PROVIDING TREATMENT INFORMATION FOR PROSTATE CANCER PATIENTS

For patients with localized disease on biopsy*

For patients with adverse pathology after prostatectomy

Contact the GenomeDx Customer Support Team 1.888.792.1601 (toll-free)
customersupport@genomedx.com
DECIPHER® PROVIDES BETTER RISK ASSESSMENT FOR MORE INDIVIDUALIZED TREATMENT FOR PATIENTS DIAGNOSED WITH LOCALIZED PROSTATE CANCER

DECIPHER PROSTATE BIOPSY TEST ACCEPTS:

NCCN Risk Categories
- Very Low/Low
- Favorable Intermediate
- Unfavorable Intermediate

DECIPHER PREDICTS THE LIKELIHOOD OF CLINICALLY USEFUL ENDPOINTS
- High Grade Disease (Gleason Grade 4 or 5)
- 5 year metastasis
- 10 year prostate cancer specific mortality

<table>
<thead>
<tr>
<th>Decipher classification</th>
<th>Patient management recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decipher Biopsy Low Risk</td>
<td><strong>Favorable prognosis</strong> - may be suitable candidate for active surveillance and may have excellent outcomes when treated with local therapy alone such as surgery or radiotherapy(^1,2)</td>
</tr>
<tr>
<td>Decipher Biopsy High Risk</td>
<td><strong>Unfavorable prognosis</strong> - may not be suitable candidate for active surveillance and may benefit from intensification with multi-modal therapy(^1,2)</td>
</tr>
</tbody>
</table>

DECIPHER BIOPSY ACCURATELY RECLASSIFIES 46% OF PATIENTS FROM NCCN RISK CATEGORY\(^*\)

References

*Decipher Prostate Biopsy is indicated for patients categorized as NCCN Very Low, Low, Favorable Intermediate or Unfavorable Intermediate.
DECIPHER BIOPSY IS AN ACCURATE PREDICTOR OF DISEASE PROGRESSION FOR NEWLY DIAGNOSED PATIENTS*

COMPARISON OF ACCURACY DURING VARIOUS STAGES

Predicting Metastasis after RP
Predictive Power Measured by Area Under the Curve (AUC)

- DECIPHER ALONE (5 yr mets): AUC = 0.87
- DECIPHER ALONE (10 yr mets): AUC = 0.80
- PRETREATMENT PSA (5 yr mets): AUC = 0.67
- BIOPSY GS (5 yr mets): AUC = 0.51

AUC > 0.7 is clinically actionable
AUC ≤ 0.5 accuracy is comparable to a coin toss

Predicting 5 Year Metastasis after First Line Radiation
Predictive Power Measured by Area Under the Curve (AUC)

- DECIPHER ALONE (5 yr mets): AUC = 0.76
- NCCN (5 yr mets): AUC = 0.63
- CAPRA (5 yr mets): AUC = 0.45

Predicting High Grade Disease At RP
Predictive Power Measured by Area Under the Curve (AUC)

- DECIPHER ALONE (High Grade Disease): AUC = 0.71
- ONCOTYPE + NCCN (High Grade Disease): AUC = 0.69
- PRETREATMENT PSA (High Grade Disease): AUC = 0.62
**CLINICAL DETAILS**

- **PSA, most recent (ng/mL):** 5.5
- **Specimen Type:** Needle Core
- **NCCN risk category:** Intermediate Risk
- **Biopsy Gleason Score:** 3+4
- **# of Positive Cores:** 3 (3 of 6 Cores)
- **Clinical Stage:** T1c

**INTERPRETATION**

Among men with a low risk Decipher prostate cancer classifier score clinical studies have shown that this cancer has a favorable prognosis. Men with a low risk Decipher score may be suitable candidates for active surveillance and may have excellent outcomes even when treated with local therapy alone.\(^1\)\(^,\)\(^2\)

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\(^1\)Average clinical risk refers to the average cohort risk of metastasis at 5 years post radical prostatectomy (RP). The average cumulative incidence of metastasis was 6.0% at 5 years post radical prostatectomy, as reported by Kames et al., 2013 from analysis of a cohort of 1,010 men with intermediate and high risk clinical features who received radical prostatectomy as first line treatment at the Mayo Clinic between 2000 and 2008.\(^1\)

\(^2\)Probability of high grade disease (primary Gleason grade 4 or 5) endpoint: Decipher uses the genomic risk score to predict the probability of primary Gleason grade 4 or 5 disease upon pathologic examination of the radical prostatectomy. Probabilities were generated using a logistic regression model in a prospective cohort of 2,342 prostate cancer patients. The model is adjusted using a prevalence of 27% for a finding of primary Gleason grade 4 or 5 on radical prostatectomy among NCCN low-, intermediate- and high-risk patients.\(^5\) Klein et al. 2016 study found Decipher biopsy predicted high grade disease at radical prostatectomy with an AUC of 0.71.\(^5\) The percent likelihood for this endpoint ranges from 6.5-45%.

