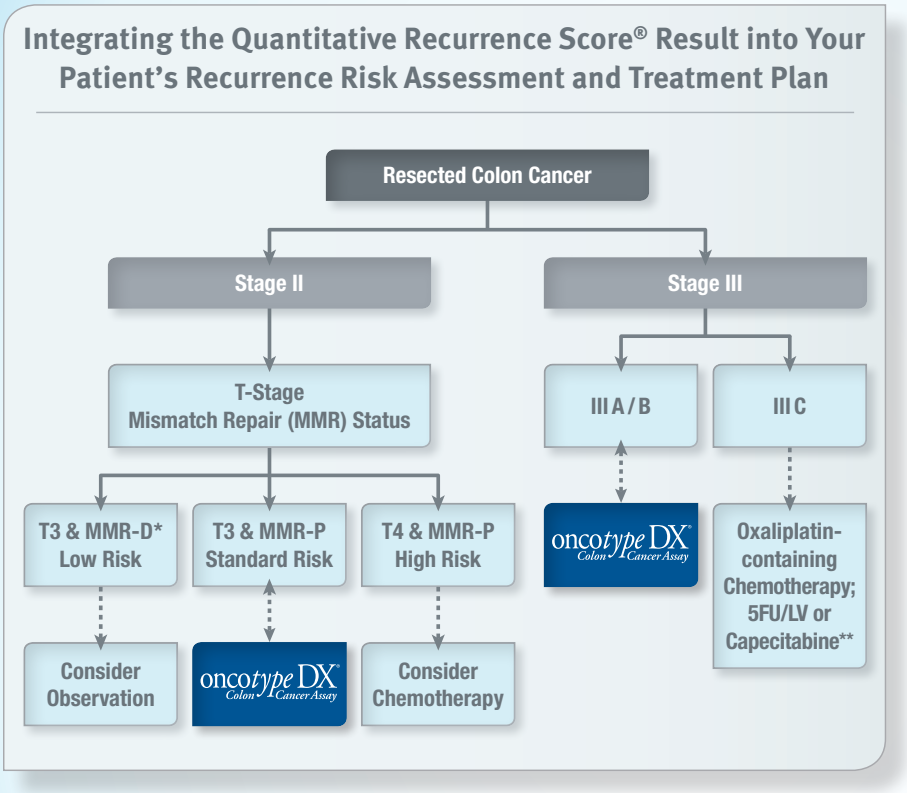
The Oncotype DX® Colon Cancer Assay: An Individualized Approach to Stage II and III Colon Cancer Treatment Planning

Integrating the Quantitative Recurrence Score® Result into Your Patient's Recurrence Risk Assessment and Treatment Plan



* MMR-D = mismatch repair deficient; MMR-P = mismatch repair proficient
**Patients not considered candidates for oxaliplatin

- Recurrence Score result predicts recurrence risk in stage II and III colon cancer, revealing underlying biology to provide value beyond conventional measures
- Recurrence Score result enables better discrimination of absolute oxaliplatin benefit as a function of risk, most notably in stage II and III A/B patients
- Incorporating the Recurrence Score result into the clinical context may better inform adjuvant therapy decisions for patients with stage II and III colon cancer

