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.

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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

• At the time of diagnosis of localized PC, patients typically undergo a prognostic risk assessment with routine clinical and pathological tests to assess the probability of subsequent progression or metastasis. These prognostic assessments help to identify lower risk patients with indolent disease who may opt for active surveillance (AS), or higher risk patients with more aggressive disease who would benefit from a treatment intervention.

• High-risk prostate cancer (PC) patients treated with radical prostatectomy (RP) also 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 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 either at the time of diagnosis of localized PC or after radical prostatectomy (RP) 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.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.⁴
- According to the manufacturer, “Decipher® uses an oligonucleotide microarray to measure the expression of up to 1.4 million RNAs (e.g., mRNA,IncRNA) extracted from formalin-fixed, paraffin-embedded (FFPE) prostate specimens. Decipher testing on tumor specimens provides the probability of high-grade disease at radical prostatectomy (biopsy specimens only), 5-year probability of clinical metastasis, and 10-year prostate cancer specific mortality. A gene expression signature is used to generate the Decipher score, which ranges from 0 to 1.0.”⁵
- Decipher Prostate Biopsy
  - Decipher Prostate Biopsy results are “intended for use as an adjunct to conventional clinical risk factors for determining metastatic potential and prognosis of patients diagnosed with localized prostate cancer.”⁶
  - “Decipher Prostate Biopsy predicts a patient’s risk for metastasis or prostate cancer mortality, as well as adverse pathology at RP, using the gene expression profile of FFPE prostate cancer tissue samples collected at biopsy. Decipher Prostate Biopsy classifies as low risk those who may be safely followed with active surveillance, or as high risk those who would potentially benefit from immediate treatment.”⁵
- Decipher Prostate Radical Prostatectomy (RP)
  - Decipher Prostate RP results are intended as “an adjunct to conventional clinical variables and models currently used for determining prognosis and treatment of prostate cancer patients after radical prostatectomy.”⁷ Clinical validity studies have evaluated patients designated as very low-, low-, favorable intermediate-, unfavorable intermediate, high, and very high risk per the National Comprehensive Cancer Network (NCCN) risk groups for prostate cancer.
  - Decipher Prostate RP “predicts a patient’s risk for metastasis or prostate cancer mortality for men with adverse pathology or PSA persistence / recurrence following RP using the gene expression profile of FFPE prostate cancer tissue
samples collected at RP. Decipher Prostate RP classifies as low risk those who may be safely observed, or as high risk those who would potentially benefit from treatment or treatment intensification.”

Guidelines and evidence

National Comprehensive Cancer Network

- The National Comprehensive Cancer Network (NCCN) 2019 Clinical Practice Guidelines on Prostate Cancer state the following regarding molecular assays:
  - “Men with low or favorable intermediate risk disease may consider the use of the following tumor-based molecular assays: Decipher, Oncotype DX Prostate, Prolaris, and Promark. Retrospective studies have shown that molecular assays performed on prostate biopsy or radical prostatectomy specimens provide prognostic information independent of NCCN or CAPRA risk groups. These include, but are not limited to, likelihood of death with conservative management, likelihood of biochemical progression after radical prostatectomy or external beam therapy, and likelihood of developing metastasis after radical prostatectomy or salvage radiotherapy.”
  - According to NCCN, the Molecular Diagnostic Services Program (MolDX) recommendations stated the following:
    - Decipher: “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. Cover post-RP for 1) pT2 with positive margins; 2) any pT3 disease; 3) rising PSA (above nadir)”
    - “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:

- “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: 

1. “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.”

Literature Review

Review of the most relevant evidence related to Decipher:

1. There is minimal low quality evidence evaluating the use of Decipher Prostate Biopsy as an adjunctive test to accurately predict the risk of progression in patients diagnosed with clinically localized prostate cancer. No definitive conclusions can be drawn about the use of Decipher Prostate Biopsy.

2. There is limited high quality evidence to support the use of Decipher Prostate RP as an adjunctive test to improve risk estimates of recurrence and likelihood of treatment response in high-risk post-radical prostatectomy patients. Majority of the available evidence consists of retrospective case-control and retrospective cohort studies evaluating the strength of the association between the Decipher score and disease recurrence (e.g., metastasis) or disease-associated mortality. Logistic regression analyses showed significant associations between the test and clinical outcome measures. Study results indicated that Decipher reliably discriminates (reasonable AUC and c-index estimates) between men at 5-year risk of metastatic disease progression after RP and in men without disease progression. A number of studies also reported reclassification rates using the Decipher test showing that patient risk could be stratified differently based on Decipher results.

3. However, available estimates are likely subject to bias and confounders due to numerous study limitations that weaken the quality of the individual studies and the evidence base as a whole for each intended use. Study limitations included: considerable patient overlap; short follow-up periods; small number of metastatic events, which lowered study power; bias associated with retrospective/case-control studies; lack of blinding; missing or flawed registry data; sampling issues; and considerable heterogeneity between cases and controls for patient demographic characteristics, disease risk factors, and treatment regimens.

4. There were no direct clinical utility studies available. Based on decision impact studies, it is not clear how results of the Decipher Prostate will impact patient disease management and treatment strategies, and if any changes will translate into improved morbidity and mortality for high-risk PC patients.

Clinical Trials

Ongoing clinical trials indicate that clinical utility studies of Decipher testing are forthcoming. Results of studies directly evaluating clinical utility may provide higher...
quality evidence to better inform clinicians regarding patient selection criteria and appropriate use of the Decipher Prostate Biopsy among patients diagnosed with clinically localized PC who may be appropriate AS candidates, and use of Decipher Prostate RP among post-RP patients who are weighing the risk and benefits of disease management and treatment options.

Ongoing clinical trials can be found at https://clinicaltrials.gov.

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


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


