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TAMIR FISHMAN

Exclusive Financial Home

~~אשר חתם~~

שמר את הרצף

מאשר שכל הדיוקן הוא

הרצף הוא הרצף כיום

31/7/23 סמל ת"פ 60 י"ר וסמל

6680-9224 - דרך ה' דין

~~שמן און~~

0203-9224
603

829 0 שים וקנה דימן 3

אשר 6 שים בים וסך

לחלקי כאלה וקנים כחל

ה' בלח

וקנים את ה' יגר סמל באיחוס פסי בלח

אין אסר על סמל השמ

1940 י"ר . י"ר

1961 קנים ש"ח
דימן

כחלית י"ר חלחל - כחלית י"ר

אשר הקנים החל

ואשר את החלחל שרר חלחל - ג' כחלית

ה' י"ר

א גיו ג האנות זם הצרפת-מ
וצרפת-מ יצרו שביכל גסת"מ האוקסוס
זם רג-טאים נאיקים וגם יצרו
פלוטצ'ים.

כשבז גפלים טזר הצנורות
זם קולט ורדזים. בזם אחת
הצ'וא מ שפך וחזק הרים הי"מ
ס/פ הדפזים. כדור 3 שים הט
נבטה.

דורו דו גיג ח' טצרה
אךלר ודיתה גצרה. נתן ידיו
לשים גסירה וכחזק
וגכנס לזור לטאר אג חזק

דילנו החלוצת סאותזיס
והדחנו אלה תהליכים.
דורפ גפ גיכלים טחומצה
אברית'ת לנזוס חימר טאני
דיגן האדלים א גנד לסחף טפ כטותים
מסל חומה
דילך לענורמים שחפכים לטח כחמה

טאטו דלמה צ'ל
טדדה מסל
מכין ס'
והרפאב
חלפה ונטורה.
שכ 4000+

Patient/ID: LEVIN, NAAMAN
Gender: Male
Date of Birth: 25-Nov-1940

Report Number: OR000823608-01
Specimen Received: 30-Aug-2016
Date Reported: 07-Sep-2016

Comments

MMR testing performed at Genomic Health Inc. 701 Galveston Drive, Redwood City, CA 94063.

Laboratory Director(s): Patrick Joseph, MD

This test was developed and its performance characteristics determined by Genomic Health, Inc. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. These results are adjunctive to the ordering physician's workup.

ID: LEVIN, NAAMAN
Sex: Male
Date of Birth: 25-Nov-1940
Internal Record/Patient #: 003531001
Date of Collection: 04-Aug-2016
Assay Type/ID: Colon/9778/8/16

Report Number: OR000823608-01
Specimen Received: 30-Aug-2016
Date Reported: 07-Sep-2016
Ordering Physician: Dr. Enat Binyat
Additional Recipient: Dr. Lior Soussan-Gulman

Mismatch Repair (MMR) Assay Results

Mismatch Repair Status = **MMR Proficient (MMR-P)**

Antibody	Clone	Result
MLH1	ES05	Expressed
MSH2	G219-1129	Expressed

Status Determination for Recurrence Risk

- MMR-Proficient (MMR-P) if both MLH1 and MSH2 are expressed
- MMR-Deficient (MMR-D) if one or both of MLH1 and MSH2 are not expressed

See comments on page 4.

Clinical Experience: MMR for Recurrence Risk Assessment in Colon Cancer

MMR deficiency (MMR-D) defines a subset of ~15% of stage II colon cancer patients who have significantly lower recurrence risk compared to patients with MMR proficient (MMR-P) tumors.^{1,2} MMR-D tumors may also have limited benefit from 5-FU based chemotherapy.¹ As reported in the QUASAR validation study, where MMR status was assessed by IHC for MLH1 and MSH2, stage II colon cancer patients with T3 MMR-D tumors had point estimates for three year recurrence risk of <7%, while stage II patients with T3 MMR-P tumors had three year recurrence risk ranging from 10% to 26%.^{3,4} Similarly, the ~10% of stage III colon cancer patients with MMR-D tumors have lower recurrence risk than stage III patients with MMR-P tumors. Assessment of MMR status using IHC for MLH1 and MSH2 is highly concordant (>95%) with microsatellite instability (MSI) using PCR, where MMR-D corresponds to high-degree MSI (MSI-H).⁵

