Decipher Prostate Cancer Classifier

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

<table>
<thead>
<tr>
<th>Procedures addressed by this guideline</th>
<th>Procedure codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decipher Prostate Cancer Classifier</td>
<td>81479</td>
</tr>
</tbody>
</table>

What are gene expression profiling tests for prostate cancer

Definition

Prostate cancer (PC) is the most common cancer and a leading cause of cancer-related deaths worldwide. It is considered a heterogeneous disease with highly variable prognosis.¹

- High-risk prostate cancer (PC) patients treated with radical prostatectomy (RP) undergo risk assessment to assess future disease prognosis and determine optimal treatment strategies. Post-RP pathology findings, such as disease stage, baseline Gleason score, time of biochemical recurrence (BCR) after RP, and PSA doubling-time, are considered strong predictors of disease-associated metastasis and mortality. Following RP, up to 50% of patients have pathology or clinical features that are considered at high risk of recurrence and these patients usually undergo post-RP treatments, including adjuvant or salvage therapy or radiation therapy, which can have serious risks and complications. According to clinical practice guideline recommendations, high risk patients should undergo 6 to 8 weeks of radiation therapy (RT) following RP. However, approximately 90% of high-risk patients do not develop metastases or die of prostate cancer, and instead may be appropriate candidates for alternative treatment approaches, including active surveillance (AS). As such, many patients may be subjected to unnecessary follow-up procedures and their associated complications, highlighting the need for improved methods of prognostic risk assessment.² ³

- Several genomic biomarkers have been commercially developed to augment the prognostic ability of currently available routine clinical and pathological tests and identify those patients most and least likely to benefit from a specific treatment strategy. Prognostic genomic tests, including gene expression profiling tests, may help to avoid overtreatment by reclassifying those men originally identified as high risk, but who are unlikely to develop metastatic disease. Genomic biomarkers may
also play a role in assisting clinicians to tailor personalized and more appropriate treatments for subgroups of PC patients, and improve overall health outcomes.\textsuperscript{2,3}

**Test information**

- Gene expression profiles (GEPs) evaluate the expression of several genes using one sample. Gene expression is determined through RNA analysis, using either reverse transcriptase (RT) polymerase chain reaction (PCR) or DNA microarrays.\textsuperscript{4}

- Decipher\textsuperscript{®} Prostate Cancer Classifier (GenomeDX Biosciences, Inc.)\textsuperscript{5}
  
  o According to the manufacturer, the Decipher test is a tissue-based tumor genomic test that predicts the probability of metastasis within 5 years of RP, and provides an independent assessment of tumor aggressiveness, information that is distinct from that provided by the Gleason score or PSA.

  o Decipher analyzes a small tissue sample removed during surgery that is routinely archived or stored by the pathology lab. This test is intended for PC patients with stage T2 disease with positive margins, stage T3 disease, or rising serum PSA after RP. The test evaluates the expression of 1.4M RNA (44,000 genes) using RNA extracted from formalin-fixed paraffin-embedded (FFPE) tumor specimens of the index lesion, defined as the highest tumor stage or Gleason score.

  o The Decipher test result is expressed as a continuous risk score; a genomic classifier (GC) that ranges from 0 (lowest) to 1 (highest). Each score is associated with the probability of 5-year metastasis.

**Guidelines and evidence**

**National Comprehensive Cancer Network**

- The National Comprehensive Cancer Network (NCCN) 2018 Clinical Practice Guidelines on Prostate Cancer state the following regarding molecular assays:\textsuperscript{6}

  o “Men with low or favorable intermediate risk disease may consider the use of the following tumor-based molecular assays: Decipher, Oncotype DX Prostate, Prolaris, Promark. Retrospective studies have shown that molecular assays performed on prostate biopsy or radical prostatectomy specimens provide prognostic information independent of NCCN risk groups.”

  o According to NCCN, the Molecular Diagnostic Services Program (MolDX) recommendations stated the following:\textsuperscript{6}
    
    - Decipher: “Cover post-RP for 1) pT2 with positive margins; 2) any pT3 disease; 3) rising PSA (above nadir)”
- Prolaris: “Cover post-biopsy for NCCN very-low, low-risk, and favorable intermediate-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy.”

- Oncotype DX Prostate: “Cover post-biopsy for NCCN very-low, low-risk, and favorable intermediate-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy.”

- ProMark: “Cover post-biopsy for NCCN very-low and low-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy.”

  "These molecular biomarker tests have been developed with extensive industry support, guidance, and involvement, and have been marketed under the less rigorous FDA regulatory pathways for biomarkers. Although full assessment of their clinical utility requires prospective randomized clinical trials, which are unlikely to be done, the panel believes that men with low or favorable intermediate disease may consider the use of Decipher, Oncotype DX Prostate, Prolaris, or ProMark during initial risk stratification. In addition, Decipher may be considered during workup for radical prostatectomy PSA persistence or recurrence (category 2B)."

