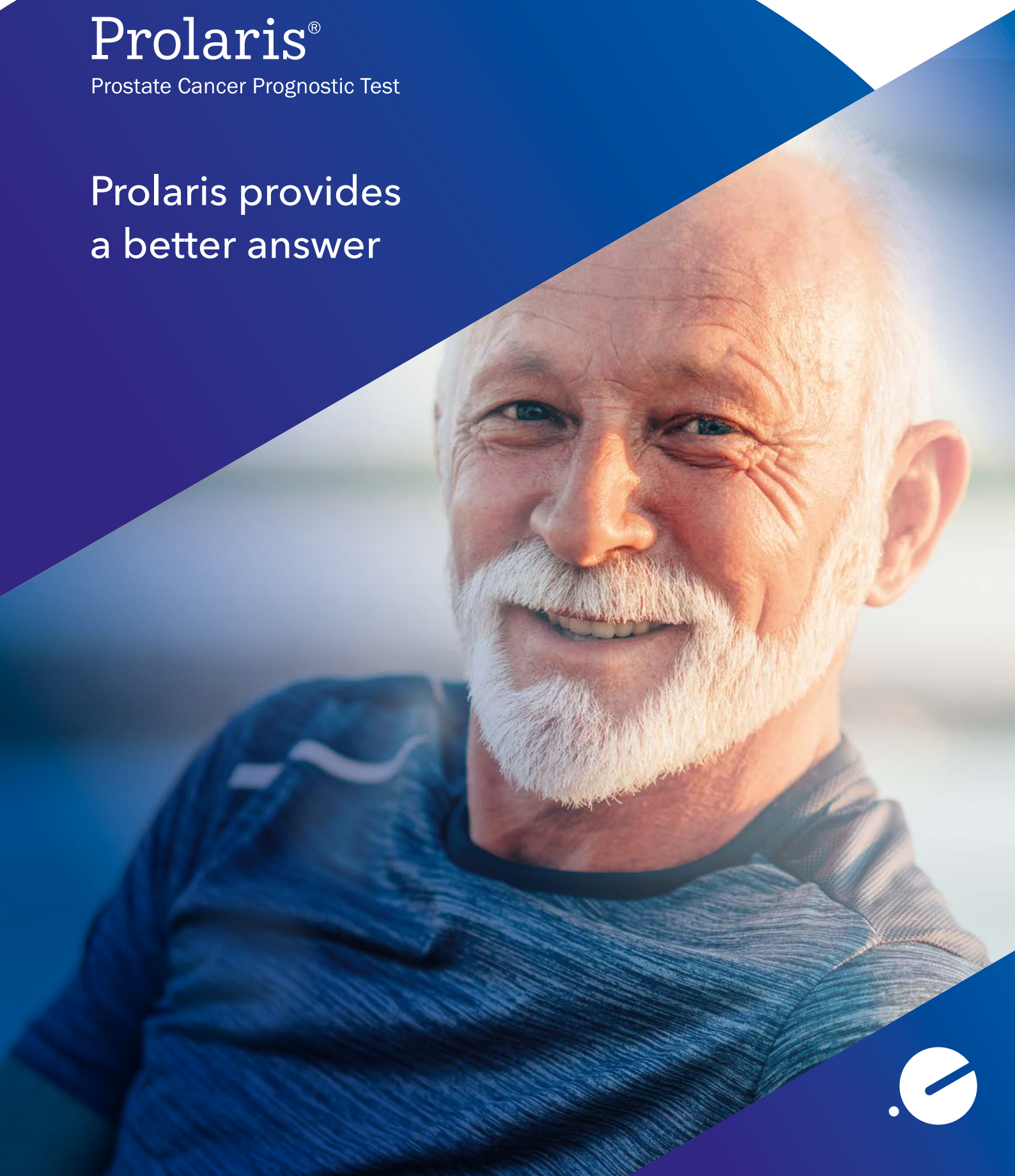
eurobio SCIENTIFIC

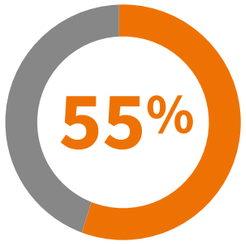
Prolaris®

Prostate Cancer Prognostic Test

Prolaris provides a better answer



CLINICAL AND PATHOLOGICAL FEATURES ARE LIMITED TO PREDICTING PATIENT OUTCOMES

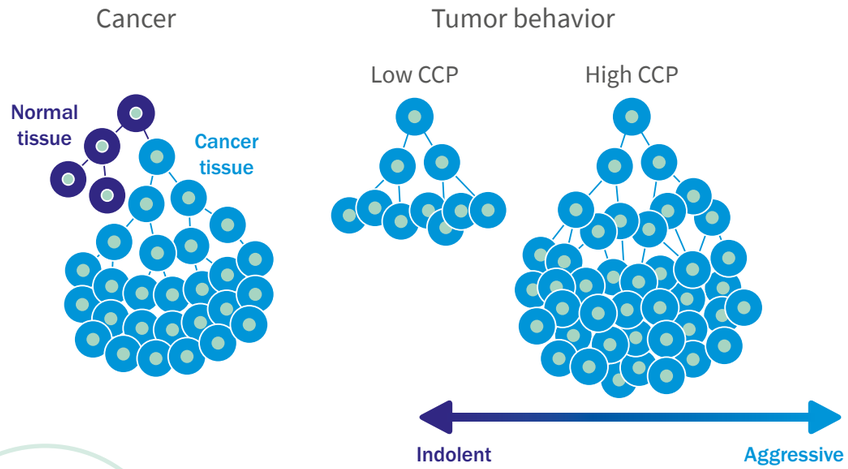


Interobserver variability impacts pathology.[1]

Biopsy Gleason scores and surgical Gleason scores are only concordant 55% of the time.[2]

Prolaris clarifies cancer aggressiveness

Prolaris looks at cell-proliferation (CCP) genes and combines it with clinical-pathological factors to determine the prostate cancer's true behavior



CCP is **2x** More prognostic than PSA and Gleason combined[3]

Prolaris has been consistently validated across all risk groups in nearly 10,000 patients[4]

PROLARIS PROVIDES A BETTER ANSWER FOR EVERY MAN IN EVERY RISK GROUP

Clinical variables

CAPRA score
Age
PSA ($p<1.5x10^{-4}$)
