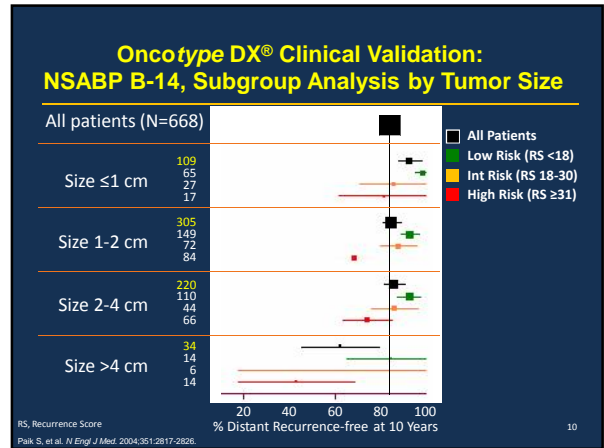
- Objective: Prospectively validate the Recurrence Score® result as a predictor of distant recurrence in node-negative, ER+ patients

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    graph TD
      Randomized --> Placebo[Placebo—not eligible]
      Randomized --> Tamoxifen1[Tamoxifen—eligible]
      Registered --> Tamoxifen2[Tamoxifen—eligible]
      Tamoxifen1 --> Tamoxifen3[Tamoxifen—eligible]
  
```

- Multicenter study with prespecified 21-gene assay, algorithm, endpoints, analysis plan

Paik S, et al. N Engl J Med. 2004;351:2817-2826. 7



Oncotype DX® Clinical Validation: NSABP B-20

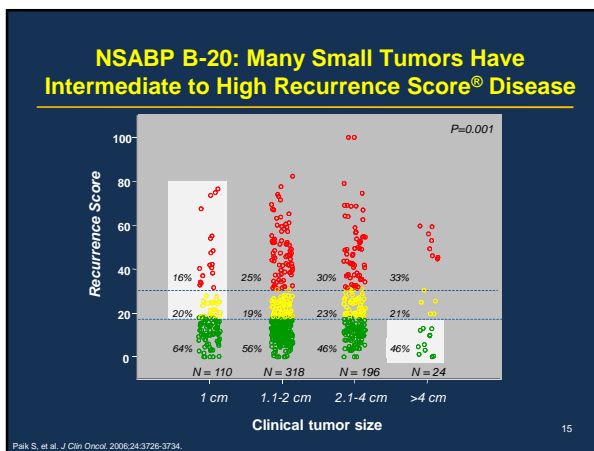
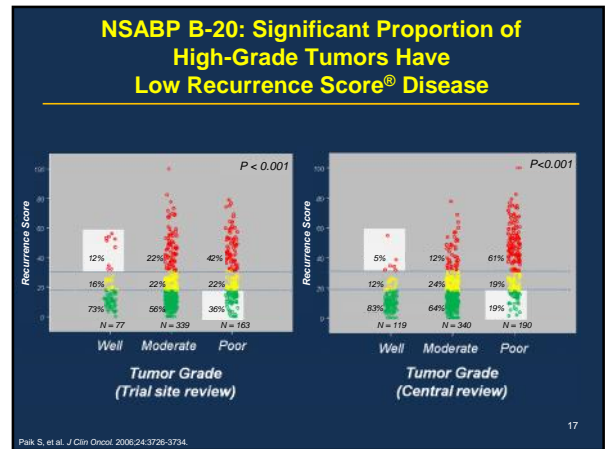
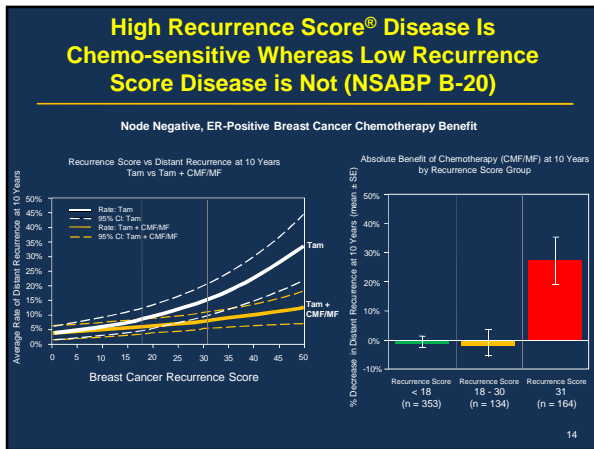
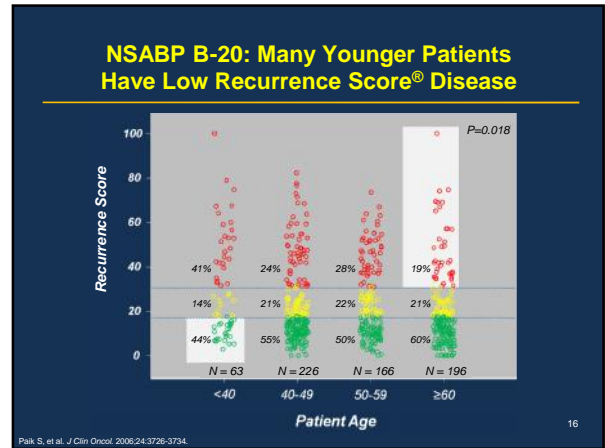
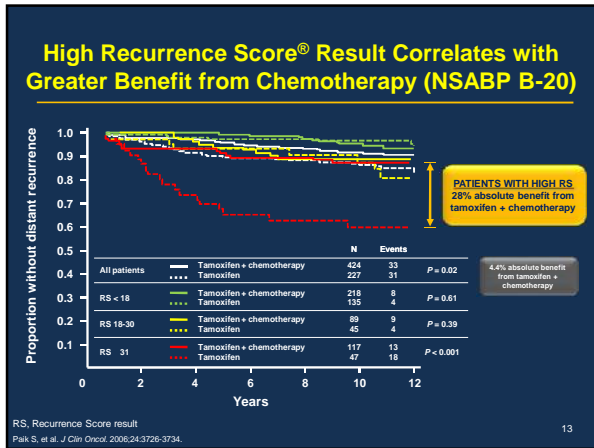
- Objective: Prospectively determine the relationship between Recurrence Score® result and chemotherapy benefit in node-negative, ER+ patients

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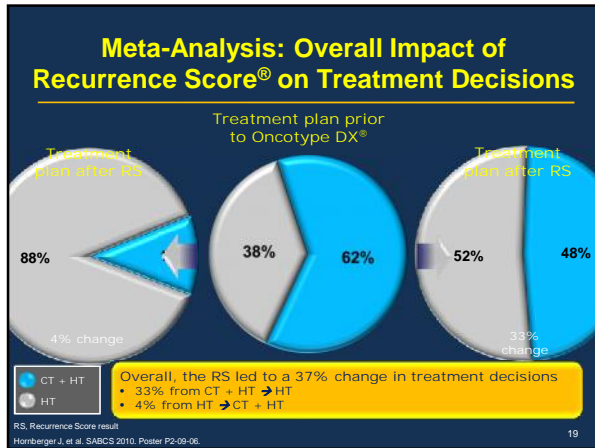
    graph TD
      Randomized --> TamMF[Tam + MF]
      Randomized --> TamCMF[Tam + CMF]
      Randomized --> Tam[Tam]
  