MMR testing using IHC as screening for hereditary cancer syndromes is typically performed by assessment of staining for MLH1, MSH2, PMS2, and MSH6, with further workup of MMR-D cases according to physician discretion and institutional guidelines. Assessment of PMS2 and MSH6 expression, which are not part of this recurrence risk assay, may identify an additional ~1-2% of colon cancers as MMR-D.^{6,7}

Sargent DJ et al., *J Clin Oncol* 2010 28; Fazio CM et al., *N Engl J Med* 2003 350; Kerr D et al., *ASCO* 2009 4; Gray RG et al., *J Clin Oncol* 2011 29; Bartagnoli MM et al., *J Clin Oncol* 2009 27; Cizek MS et al., *J Mol Diagn* 2011 13; Hampel H et al., *J Clin Oncol* 2008 26

Immunohistochemistry (IHC) Methodology and Scoring

Antigen detection is performed using a biotin-free, polymer based IHC methodology with the antibodies listed above on fixed, paraffin embedded tissue sections. Results for MLH1 and MSH2 are scored as expressed if any fraction of tumor cells are immunoreactive, or not expressed if no tumor cells are found to be immunoreactive. The internal and external tissue and reagent controls are reviewed and determined to be satisfactory.

Reviewing Pathologist: Anil Pingitore

Laboratory Director(s): Patrick Joseph, MD

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Colon Cancer Assay

Stage II Colon Cancer Report Following Surgery Alone

Genomic Health, Inc.
 301 Peninsula Drive, Redwood City, CA 94063 USA
 USA/Canada: +1.866.ONCOTYPE
 International: www.oncotypedx.com/contact
 www.oncotypedx.com
 CLIA Number 05D1018272

Patient/ID: LEVIN, NAAMAN
 Gender: Male
 Date of Birth: 25-Nov-1940
 Medical Record/Patient #: 003531001
 Date of Collection: 04-Aug-2016
 Specimen Type/ID: Colon/9778/616

Report Number: OR000823608-01
 Specimen Received: 30-Aug-2016
 Date Reported: 07-Sep-2016
 Ordering Physician: Dr. Enat Binyat
 Additional Recipient: Dr. Lior Soussan-Gutman

Recurrence Score[®] Result

17

OncoType DX[®] Colon Cancer Assay uses RT-PCR to determine the expression of a panel of 12 genes in tumor tissue. The Recurrence Score[®] result is calculated from the gene expression results, and ranges from 0-100.

These findings are applicable to stage II patients with adenocarcinoma or mucinous carcinoma limited to the colon. It is unknown whether the findings apply to other patients outside these criteria.

Clinical Experience is based on a prospectively-designed validation study with a pre-specified analysis of the Recurrence Score result, in the context of T-Stage and MMR status (MMR proficient (MMR-P) or MMR deficient (MMR-D)), using patients from the surgery-alone arm of the QUASAR study (N=711).

Note: Determination of MMR status is important for treatment decision-making in stage II colon cancer. In this validation study, stage IIA MMR-D patients had a 3-year recurrence risk ranging from 3% to 7% across Recurrence Score results and are expected to have little if any clinical benefit from 5FU/LV adjuvant therapy. Use of this assay is generally not recommended for stage II MMR-D patients.

Relevance for Chemotherapy Benefit: Based on the results in QUASAR (N=1,436) that randomized patients to surgery or surgery+5FU/LV, the proportional reductions in recurrence risk with 5FU/LV were similar across the range of Recurrence Score results, with larger absolute benefit at higher Recurrence Score results. In the parent QUASAR trial, 5FU/LV treatment resulted in ~20% relative risk reduction of cancer recurrence.

See comments on page 4.

