A Gene Expression Test to Predict Prostate Cancer Aggressiveness

Use Prolaris® testing as a guide in your medical and surgical management

Prolaris®
A prognostic medicine product for prostate cancer.
Prostate cancer (PCa) is now the second most frequently diagnosed cancer and the sixth most common cause of cancer-related mortality in men worldwide.\(^1\)

An estimated 1.1 million men were diagnosed with prostate cancer across the world in 2012.\(^2\) Only 3% of men diagnosed with prostate cancer will die from it.\(^3\)

Prostate cancer natural history is highly variable and difficult to predict, with most men having indolent disease that could be safely followed without immediate treatment, and others having a more aggressive disease requiring immediate intervention.

Prolaris\(^4\) (also called CCP in clinical publications) is the first prognostic test that offers a look inside the molecular biology of prostate cancer to help physicians determine its aggressiveness. In combination with other variables, such as Gleason score and PSA, Prolaris provides a personalized assessment of risk.

**What is Prolaris®?**

- A novel genetic test developed to help doctors predict prostate cancer aggressiveness, together with other clinical variables
- A direct molecular measure of prostate cancer tumor biology
- An RNA expression signature based on cell cycle progression (CCP) genes
- A 46 gene panel and integrative algorithms to assess prostate cancer aggressiveness
- 31 genes across multiple cell cycle progression pathways
- 15 housekeeper genes
- Prolaris testing results provide a Prolaris Score\(^\text{TM}\). Prolaris Scores can range from -3 to 7 (technical range). Each 1-unit increase in the Prolaris Score represents a doubling (or halving) of risk. Higher Prolaris Scores represent more aggressive cancers
- Prolaris testing can be done:
  - following affirmative biopsy and prostate cancer diagnosis
  - following radical prostatectomy
- Prolaris testing provides greater prognostic information than Gleason score or PSA
- Prolaris testing provides personalized risk assessment:
  - prognostic for biochemical recurrence (BCR), metastasis and PCA mortality

### THE PROLARIS 46-GENE PANEL

**31 Cell Cycle Progression Genes**

- FOXM1
- COC2
- COKN3
- RPL38
- UBA52
- PSMC1
- BIRCS
- KIF20A\(^\text{BP1}\)
- PLK1
- RPL13A
- PPP2CA
- MRFAP1
- NUSAP1
- CENPF
- ASPM
- SLC25A3
- CLTC
- TXNL1
- ASF1B
- C18orf24
- RAD54L
- DTL
- CEPT55
- RAD51
- COC2
- KIF11
- KIAA0101
- RPL4
- RPL37
- RPS29
- TOP2A
- TK1
- PBK
- BUB1B
- RRM2
- DULGAPS
- PSMA1
- RPL8
- MMADHC
- PTTG1
- MCM10
- PRC1
- CENPM
- COCA3
- COCA8
- ORC6L

**15 Housekeeper Genes**

- Highly correlated and provide a reproducible measure of cell proliferation
- Normalize the expression of the cell proliferation genes

Prolaris\(^4\) provides unique and independent information from current clinical and pathological features
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The Prolaris 46-Gene Panel

- 31 Cell Cycle Progression Genes
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Prolaris® provides unique and independent information from current clinical and pathological features.
In a study of 349 conservatively managed prostate cancer patients diagnosed using needle biopsy, Prolaris Score™ was found to be the strongest independent predictor of prostate cancer-related death and provided more information than either Gleason score or PSA. A study of 582 patients evaluated the prognostic utility of the Prolaris Score derived from biopsy specimens in men who were treated by radical prostatectomy. Results from this study indicate that Prolaris can be used at disease diagnosis to better define patient prognosis and enable more appropriate clinical care. Prolaris Score™ was found to be the strongest independent predictor of prostate cancer-related death and provided more information than either Gleason score or PSA.

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Prolaris: Extensive Validation in both Biopsy and Radical Prostatectomy Settings

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Scatter Plot of Predicted 10-year Risk of Death From Prostate Cancer for Combined Risk Score versus Clinical Risk Score*

• Study demonstrates that Prolaris (CCP) Score predicts survival from prostate cancer.

10-year Estimated Prostate Cancer Death According to Prolaris (CCP) Score

• Combining Prolaris (CCP) Score with Gleason score and PSA values improves the 10-year survival prediction compared to clinical parameters alone.

10-year Estimated Biochemical Recurrence Progression-free Survival

• Prolaris (CCP) Score correlates with the probability of biochemical recurrence and was the strongest predictor of metastatic disease.

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Scatter Plot of Predicted 5-year Risk of BCR for Combined Risk vs Clinical Risk*

• Prolaris (CCP) Score provided prognostic information that was not provided by standard clinical parameters.

