WHY?

The GPS™ assay is critical for management of Gleason 3+3 (GG1) and 3+4 patients (GG2)
Is the biopsy sample representative of the extent of the disease in your patient with clinically low-risk prostate cancer?
### Limitations of the Prostate Biopsy

<table>
<thead>
<tr>
<th>Biopsy</th>
<th>RP registry (n=8095)</th>
<th>3+3=6</th>
<th>3+4=7</th>
<th>&gt;3+4</th>
<th>Non-organ confined</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>74.4%</td>
<td>19.8%</td>
<td>3.3%</td>
<td>6.1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Biopsy</th>
<th>3+3=6 (GG1) (n=6360)</th>
<th>22.3%</th>
<th>63.6%</th>
<th>12.3%</th>
<th>17.4%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In a substantial number of cases, Biopsy Gleason differs from pathological Gleason. Biopsy Gleason Score may not accurately reflect the true nature of the tumor. Undermines confidence in decision making.

Genomic testing gives you critical information to help guide management decisions.

Gearman et al., J Urol 2017
Two patients with NCCN® Low Risk Disease with the same clinicopathological features:

<table>
<thead>
<tr>
<th>Michael</th>
<th>68 year old</th>
<th>African American, healthy man</th>
</tr>
</thead>
<tbody>
<tr>
<td>George</td>
<td>65 year old</td>
<td>Caucasian American, healthy man</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Unit</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gleason</td>
<td>3+3=6</td>
</tr>
<tr>
<td>PSA</td>
<td>5.4 ng/mL</td>
</tr>
<tr>
<td>PSAD</td>
<td>.18 ng/mL/cc</td>
</tr>
<tr>
<td>Cores Positive</td>
<td>2/12, &lt;50% Positive</td>
</tr>
<tr>
<td>Volume</td>
<td>30cc</td>
</tr>
<tr>
<td>NCCN® Risk Category</td>
<td>Low</td>
</tr>
<tr>
<td>Stage</td>
<td>cT1c</td>
</tr>
</tbody>
</table>

Patient names, images, and pathology photos are illustrative. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
Many patients with low-risk cancer are unnecessarily treated\(^1,2\)

Some patients who have unrecognized high-risk disease are undertreated and may miss a chance for a cure\(^3\)

Currently available clinical risk factors have limitations\(^4\)
The GPS™ assay reports short and long-term outcomes

**WHAT**

*Does the GPS assay report?*

**AP**

*Adverse Pathology at RP*¹²

*Provides an immediate and actionable endpoint*

**METS**

*At 10 years after RP*³

*Helps patients understand their long-term prognosis*

---


AP: Adverse Pathology, RP: Radical Prostatectomy
**INCLUSION OF GENOMIC TESTING WITHIN NCCN GUIDELINES® IS A SIGNIFICANT ADVANCEMENT IN PROVIDING PATIENT CARE FOR NEWLY DIAGNOSED PROSTATE CANCER PATIENTS**

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Clinical/pathologic features</th>
<th>Imaging</th>
<th>Molecular testing of tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>• T1-T2a AND</td>
<td>Not indicated</td>
<td>Consider if life expectancy ≥10y</td>
</tr>
<tr>
<td></td>
<td>• Gleason score ≤6/grade group 1 AND</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• PSA &lt;10 ng/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Favorable intermediate</td>
<td>• T2b-T2c OR</td>
<td></td>
<td>Consider if life expectancy ≥10y</td>
</tr>
<tr>
<td></td>
<td>• Gleason score 3+4=7/grade group 2 OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• PSA 10-20 ng/mL</td>
<td>• Bone imaging: not recommended for staging</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• AND</td>
<td>• Pelvic ± abdominal imaging: recommended if nomogram predicts &gt;10% probability of pelvic lymph node involvement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Percentage of positive biopsy cores &lt;50%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**GPS® Assay is included within NCCN guidelines as a molecular testing option for consideration in prostate cancer patients with clinically low-risk and favorable intermediate disease**