Clinical T stage
% biopsy cores
Gleason score ($p<2.1x10^{-7}$)

\+

Prolaris Molecular Score

Cell cycle proliferation ($p<3.7x10^{-15}$)

2x more predictive than PSA and Gleason[3]

=

Combined Clinical Risk Score

Patient's 10-year Disease Specific Mortality (DSM) risk after conservative management

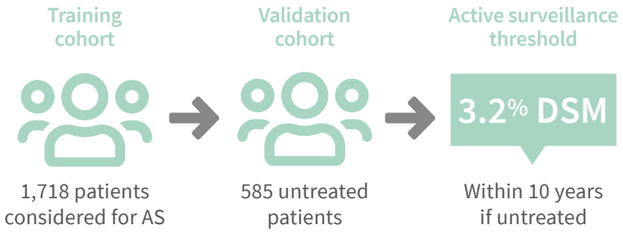
Patient's 10-year Metastasis (Mets) risk after definitive treatment

Active surveillance	Single-modal treatment	Multi-modal treatment
1	2	3

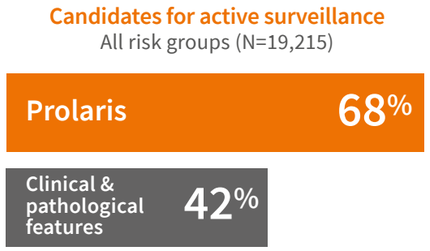
1. Men safe for active surveillance
2. Men not safe for active surveillance ➔ candidates for single-modal therapy
3. Men not safe for single-modal therapy ➔ candidates for multi-modal therapy

PROLARIS IMPROVES ACTIVE SURVEILLANCE DECISIONS

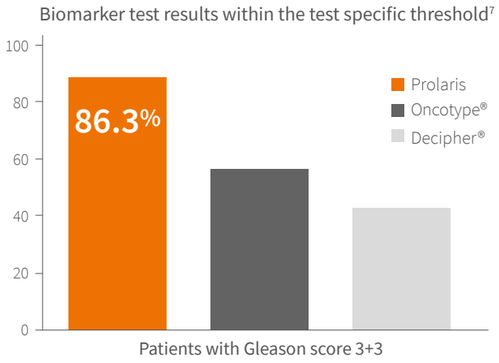
The Prolaris active surveillance threshold was validated and proven to work in untreated patients[6]