Stage II Recurrence Risk Following Surgery Alone

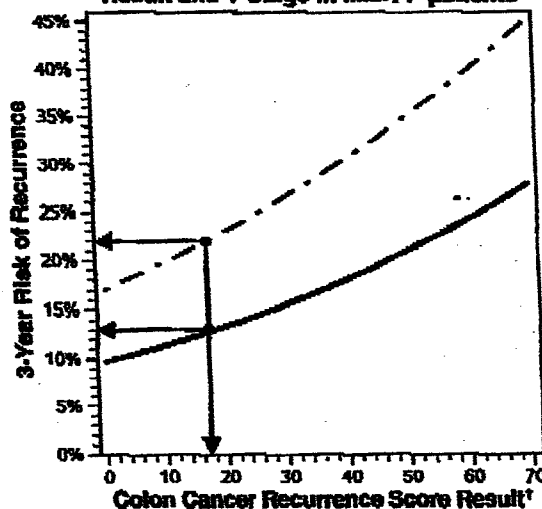
22%

— · — · — T4, MMR-P
 (95% CI: 15%-32%)

13%

———— T3, MMR-P*
 (95% CI: 10%-17%)

3-Year Recurrence Risk by Recurrence Score Result and T-Stage in MMR-P patients



* 2% of all patients with T4, MMR-D tumors had estimated recurrence risks that approximated (with large confidence intervals) those for patients with T3 stage, MMR-P tumors and were not included in this figure.

† In the clinical validation studies, very few patients had Recurrence Score results > 70.

Impact of Nodes Assessed: For patients with ≥ 12 nodes examined the 3-year recurrence risk was lower than that shown in the Figure. For T3 MMR-P patients the reduction in risk ranged from 2% for low to 6% for high Recurrence Score results. For T4 MMR-P patients the reduction in risk ranged from 4% to 10%, respectively. For all MMR-P patients with < 12 nodes examined, the recurrence risk was 2-3% higher.

1. Gray RG et al. J Clin Oncol. 2011.

Laboratory Director(s): Patrick Joseph, MD

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Colon Cancer Assay

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 International: www.oncotypedx.com/contact
 www.oncotypedx.com
 CLIA Number 05D1018272

Stage II Colon Cancer Report Following Adjuvant Chemotherapy

Patient ID: LEVIN, NAAMAN
 Gender: Male
 Date of Birth: 25-Nov-1940

Report Number: OR000823608-01
 Specimen Received: 30-Aug-2016
 Date Reported: 07-Sep-2016

Recurrence Score[®] Result

OncoType DX[®] Colon Cancer Assay uses RT-PCR to determine the expression of a panel of 12 genes in tumor tissue. The Recurrence Score[®] result is calculated from the gene expression results, and ranges from 0-100.

These findings are applicable to stage II patients with adenocarcinoma or mucinous carcinoma limited to the colon. It is unknown whether the findings apply to other patients outside these criteria.

Clinical Experience is based on a prospectively-designed clinical validation study (NSABP C-07) which randomized patients to 5FU/LV versus 5FU/LV+oxaliplatin, in which 264 patients were stage II, including 247 (94%) with T3 tumors. Out of 213 patients with available MMR status, 82% were MMR-P.

See comments on page 4.

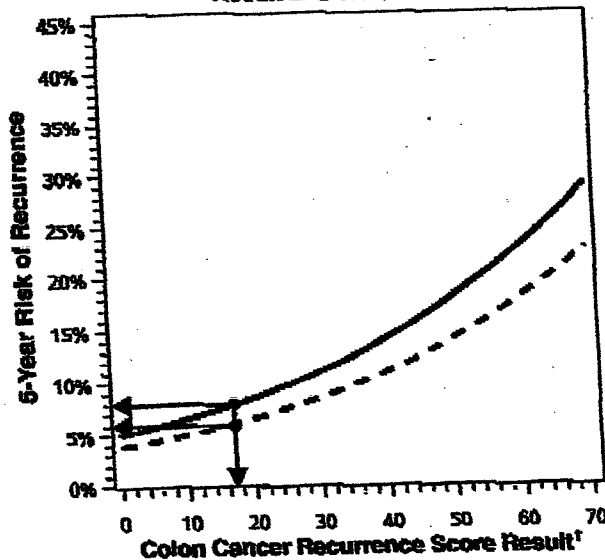
17

Stage II Recurrence Risk Following Adjuvant Chemotherapy

8% ——— 5FU/LV
 (95% CI: 5%-12%)

6% - - - - 5FU/LV + oxaliplatin
 (95% CI: 4%-9%)

5-Year Recurrence Risk by Recurrence Score Result and Treatment



[†] In the clinical validation studies, very few patients had Recurrence Score results > 70.

Impact of MMR Status: Consistent with previous studies, patients with MMR-D tumors had generally lower recurrence risk than patients with MMR-P tumors. These results are not shown on the graph due to low number of events (6 recurrences in the 18% of stage II patients with MMR-D tumors).

