MMM998461

AMENDED

Prolaris®
Prostate Cancer Prognostic Test

Prolaris Biopsy Test Result | Summary Findings

Ordering physician	Specimen		Patient	
Bob Doctor PhD	Tissue:	**Prostate**	Legal name:	**Pt Last Name**
Institution	Biopsy date:	**Jul 24, 2018**		**Pt First Name**
123 Fara Wat	TRF received:	**Aug 3, 2018**	Date of birth:	**Jun 22, 1959**
Anywhere, UT 84010	Sample received:	**Aug 8, 2018**	Patient ID:	**123**
	First report date:	**Sep 17, 2019**	Sex at birth:	**M**
Pathology: Joe Pathologist PhD	Final Report date:	**Dec 15, 2022**	Accession #:	**02923748-BLD**
			Requisition #:	**06700033**

Block(s) analyzed:

Prolaris test result summary

Based on a 10-year Disease Specific Mortality (DSM) risk of 0.9% with conservative management, this patient is a candidate for Active Surveillance.

Defined as either radiation with androgen deprivation or surgery with intensified therapy per guideline recommendations.

The Active Surveillance Threshold was validated in a cohort of conservatively managed men (n=585). Men with scores above the threshold had significantly different risk profiles compared to men below the threshold. No prostate cancer-related deaths were observed in men with scores at or below the threshold within 10 years of diagnosis. [4]

For information about prostate cancer treatments go to https://prolaris.com/prostate-cancer-symptoms-treatment-options

Myriad genetics

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prolaris.com

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Prolaris Biopsy Test Result | Risk Assessment Details

Legal name:	**Pt Last Name** **Pt First Name**	Date of birth: Accession #:	**Jun 22, 1959** **02923748-BLD**	Biopsy date: Report date:	**Jul 24, 2018** **Dec 15, 2022**

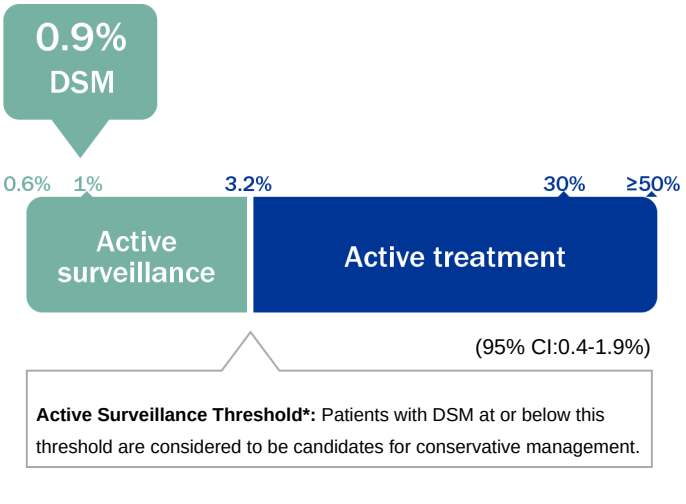
Block(s) analyzed:

Patient's risk assessment - two treatment scenarios

Prolaris Score and clinical variables **are combined** in a clinically validated weighted algorithm.

Risk when pursuing active surveillance†

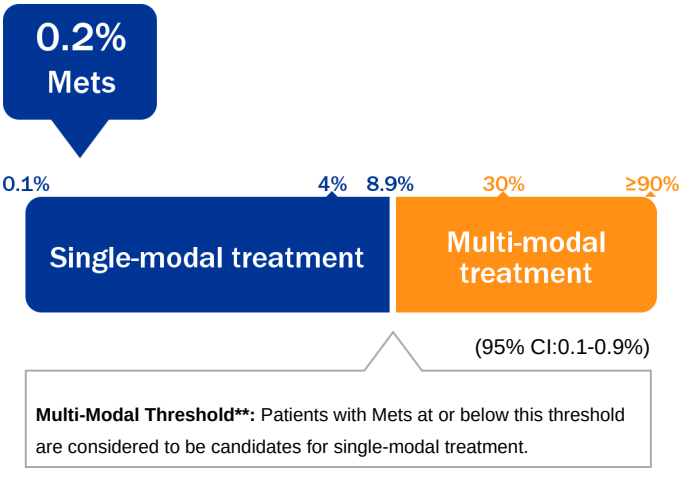
This patient's 10-year prostate cancer Disease Specific Mortality (DSM) risk with conservative managment is:



Active Surveillance Threshold*: Patients with DSM at or below this threshold are considered to be candidates for conservative management.

Risk when pursuing active treatment‡

This patient's 10-year prostate cancer Metastasis (Mets) risk with single-modal treatment is:



Multi-Modal Threshold:** Patients with Mets at or below this threshold are considered to be candidates for single-modal treatment.

Prolaris molecular score

A measure of cell proliferation, independent of clinical variables.