Prolaris identifies more men for active surveillance than clinical-pathological features alone[6]

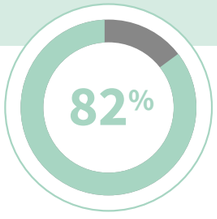


Prolaris outperforms other biomarkers in identifying appropriate patients for AS in independent study[7]



86% of low-risk 3+3 patients were below the Prolaris AS threshold

Prolaris provides peace of mind[8]



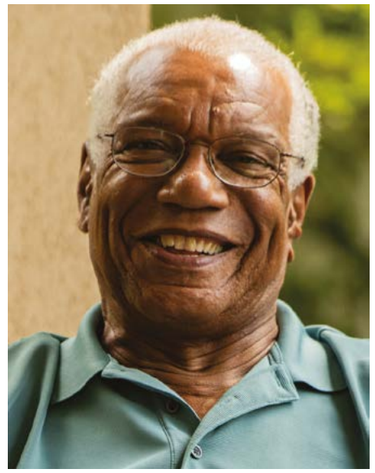
82% of low-risk men below the active surveillance threshold selected active surveillance

No events (biochemical recurrence and metastasis) occurred in 99.6% of men who selected AS after 2.2 years of follow-up

CASE EXAMPLE 1

Patient clinical profile

Age at biopsy	65
PSA prior to this biopsy	5.2
Clinical T-Stage	T1c
% Positive cores	<34%
Gleason score	3+4=7
Life expectancy	10 years
Imaging	PI-RADS 2
NCCN Risk Group	Favorable intermediate



Potential initial treatment options:

- Active surveillance
- External Beam Radiation Therapy (EBRT)
- Brachytherapy
- Radical Prostatectomy (RP) without pelvic lymph node dissection
- RP plus pelvic lymph node dissection*

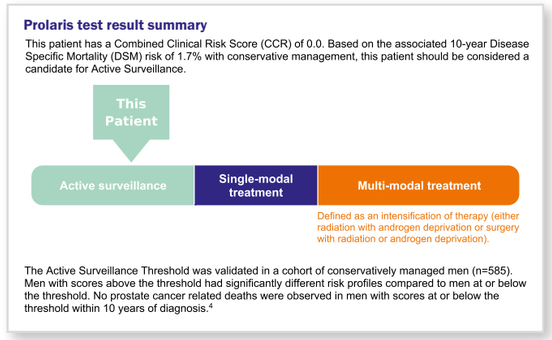
*Regional or extended PLND

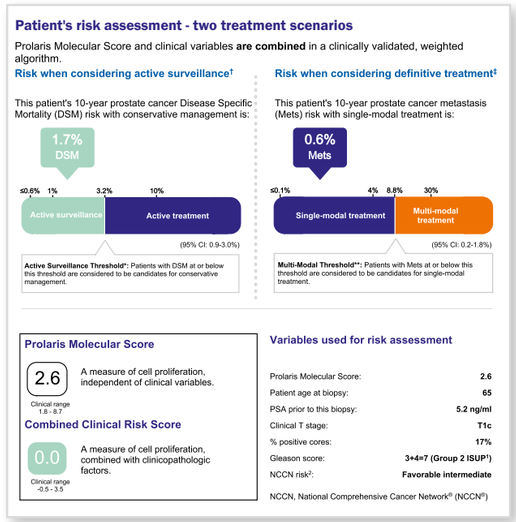
CASE EXAMPLE 1

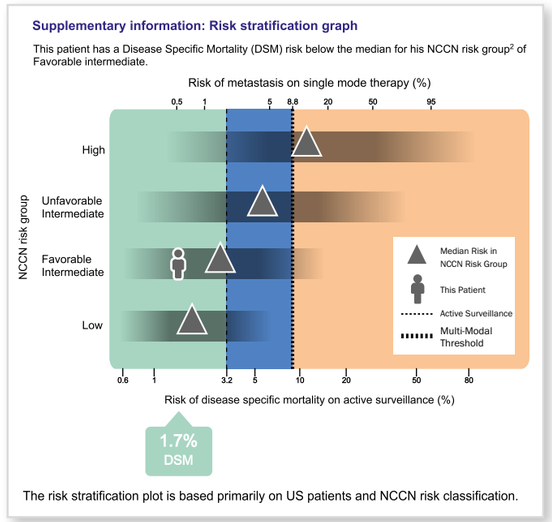
How would this Prolaris result impact your treatment decision?