```

- Multicenter study with prespecified 21-gene assay, algorithm, endpoints, analysis plan

Paik S, et al. J Clin Oncol. 2006;24:3726-3734. 12



Does the Recurrence Score® Impact Treatment Decisions?



The Oncotype DX® Assay

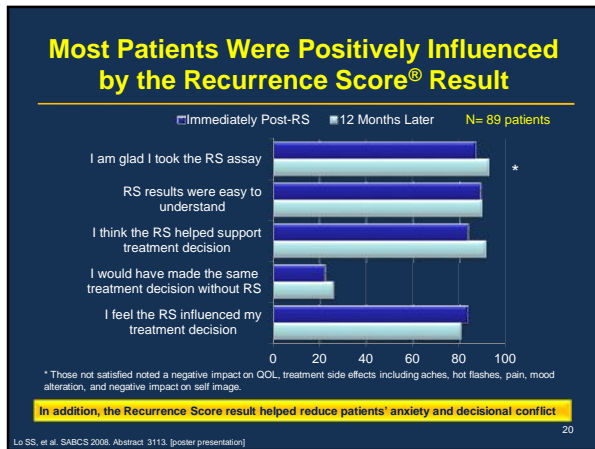
The Only Multi-gene Assay Incorporated into 4 Major Guidelines to Predict Adjuvant Chemotherapy Benefit in ER+, HER2- Early Stage Breast Cancer

NCCN Guidelines* <small>> 0.5 cm, node negative, N1mi</small>	Quantifies risk of recurrence as a continuous variable and predicts responsiveness to both tamoxifen and chemotherapy ¹
ASCO® Guidelines <small>Node negative</small>	Predicts the risk of recurrence and may be used to identify patients likely to benefit from tamoxifen or chemotherapy ²
St Gallen Consensus <small>Node negative, node positive</small>	Provides not only prognostic but also predictive information regarding the utility of cytotoxic therapy in addition to endocrine therapy ³
NICE <small>Node negative</small>	Recommended as an option for guidance of chemotherapy decisions in patients at intermediate risk ⁴ of distant recurrence ⁴

1 NCCN Practice Guidelines in Oncology, V.3.2013.
 2 Harris B, et al. J Clin Oncol 2005.
 3 Gosselin A, et al. Ann Oncol 2011.
 4 NICE Clinical Guideline 2011.

ASCO is a trademark of the American Society of Clinical Oncology. NCCN and NCCN Guidelines are trademarks of the National Comprehensive Cancer Network. The guidelines do not endorse particular therapies.
 *Intermediate risk of distant recurrence is defined as Nottingham Prognostic Index score above 3.4 or being at intermediate risk by other decision making tools or protocols.

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Patient Cases

Is the Oncotype DX® Assay Included in Treatment Guidelines?

Can You Guess the Recurrence Score®?

