Test Specific Guidelines

DecisionDx Uveal Melanoma

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Introduction

DecisionDX testing for uveal melanoma is addressed by this guideline.

Procedures Addressed

The inclusion of any procedure code in this table is provided for informational purposes and is not a guarantee of coverage nor an indication that prior authorization is required.

Procedures addressed by this guideline	Procedure codes
DecisionDx-PRAME	81401
DecisionDx-UMSeq	81479
DecisionDx Uveal Melanoma	81552

What Is Uveal Melanoma?

Definition

Uveal melanoma (UM) is a rare cancer of the eye, arising in the choroid, ciliary body or iris of the eye, with about 1500 new cases per year in the US. It accounts for about 5% of all melanomas in the US.[1]

The diagnosis is usually established by clinical assessment combined with ancillary diagnostic testing, using fluorescein angiography and ultrasonography.[2]

Despite relatively high cure rates of the primary tumor following treatment,[3] metastatic disease to the liver has been reported to occur in 20 to 50% of individuals with UM. Median survival after metastasis detection has been reported to be approximately 9 months.[4]

As a result, accurate prognostic assessment for metastatic risk is considered crucial for patient survival. Conventional prognostic evaluation of UM involves clinical and pathologic criteria, such as age, tumor diameter, tumor thickness, ciliary body involvement, tumor cell morphology, and extraocular tumor extension.[4,5]

Some experts have questioned the accuracy of these methods to predict metastasis.[6,7] As such, new molecular techniques examining the genetic composition of tumor cells have been introduced to improve prognostic evaluations potentially allowing for more targeted surveillance and treatment

options for UM. Additionally, it may also facilitate referral of high risk individuals to clinical trials.[7,8]

Test Information

Introduction

DecisionDx-UM is a 15 gene panel that measures gene expression of 12 genes present in ocular melanoma (CDH1, ECM1, EIF1B, FXR1, HTR2B, ID2, LMCD1, LTA4H, MTUS1, RAB31, ROBO1, and SATB1) and 3 control genes (MRPS21, RBM23, and SAP130). This test is designed to assess the risk of metastasis within 5 years.[9]

DecisionDx-UM test results are reported as follows:[9,10]

Class 1A – very low risk (2%) of metastasis within 5 years

Class 1B – intermediate risk (21%) of metastasis within 5 years

Class 2 – high risk (72%) of metastasis within 5 years

DecisionDx-PRAME is a test that can be added on to the DecisionDx-UM assay for additional information regarding prognosis. According to Castle Biosciences,"PRAME [preferentially expressed antigen in melanoma] is usually not expressed in normal adult tissues, but in some cancers, PRAME expression is elevated. Studies have suggested that elevated PRAME expression ("PRAME positive") in a Class 1 uveal melanoma tumor may be associated with an increased risk of metastasis compared to a Class 1 tumor that does not express PRAME ("PRAME negative")." [11]

The manufacturer also offers the DecisionDX-UMSeq test, which is gene sequencing panel including 7 genes (GNAQ, GNA11, CYSLTR2, PLCB4, EIF1AX, SF3B1, and BAP1).[12,13] "This genomic information can be used to help guide your care, and may also become useful in the future as UM scientific research and therapeutics evolve." [12]

Guidelines and Evidence

Introduction

This section includes relevant guidelines and evidence pertaining to DecisionDx testing for uveal melanoma.

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN, 2021) stated the following regarding gene expression for uveal melanoma.[8]

"Biopsy of the primary tumor may provide prognostic information that can help inform frequency of follow-up and may be needed for eligibility for clinical trials.

If biopsy is performed, molecular/chromosomal testing for prognostication is preferred over cytology alone. The risk/benefits of biopsy for prognostic analysis should be carefully considered and discussed."

"For patients who had a biopsy of their primary tumor, both cell histology and certain molecular features have been shown to be prognostic for risk of distant spread and should be used for risk stratification."

Gene expression profiling as described by Onken et al[20] was recommended as part of the stratification in determining the class of the tumor [Class 1A (low risk), Class 1B (medium risk), or Class 2 (high risk)]. This can assist with informing the risk of distant metastasis and recommended surveillance imaging.

"Multivariate analyses have found that class 2 is associated with a 5-fold to 20-fold higher risk of metastasis than class 1."

"PRAME expression, present in about a third of uveal melanomas has also been associated with increased risk of metastasis… [and can be] an indicator of high risk to be used to inform frequency of follow-up."

Selected Relevant Publications

Based on the review of the available peer-reviewed published literature, the DecisionDx-UM 15-gene assay has sufficient evidence for use as a prognostic test in individuals diagnosed with primary, localized uveal melanoma to assist clinicians with predicting disease severity and improving disease management strategies.[3,14-25]

DecisionDX PRAME and DecisionDX-UMSeq

There is currently insufficient evidence regarding use of DecisionDX PRAME.[26-28] No clinical validity or clinical utility studies were identified. There is also no evidence evaluating use of DecisionDX-UMSeq. As a result, no conclusions can be drawn regarding the value and usefulness of these two additional tests.

Criteria

Introduction

Requests for DecisionDX testing for uveal melanoma are reviewed using these criteria.

DecisionDX-UM

DecisionDx-UM testing is considered medically necessary when the following criteria are met:

No previous DecisionDx-UM testing performed after current diagnosis when a result was successfully obtained, AND

Member has primary, localized uveal melanoma, AND

No evidence of metastatic disease, AND

Rendering laboratory is a qualified provider of service per the Health Plan policy.

DecisionDx-PRAME

This test is considered investigational and/or experimental.

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.

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.

DecisionDx-UMSeq

This test is considered investigational and/or experimental.

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.

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