Clinical Utility: Lessons from Oncotype DX in Breast, Colon, and Prostate

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Genomic Health
Genomic Health Strategy in 2001 Was Founded on Four Strategic Imperatives

• Most important – “Fit for Purpose”
  • Delivering what patients, physicians, regulators, and payors need, relevant to a specific use
  • Actionable and patient oriented
  • Requires multiple studies
  • Clear value beyond existing measures

• Technical innovation brought to standardized implementation

• Collaboration, and the skills, processes, and resources to do it right – think industry-academic partnerships

• Commitment to continued research
Clinical and pathologic context greatly impacts biomarker clinical utility

• Alteration of the same gene(s) or pathway(s) in a different tumor context often has a significantly different clinical impact
  • K-Ras alterations in colon cancer and lung cancer
  • Oncotype DX Recurrence Score in ER- and ER+ breast cancer
  • Oncotype DX Proliferation gene group in breast cancer and colon cancer
  • Genomic Prostate Score needs to be integrated with biopsy Gleason Grade for appropriate interpretation
  • Too many other examples to count
Three Examples Relevant to Clinical Practice

• Relevance to an actionable decision
  • Oncotype DX and MammaPrint clinical validation study populations and endpoints

• Assay reproducibility for individual patients
  • Oncotype DX Recurrence Score and Tumor Grade

• Documentation of change in physician behavior and value to the health care system
  • Treatment decision studies and health economic analysis
MammaPrint and Oncotype DX in 67 Patients (Poulet et al, SABCS 2012)

MammaPrint Risk vs RS

Oncotype DX ER vs MammaPrint Risk

Multi-gene assays are not the same

Assays developed on patients without systemic treatment may not be clinically useful when the need is to select between Rx’s (eg, HT vs HT + CT)
Clinical Utility: Assay Reproducibility for Individual Patients

Tumor Grade\(^1\)
Stanford, UCSF, and NSABP Pathologists

<table>
<thead>
<tr>
<th>Pathologist A</th>
<th>Well</th>
<th>Moderate</th>
<th>Poor</th>
</tr>
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<tbody>
<tr>
<td>Well</td>
<td>105</td>
<td>114</td>
<td>5</td>
</tr>
<tr>
<td>Moderate</td>
<td>24</td>
<td>241</td>
<td>31</td>
</tr>
<tr>
<td>Poor</td>
<td>3</td>
<td>82</td>
<td>63</td>
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Concordance = 61%

<table>
<thead>
<tr>
<th>Pathologist C</th>
<th>Well</th>
<th>Moderate</th>
<th>Poor</th>
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<tbody>
<tr>
<td>Well</td>
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<td>50</td>
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<tr>
<td>Moderate</td>
<td>74</td>
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<tr>
<td>Poor</td>
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Concordance = 65%

<table>
<thead>
<tr>
<th>Pathologist C</th>
<th>Well</th>
<th>Moderate</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well</td>
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<td>31</td>
<td>0</td>
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<tr>
<td>Moderate</td>
<td>140</td>
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<td>52</td>
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<tr>
<td>Poor</td>
<td>8</td>
<td>44</td>
<td>96</td>
</tr>
</tbody>
</table>

Concordance = 59%

Standardized Oncotype DX\(^2\)
38 RS Measures on 5 Days

![Graph showing recurrence score over time](image)

1 Paik et al, NEJM 2004 (supplemental data)
2 Genomic Health data on file
Clinical Utility: Importance of Treatment Decision Studies

Payors Want to Know – Will Test Change Clinical Practice?

Hornberger et al, St. Gallen 2011