2.0

Clinical range 1.8-8.7

Variables used for risk assessment

Prolaris molecular score:	**2.0**
Patient age at biopsy:	**59**
Total PSA prior to this biopsy:	**4.6**
Clinical t stage:	**T1c**
% Positive cores:	**< 34%**
Gleason score:	**3+3=6 (Group 1 (ISUP[1]))**
NCCN risk[2]:	**Very Low/Low**

For information about the Prolaris Test Result go to https://prolaris.com/understanding-the-prolaris-report/

NCCN, National Comprehensive Cancer Network® (NCCN®)

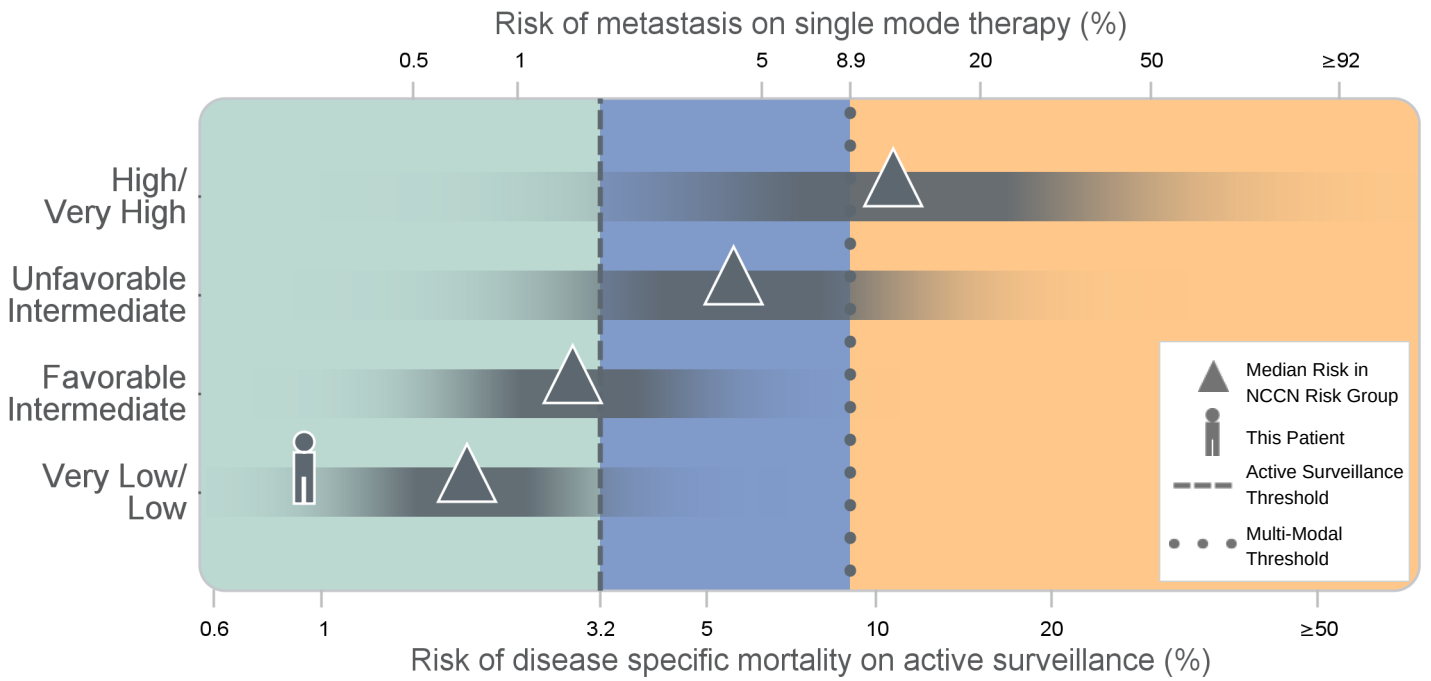
Prolaris Biopsy Test Result | Risk Stratification Details

Legal name:	**Pt Last Name** **Pt First Name**	Date of birth: Accession #:	**Jun 22, 1959** **02923748-BLD**	Biopsy date: Report date:	**Jul 24, 2018** **Dec 15, 2022**

Block(s) analyzed:

Risk stratification graph

This patient has a Disease Specific Mortality (DSM) risk in the 3rd percentile§ for his NCCN risk group[2] of Very Low/Low.



0.9%
DSM

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Prolaris Biopsy Test Result

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Legal name:	**Pt Last Name** **Pt First Name**	Date of birth: Accession #:	**Jun 22, 1959** **02923748-BLD**	Biopsy date: Report date:	**Jul 24, 2018** **Dec 15, 2022**

Block(s) analyzed:

Test description

Prolaris utilizes quantitative PCR analysis to measure the mRNA expression levels of 31 cell cycle progression genes and 15 control genes from which a molecular score is calculated. Prolaris Scores are initially calculated as previously described and then adjusted by +4 units for the patient results. The Prolaris Score is combined with a patient's CAPRA score, resulting in a personalized combined clinical risk (CCR) score, which is used to estimate the 10-year risk of both metastatic disease (Mets) and prostate cancer disease specific mortality (DSM).[3,5-7] When counting prostate biopsy sites/cores for CAPRA calculations, the default will be to align with the NCCN guidelines[2]. In situations where the pathology report and the Test Request Form do not align on biopsy sites/cores, default will be to the pathology report.

