PLASMA CELL PROLIFERATIVE DISORDERS

PHYSICIAN CHOICE GUIDED BY MAYO STRATIFICATION FOR MYELOMA AND RISK-ADAPTED THERAPY (mSMART)
STRATIFYING RISK AND INDIVIDUALIZING TREATMENT

Multiple myeloma is increasingly recognized as more than one disease, characterized by marked cytogenetic, molecular, and proliferative heterogeneity.

The Mayo Stratification for Myeloma and Risk-Adapted Therapy (mSMART) algorithm stratifies patients into low, intermediate, standard or high-risk categories. This genetically determined risk classification also plays an important role in individualizing a patient’s treatment strategy.

PATIENTS WITH MONOCLONAL PROTEIN DISORDERS

### MONOCLONAL PROTEIN ISOTYPE

- **In addition to the below differential diagnoses, also consider B-Cell Lymphoproliferative Disorders or Waldenström Macroglobulemia**

#### CHARACTERISTICS

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>PREVALENCE IN PATIENTS WITH MONOCLONAL GAMMOPATHY</th>
<th>PROGRESSION TO MULTIPLE MYELOMA</th>
<th>BONE MARROW MONOCLONAL PLASMA CELLS</th>
<th>SERUM M-SPIKE</th>
<th>END-ORGAN MANIFESTATIONS (CRAB)**</th>
<th>TREATMENT REQUIRED</th>
<th>OTHER PLASMA CELL DISORDERS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE (MGUS)</strong></td>
<td>58%</td>
<td>10 - 15% within 10 years</td>
<td>&lt;10%</td>
<td>&lt;3g/dL</td>
<td>No</td>
<td>No</td>
<td>Amyloidosis, Lymphoplasmocytic disorders, Plasmacytoma and POEMS syndrome</td>
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<tr>
<td><strong>SMOLDERING MULTIPLE MYELOMA (SMM)</strong></td>
<td>4%</td>
<td>50% over 5 years</td>
<td>≥10%</td>
<td>≥3g/dL</td>
<td>No</td>
<td>Clinical trials available</td>
<td></td>
</tr>
<tr>
<td><strong>MULTIPLE MYELOMA (MM)</strong></td>
<td>17.5%</td>
<td>5 year survival rate is ~30%</td>
<td>≥10%*</td>
<td>Variable (typically ≥3g/dL)</td>
<td>Yes</td>
<td>Yes</td>
<td>Plasma cell leukemia</td>
</tr>
<tr>
<td><strong>AMYLOIDOSIS</strong></td>
<td>10%</td>
<td>Uncommon</td>
<td>Any %</td>
<td>Any amount</td>
<td>Yes</td>
<td></td>
<td>NA</td>
</tr>
</tbody>
</table>

*PATIENTS WITH ANY ONE OF THESE 3:*
- >60% plasma cells
- >100 Kappa/Lambda Free Light Chain ratio
- >1 MRI lesion

**KEY**
- C - Hypercalcemia
- R - Renal Insufficiency
- A - Anemia
- B - Bone Disease
**PHYSICIAN CHOICE GUIDED BY MAYO STRATIFICATION FOR MYELOMA AND RISK-ADAPTED THERAPY (MSMART)**

**TRADITIONAL APPROACH**

- Chromosome Analysis
- FISH
- Flow Cytometry
- Gene Expression Profile (GEP)

Physician consolidates test results

Physician selects treatment option

Treatment/Therapy Options

VCD  VTD  VMP  MPR  MPT  VTD  VMP

**MAYO CLINIC APPROACH**

- mSMART

Includes flow cytometry and FISH testing

Risk Stratification
- High
- Intermediate
- Low

mSMART guides physician to best treatment option***

**INCLUDED IN THE mSMART TEST (MAYO ID: MSMRT):**

a. Plasma cell DNA content and proliferation flow cytometry testing (PCPRO) provide:
   - Plasma cell clonality
   - Plasma cell proliferation
   - DNA index
   - Percent polyclonal plasma cells in total plasma cells

b. Plasma Cell Proliferative FISH testing using cytoplasmic immunoglobulin staining method and probes to detect:
   - t(11;14)(q13;q32) / +11
   - 14q32 / IGH rearrangement
   - Reflex: t(4;14)(p16.3;q32)
   - Reflex: t(6;14)(p21;q32)
   - Reflex: t(14;16)(q32;q23)
   - Reflex: t(14;20)(q32;q12)
   - +3 / +7
   - +9 / +15
   - -17 / 17p deletion / +17
   - 1q gain / 1p loss / +1
   - 8q24 / MYC rearrangement
   - -13 / 13q deletion

Notes: FISH testing will only be performed if PCPRO testing identifies sufficient plasma cells

Chromosome analysis is available to rule out therapy-related MDS

**RISKS WITH TRADITIONAL APPROACH**

- Wrong risk stratification identified
- Suboptimal treatment option selected
- Wasted health care expenses
- Chromosome Analysis is poorly reimbursed

**KEY**

- VCD - bortezomib + cyclophosphamide + dexamethasone
- VRD - bortezomib + lenalidomide + dexamethasone
- Rd - lenalidomide + low-dose dexamethasone
- KRD - carfilzomib + lenalidomide and dexamethasone
- VD - bortezomib + dexamethasone
- VTD - bortezomib + thalidomide + dexamethasone
- MPT - melphalan + prednisone + thalidomide
- MPR - melphalan + prednisone + lenalidomide
- VMP - bortezomib + melphalan + prednisone

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COLLEGIAL ACCESS TO MAYO CLINIC CLINICIANS, LABORATORIANS, AND GENETIC COUNSELORS

Mayo Medical Laboratories supports the local delivery of health care services, so when assistance with testing options, result interpretation, or case review and coordination is needed, Mayo Clinic clinicians, laboratorians, and genetic counselors are available to provide assistance. This rapport also provides the opportunity for general practice discussions among colleagues.

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FOR MORE INFORMATION ABOUT mSMART TESTING, VISIT  
MayoMedicalLaboratories.com/myeloma