mSMART

*Mayo Stratification for Myeloma And Risk-adapted Therapy*

Newly Diagnosed Myeloma
mSMART

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

• The result is widely varied outcome ranging from low to very high risk.

• Treatment is evolving rapidly as more effective agents and combinations become available.

• mSMART (Mayo Stratification for Myeloma And Risk-adapted Therapy) is a consensus opinion that takes into account genetically determined risk status and the various treatment strategies currently available.

• Risk stratification and individualizing treatment options is complex and based not just on the cytogenetic classification presented here, but also on various host factors, disease stage, and a variety of other prognostic factors.

• Therefore we recommend all patients with newly diagnosed myeloma be seen at least once at a referral center with expertise in the disease.

mSMART

• The general approach is presented below (mSMART – off-study). However, clinical trials must be considered and are preferred at every level (mSMART – on-study).

• Management decisions are also varied depending on renal function and presence or absence of coexisting amyloidosis.
mSMART 2.0: Classification of Active MM

High-Risk
- FISH
  - Del 17p
  - t(14;16)
  - t(14;20)
- GEP
  - High risk signature

Intermediate-Risk$^a$
- FISH
  - t(4;14)$^d$
  - 1q gain
  - High PC S-phase$^f$

Standard-Risk$^{a,b}$
- All others including:
  - Trisomies
  - t(11;14)$^e$
  - t(6;14)

$a$ Note that a subset of patients with these factors will be classified as high-risk by GEP
$b$ LDH >ULN and beta-2 M > 5.5 may indicate worse prognosis; $^c$Trisomies may ameliorate
$d$ Prognosis is worse when associated with high beta-2 M and anemia
$e$ t(11;14) may be associated with plasma cell leukemia; $^f$ Cut-offs vary

In patients treated initially with Rd, continuing treatment until progression is an option for patients responding well with low toxicities; 

Dex is usually discontinued after first year

Clinical trials strongly recommended as the first option

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mSMART – Off-Study

Transplant Eligible

<table>
<thead>
<tr>
<th>Standard-Risk</th>
<th>Intermediate-Risk</th>
<th>High-Risk</th>
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</thead>
<tbody>
<tr>
<td>t(11;14), t(6;14), Trisomies</td>
<td>t(4;14)</td>
<td>Del 17p, t(14;16), t(14;20)</td>
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- 4 cycles of VRd
- Collect Stem Cells
- Autologous stem cell transplant (preferred)
- Len maintenance for at least 2 years
- VRd x 4 cycles
- Autologous Stem Cell Transplant (ASCT); Consider tandem ASCT
- Bortezomib-based maintenance for 2 years
- Carfilzomib or Bortezomib-based maintenance for 2 years

**a** If age > 65 or > 4 cycles of VRd, consider mobilization with G-CSF plus cytoxan or plerixafor

**b** Duration based on tolerance; consider risks and benefits for treatment beyond 2 years

**c** Continuing Rd for patients responding to Rd and with low toxicities