Potential initial treatment options:

- Active surveillance
- EBRT
- Brachytherapy
- RP without pelvic lymph node dissection
- RP plus pelvic lymph node dissection*







*Regional or extended PLND

PROLARIS MAKES ACTIVE TREATMENT DECISIONS EASIER

The Prolaris multi-modal threshold was developed and double-validated to predict the risk of metastasis and identify men who may safely forego multi-modal therapy[5,9]

Multi-modal treatment

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

Training cohort	Validation cohort	Multi-modal threshold
15,669 unfavorable intermediate- and high-risk patients	n=718[9] and n=741[5] intermediate- and high-risk men who received single- or multi-modal treatment	8.8% METs Within 10 years if treated with single-modal therapy

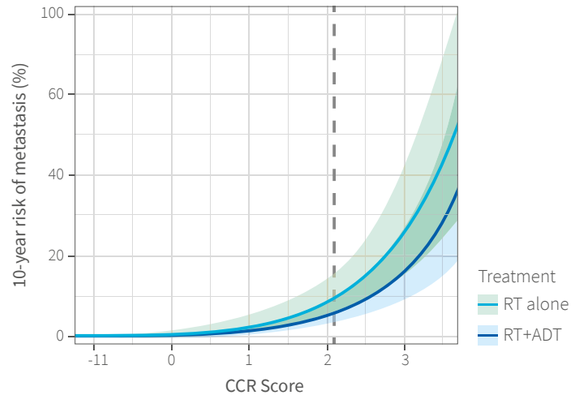
There was little to no benefit of multi-modal therapy for patients below the threshold, whereas those above the threshold had benefit

MULTIMODAL TREATMENT: CAN THE BENEFIT BE QUANTIFIED?

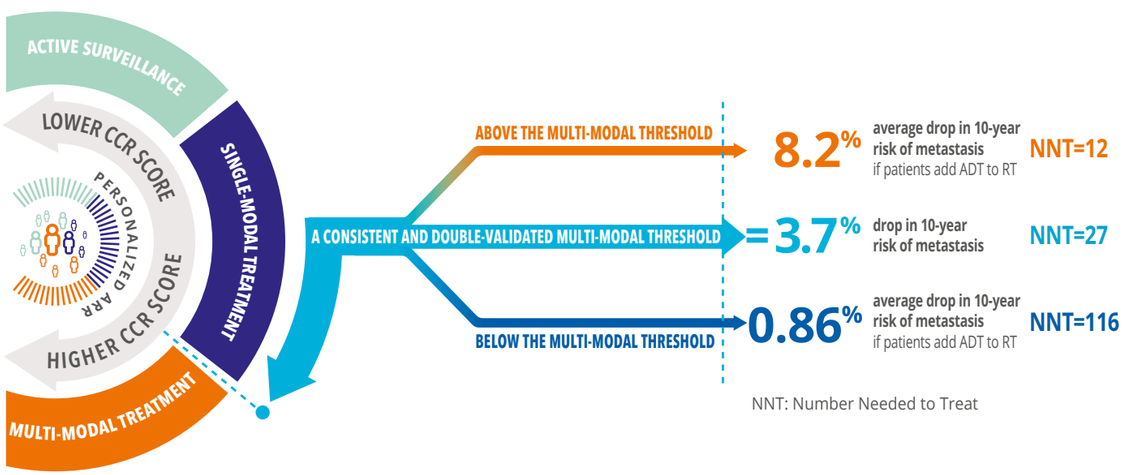
Men in each NCCN risk group who can avoid ADT when receiving dose-escalated RT[10]

FAVORABLE INTERMEDIATE RISK	UNFAVORABLE INTERMEDIATE RISK	HIGH RISK	VERY HIGH RISK
1 in 80	**1/2**	**1 in 5**	**1 in 20**
would benefit from ADT	could avoid ADT	could avoid ADT	could avoid ADT

Risk of metastasis with RT +/- ADT[11,12]



The answer to ADT decision[12]

