A number of new diagnostic assays are being developed to improve risk stratification in prostate cancer (PCa), but their performance in “real-life” clinical practice remains to be determined.

The Genomic Prostate Score – GPS (Genomic Health, Inc.) – is a biopsy-based 17-gene test that has been clinically validated as a predictor of favorable pathology and is intended to help guide use of active surveillance for men with very low, low, and low-intermediate risk PCa (Figure 1 and 2).

Here we report the early experience with the assay for prostate biopsy specimens tested in the Genomic Health Clinical Laboratory.

**Figure 1. 17-Gene Oncotype DX Genomic Prostate Score**

<table>
<thead>
<tr>
<th>Stromal Response</th>
<th>Cellular Organization</th>
<th>Androgen Signaling</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>BGN, COL1A1, SFRP4</td>
<td>FLNC, GSN, GSTM2, TPM2</td>
<td>AZGP1, FAM13C, KLK2, SRD5A2</td>
<td>ARF1, ATP5E, CLTC, GPS1, PGK1</td>
</tr>
</tbody>
</table>

GPS (scaled 0-100) =

- {Stromal Response Group} + {Androgen Signaling Group} + {Cellular Organization Group} + {Proliferation}

Each gene is individually weighted in the final algorithm.

**Figure 2. Relationship of GPS with Likelihood of Favorable Pathology Adjusted for NCCN Risk Group (categorical)**

Top panel - the dot on each curve represents the point estimate for each NCCN clinical risk group

Bottom panel – scatterplot of GPS distribution by NCCN risk group
**METHODS**

- We report on the first 750 patient samples tested since the assay was made available on 5/8/2013 that met clinical and pathology submission criteria.
- NCCN risk group classification was provided by submitting physicians.
- All submitted biopsy samples were centrally reviewed for Gleason score and tumor length at Genomic Health.
- The 17-gene assay (12 cancer-related genes and 5 reference genes) was performed, and the GPS was calculated.

**RESULTS**

Table 1. NCCN Risk Group by GPS Risk Group

<table>
<thead>
<tr>
<th>Submitted NCCN Risk Group</th>
<th>GPS Biologic Risk Grouping</th>
<th>Very Low</th>
<th>Low</th>
<th>Low-Intermediate</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Low</td>
<td>Very Low</td>
<td>167</td>
<td>14</td>
<td>1 &lt;1%</td>
<td>182</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>91</td>
<td>157</td>
<td>31 11%</td>
<td>279</td>
</tr>
<tr>
<td></td>
<td>Low-Intermediate</td>
<td>0</td>
<td>15</td>
<td>210 93%</td>
<td>225</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>258</td>
<td>186</td>
<td>242</td>
<td>686*</td>
</tr>
</tbody>
</table>

*NCCN risk was not designated at submission for 54 patients and an additional 10 patients did not have a GPS result from which to derive a biologic risk grouping.

- Of 750 samples that met submission criteria, 99% yielded a GPS result, including 96% of samples at the minimum acceptable tumor length (1 mm). The median patient age was 64 (range 42–89).
- 25%, 38%, and 30% of patients were classified by the submitting physician as NCCN very low, low, and low-intermediate risk respectively (7% no NCCN designation) (Table 1).
- In 33% of NCCN low risk patients, GPS indicated a higher likelihood of favorable pathology than predicted by clinical risk alone, consistent with NCCN very low risk. Conversely, in 11% of NCCN low risk patients, the assay predicted a lower likelihood of favorable pathology than expected by clinical risk alone, consistent with NCCN intermediate risk.

Figure 3. Distribution of GPS Results in Patients with 1mm Samples

- GPS results ranged from 2–67 for patients with 1 mm samples (Figure 3).
A wide range of GPS values was observed within each NCCN risk group: range 3–67 very low, 2–67 for low, and 1–67 for low-intermediate (Figure 4).
RESULTS (cont.)

Figure 5. Patient Example: Gleason Score 3+3 (NCCN Low Risk)

- Two patients, both presenting with Gleason score 3+3 and NCCN low risk disease, and their respective differing GPS results.

CONCLUSIONS

- The specimens tested to date are contemporary very low, low and low-intermediate risk PCa cases with GPS distribution very similar to that observed in the clinical validation study of the assay.
- A wide range of GPS values was observed in each NCCN risk group and in tumors with only 1 mm of tumor length, enabling clinically meaningful refinement of risk, which should help physicians and patients make initial treatment decisions more confidently.
- The high rate of analytical success (96%) with small samples enables broad use of the GPS even with limited available tissue.

REFERENCES AND ACKNOWLEDGMENTS