\(^3\)Five-year probability of metastasis endpoint: Decipher uses the genomic risk score to predict the 5-year probability of metastasis from the time of radical prostatectomy. Probabilities were generated from a Cox proportional hazards model based upon a cohort of 1,010 men with intermediate and high risk clinical features with a median 6.9 years of follow-up.\(^4\) In a separate cohort, Klein et al. 2016 reported that Decipher biopsy predicted 5-year metastasis with an AUC of 0.874. Subsequently, in another independent cohort, Decipher biopsy predicted 5-year metastasis with an AUC of 0.76 and similarly found that Decipher biopsy was the only significant variable that predicted metastatic onset in multivariable analysis with clinical risk factors.\(^6\) The average concordance between Decipher biopsy and radical prostatectomy specimens is 84%.

\(^4\)Ten-year probability of prostate specific mortality (PCSM) endpoint: Decipher uses the genomic risk score to predict the 10-year probability of PCSM from the time of radical prostatectomy. Probabilities are generated from a logistic regression analysis based upon a cohort of 557 patients with 112 prostate cancer deaths within 10 years post radical prostatectomy. These probabilities are adjusted for a PCSM cumulative incidence of 5% at 10 years post radical prostatectomy.\(^9\) All non-PCSM patients in the study had at least 10 years of follow-up. In a validation study with a biopsy cohort of 175 patients, Decipher was a significant predictor of PCSM at diagnosis with a hazard ratio (HR) of 157 (95% CI 1.07-2.40) per 10% increase for Decipher score (p=0.02).\(^9\) The percent likelihood for this endpoint ranges from 0.7-30.5%.
DECIPHER BIOPSY REPORT

PATIENT DETAILS
Patient Name: [Redacted]
Medical Record Number: [Redacted]
Date of Birth: [Redacted]
Date of Biopsy: [Redacted]
Pathology Laboratory: D
Pathologist: [Redacted]
Address:

ORDER INFORMATION
Order Date: [Redacted]
Specimen Received Date: [Redacted]
GenomeDx Accession ID:
Specimen ID:
Ordering Physician:
Clinic/Hospital Name:
Clinic/Hospital Address:
Additional Physician:

CLINICAL DETAILS
PSA, most recent (ng/mL): 1.9
Specimen Type: Needle Core
NCCN risk category: Intermediate Risk
# of Positive Cores: 3 (3 of 9 Cores)
Biopsy Gleason Score: 3+4
Clinical Stage: T1c

YOUR DECIPHER RESULT – GENOMIC HIGH RISK

DECIPHER SCORE 0.72

Risk at RP - Percent Likelihood
High Grade Disease (primary Gleason grade 4 or 5): 39.7%
5-Year Metastasis: 18.5%
10-Year Prostate Cancer Specific Mortality: 12.4%

INTERPRETATION
Among men with a high risk Decipher prostate cancer classifier score clinical studies have shown that this cancer has an unfavorable prognosis. Men with a high risk Decipher score may not be suitable candidates for active surveillance and may benefit from intensification with multi-modal therapy.1-3

GenomeDx Medical Director (Name & Signature)

Disclaimer: The Decipher test was developed and its performance characteristics were determined by GenomeDx Biosciences Laboratory. The GenomeDx Biosciences Laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88) to perform high complexity testing. This test has not been cleared or approved by the U.S. Food and Drug Administration. Summary of surgical pathology report provided for convenience of Ordering Physician. Please refer to Referring Pathologist’s original pathology report to guide treatment decisions.
DECIPHER CLASSIFIES POST-SURGERY PATIENTS* INTO GENOMIC RISK CATEGORIES FOR METASTASIS WITH 98.5% NEGATIVE PREDICTIVE VALUE (NPV)