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Prolaris adds Precisions to Conventional Risk Assessment

- With AUA (D’Amico) risk categories alone, all patients within one group (low, intermediate or high risk) are assigned the same risk.

- The addition of Prolaris Score will help physicians:
  - differentiate patients with similar AUA (D’Amico) risk profiles
  - better assess the near-term risk profile of patients
  - make more confident treatment decisions with patients.

A study of 366 patients showed that in patients who had undergone radical prostatectomy, a high Prolaris Score was predictive of Biochemical Recurrence (BCR). The Prolaris Score was predictive of death after disease progression and provided substantially more prognostic information than clinical variables alone.

Prolaris was predictive of death after disease progression.

A study of 413 patients concluded that Prolaris Score after radical prostatectomy provided independent prognostic information beyond clinico-pathological parameters and could be useful in helping guide decisions with respect to adjuvant treatment and in stratifying men for future adjuvant therapy studies.

- The proportion of patients who develop biochemical recurrence at different follow-up times increases as the Prolaris (CCP) Score increases.

- Prolaris (CCP) Score stratified patients in terms of risk of biochemical recurrence. Prolaris’s ability to stratify risk was conserved when separating out low risk from intermediate/high risk patients (CAPRA-S score, 0 to 2) by clinical characteristics.

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Prolaris significantly modifies treatment decisions in prostate cancer:

A prospective study evaluated the impact of the Prolaris testing on physician recommendations for Prostate Cancer Treatment. Clinicians ordering Prolaris test were asked how influential the test result was in making therapeutic decisions.

- In 65% of cases, there was a change recorded between the therapy initially planned and the therapy actually selected (40% decrease and 25% increase).
- In 40% of cases, clinicians indicated they would reduce the intended therapeutic burden post Prolaris test.
- In 88% of cases, the influence of Prolaris on therapeutic treatment recommendations was moderate to very high.

Based on the judgment of ordering physicians, the Prolaris Score adds meaningful new information to risk assessment for localized prostate cancer patients.

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10 year Biochemical Recurrence Rates

- Patients with biochemical recurrence (%)
- Time since surgery (years)
- CCP score
  - CCP score < 0 (n=6)
  - CCP score 0 to ≤ 2 (n=50)
  - CCP score > 0 to ≤ 1 (n=161)
  - CCP score > 1 (n=149)

10 year Biochemical Progression-free Survival (Probability)

- CCP score
  - CCP score ≤ 0
  - CCP score > 0

Prolaris® Further Stratifies Patients within Each AUA Biopsy Risk Category

- AUA PCa Mortality Risk (%)
- Prolaris PCa Mortality Risk (%)
- 3.9% risk of PCa death vs. 11% with AUA alone
- 1.8% risk of PCa death vs. 4.8% with AUA alone
- 6.7% risk of PCa death vs. 4.8% with AUA alone

100
50
5
2
1
0
80
60
40
20
0
2
4
6
8
10
Time (years)

Biochemical Progression-free Survival (Probability)

10-year Estimated Biochemical Recurrence Rates

10-year Estimated Biochemical Recurrence Rates

Patients with biochemical recurrence (%) Time since surgery (years) CCP score

Change in Intended Therapeutic Options (pre-CCP Test to Post - CCP Test) Total (n=305)

<table>
<thead>
<tr>
<th>Change</th>
<th>Reduction</th>
<th>No Change</th>
<th>Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>122 (40.0%)</td>
<td>107 (35.1%)</td>
<td>76 (24.9%)</td>
</tr>
</tbody>
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150 Clinicians Completed Surveys on the Influence of the Prolaris (CCP) Test in 305 Cases

- Reduction
- No Change
- Increase

- Reduction
- No Change
- Increase

100
50
20
10
5
2
1
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1.0
0.8
0.6
0.4
0.2
0
- CCP score
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Prolaris® Benefits:

Prolaris® addresses a currently unmet need in prostate cancer by providing the clinician with direct information about prostate tumor aggressiveness that may be used to make more confident management decisions.

1. For example, at the time of diagnosis, a low Prolaris Score™ in the context of low-risk clinico-pathologic features may more accurately identify patients who are the best candidates for active surveillance.

2. Alternatively, a high Prolaris Score in patients with an intermediate risk profile may alter the management with additional staging and more aggressive (combination) therapy.

Prolaris also provides information that may be used to guide the extent of adjuvant treatment after primary therapy.

3. For example, a high Prolaris Score in the context of high-risk pathologic findings after radical prostatectomy may help identify patients who are appropriate candidates for adjuvant radiation.

“It seems certain that, particularly in men in whom the management approach is uncertain… there is a lot of information in this test to help you decide whether you need more aggressive therapy or can manage them more conservatively.”

Prof. Jack Cuzick, Queen Mary, University of London, UK

References:


