A Gene Expression Test to Predict Prostate Cancer Aggressiveness

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

MYRIAD®

What is Prolaris?

- 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

PROLARIS HELPS YOU TO MAKE BETTER TREATMENT DECISIONS BY IDENTIFYING PATIENTS:

- With aggressive disease who would benefit from immediate treatment
- With slow growing cancer appropriate for active surveillance
- At high risk of cancer recurrence
- Who are candidates for closer observation or additional treatment

Demontrated in studies of over 1.500 patients undergoing TURP, biopsy and radical prostatectomy:

- Predicted clincal progression in four different cohorts
- Stronger predictor of clinical outcome than any other clinical/pathological variable such as PSA and Gleason

PROLARIS® PROVIDES UNIQUE AND INDEPENDENT INFORMATION FROM CURRENT CLINICAL AND PATHOLOGICAL FEATURES

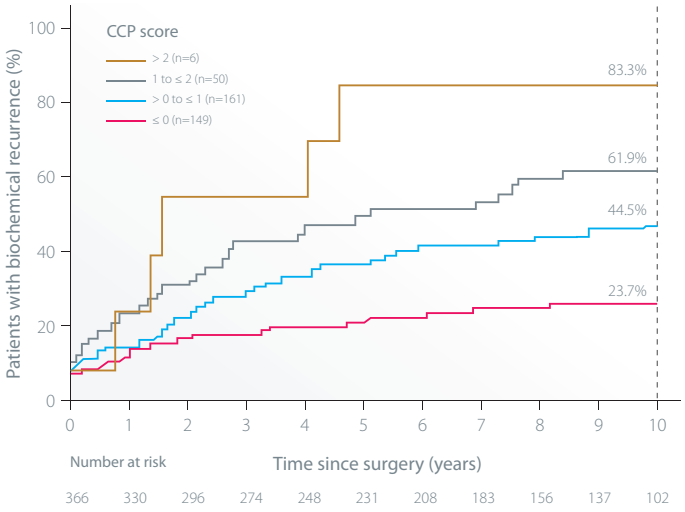
Prostate Cancer Biopsy	Prostate Cancer Post-Prostatectomy
Gleason score	Gleason score
PSA	PSA
Clincal T-stage	Seminal Vesicle Invasion (SVI)
	Extracapsular Extension (ECE)
	Lymph Node Involvement (LNI)
	Surgical Margins

Prognostic value of an RNA expression signature derived from cell cycle proliferation genes in patients with prostate cancer: a retrospective study[1]

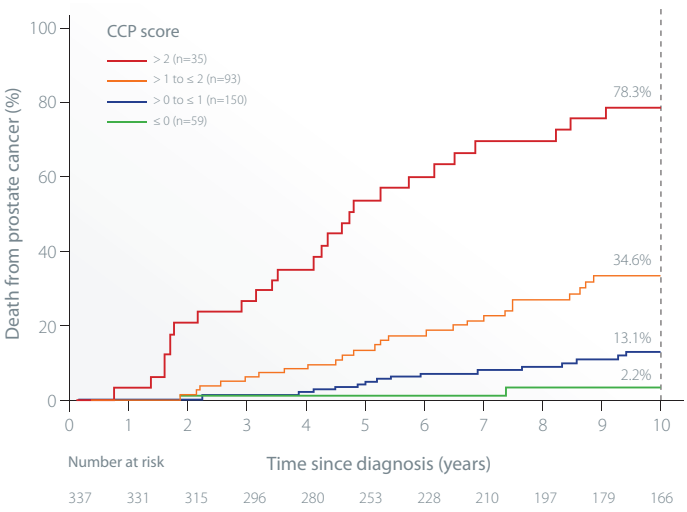
TWO PATIENTS COHORT – RADICAL PROSTATECTOMY AND TURP[1]

	RP	TURP
Patients	366	337
Endpoint	Time to Biochemical Recurrence	Death from Prostate Cancer
Events	36%	20%
Median years Fu	9.4	9.8
Median age	68	70.3
Median PSA (ng/ml)	6.9	8.3
Gleason score < 7	65.6%	51.0%
Gleason score = 7	30.0%	21.7%
Gleason score > 7	4.4%	23.7%

10-year Estimated Biochemical Recurrence Rates (RP)



10-year estimated prostate cancer death rates for each group (TURP)