POST RADICAL PROSTATECTOMY (RP) INDICATIONS FOR DECIPHER TEST

- Patient with prostate cancer who has undergone a RP within the previous 60 months and is being considered for postoperative secondary therapy due to one or more cancer-recurrence risk factors, and
- Patient must have achieved initial PSA nadir (defined as undetectable PSA) within 30 days of RP surgery, and
- Patient must not have any evidence of distant metastasis, and
- Patient must not have received any neo-adjuvant treatment prior to surgery, and
- Decipher is performed on a patient’s RP specimen, and
- Patient’s surgical pathology report or medical records must have documented presence of adverse pathology:
  - Pathological stage T2 disease with a positive surgical margin,** or
  - Pathological stage T3 disease (e.g., extraprostatic extension, seminal vesicle invasion, bladder neck invasion),** or
  - Rising PSA after initial PSA nadir,** and
- Testing has been ordered by a physician who is certified in the GenomeDX Decipher Certification and Training Registry (CTR)

<table>
<thead>
<tr>
<th>Decipher classification</th>
<th>Treatment recommended post-surgery(^{5,6})</th>
<th>Treatment recommended post-surgery after PSA rise or biochemical recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genomic Low Risk</td>
<td>Observation with PSA monitoring until detectable PSA rise, if any/ever(^{2})</td>
<td>Radiation alone is sufficient. Concurrent hormone therapy may be avoided(^{7})</td>
</tr>
<tr>
<td></td>
<td>98.5% 5 year metastasis-free survival(^{4})</td>
<td></td>
</tr>
<tr>
<td></td>
<td>95% 10 year prostate cancer-specific survival(^{4})</td>
<td></td>
</tr>
<tr>
<td>Genomic High Risk</td>
<td>80% reduction in metastasis risk in Decipher high-risk patients who receive adjuvant or early radiation(^{12})</td>
<td>Radiation alone is insufficient. Intensification of treatment may be needed(^{3})</td>
</tr>
</tbody>
</table>

References


* Clinically high risk patients with one or more of the “Post radical prostatectomy (RP) indications for Decipher test” listed above.
** Covered for Medicare patients whose physicians are registered in the Decipher CTR (Certification and Training Registry)
**DECIPHER. KNOW WHAT TREATMENT. AND WHEN TO TREAT.**

NCCN GUIDELINES HIGHLIGHT DECIPHER AS A CLINICALLY AVAILABLE TISSUE-BASED TEST FOR PROSTATE CANCER

**DECIPHER FOR PATIENTS AFTER PROSTATE SURGERY**

*Decipher low-risk* patients may be managed safely with observation until PSA rise

*Decipher high-risk* patients may experience lower rates of metastasis when treated with adjuvant radiation post-RP

Patients treated with salvage radiotherapy*

*No concurrent hormone therapy given

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**DECIPHER FOR PATIENTS AFTER PROSTATE SURGERY WITH PSA RISE OR BIOCHEMICAL RECURRENCE**

*Decipher low-risk* patients have excellent prognosis with salvage radiation and may avoid concurrent hormonal therapy, as incidence of metastasis remains low.

*Decipher high-risk* patients may require intensification of therapy beyond radiation as incidence of metastasis remains high.


Radiation (ART Better Results Than SRT)¹

OBSERVATION

PSA RISE/BCR

Excellent prognosis with SRT and may avoid concurrent hormone therapy³

May require intensification of therapy beyond radiation³

DECIPHER HIGH RISK

DECIPHER LOW RISK

Excellent prognosis with SRT and may avoid concurrent hormone therapy³
PATIENT DETAILS

Patient Name: 
Medical Record Number: 
Date of Birth: 
Date of Prostatectomy: 
Pathology Laboratory: 
Pathologist: 
Address: 

ORDER INFORMATION

Order Date: 
Specimen Received Date: 
GenomeDx Accession ID: 
Specimen ID: 
Ordering Physician: 
Clinic/Hospital Name: 
Clinic/Hospital Address: 
Additional Physician: 

CLINICAL DETAILS

PSA, most recent (ng/mL): 4.9 
Gleason Score: 4+3 
Specimen Type: 