oncotype DX® Colon Cancer Assay

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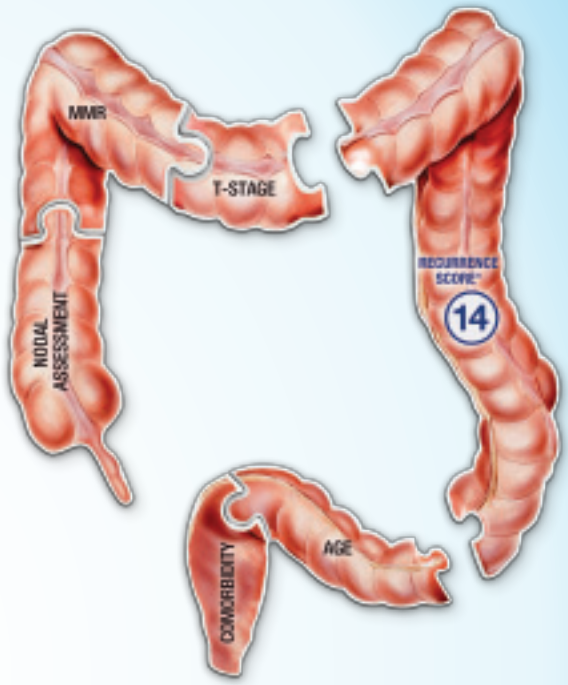
The Onco*type* DX® Colon Cancer Assay is a Prospectively Defined Clinical Gene Expression Commercial Test That Independently Predicts Recurrence Risk in Stage II and III Colon Cancer



- Traditional clinical and pathologic measures are insufficient to guide the decision to add or withhold oxaliplatin for adjuvant treatment
- In stage III colon cancer, the Recurrence Score result predicts risk of recurrence after 5FU/LV or 5FU + oxaliplatin
  - Higher absolute benefit of oxaliplatin with higher Recurrence Score results
- Expanding payor coverage including both public and private payors (Stage II)
- Patients can receive assistance regarding insurance benefits and referral to financial aid, if qualified, through the Genomic Access Program

For more information regarding the Onco*type* DX Colon Cancer Assay, please contact customer service at 866-ONCOTYPE (866-662-6897) in the US, or 001-650-569-2080 outside the US

www.onco*type*DX.com

References: 1. Gray RG, Quirke P, Handley K, et al. Validation study of a quantitative multigene reverse transcriptase-polymerase chain reaction assay for assessment of recurrence risk in patients with stage II colon cancer. *J Clin Oncol.* 2011;29(35):4611-9. **2.** Venook AP, Niedzwiecki D, Lopatin M, et al. Validation of a 12-gene colon cancer recurrence score in stage II colon cancer patients from CALGB 9581. Presented at the American Society of Clinical Oncology annual meeting; June 2011; Chicago, IL. **3.** O'Connell MJ, Lee M, Lopatin M, et al. Validation of the 12-gene colon cancer Recurrence Score (RS) in NSABP C-07 as a predictor of recurrence in stage II and III colon cancer patients treated with 5FU/LV (FU) and 5FU/LV + oxaliplatin (FU+Ox). Presented at the American Society of Clinical Oncology annual meeting; June 2012; Chicago, IL. **4.** Kuebler JP, Wieand HS, O'Connell MJ, et al. Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07. *J Clin Oncol.* 2007;25(16):2198-204.