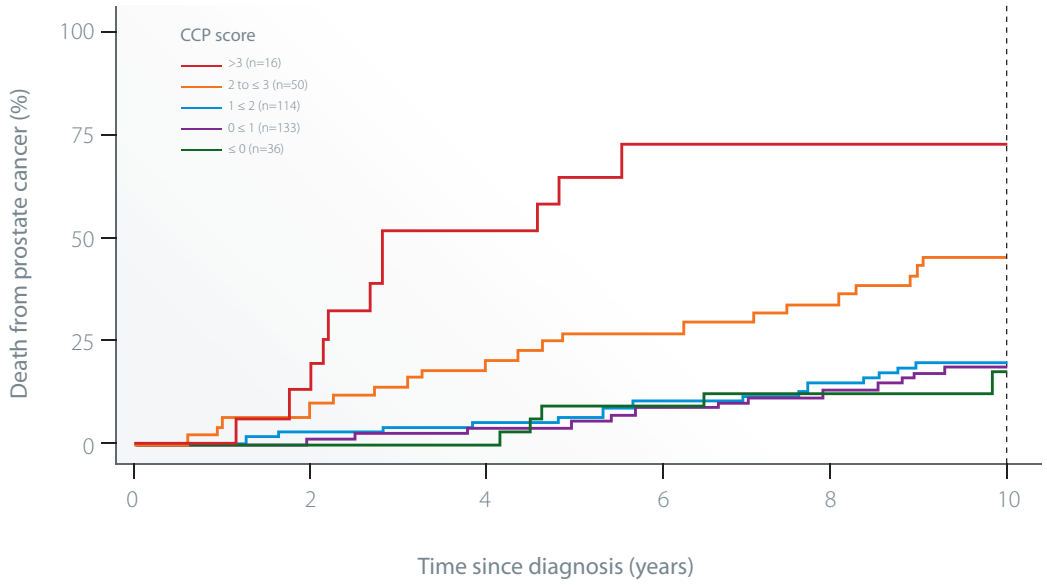


- In the multivariate analysis CCP and PSA concentration were the most significant predictors of biochemical recurrence (RP) and or death (TURP)
- CCP and PSA provided more prognostic information than any other variable
- CCP score was only weakly correlated with other variables
- Hazard Ratio increased 1.89 per 1 unit change in CCP score (RP) and 2.57 per 1 unit (TURP)

Prognostic value of a cell cycle progression signature for prostate cancer death in a conservatively managed needle biopsy cohort

Biopsy Patient Cohort	
Patients	349
Endpoint	Death from Prostate Cancer
Median years Fu	11.8
Median age	70.5
Median PSA (ng/ml)	21.4
Gleason score < 7	30.4%
Gleason score = 7	43.6%
Gleason score > 7	26.1%
10-year death from Prostate Cancer	27.1%

10-year Estimated Prostate Cancer Death According to CCP score



- In the pre-planned multivariate analysis, extent of disease, age, clinical stage, and use of hormones were not statistically significant. Only CCP score, Gleason grade and PSA remained significant
- CCP was a stronger prognostic factor than either Gleason grade or PSA
- CCP score was only weakly correlated with other variables
- Hazard Ratio increased 1.65 per 1 unit change in CCP score

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Prolaris benefits:

1. 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.

   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.

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

   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

Technical information

Prolaris is a gene expression test to predict prostate cancer aggressiveness. The Prolaris assay has been validated in two clinical settings: the **newly diagnosed prostate cancer patient** and the **post-prostatectomy patient**.

Newly diagnosed prostate cancer patient:

- Prolaris provides a rapid and reliable method of predicting prostate cancer-specific mortality.
- Over 60% of men diagnosed with prostate cancer are older than 65 and the disease often progresses slowly. While these men could have their disease monitored by active surveillance, many individuals with localized disease choose aggressive clinical treatment, including radical prostatectomy or radiation treatment, which are associated with morbidity. Prognostic markers, combined with clinical information can further stratify indolent versus aggressive rostate cancer and can aid in the treatment choice best for that patient.

Post-prostatectomy patient:

- Prolaris provides a rapid and reliable method of determining the risk of post-prostatectomy biochemical recurrence.
- Approximately 30% of men post- prostatectomy experience biochemical recurrence. Adjuvant therapies such as radiation treatment, hormonal ablation, medical castration with an LHRH agonist, and bilateral orchiectomy significantly reduce recurrence risk but are associated with significant morbidity and adverse side effects. Prognostic markers identifying individuals at high risk for recurrence can be used to provide more individualized treatment after surgery.

The Prolaris assay is performed on formalin-fixed paraffin-embedded (FFPE) tissue obtained from blocks or slides from prostatectomy specimens or prostatic adenocarcinoma biopsies. The expression of 31 cell cycle genes, normalized to that of 15 housekeeping genes, is measured in triplicate to generate a Prolaris Score™. The Prolaris Score is combined with clinical and pathological features to generate patient-specific outcome predictions.

Prolaris provides additional information for the newly diagnosed prostate cancer patient:

- AUA risk category: Based on the patient's clinical variables, he is assigned a risk category based on American Urological Association (AUA). The Prolaris Score indicates whether the patient's prostate cancer is more or less aggressive for that specific AUA risk category in the U.S. population. There is approximately a 2-fold change in risk of prostate cancer mortality between intervals, which is the hazard ratio corresponding to a 1-unit change in the Prolaris Score™.
- 10-year prostate cancer specific mortality: A combined analysis, incorporating Prolaris and CAPRA Scores, generates the likelihood of 10-year risk of prostate cancer-specific mortality.

Prolaris provides additional information for the post-prostatectomy patient:

- The Prolaris Score™ is combined with CAPRA-S Score to generate the Prolaris Combined Score. This combined score is used to estimate the 10-year risk of biochemical recurrence, and it can be compared with the Prolaris Combined Scores of other patients within a U.S. distribution of scores previously observed by Myriad Genetic Laboratories, Inc. This will indicate the patient at higher or lower risk of biochemical recurrence than other patients with a similar CAPRA-S risk profile.

References:

1. Cuzick et.al; *Lancet Oncol* 2011;12:245-55

Prolaris®

A prognostic medicine product for prostate cancer.

Prolaris™ testing assesses the prostate cancer aggressiveness in conjunction with other clinical parameters. Prolaris measures the expression level of genes involved with cell cycle progression (CCP) in tumor specimens to predict disease outcome.

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