(life expectancy ≥ 10 years)
Does my patient have Occult High-risk Disease?
Adverse Pathology is the likelihood your patient is harboring aggressive disease (dominant pattern 4, any pattern 5 or pT3)\(^1\) and is pivotal in the risk assessment when selecting a management decision in clinically low-risk prostate cancer patients.
The GPs™ assay is rigorously developed, validated and studied in over 4,500 patients, including:

**Development**
- Study 1 (n = 441)
  - Cleveland Clinic
  - (Prostatectomy study)
  - Bx GS 6 70%
  - Bx GS 7 25%

- Study 2 (n = 167)
  - Cleveland Clinic
  - (Biopsy study)
  - L 57%, Int 43%

**Validation**
- Study 1 (n = 395)
  - University of California, San Francisco
  - Bx GS 6 70%
  - Bx GS 7 25%

- Study 2 (n = 402)
  - Center for Prostate Disease Research (VA)
  - VL 11%, L 54%, Int 35%

- Study 3 (n = 259)
  - Kaiser Northern California
  - VL 3%, L 21%, Int 67%

**Utility**
- Study 1 (n = 158)
  - Columbia University
  - VL 22%, L 45%, Int 33%

- Study 2 (n = 124)
  - University of California Davis
  - VL 42%, L 40%, Int 17%

- Study 3 (n = 258)
  - 22 US Community Practice Sites
  - VL 39%, L 28%, Int 34%

- Study 4 (n = 80)
  - Excellus BCBS Payor Utility study

- Study 5 (n = 375)
  - OPTUM Payer Utility Study

References:
**DEVELOPMENT STUDY OVERVIEW OF THE GPS™ ASSAY**

- **727** candidate genes
- **374** genes Primary Gleason Sample
- **367** genes Highest Gleason Sample
- **288** genes
- **17** genes
Development Studies

- The expression of 727 cancer specific genes was quantified independently in tissue from the primary and highest Gleason patterns in prostatectomy specimens.

- Only genes predictive of clinical recurrence in both specimens were selected for further development in biopsy specimens.
The GPS™ assay is a synthesis of multiple pathways

<table>
<thead>
<tr>
<th>Androgen Signaling</th>
<th>Cellular Organization</th>
<th>Stromal Response</th>
<th>Cellular Proliferation</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZGP1, FAM13C, KLK2, SRD5A2</td>
<td>FLNC, GSN, GSTM2, TPM2</td>
<td>BGN, COL1A1, SFRP4</td>
<td>TPX2</td>
<td>ARF1, ATP5E, CLTC, GPS1, PGK1</td>
</tr>
</tbody>
</table>

Associated with a better outcome

Associated with a worse outcome

12 genes in 4 pathways specific to prostate cancer
The GPs™ assay is validated as an independent predictor of adverse pathology.

Are these the ideal patients for Radical Prostatectomy?

Are these the ideal patients for Active Surveillance?

48% of NCCN low-risk patients had a different biological risk group than their NCCN risk group (consistent results with published validation cohort)

GPS
Characterizes a patient’s tumor biology and refines the population-based clinical risk with a more personalized risk assessment

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Percentages do not calculate to 100 due to rounding
In a Kaiser Northern California cohort of 6000 surgically treated patients, GPS™ assay was validated as a predictor of death and metastasis at 10 years.

In the clinical validation study, including patients with NCCN® very low, low and intermediate-risk, no patient with a GPS result <20 had metastasis or died from prostate cancer within 10 years.
Results are from a multivariable model adjusting for NCCN risk group
HR – Hazard Ratio
In the largest study of active surveillance utilization, the GPS™ assay is associated with significantly higher AS rates.