[ ] SM+ 
[ ] EPE 
[ ] SVI 
[ ] LNI 
[ ] BCR 
[ ] Tertiary Gleason 5 

YOUR DECIPHER RESULT – GENOMIC LOW RISK

<table>
<thead>
<tr>
<th>DECIPHER SCORE 0.3</th>
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</thead>
<tbody>
<tr>
<td>5-Year Metastasis</td>
</tr>
<tr>
<td>10-Year Prostate Cancer Specific Mortality</td>
</tr>
</tbody>
</table>

INTERPRETATION

Clinical studies concluded that Decipher low risk results in men with adverse pathology have good prognosis overall and may be optimally managed with observation after surgery.1-3,12 Upon PSA rise, these patients may be treated with delayed radiotherapy without concurrent hormone therapy.4,11

Relevant findings from published clinical studies: Patients with Decipher low risk had >97% 5-year metastasis free survival and >94.7% 10-year cause specific survival.1,2,3 For these patients there were no significant differences in metastasis free survival with adjuvant, early or late salvage postoperative radiotherapy treatment.5,6,11

In patients with PSA rise or biochemical recurrence after surgery that received salvage radiotherapy, >97% 5-year metastasis free survival was observed with or without concurrent hormone therapy.4

*Average clinical risk refers to the average cohort risk of metastasis at 5 years post radical prostatectomy. The average cumulative incidence of metastasis was 6.0% at 5 years post radical prostatectomy, as reported by Karnes et al., 2013 from analysis of a cohort of 1,010 men with intermediate and high risk clinical features who received radical prostatectomy as first line treatment at the Mayo Clinic between 2000 and 2008.5

Five-year probability of metastasis endpoint: Decipher uses the genomic risk score to predict the 5-year probability of metastasis from the time of radical prostatectomy. Probabilities were generated from a Cox proportional hazards model based upon a cohort of 1,010 men with intermediate and high risk clinical features with a median 6.9 years of follow up. Decipher had an AUC of 0.76-0.85 in multiple clinical validation studies for prediction of metastasis.4,7,10 Percent likelihood for this endpoint ranges from 0.3-67%.

Ten-year probability of prostate cancer specific mortality (PCSM) endpoint: Decipher uses the genomic risk score to predict the 10-year probability of PCSM from the time of radical prostatectomy. Probabilities are generated from a logistic regression analysis based upon a cohort of 557 patients with 112 prostate cancer deaths within 10 years post radical prostatectomy. These probabilities are adjusted for a PCSM cumulative incidence of 5% at 10 years post radical prostatectomy. All non-PCSM patients in the study had at least 10 years of follow-up. Decipher had an AUC of 0.72 in predicting PCSM.1,7,12 Percent likelihood for this endpoint ranges from 0.7-30.5%.
DECIPHER POST-OPERATIVE REPORT

PATIENT DETAILS
Patient Name: [redacted]
Medical Record Number: [redacted]
Date of Birth: [redacted]
Date of Prostatectomy: [redacted]
Pathology Laboratory: [redacted]
Pathologist: [redacted]
Address: [redacted]

ORDER INFORMATION
Order Date: [redacted]
Specimen Received Date: [redacted]
GenomeDx Accession ID: [redacted]
Specimen ID: [redacted]
Ordering Physician: [redacted]
Clinic/Hospital Name: [redacted]
Clinic/Hospital Address: [redacted]
Additional Physician: [redacted]

CLINICAL DETAILS
PSA, most recent (ng/mL): 4.2
Gleason Score: 4+3
Specimen Type:
- SM+:
- EPE: [redacted]
- SVI: [redacted]
- LNI: [redacted]
- BCR: [redacted]
- Tertiary Gleason 5: [redacted]

YOUR DECIPHER RESULT – GENOMIC HIGH RISK

DECIPHER SCORE 0.7

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>5-Year Metastasis</th>
<th>10-Year Prostate Cancer Specific Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk - Percent Likelihood</td>
<td>16.4%</td>
<td>11.4%</td>
</tr>
</tbody>
</table>

INTERPRETATION

Clinical studies concluded that Decipher high risk men with adverse pathology have a poor prognosis overall. These men may benefit from adjuvant or early salvage radiotherapy and consideration for clinical trials.

Relevant findings from published clinical studies: Patients with Decipher high risk had 77.5% 5-year metastasis-free survival and 76.6% 10-year cause specific survival. For these patients there was improved metastasis-free survival favoring adjuvant and early salvage postoperative radiotherapy compared to postoperative observation.

