Treatment of Relapsed Myeloma
Mayo Consensus

Scottsdale, Arizona
Rochester, Minnesota
Jacksonville, Florida
mSMART

Mayo Stratification for Myeloma And Risk-adapted Therapy

Relapsed Myeloma
Multiple myeloma is increasingly recognized as a heterogenous disease, characterized by marked cytogenetic, molecular, and proliferative variability.

Availability of novel agents are rapidly redefining the treatment paradigm for patients with myeloma and with multiple available treatment options.

This is a consensus opinion that takes into account the various risk factors and the treatment strategies currently available.

The general approach is presented below. However, clinical trials must be considered and are preferred at every level.

Management decisions should take into account the age as well as other co-morbidities such as renal failure, diabetes and presence or absence of coexisting amyloidosis.
## mSMART 2.0: Classification of Relapsed MM

<table>
<thead>
<tr>
<th>High-Risk</th>
<th>Intermediate-Risk</th>
<th>Standard-Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Relapse &lt;12 months from transplant or progression within first year of diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- FISH</td>
<td>- FISH</td>
<td>All others including:</td>
</tr>
<tr>
<td>- Del 17p</td>
<td>- t(4;14)</td>
<td>- Trisomies</td>
</tr>
<tr>
<td>- t(14;16)</td>
<td>- 1q gain</td>
<td>- t(11;14)</td>
</tr>
<tr>
<td>- t(14;20)</td>
<td>- High PC S-phase</td>
<td>- t(6;14)</td>
</tr>
<tr>
<td>- High risk GEP</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

Abbreviations for Major Regimens

• KRd, carfilzomib, lenalidomide, dexamethasone
• KPd, carfilzomib, pomalidomide, dexamethasone
• CyBord, cyclophosphamide, bortezomib, dexamethasone
• IRd, ixazomib, lenalidomide, dexamethasone
• ICd, ixazomib, cyclophosphamide, dexamethasone
• Rd-Elo, lenalidomide, dexamethasone, elotuzumab
• Pom-dex, pomalidomide, dexamethasone
• PVd, pomalidomide, bortezomib, dexamethasone
• Dara, daratumumab
• DVd, daratumumab, bortezomib, dexamethasone
• DRd, daratumumab, lenalidomide, dexamethasone
First Relapse Off-Study

On maintenance

Fit Patients*

KPd or DVd if Rev maintenance
DRd if Vel maintenance

Indolent Relapse* or Frail patients

DVd or ICd if Rev maintenance
IRd or DRd if Vel maintenance

Off-therapy/ Unmaintained*

Fit Patients*

KRd or DRd

Indolent Relapse* or Frail patients

IRd or ERd

*Consider salvage auto SCT in patients eligible for ASCT who have not had transplant before; Consider 2nd auto SCT if eligible and >18 months unmaintained or >36 months maintained response to first auto

### Second or later Relapse Off-Study

**Not Plasma Cell Leukemia (PCL) or Similar extramedullary disease (EMD)**

<table>
<thead>
<tr>
<th>Category</th>
<th>Regimen Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single Refractory</strong>*</td>
<td>Refractory to Imid or PI but not both</td>
</tr>
<tr>
<td></td>
<td>- Bortezomib and/or Ixazomib</td>
</tr>
<tr>
<td></td>
<td>- Lenalidomide</td>
</tr>
<tr>
<td></td>
<td>DVd if refractory to Imid</td>
</tr>
<tr>
<td></td>
<td>DRd if refractory to PI</td>
</tr>
<tr>
<td><strong>Dual Refractory</strong>*</td>
<td>Pom-based regimen (Pom-Dex or Pom-Cyclo-Dex) plus daratumumab**</td>
</tr>
<tr>
<td></td>
<td>Or</td>
</tr>
<tr>
<td></td>
<td>KPD/KRD</td>
</tr>
<tr>
<td><strong>Triple Refractory</strong>*</td>
<td>Pom-based regimen (Pom-Dex or Pom-Cyclo-Dex) plus daratumumab**</td>
</tr>
<tr>
<td></td>
<td>Or</td>
</tr>
<tr>
<td></td>
<td>KPd/KRd</td>
</tr>
<tr>
<td></td>
<td>Dara-based regimen;**</td>
</tr>
<tr>
<td></td>
<td>or</td>
</tr>
<tr>
<td></td>
<td>Alkylator-based regimen if alkylator naïve; or</td>
</tr>
<tr>
<td></td>
<td>Proteasome inhibitor plus panobinostat</td>
</tr>
</tbody>
</table>

*Auto transplant is an option, if transplant candidate and feasible; **If known to be refractory to Daratumumab as single agent, use elotuzumab instead

---

Second or later Relapse – Off-Study

Quadruple-refractory (Lenalidomide, Pomalidomide, Bortezomib, and Carfilzomib)

VDT-PACE* x 2 cycles if possible.*
Auto transplant if transplant candidate; if not, treat with regimens that the patient is not known to be refractory to (eg., daratumumab-containing regimen; panobinostat-containing regimen; bendamustine; alkylator-containing combination if not alkylator refractory; or anthracycline containing regimen such as RAD, VDD, PAD, or CHOP)

*CVAD or similar regimen can be used in place of VDT-PACE in older patients or patients with poor functional status

Second or later Relapse – Off-Study

Secondary PCL or extensive EMD

VDT-PACE x 2 cycles;*
Auto transplant if transplant candidate; if not maintain with one of the regimens listed that the patient is not known to be refractory to (eg., daratumumab-containing regimen; alkylator-containing combination if not alkylator refractory; or anthracycline containing regimen such as RAD, VDD, PAD, or CHOP)

*CVAD or similar regimen can be used in place of VDT-PACE in older patients or patients with poor functional status