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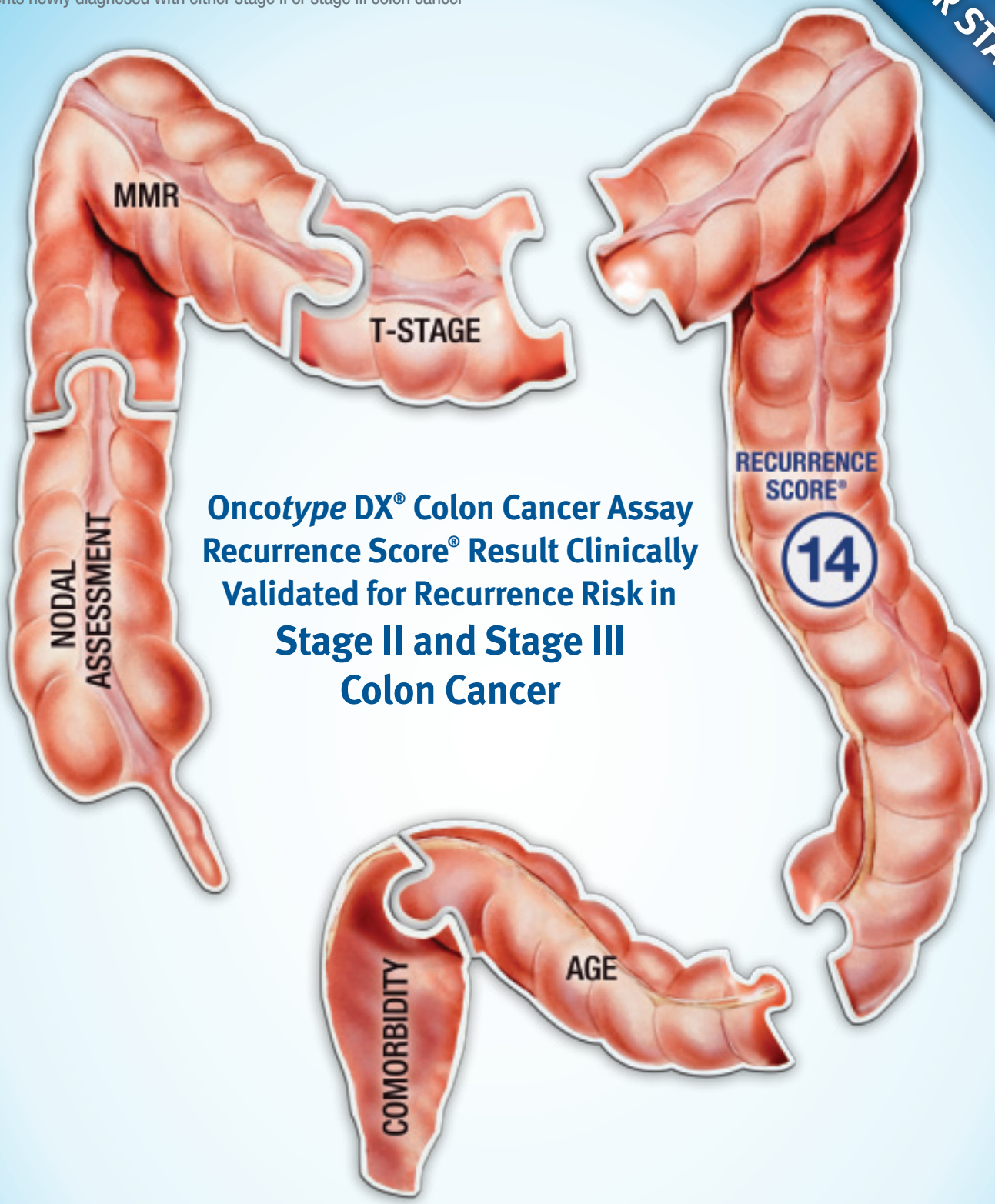
Genomic Health™

oncotype DX® Colon Cancer Assay

For patients newly diagnosed with either stage II or stage III colon cancer

NOW AVAILABLE FOR STAGE III



Oncotype DX® Colon Cancer Assay Recurrence Score® Result Clinically Validated for Recurrence Risk in Stage II and Stage III Colon Cancer

The Oncotype DX Colon Cancer Assay

Is the first commercial test to provide a quantitative Recurrence Score result to give you a more complete assessment of recurrence risk. Now you can individualize treatment for both your stage II and stage III colon cancer patients.[1,2,3]

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Oncotype DX® Colon Cancer Assay Recurrence Score® Result Clinically Validated for Recurrence Risk in Stage II and Stage III Colon Cancer

