Correlation of Breast Cancer Index (BCI) Risk Classification with Tumor Grade and Ki-67 in a Large Series of Patients with Early-stage, ER+ Breast Cancer

Hatem Soliman,1 Brock E. Schroeder,2 Yi Zhang,2 Anthony M. Magiocco,2 Catherine A. Schnabel2

1Moffitt Cancer Center, Tampa, FL; 2Biotheranostics, Inc., San Diego, CA

RESULTS

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Total Number of Cases</th>
<th>N=1339</th>
<th>Age, mean/median</th>
<th>57y/ 58y</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER status (N=905)</td>
<td></td>
<td>Positive</td>
<td>894 (99%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>PR status (N=989)</td>
<td></td>
<td>Positive</td>
<td>801 (89%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Her2 status (N=858)</td>
<td></td>
<td>Negative Positive</td>
<td>774 (90%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>Nodal status (N=1359)</td>
<td></td>
<td>Negative</td>
<td>1359 (100%)</td>
</tr>
<tr>
<td>Tumor size (N=1347)</td>
<td></td>
<td>≤1 cm</td>
<td>356 (26%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;1-5 cm</td>
<td>656 (49%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;5-15 cm</td>
<td>308 (23%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;15 cm</td>
<td>27 (2%)</td>
</tr>
<tr>
<td>Tumor grade (N=1335)</td>
<td></td>
<td>Low (≤10%)</td>
<td>137 (37%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intermediate (11-20%)</td>
<td>91 (24%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High (&gt;20%)</td>
<td>145 (39%)</td>
</tr>
</tbody>
</table>

Table 2. BCI Prognostic Risk Classification vs Grade (N=1335)

<table>
<thead>
<tr>
<th>Grade</th>
<th>N (N=589)</th>
<th>N (N=711)</th>
<th>N (N=255)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>104</td>
<td>104</td>
<td>104</td>
</tr>
<tr>
<td>Intermediate</td>
<td>204</td>
<td>204</td>
<td>204</td>
</tr>
<tr>
<td>High</td>
<td>231</td>
<td>231</td>
<td>231</td>
</tr>
</tbody>
</table>

Table 3. BCI Prognostic Risk Classification vs Ki-67 (N=372)

<table>
<thead>
<tr>
<th>Ki67 Low (N=137)</th>
<th>Ki67 Intermediate (N=91)</th>
<th>Ki67 High (N=414)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk (N=196)</td>
<td>109</td>
<td>47</td>
</tr>
<tr>
<td>Intermediate Risk (N=102)</td>
<td>21</td>
<td>36</td>
</tr>
<tr>
<td>High Risk (N=74)</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 4. MGI Risk Classification vs Grade (N=1335)

<table>
<thead>
<tr>
<th>Grade</th>
<th>N (N=389)</th>
<th>N (N=711)</th>
<th>N (N=235)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MGI Low Risk (N=624)</td>
<td>294</td>
<td>295</td>
<td>35</td>
</tr>
<tr>
<td>MGI High Risk (N=711)</td>
<td>95</td>
<td>416</td>
<td>200</td>
</tr>
</tbody>
</table>

Table 5. MGI Risk Classification vs Ki-67 (N=372)

<table>
<thead>
<tr>
<th>Ki67 Low (N=137)</th>
<th>Ki67 Intermediate (N=91)</th>
<th>Ki67 High (N=414)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MGI Low Risk (N=165)</td>
<td>104</td>
<td>40</td>
</tr>
<tr>
<td>MGI High Risk (N=207)</td>
<td>32</td>
<td>51</td>
</tr>
</tbody>
</table>

RESULTS

- BCI Prognostic Risk Classification variables: continuous variables
- MGI Prognostic Risk Classification variables: continuous variables

REFERENCES

In this study, correlative analyses of risk stratification by BCI Prognostic and Molecular Grade Index (MGI; 5 genes making up the proliferative component of BCI) vs tumor grade and Ki67 were performed to characterize their relationship to other markers of proliferation. Discordance between both BCI Prognostic and MGI to tumor grade and Ki67 were statistically significant. Data from this large retrospective analysis indicate that BCI Prognostic and MGI are capturing distinct information related to tumor proliferative status compared with tumor grade and Ki67.

The algorithmic combination of the mitogenic (MGI) and endocrine response (H/I) gene signatures within BCI Prognostic has been demonstrated to be a superior prognostic factor to clinicopathologic variables in previous multivariate analyses.

### Highlights:
- In this study, correlative analyses of risk stratification by BCI Prognostic and Molecular Grade Index (MGI; 5 genes making up the proliferative component of BCI) vs tumor grade and Ki67 were performed to characterize their relationship to other markers of proliferation.
- Discordance between both BCI Prognostic and MGI to tumor grade and Ki67 were statistically significant.

### Reclassification by BCI and MGI

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Ki67 Low</th>
<th>Ki67 Intermediate</th>
<th>Ki67 High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reclassification by BCI</td>
<td>4% BCI High</td>
<td>51% BCI Low</td>
<td>18% BCI High</td>
<td>18% BCI Low</td>
<td>4% BCI High</td>
</tr>
<tr>
<td></td>
<td>52% BCI Low</td>
<td>9% BCI High</td>
<td>28% BCI Low</td>
<td>56% MGI High</td>
<td>14% MGI Low</td>
</tr>
<tr>
<td>Reclassification by MGI</td>
<td>24% MGI High</td>
<td>41% MGI Low</td>
<td>59% MGI High</td>
<td>15% MGI Low</td>
<td>24% MGI High</td>
</tr>
<tr>
<td></td>
<td>44% MGI Low</td>
<td>56% MGI High</td>
<td>14% MGI Low</td>
<td>51% MGI Low</td>
<td>18% MGI High</td>
</tr>
</tbody>
</table>

- Data from this large retrospective analysis indicate that BCI Prognostic and MGI are capturing distinct information related to tumor proliferative status compared with tumor grade and Ki67.
- The algorithmic combination of the mitogenic (MGI) and endocrine response (H/I) gene signatures within BCI Prognostic has been demonstrated to be a superior prognostic factor to clinicopathologic variables in previous multivariate analyses.