### Proportion of AS Persistence at 6 and 12-Month Follow-up¹

<table>
<thead>
<tr>
<th></th>
<th>6-mo</th>
<th>12-mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>No GPS or MRI</td>
<td>60%</td>
<td>56%</td>
</tr>
<tr>
<td>(n = 7446)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GPS</td>
<td>89%</td>
<td>84%</td>
</tr>
<tr>
<td>(n = 300)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P < 0.001

**Absolute Increase in Active Surveillance Among GPS Tested**

30%

### GPS™ Assay Drives Adherence to Guideline Based Care


*Adjusted for demographic and background characteristics.

AS - Active Surveillance
mpMRI is a breakthrough improvement and has the potential to improve both screening and management of prostate cancer

- More likely to diagnose significant prostate cancer¹

However; significant limitations exist, including but not limited to:
- Poor sensitivity for extraprostatic extension²
- Potential for interobserver/intraobserver variability in interpretation³
- Marginal positive predictive value in some studies⁴
- Potentially underestimates tumor volume¹

The Oncotype DX® GPS™ assay provides objective, molecular data that has been validated as an independent predictor of clinically relevant outcomes.

YOUR VERY LOW, LOW AND INTERMEDIATE RISK PCA PATIENTS NEED GUIDANCE IN SELECTING THE RIGHT MANAGEMENT DECISION

Michael, 68  
Healthy man

George, 65  
Healthy man

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What were Michael’s and George’s results?

How would you proceed?
Michael’s Physician Explains His Results

**GPS + NCCN**: Very Low Risk

- Top-line results integrate clinical variables into a single composite risk estimate

**NCCN Risk Group**: Low

**Physician-Provided Information**:  
- Gleason Score: 3+3  
- PSA (ng/mL): 5.4  
- Clinical Stage: T1  
- Max. % of tumor involvement in any core: ≤ 50%  
- Number of cores collected: 12

- Baseline clinical data highlighted for ease of reference during discussion with your patient

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Risk for specific outcomes clearly articulated on a slider bar

The combination of GPS and clinical features predicts that this patient’s risk is consistent with NCCN Very Low Risk disease.²

In a clinical validation study including patients with NCCN Very Low, Low, and Intermediate Risk, no patient with a GPS result <20 had metastasis or died from prostate cancer within 10 years.¹

Michael, 68
Healthy man

Risk for specific outcomes clearly articulated on a slider bar

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His physician recommended that Michael go on Active Surveillance and GPS gave Michael confidence to pursue this management recommendation.
George's physician found value in using the second page of the GPS™ report to guide treatment.

GPS Distribution in NCCN® Low Risk

Group Average: 25

This patient has a GPS result that is higher than the average GPS result for NCCN Low Risk.

Pathology Endpoints**

<table>
<thead>
<tr>
<th>Disease Description</th>
<th>Individualized Risk (95% Confidence Interval [CI])</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-Grade Disease (Gleason ≥4+3)</td>
<td>45% (95% CI: 31% - 59%)</td>
</tr>
<tr>
<td>Non-Organ-Confined Disease (pT3a)</td>
<td>62% (95% CI: 47% - 74%)</td>
</tr>
</tbody>
</table>

His physician recommended that George proceed with a prostatectomy. Final pathology was demonstrative of Gleason 4+3 (75% pattern 4), focal EPE.
Gleason 3+3=6 (GG1)
- PSA of 5.4 ng/mL
- PSAD of 0.18 ng/mL/cc
- Volume of 30 cc
- 2/12 Cores Positive
- cT1c

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Adverse Pathology Remains the Immediate and Actionable Endpoint

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**INCORPORATING THE GPS™ ASSAY INTO PRACTICE**

Oncotype DX GPS Assay is supported by numerous studies1-8

- The Oncotype DX GPS test helps predict short- AND long-term risks
  - Adverse Pathology at the time of diagnosis2,3
  - Metastasis within 10 years after RP6
  - Prostate cancer death within 10 years after RP6

- Medicare covers the GPS™ assay for patients with NCCN® very low, low-risk
  and favorable intermediate prostate cancer patients
  - Private coverage varies by plan

- Genomic Access Program was created to help your eligible patients determine payment options for our tests, including Oncotype DX GPS

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