Microarray-Based Gene Expression Profile Testing for Multiple Myeloma Risk Stratification

Description

Multiple myeloma is a genetically complex-and invariably fatal-disease. A host of well-characterized factors related to tumor biology, tumor burden, and patient-centered characteristics are used to stratify patients into high-, intermediate-, and standard-risk categories for prognostic purposes, as well as determining treatment intensity. However, clinical outcomes have varied among patients in the same risk category who received similar therapy. Thus, more specific methods have been sought to classify multiple myeloma; one such method being proposed is the utilization of a microarray-based gene expression profile (GEP) analysis, which serves to reveal the underlying activity of cellular biologic pathways. This method lends itself to a variety of benefits including the ability to risk-stratify patients with multiple myeloma, as well as guide treatment decisions.

OBJECTIVE

The objective of this evidence review is to determine whether risk stratification using a gene expression profile risk score improves the net health outcome in individuals with multiple myeloma.

POLICY STATEMENT

Microarray-based gene expression profile testing for multiple myeloma is considered investigational for all indications.
POLICY GUIDELINES

According to Mayo Clinic recommendations, a large number of prognostic factors have been validated and categorized into 3 main groups: tumor biology, tumor burden, and patient-related factors. These factors must be considered to individualize the choice of therapy in multiple myeloma patients (see Table PG1).

Table PG1. Prognostic Factors in Multiple Myeloma

<table>
<thead>
<tr>
<th>Tumor Biology</th>
<th>Tumor Burden</th>
<th>Patient-Related</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Ploidy</td>
<td>● Durie-Salmon stage</td>
<td>● ECOG Performance Status</td>
</tr>
<tr>
<td>● 17p (p53 deletion)</td>
<td>● International Staging System stage</td>
<td>● Age</td>
</tr>
<tr>
<td>● t(14;16)</td>
<td>● Extramedullary disease</td>
<td>● Renal function</td>
</tr>
<tr>
<td>● t(14;20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● t(4;14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● Deletion 13 on conventional cytogenetics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● Alterations in chromosome 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● t(11;14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● t(6;14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● Lactate dehydrogenase levels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● Plasma cell proliferative rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● Presentation as plasma cell leukemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● High-risk GEP signature(^a)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Mikhael et al (2013).
ECOG: Eastern Cooperative Oncology Group; GEP: gene expression profile.

\(^a\) The Mayo Clinic does not currently recommend or routinely perform GEP analysis in a non-research setting. However, Mikhael et al (2013) have suggested GEP analysis will likely play a greater role in the management of multiple myeloma as evidence develops.

BENEFIT APPLICATION

Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.

Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient's existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.

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FDA REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. The MyPRS™/MyPRS Plus™ GEP70 test was acquired by Quest Diagnostics in December 2016. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

RATIONALE

Summary of Evidence

For individuals who have multiple myeloma who received risk stratification using a gene expression profile (GEP) test, the evidence includes retrospective series that correlate risk scores with survival. Relevant outcomes are progression free survival (PFS), overall survival (OS), disease-specific survival, test validity, and other test performance measures. The microarray-based GEP70 test (MyPRS/MyPRS Plus) has been reported to risk-stratify multiple myeloma patients. Some predictive models in the body of evidence combine risk status as determined by GEP70 test with additional clinical or genetic variables. Patients with a high GEP70 risk score have a substantially increased risk of mortality compared with patients without a high score. However, there is no evidence (from available studies) that this test would add incremental value to existing risk stratification methods; nor have any studies demonstrated the need to prospectively allocate patients to risk-based therapies based on the GEP70 score. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Comprehensive Cancer Network

The National Comprehensive Cancer Network practice guidelines (v.4.2020) on multiple myeloma state that "although GEP [gene expression profiling] is not currently routinely used in clinical practice during diagnostic workup, GEP is a useful tool and may be helpful in selected patients to estimate the aggressiveness of the disease and individualize treatment." The Network offered no specific recommendation for the use of the MyPRS GEP70 test.

Mayo Clinic Stratification of Multiple Myeloma and Risk-Adapted Therapy

Guidelines from the Mayo Clinic (2017) have stated that "if indicated, gene expression profiling may be performed to further understand the behavior of the disease and guide therapy."
U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

Medicare does not have a national coverage determination for this testing. Novitas Solutions retired its local coverage decision on the MyPRS test (L32636) in 2014.32

REFERENCES

32. Novitas Solutions. Medical Policy Update History for Jurisdiction H. 2018; https://www.novitas-solutions.com/webcenter/portal/MedicareJL/pagebyid;jsessionid=BpHN6XYcFavHcd_h7c0VzIvyI46lXrKu1tDjsqFb9UcLQxT2JMnF15284083341-2108564542?contentId=00006151&afrlLoop=4267576608061424%40%40%3F_afrlLoop%3D4267576608061642%26centerWidth%3D100%262525%26contentId%3D00006151%26leftWidth%3D0%262525%26rightWidth%3D0%26525%26showFooter%3Dfalse%26showHeader%3Dfalse%2626_adf.ctrl-state%3Dz281w4k0y_4 Accessed August 20, 2020.