Impact of Nodes Assessed: The recurrence risk for patients with ≥ 12 nodes examined was lower than the risk for those with < 12 nodes examined.

1. Yamaoka G, et al. J Clin Oncol. 2013.

Laboratory Director(s): Patrick Joseph, MD

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Patient/ID: LEVIN, NAAMAN
Gender: Male
Date of Birth: 25-Nov-1940
Medical Record/Patient #: 003531001
Date of Collection: 04-Aug-2016
Specimen Type/ID: Colon/9778/6/16

Report Number: OR000823608-01
Specimen Received: 30-Aug-2016
Date Reported: 07-Sep-2016
Ordering Physician: Dr. Einat Binyat
Additional Recipient: Dr. Lior Soussan-Gutman

Mismatch Repair (MMR) Assay Results

Mismatch Repair Status = **MMR Proficient (MMR-P)**

Antibody	Clone	Result
MLH1	ES05	Expressed
MSH2	G219-1129	Expressed

MMR Status Determination for Recurrence Risk:

- MMR-Proficient (MMR-P) if both MLH1 and MSH2 are expressed
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See comments on page 4.

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MMR testing using IHC as screening for hereditary cancer syndromes is typically performed by assessment of staining for MLH1, MSH2, PMS2, and MSH6, with further workup of MMR-D cases according to physician discretion and institutional guidelines. Assessment of PMS2 and MSH6 expression, which are not part of this recurrence risk assay, may identify an additional ~1-2% of colon cancers as MMR-D.^{6,7}

1. Sargent DJ et al., *J Clin Oncol*. 2010 2. Ribic CM et al., *N Engl J Med*. 2003 3. Kerr D et al., *ASCO* 2009 4. Gray RG et al., *J Clin Oncol*. 2011 5. Bertagnolli MM et al., *J Clin Oncol*. 2009 6. Ciolek MS et al., *J Mol Diagn*. 2011 7. Hampel H et al., *J Clin Oncol*. 2008

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Reviewing Pathologist: Andi Pingitore

Laboratory Director(s): Patrick Joseph, MD

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Colon Cancer Assay

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CLIA Number 05D1018272

Page 4 of 4

Patient/ID: LEVIN, NAAMAN
Gender: Male
Date of Birth: 25-Nov-1940

Report Number: OR000823608-01
Specimen Received: 30-Aug-2016
Date Reported: 07-Sep-2016

Comments

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Laboratory Director(s): Patrick Joseph, MD

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Stage II Colon Cancer Report Following Surgery Alone

Patient ID: LEVIN, NAAMAN
 Gender: Male
 Date of Birth: 25-Nov-1940
 Medical Record/Patient #: 003531001
 Date of Collection: 04-Aug-2016
 Specimen Type/ID: Colon/9778/6/16

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 CLIA Number 05D1018272

Report Number: OR000823608-01
 Specimen Received: 30-Aug-2016 ✓
 Date Reported: 07-Sep-2016 ✓
 Ordering Physician: Dr. Einat Binyat
 Additional Recipient: Dr. Lior Soussan-Gutman

Recurrence
 Score[®]
 Result

17

Oncotype DX[®] Colon Cancer Assay uses RT-PCR to determine the expression of a panel of 12 genes in tumor tissue. The **Recurrence Score[®]** result is calculated from the gene expression results, and ranges from 0-100. These findings are applicable to stage II patients with adenocarcinoma or mucinous carcinoma limited to the colon. It is unknown whether the findings apply to other patients outside these criteria.

Clinical Experience is based on a prospectively-designed validation study with a pre-specified analysis of the Recurrence Score result, in the context of T-Stage and MMR status (MMR proficient (MMR-P) or MMR deficient (MMR-D)), using patients from the surgery-alone arm of the QUASAR study (N=711).

Note: Determination of MMR status is important for treatment decision-making in stage II colon cancer. In this validation study, stage IIA MMR-D patients had a 3-year recurrence risk ranging from 3% to 7% across Recurrence Score results and are expected to have little if any clinical benefit from 5FU/LV adjuvant therapy. Use of this assay is generally not recommended for stage II MMR-D patients.