* Active Surveillance Threshold Validation Analysis: The Prolaris Score distribution was determined in a training cohort of men (N=505) who, based on clinical parameters (Gleason score 3+4; PSA < 10 ng/ml; <25% cores positive; and clinical stage T2a), might be considered for active surveillance. A predefined combined clinical risk score was selected such that 90% of the men in the training cohort had lower scores. Two independent cohorts of conservatively managed men (N=765) were evaluated and there were no observed prostate cancer-specific deaths in patients with lower scores. This predefined clinical risk score was associated with a 3.2% (95% CI: 2.0, 5.2) 10-year risk of prostate cancer-specific mortality in the combined cohort.[3-6]

** Multi-Modal Threshold Validation Analysis: The Combined Clinical Risk (CCR) score and a predefined CCR-based threshold were evaluated in two cohorts of men with NCCN intermediate- or high-risk localized disease (N=718 [11] and N=741[12]) who received either single or multimodality therapy with known outcomes. Multimodality therapy was defined as either radiation or surgery with androgen deprivation, or surgery with adjuvant radiation. Studies have shown that surgery with adjuvant radiation has equivalent outcomes to early salvage.[13, 14] Single modality therapy included surgery, external beam radiation therapy (with or without brachytherapy). Median follow-up in the cohort was 5.4 years. A predefined multimodality threshold was selected such that the number of men who would be above the threshold would be similar to the number considered high-risk by NCCN clinicopathologic criteria. The predefined CCR threshold was associated with an 8.9% (95% CI: 5.3, 14.7) 10-year risk of metastasis for men on single mode therapy (N=912) at the threshold. The CCR-based multimodality threshold is a significant univariable prognosticator of risk in patients treated with single mode therapy (HR 10.77, 95% CI (5.16, 25.26), $p = 1.2 \times 10^{-11}$).[3, 11, 12]

† Patients with similar clinicopathologic features, as determined by their CAPRA score, have the same a priori 10-year prostate cancer-specific mortality risk. The addition of the Prolaris Score further differentiates this risk.[3-6]

‡ Patients undergoing definitive therapy, defined as radical prostatectomy or primary radiation therapy, with similar clinicopathologic features, as defined by their CAPRA score, have the same a priori risk of developing metastases. The addition of the Prolaris Score further differentiates this risk.[3,8-10]

§ Risk Percentile Calculation: The percentile of each clinically reportable CCR score was calculated as the percentile from a normal distribution of CCR scores from a commercial cohort in the same NCCN risk category as the patient. The reported percentile is rounded to the nearest whole percentage, except for "<1%" and ">99%" reported when the unrounded percentile is "<1" or ">99%", respectively.

Sex assigned at birth refers to the classification of an individual as male or female, often based on physical characteristics at birth. The terms "male", "men", and "his" refer to sex assigned at birth.

Please contact Myriad Medical Services at 1-800-469-7423 x3850 to discuss any questions regarding this result.

References

1. Epstein JI, et al. The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma: Definition of Grading Patterns and Proposal for a New Grading System. *The American Journal of Surgical Pathology*. 2016;40(2):244-52.
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.1.2022.© National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed [November 19, 2021]. To view the most recent and complete version of the guideline, go online to https://www.nccn.org/. 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.
3. Data on file. Myriad Genetics, Inc.
4. Lin DW, et al. Identification of men with low-risk biopsy-confirmed prostate cancer as candidates for active surveillance. *Urologic Oncology: Seminars and Original Investigations*. 2018;36(6). doi:10.1016/j.urolonc.2018.03.011
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14. Vale CL, et al. LBA48_PR - Adjuvant or salvage radiotherapy for the treatment of localized prostate cancer? A prospectively planned aggregate data meta-analysis. Annals of Oncology. 2019; 30(5):v883. doi:10.1093/annonc/mdz394.041

Note: Myriad deems information provided on the Test Request Form to be definitive, and to supersede information provided in any other form (e.g., pathology report). Clinicopathologic parameters provided by the healthcare provider(s), in whatever form, have not been verified by Myriad.

Authorized Signature:

Benjamin B. Roa, Ph.D. Diplomate ABMGG Laboratory Director	**Karla R. Bowles, Ph.D.** Diplomate ABMGG Laboratory Director	**David Mehr, M.D.** Laboratory Director Anatomic Pathology

The Technical Specifications summary (available at https://prolaris.com/prolaris-sample-requirements-technical-specifications/) describes the analysis, method, performance characteristics, nomenclature, and interpretive criteria of this test. This test may be considered investigational in some states. This test was developed and its performance characteristics determined by Myriad Genetic Laboratories. It has not been reviewed by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.