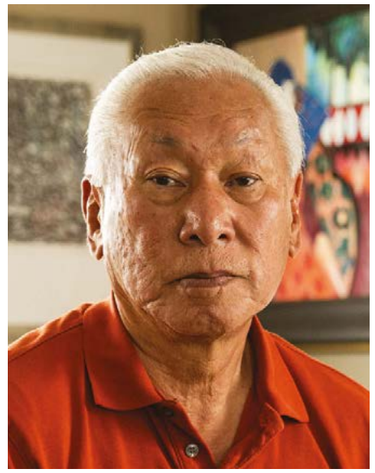


NNT: Number Needed to Treat

CASE EXAMPLE 2

Patient clinical profile

Age at biopsy	66
PSA prior to this biopsy	7.0
Clinical T-Stage	T2a
% Positive cores	<34%
Gleason score	4+3=7
Life expectancy	10 years
Imaging	PI-RADS 4
NCCN Risk Group	Unfavorable intermediate



Potential initial treatment options:

- RP without pelvic lymph node dissection
- RP plus pelvic lymph node dissection*
- EBRT with ADT (4-6 months)
- EBRT + brachytherapy with ADT (4-6 months)
- EBRT + brachytherapy without ADT

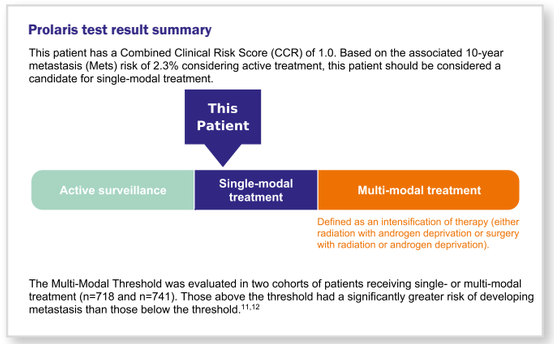
*Regional or extended PLND

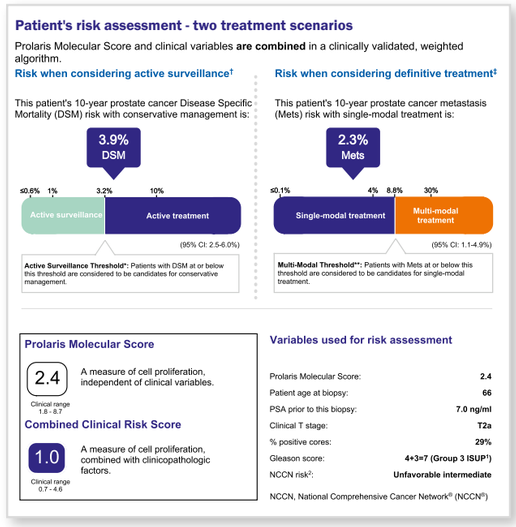
CASE EXAMPLE 2

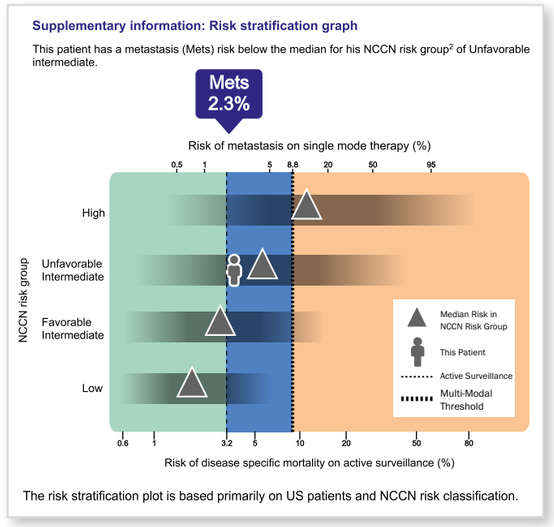
How would this Prolaris result impact your treatment decision?

Potential initial treatment options:

- RP without pelvic lymph node dissection
- RP plus pelvic lymph node dissection*
- EBRT with ADT (4-6 months)
- EBRT + brachytherapy with ADT (4-6 months)
- EBRT + brachytherapy without ADT







*Regional or extended PLND

PROLARIS PROVIDES A BETTER ANSWER FOR EVERY MAN WITH PROSTATE CANCER

How aggressive should initial treatment be?

Is active surveillance safe for me?