Relevance for Chemotherapy Benefit: Based on the results in QUASAR (N=1,436) that randomized patients to surgery or surgery+5FU/LV, the proportional reductions in recurrence risk with 5FU/LV were similar across the range of Recurrence Score results, with larger absolute benefit at higher Recurrence Score results. In the parent QUASAR trial, 5FU/LV treatment resulted in ~20% relative risk reduction of cancer recurrence.

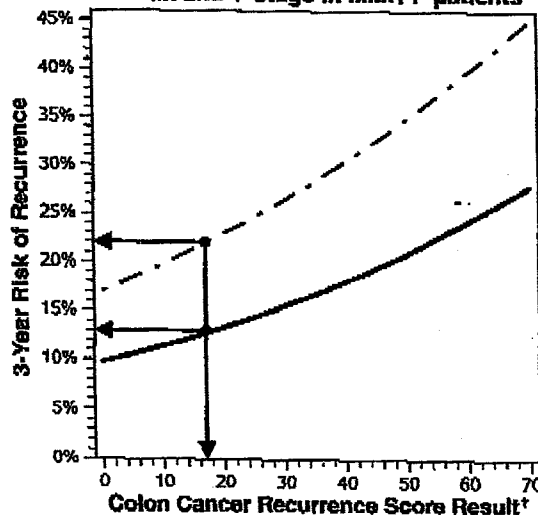
See comments on page 4.

Stage II Recurrence Risk Following Surgery Alone

22% — T4, MMR-P
 (95% CI: 15%-32%)

13% ————— T3, MMR-P*
 (95% CI: 10%-17%)

3-Year Recurrence Risk by Recurrence Score Result and T-Stage in MMR-P patients



Colon Cancer Recurrence Score Result[†]

[†] In the clinical validation studies, very few patients had Recurrence Score results > 70.

* 2% of all patients with T4, MMR-D tumors had estimated recurrence risks that approximated (with large confidence intervals) those for patients with T3 stage, MMR-P tumors and were not included in this figure.

Effect of Nodes Assessed: For patients with ≥ 12 nodes examined the 3-year recurrence risk was lower than that shown in the Figure. For T3 MMR-P patients the reduction in risk ranged from 2% for low to 6% for high Recurrence Score results. For T4 MMR-P patients the reduction in risk ranged from 4% to 10%, respectively. For all MMR-P patients with < 12 nodes examined, the recurrence risk was 2-3% higher.

RG et al., J Clin Oncol. 2011.

Laboratory Director(s): Patrick Joseph, MD

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Genomic Health[®] | **oncotype DX[®]**
Colon Cancer Assay

Stage II Colon Cancer Report Following Adjuvant Chemotherapy

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International: www.oncotypedx.com/contact
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CLIA Number 05D1018272

Patient ID: LEVIN, NAAMAN
Gender: Male
Date of Birth: 25-Nov-1940

Report Number: OR000823608-01
Specimen Received: 30-Aug-2016
Date Reported: 07-Sep-2016 ✓

Recurrence Score[®] Result

17

Oncotype DX[®] Colon Cancer Assay uses RT-PCR to determine the expression of a panel of 12 genes in tumor tissue. The Recurrence Score[®] result is calculated from the gene expression results, and ranges from 0-100.

These findings are applicable to stage II patients with adenocarcinoma or mucinous carcinoma limited to the colon. It is unknown whether the findings apply to other patients outside these criteria.

Clinical Experience is based on a prospectively-designed clinical validation study (NSABP C-07) which randomized patients to 5FU/LV versus 5FU/LV+oxaliplatin, in which 264 patients were stage II, including 247 (94%) with T3 tumors. Out of 213 patients with available MMR status, 82% were MMR-P.[†]

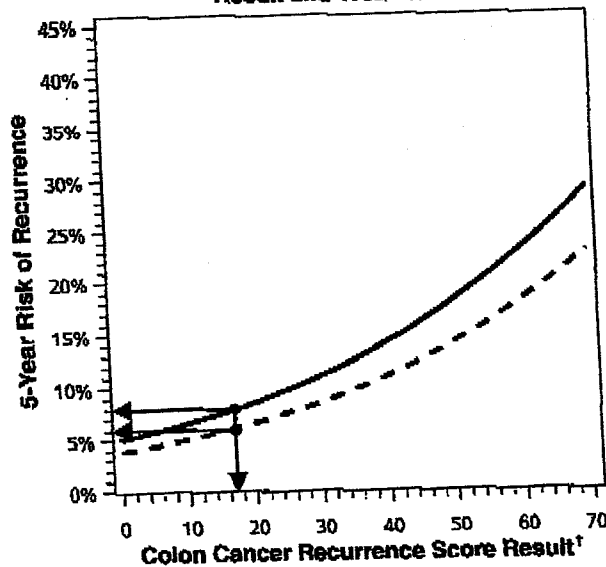
See comments on page 4.