In patients with PSA rise or biochemical recurrence after surgery that received salvage radiotherapy, only 66.9% remained metastasis free after 5 years.

*Average clinical risk refers to the average cohort risk of metastasis at 5 years post radical prostatectomy. The average cumulative incidence of metastasis was 6.0% at 5 years post radical prostatectomy, as reported by Kames et al., 2013 from analysis of a cohort of 1,010 men with intermediate and high risk clinical features who received radical prostatectomy as first line treatment at the Mayo Clinic between 2000 and 2008.

Five-year probability of metastasis endpoint: Decipher uses the genomic risk score to predict the 5-year probability of metastasis from the time of radical prostatectomy. Probabilities were generated from a Cox proportional hazards model based upon a cohort of 1,010 men with intermediate and high risk clinical features with a median 6.9 years of follow up.

Ten-year probability of prostate cancer specific mortality (PCSM) endpoint: Decipher uses the genomic risk score to predict the 10-year probability of PCSM from the time of radical prostatectomy. Probabilities are generated from a logistic regression analysis based upon a cohort of 557 patients with 112 prostate cancer deaths within 10 years post radical prostatectomy. These probabilities are adjusted for a PCSM cumulative incidence of 6% at 10 years post radical prostatectomy. All non-PCSM patients in the study had at least 10 years of follow-up. Decipher had an AUC of 0.72 in predicting PCSM. Percent likelihood for this endpoint ranges from 0.7-30.5%.

GenomeDx Medical Director (Name & Signature)
Medical Directors: Timothy J. Triche, MD, PhD & Doug Dolginow, MD

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Decipher Prostate Cancer Classifier represents 22 biomarkers specific to prostate cancer representing multiple biological pathways.

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<tr>
<th>BIOLOGICAL PATHWAY</th>
<th>PROSTATE-SPECIFIC BIOMARKERS</th>
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<tr>
<td>Androgen-Signaling</td>
<td>ANO7, PCAT-32, UBE2C</td>
</tr>
<tr>
<td>Cell Cycle Progression</td>
<td>NFI1, NUSAP1, ZWILCH</td>
</tr>
<tr>
<td>Cell Proliferation, Differentiation</td>
<td>CAMK2NI, MYBPCI, PBX1, THBS2, UBE2C</td>
</tr>
<tr>
<td>Cell Structure, Adhesion, Motility</td>
<td>ANO7, EPPK1, IQGAP3, LASP1, MYBPCI, PCDH7, RABGAP1</td>
</tr>
<tr>
<td>Immune System Modulation</td>
<td>GLYATL1P4, SIPR4, TNFRSF19, TSBP</td>
</tr>
</tbody>
</table>

A tissue sample is precious and finite. Use a molecular test that provides the most comprehensive assessment of your patient’s tumor. The Decipher testing platform collects over 1.4 million data points to help better understand the tumor biology. The GRID research program provides exclusive access to this valuable information by sharing an in-depth, personalized Tumor RNA Expression Profile for your Decipher patient. This research use only (RUO) information can provide insights. In addition, the GRID research program aims to foster collaborations among researchers by collectively sharing this wealth of data to facilitate new genomic discoveries. To learn more, visit DecipherGRID.com.

Decipher Prostate Cancer Classifier helps determine who:

- May be suitable candidates for active surveillance
- May be treated with local therapy alone
- May benefit from intensification with multimodal therapy

Decipher Prostate Cancer Classifier represents 22 biomarkers specific to prostate cancer representing multiple biological pathways.

- Androgen-Signaling: ANO7, PCAT-32, UBE2C
- Cell Cycle Progression: NFI1, NUSAP1, ZWILCH
- Cell Proliferation, Differentiation: CAMK2NI, MYBPCI, PBX1, THBS2, UBE2C
- Cell Structure, Adhesion, Motility: ANO7, EPPK1, IQGAP3, LASP1, MYBPCI, PCDH7, RABGAP1
- Immune System Modulation: GLYATL1P4, SIPR4, TNFRSF19, TSBP

Access for all patients:

- Medicare Coverage (Mol Dx LCD ID L36345): Decipher post-op test covered for Medicare beneficiaries
- Private Insurance Coverage
- Proven and comprehensive financial assistance for patients

Contact the GenomeDx Customer Support Team 1.888.792.1601 (toll-free)
customersupport@genomedx.com

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