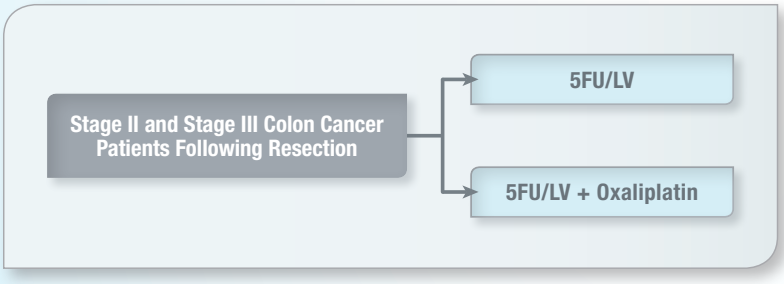
Traditional clinical and pathologic measures are insufficient to guide the decision to add or withhold oxaliplatin for adjuvant treatment of resected colon cancer

Validated in the NSABP C-07 Study

Prospective analysis of archived paraffin embedded samples from a landmark phase III randomized clinical trial that demonstrated benefit of adding oxaliplatin to adjuvant 5FU/LV chemotherapy[4]

The first standardized, clinically validated, commercially available genomic test to differentiate risk of recurrence for patients with stage III disease and in the context of oxaliplatin-containing adjuvant therapy

The third independent confirmatory study demonstrating the value of the Recurrence Score result in stage II disease[1,2]



Included 892 stage II and III colon cancer patients randomized to 5FU/LV or 5FU/LV + oxaliplatin[3]

- 30% stage II, 46% stage III A/B, 24% stage III C
- 18% MMR-D tumors in stage II, 9% MMR-D tumors in stage III

Recurrence Score results predict recurrence risk in stage II and III colon cancer in patients from NSABP C-07, revealing underlying tumor biology to provide risk information not available with conventional factors

Recurrence Score results enable better discrimination of absolute oxaliplatin benefit for the patient as a function of risk

- Patients with higher Recurrence Score values are expected to have greater absolute benefit from the addition of oxaliplatin than patients with lower Recurrence Score values

NSABP C-07: The Continuous Recurrence Score® Result Predicts Risk of Recurrence Beyond Traditional Clinical and Pathologic Covariates

Recurrence Score Result is a Highly Significant Predictor of Recurrence Risk[3]

Variable	Value	HR*	HR 95% CI	P Value
Stage	Stage III A/B vs II	2.53	(1.70,3.78)	<0.001
	Stage III C vs II	5.29	(3.54,7.90)	
Treatment	5FU/LV + Oxaliplatin vs 5FU/LV	0.76	(0.59,0.98)	0.033
Recurrence Score Result	**Continuous per 25 Units**	**1.96**	**(1.50,2.55)**	**<0.001**

*HR = Hazard Ratio

- Recurrence Score result was significantly associated with risk of recurrence after controlling for stage and treatment (HR=1.96 per 25 Recurrence Score units; 95% CI 1.50–2.55, p < 0.001)
- Recurrence Score performance was similar for both stage II and III colon cancer patients (interaction p=0.90)

Pre-specified Multivariate Analysis

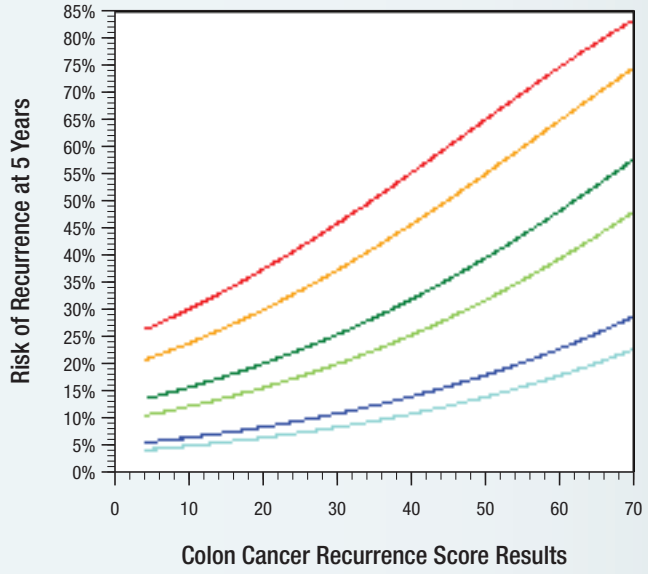
Variable	Value	HR	HR 95% CI	P Value
Stage	Stage III A/B vs II	0.97	(0.55,1.71)	<0.001
	Stage III C vs II	2.07	(1.16,3.68)	
Treatment	5FU/LV + Oxaliplatin vs 5FU/LV	0.82	(0.64,1.06)	0.122
MMR*	MMR-D vs MMR-P	0.27	(0.12,0.62)	<0.001
T-stage	T4 St. II & T3-T4 St. III vs All Other	3.04	(1.84,5.02)	<0.001
Nodes Examined	<12 vs ≥12	1.51	(1.17,1.95)	0.002
Tumor Grade	High vs Low	1.36	(1.02,1.82)	0.041
Recurrence Score Result	**Continuous per 25 Units**	**1.57**	**(1.19,2.08)**	**0.001**