Stage II Recurrence Risk Following Adjuvant Chemotherapy

8% ——— 5FU/LV
(95% CI: 5%-12%)

6% - - - - - 5FU/LV + oxaliplatin
(95% CI: 4%-9%)

5-Year Recurrence Risk by Recurrence Score
Result and Treatment



[†] In the clinical validation studies, very few patients had Recurrence Score results > 70.

Impact of MMR Status: Consistent with previous studies, patients with MMR-D tumors had generally lower recurrence risk than patients with MMR-P tumors. These results are not shown on the graph due to low number of events (6 recurrences in the 18% of stage II patients with MMR-D tumors).

Impact of Nodes Assessed: The recurrence risk for patients with ≥ 12 nodes examined was lower than the risk for those with < 12 nodes examined.

1. Yamahara G, et al. J Clin Oncol. 2013.

Laboratory Director(s): Patrick Joseph, MD

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Genomic Health | oncotype DX[®]

Colon Cancer Assay

Stage II Colon Cancer Report Following Surgery Alone

Patient/ID: LEVIN, NAAMAN
Gender: Male
Date of Birth: 25-Nov-1940
Medical Record/Patient #: 003531001
Date of Collection: 04-Aug-2016
Specimen Type/ID: Colon/9778/6/16

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Specimen Received: 30-Aug-2016 ✓
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Ordering Physician: Dr. Einat Binyat
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Recurrence Score[®] Result

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Note: Determination of MMR status is important for treatment decision-making in stage II colon cancer. In this validation study, stage IIA MMR-D patients had a 3-year recurrence risk ranging from 3% to 7% across Recurrence Score results and are expected to have little if any clinical benefit from 5FU/LV adjuvant therapy. Use of this assay is generally not recommended for stage II MMR-D patients.

Relevance for Chemotherapy Benefit: Based on the results in QUASAR (N=1,436) that randomized patients to surgery or surgery+5FU/LV, the proportional reductions in recurrence risk with 5FU/LV were similar across the range of Recurrence Score results, with larger absolute benefit at higher Recurrence Score results. In the parent QUASAR trial, 5FU/LV treatment resulted in ~20% relative risk reduction of cancer recurrence.

See comments on page 4.

Stage II Recurrence Risk Following Surgery Alone

22% ——— T4, MMR-P
(95% CI: 15%-32%)

3% ——— T3, MMR-P*
(95% CI: 10%-17%)

* 2% of all patients with T4, MMR-D tumors had estimated recurrence risks that approximated (with large confidence intervals) those for patients with T3 stage, MMR-P tumors and were not included in this figure.

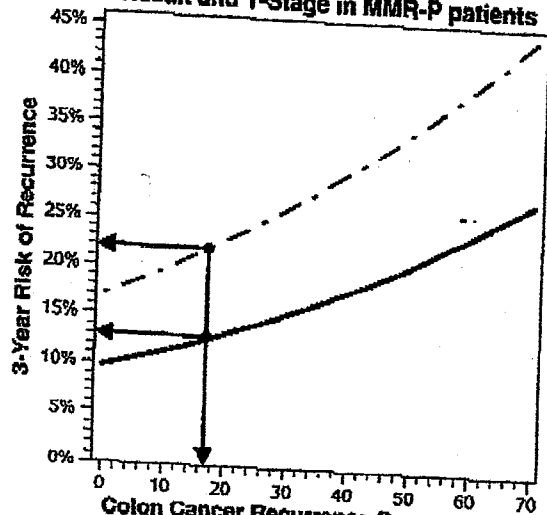
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et al., J Clin Oncol. 2011.

Laboratory Director(s): Patrick Joseph, MD

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3-Year Recurrence Risk by Recurrence Score Result and T-Stage in MMR-P patients



† In the clinical validation studies, very few patients had Recurrence Score results > 70.