**American Association of Clinical Urologists**

The American Association of Clinical Urologists has issued a position statement on genomic testing in prostate cancer that states the following: 7

- “The AACU supports the use of tissue-based molecular testing as a component of risk stratification in prostate cancer treatment decision making.”

**American Urological Association, ASTRO, and the Society of Urologic Oncology**

The AUA/ASTRO/SUO guideline for clinically localized prostate cancer states the following: 8

- “Among most low-risk localized prostate cancer patients, tissue based genomic biomarkers have not shown a clear role in the selection of candidates for active surveillance.”

**Decipher**

Decipher Literature Review 9-34

- There is currently limited evidence in the peer-reviewed literature to support the widespread use of the Decipher test to accurately provide prognostic risk stratification among patients with prostate cancer who have undergone RP in
routine clinical practice. The relatively large evidence base, published primarily by the test manufacturer, consists of retrospective case-control and retrospective cohort studies evaluating the strength of the association between the Decipher score and incidence of disease recurrence (e.g., biochemical recurrence, metastasis) or PC-associated mortality. Hazard and odds ratios from univariate and multivariate logistic regression analyses show significant associations between the test and clinical endpoint. Also, study results indicate that Decipher consistently discriminates between men at 5-year risk of metastatic disease progression after RP and men without disease progression with reasonable AUC and c-index estimates. Several studies reported reclassification rates using the Decipher test, indicating that patient risk could be stratified differently based on Decipher results. These types of reclassification calculations are useful since the clinical usefulness of a prognostic test has been reported to be reliant on its ability to categorize patients into different and more accurate prognostic groups, providing accurate predictions about their future disease state, and ultimately guiding optimal treatment regimens. However, these various estimates may be subject to bias and confounders given the several limitations that weaken the quality of the individual studies, including publication bias; patient overlap; insufficient follow-up periods and small number of metastatic event cases; bias associated with retrospective analyses; lack of observer or investigator blinding; missing or flawed registry data; Decipher sampling issues; and considerable heterogeneity between cases and controls for various demographic, disease risk factors, and treatment regimens.

- It is not clear how results of the Decipher test will impact patient disease management and treatment strategies, and if any changes will translate into improved morbidity and mortality for high-risk PC patients. Results of new peer-reviewed studies of clinical utility will potentially provide higher quality evidence to better inform clinicians regarding patient selection criteria and appropriate use of the Decipher test among high-risk PC patients who are weighing the risk and benefits of various treatment options.

- Results of a meta-analyses of 5 studies showed that Decipher moderately correlates with clinicopathologic measures and does appear to add benefit more than standard clinicopathologic measures to accurately assess prognosis and predict metastases in men who have undergone RP.

**Clinical Trials**

Observational prospective cohort study: A Validation Study on the Impact of Decipher® Testing on Treatment Recommendations in African-American and Non-African American Men With Prostate Cancer (VANDAAM Study)\(^{35}\)

- “The primary purpose of this study is to determine whether a tumor test recently developed by GenomeDx Biosciences known as Decipher® can predict aggressive prostate cancer with the same accuracy in African-American men (AAM) as in non-African-American men (NAAM).”
  - NCT02723734
• Recruiting

Observational patient registry study: Decipher Genomics Resource Information Database (GRID)\textsuperscript{36}

• “To prospectively evaluate the utility of genomic expression data as a tool to better characterize the tumors of individual patients, and to understand how genomic information from individual patients undergoing routine clinical testing can be used in population-level analysis to improve treatment and outcomes.”

• NCT02609269

• Recruiting

Genomics in Michigan Impacting Observation or Radiation (G-MINOR)\textsuperscript{37}

• “To determine the impact of Decipher test results on adjuvant treatment decisions of high-risk post-RP patients with undetectable post-op prostate specific antigen (PSA) compared to clinical factors alone.”

• NCT02783950

• Active, not yet recruiting

Criteria

• This test is considered investigational and/or experimental.

  o Investigational and experimental (I&E) molecular and genomic (MolGen) tests refer to assays involving chromosomes, DNA, RNA, or gene products that have insufficient data to determine the net health impact, which typically means there is insufficient data to support that a test accurately assesses the outcome of interest (analytical and clinical validity), significantly improves health outcomes (clinical utility), and/or performs better than an existing standard of care medical management option. Such tests are also not generally accepted as standard of care in the evaluation or management of a particular condition.

  o In the case of MolGen testing, FDA clearance is not a reliable standard given the number of laboratory developed tests that currently fall outside of FDA oversight and FDA clearance often does not assess clinical utility.

References


2. Marrone M, Potosky AL, Penson D, Freedman AN. A 22 Gene-expression Assay, Decipher\textsuperscript{\textregistered} (GenomeDx Biosciences) to Predict Five-year Risk of Metastatic


5. Decipher website. Available at: http://deciphertest.com/


