A Tale of Two Cancers or
How Genomics Can Guide Treatment Decisions

Bela S. Denes, MD, FACS
Genomic Health, Inc.
Redwood City, CA
Decisions for a Man with Clinically Low Risk Prostate Cancer

If I choose surgery or radiation, I worry about ED...if I choose surveillance, I worry about cancer spreading.

Surgery
- Robotic radical prostatectomy
- Open radical prostatectomy
- Focal Therapy (cryotherapy, HIFU, etc.)

Radiation
- External beam radiotherapy

Brachytherapy

Active surveillance
NCCN Guideline for Management of LOW RISK CaP

<table>
<thead>
<tr>
<th>RISK GROUP</th>
<th>EXPECTED PATIENT SURVIVAL</th>
<th>INITIAL THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 10 y Low</td>
<td></td>
<td>EBRT or brachytherapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RP + PLND if predicted probability of lymph node metastasis ≥ 2%</td>
</tr>
<tr>
<td>&lt; 10 y Low</td>
<td></td>
<td>Observation</td>
</tr>
</tbody>
</table>

*Active surveillance involves actively monitoring the course of disease with the expectation to intervene with potentially curative therapy if the cancer progresses. See Principles of Active Surveillance and Observation (PROS-C).*
Why All the Confusion?????

The Challenge of Random Biopsies

Final Pathology – GS 7 (3 + 4)
The Importance of Getting It Right

CLINICALLY LOW-RISK BIOPSY

Does my patient have aggressive disease?

60-70%

Favorable Pathology @ RP
Organ Confined Gleason 3+3 OR Gleason 3+4

Adverse Pathology @ RP
Gleason ≥4+3 and/or ≥pT3

30-40%

Progression-free Survival (Time 0)
Biochemical Recurrence (5 years)
Metastasis (10 years)
Prostate Cancer–specific Mortality (15 years)

Michael is NCCN Low Risk has Been Advised to Have Radiation

- PSA of 6.0
- PSAD of 0.30 ng/mL
- Prostate Volume of 20cc
- Biopsy revealed Gleason score 6 (3+3), 1/12 positive cores
- By NCCN® clinical factors alone he has NCCN® low-risk cancer and is interested in Active Surveillance
- His physician ordered GPS to assess the risk of occult higher-risk disease
Based on GPS his physician recommended that Michael proceed with **Active Surveillance**.

No patients with GPS < 20 in the validation study experienced metastasis or prostate cancer death.

This phrase appears only in reports with GPS < 20.

---

**GPS + NCCN®: Very Low Risk**

- **GPS 12**
- **Very Low Risk**

<table>
<thead>
<tr>
<th>Clinical Interpretation</th>
<th>Clinical Endpoints</th>
<th>Individualized Risk (95% Confidence Interval [CI])</th>
</tr>
</thead>
<tbody>
<tr>
<td>The combination of GPS and clinical features predicts that this patient’s risk is consistent with NCCN Very Low Risk disease.</td>
<td>Prostate Cancer Death Within 10 Years</td>
<td>&lt;1% (99% CI: 1% - 4%)</td>
</tr>
<tr>
<td>In a clinical validation study including patients with NCCN Very Low, Low, and Intermediate Risk, no patient with a GPS result &lt;20 had metastasis or died from prostate cancer within 10 years.</td>
<td>Metastasis Within 10 Years</td>
<td>1% (95% CI: 1% - 4%)</td>
</tr>
<tr>
<td>Adverse Pathology (Gleason ≥ 4+3 and/or pT3+)</td>
<td></td>
<td>16% (95% CI: 12% - 21%)</td>
</tr>
</tbody>
</table>
George is NCCN Risk and has Been Advised to Pursue Active Surveillance

- PSA of 5.4
- PSAD of 0.18 ng/mL
- Prostate Volume of 30cc
- Biopsy revealed Gleason score 6 (3+3), 2/12 positive cores
- By NCCN® clinical factors alone he has NCCN® low-risk cancer and is not sure what to do next
- His physician ordered Oncotype DX GPS to assess the risk of occult higher-risk disease

George 58-year-old healthy man; Negative family hx.

Patient names, images, and pathology photos are illustrative. American Society of Clinical Oncology (ASCO) and ASCO are registered trademarks of ASCO; National Comprehensive Cancer Network (NCCN) and NCCN are registered trademarks of NCCN. ASCO and NCCN do not endorse any product or therapy.
His physician recommended that George proceed with a prostatectomy.

Final pathology:
How Oncotype DX® GPS Can Help Decision Making

**Favorable Pathology**
- Organ Confined
- Gleason 3+3 OR Gleason 3+4

**Adverse Pathology**
- Gleason ≥4+3 and/or ≥pT3

**Key Decision Point**
Likelihood of Adverse Pathology is pivotal in the risk assessment of PCa and initial treatment selection.

**GPS = 12**
- AP = 16%
- Active Surveillance

**GPS = 61**
- AP = 65%
- Surgery
Endpoints Driving Treatment decisions

GPS CAN HELP GUIDE TREATMENT DECISIONS BASED ON CANCER BIOLOGY
Don’t get into a car with a stranger

ONLY politicians can become US President

Gleason Score accurately stages CaP
Thank You

bdenes@genomichealth.com