*MMR-D = mismatch repair deficient; MMR-P = mismatch repair proficient

- Recurrence Score value predicts recurrence independently of traditional clinical and pathologic covariates: T-stage, MMR status, nodes examined, and grade

Absolute Benefit From the Addition of Oxaliplatin Was Greater in the High Recurrence Score® Group than in the Low Recurrence Score Group

Risk of Recurrence at 5 Years by Recurrence Score Result, Stage and Treatment



Stage III C (24% of Study Patients)
- 5FU/LV
- 5FU/LV + Oxaliplatin

Stage III A/B (46% of Study Patients)
- 5FU/LV
- 5FU/LV + Oxaliplatin

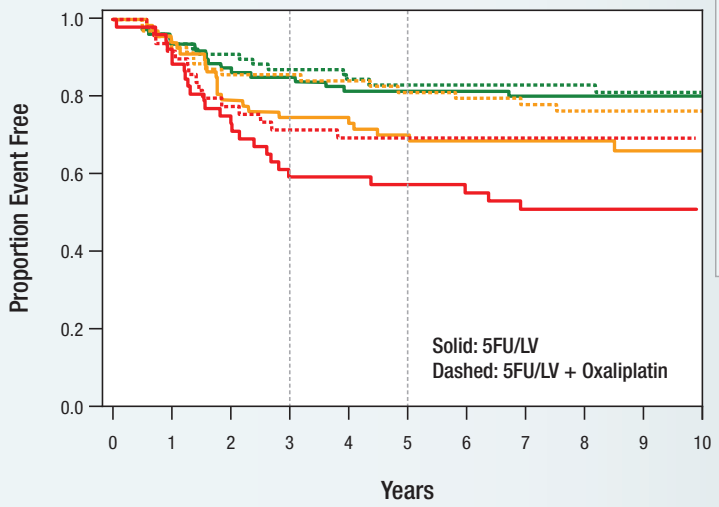
Stage II (30% of Study Patients)
- 5FU/LV
- 5FU/LV + Oxaliplatin

Relative benefit of oxaliplatin was similar across the range of Recurrence Score values (interaction p=0.48)

- Absolute benefit from the addition of oxaliplatin increased with higher Recurrence Score values, most apparently in stage II and stage III A/B patients

Differentiation of Risk and Absolute Oxaliplatin Benefit by Recurrence Score Group

Kaplan-Meier (KM) Analysis in Stage III A/B Patients



Recurrence Score Risk Group	Patients (n)	Events (n)	Recurrence Risk at 5 Years KM Estimates (95% CI) 5FU/LV	5FU/LV + Oxaliplatin
Low (<30)	169	31	19% (12%, 28%)	17% (10%, 27%)
Intermediate (≥30)	138	38	30% (20%, 42%)	19% (11%, 30%)
High (≥41)	102	40	43% (31%, 57%)	31% (20%, 46%)

- Absolute benefit from the addition of oxaliplatin was greater in the high Recurrence Score group than in the low Recurrence Score group

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