NCCN risk group	Low-risk	Favorable intermediate-risk	Unfavorable intermediate-risk	High-risk
Tumor aggression	Prolaris® Prostate Cancer Prognostic Test	Prolaris® Prostate Cancer Prognostic Test	Prolaris® Prostate Cancer Prognostic Test	Prolaris® Prostate Cancer Prognostic Test

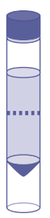
NCCN support for biomarkers[13]

Patients with NCCN low, favorable intermediate, unfavorable intermediate, or high-risk disease and life expectancy 10 years may consider the use of tumor based molecular assays.

CE-IVD kit for decentralized testing

1. Sample preparation
2. RNA extraction
3. RNA analysis
3. RNA analysis

FFPE tissue preparation:
- 5 µm section
- 60% tumor content
- Adjacent HE slide



RNA isolation:
- miRNeasy FFPE Kit

Prolaris test:
- RT/pre-amp
- qPCR

Analysis and report:
- Upload data
- Quality control
- Report print-out• qPCR

Prolaris®

Prostate Cancer Prognostic Test

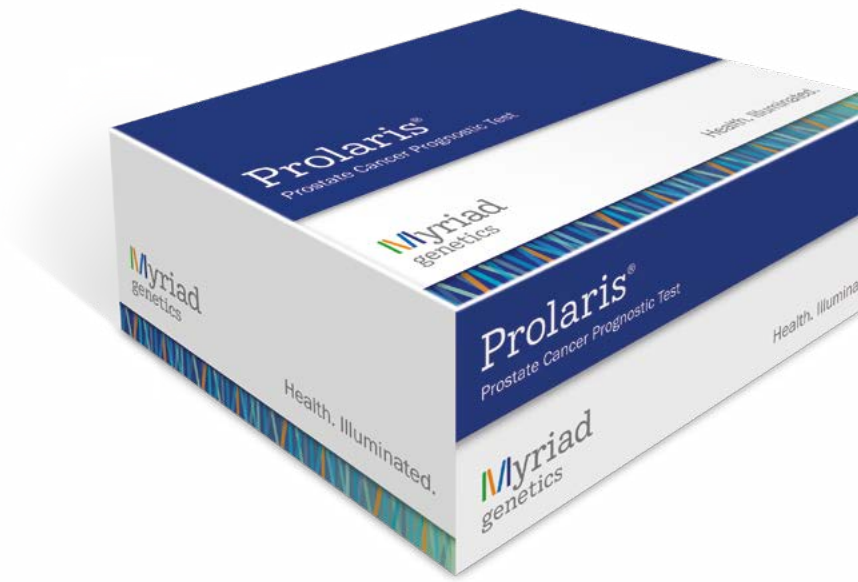
Prolaris clarifies prostate cancer aggressiveness

Prolaris provides a better answer for every man in every risk group

Prolaris improves active surveillance decisions

Prolaris makes active treatment decisions easier

Prolaris is a CE marked IVD kit performed in local laboratories in several countries



References:
1. Allsbrook W. C. et al., Human Pathology 2001 **2.** Schreiber D. et al., Journal of Clinical Pathology 2015 **3.** Cuzick J. et al., British Journal of Cancer 2012 **4.** https://prolaris.com/posters-and-medical-publications/#!#home **5.** Tward J.D. et al., International Journal of Radiation Oncology, Biology, Physics 2021. **6.** Lin D.W. et al., Urologic Oncology: Seminars and Original Investigations 2018 **7.** Hu J.C. et al., Journal of Clinical Oncology Precision Oncology 2018 **8.** Kaul S. et al., Per Med 2019 **9.** Tward J.D. et al., Journal of Clinical Oncology 2020 **10.** Tward J.D. et al., International Journal of Radiation Oncology - Biology - Physics 2022 **11.** Kishan A.U. et al., Lancet Oncology 2022 **12.** Tward JD et al., Journal of Clinical Oncology 2023 **13.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.4.2023.© National Comprehensive Cancer Network, Inc 2023. All rights reserved. Accessed September 28, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org. (PROS-D 2 of 4)

eurobio SCIENTIFIC

Eurobio Scientific GmbH
Nattermannallee 1, Building S19
50829 Köln
Germany

info-INT@eurobio-scientific.de
www.eurobio-scientific.de

PROL_MD_KIT_BR_10_24_EN