68 & 69 year-old patients, small node-negative tumors, grade 2 & 3

PATIENT A 68-year-old patient with 1.1-cm tumor Menopausal Status: Postmenopausal Tumor Type: Infiltrating Ductal Carcinoma (IDC) Tumor Size: 1.1 cm ER Status (IHC): Positive PR Status (IHC): Positive HER2/neu Status: Negative Histologic Grade: 2 Lymph Node Status: Negative General Health: Fair	PATIENT B 69-year-old patient with 1.3-cm tumor Menopausal Status: Postmenopausal Tumor Type: Infiltrating Ductal Carcinoma (IDC) Tumor Size: 1.3 cm ER Status (IHC): Positive (2) PR Status (IHC): Positive (2) HER2/neu Status: Negative (IHC) Histologic Grade: 3 Lymph Node Status: Negative General Health: PS 0
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CASE SUBMITTED BY:
 Victor G. Vogel, MD

CASE SUBMITTED BY:
 Ella Tepper, MD

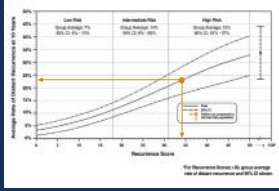
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Can You Guess the Recurrence Score®?

68 & 69 year-old patients, small node-negative tumors, grade 2 & 3

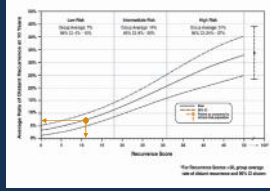
PATIENT A RESULTS
Clinical Experience

Patients with a Recurrence Score of **34** in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of **23% (95% CI: 18%-28%)**.



PATIENT B RESULTS
Clinical Experience

Patients with a Recurrence Score of **11** in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of **7% (95% CI: 5%-10%)**.



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Conclusions

Can You Guess the Recurrence Score®?

45 & 46 year-old patients, small node-negative tumors, grade 2 & 3

PATIENT A
45-year-old patient with 0.9-cm tumor

Menopausal Status: Premenopausal
Tumor Type: Infiltrating Ductal Carcinoma (IDC)
Tumor Size: 0.9 cm
ER Status (IHC): Positive (99%)
PR Status (IHC): Positive (13%)
HER2/neu Status: Negative (1.7 by FISH)
Ki-67: 38%
Histologic Grade: 2
Lymph Node Status: Negative (0/2 SLNs)

CASE SUBMITTED BY:
Barbara Schwartzberg, MD

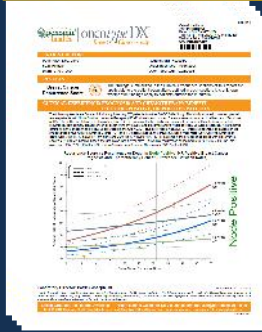
PATIENT B
46-year-old patient with 0.7-cm tumor

Menopausal Status: Premenopausal
Tumor Type: Infiltrating Ductal Carcinoma (IDC)
Tumor Size: 0.7 cm
ER Status (IHC): Positive (91%)
PR Status (IHC): Positive (99%)
HER2/neu Status: Negative (0.7 by FISH)
Ki-67: 35%
Histologic Grade: 3
Lymph Node Status: Negative

CASE SUBMITTED BY:
Barbara Schwartzberg, MD

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The Oncotype DX® Report Provides Valuable Information Along a Continuum of ER+ Breast Cancer



- The Oncotype DX report provides valuable information on:
 - Node-negative prognosis
 - Node-negative predicted chemotherapy benefit
 - Quantitative data on ER/PR/HER2
- Node-positive report contains an additional page with prognosis and predicted chemo benefit information specific to node-positive patients

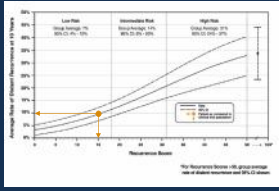
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Can You Guess the Recurrence Score®?

45 & 46 year-old patients, small node-negative tumors, grade 2 & 3

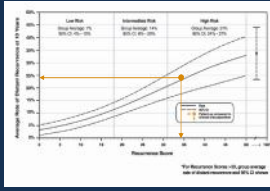
PATIENT A RESULTS
Clinical Experience

Patients with a Recurrence Score of **15** in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of **10% (95% CI: 7%-12%)**.



PATIENT B RESULTS
Clinical Experience


Patients with a Recurrence Score of **35** in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of **24% (95% CI: 18%-30%)**.



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The Oncotype DX® Breast Cancer Assay

- Quantitatively predicts the likelihood of breast cancer recurrence and assesses the benefit from both hormonal therapy and chemotherapy (Level I Evidence)
- High and low Recurrence Score® results reflect different intrinsic tumor biology
- You cannot predict the risk of distant recurrence or chemotherapy benefit by relying on clinical and pathological variables
- Changes treatment decisions based on traditional measures 37% of the time, sparing patients the negative health and QOL impact of unnecessary chemotherapy and resulting in cost savings
- Only assay incorporated into ASCO®, NCCN® and St Gallen's clinical practice guidelines
- Longest history of commercial genomic assays with over 200,000 patients tested worldwide



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