

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 3.0: Classification of Active MM

High-Risk

■ High Risk genetic Abnormalities ^{a,b}

- t(4;14)
- t(14;16)
- t(14;20)
- Del 17p
- p53 mutation
- Gain 1q

- RISS Stage 3
- High Plasma Cell S-phase^c
- GEP: High risk signature

- Double Hit Myeloma: Any 2 high risk genetic abnormalities
- Triple Hit Myeloma: 3 or more high risk genetic abnormalities

Standard-Risk^a

All others including:

- Trisomies
- t(11;14)^d
- t(6;14)

^aTrisomies may ameliorate

^b By FISH or equivalent method

^c Cut-offs vary

^d t(11;14) may be associated with plasma cell leukemia

Abbreviations for Major Regimens

- VRd, bortezomib, lenalidomide, dexamethasone
- DRd, daratumumab, lenalidomide, dexamethasone
- Dara-VRd, daratumumab, bortezomib, lenalidomide, dexamethasone

Dosing for Major Regimens

- Please refer to: <https://onlinelibrary.wiley.com/doi/full/10.1002/ajh.25791>

mSMART – Off-Study *Transplant Ineligible*

t(11;14), t(6;14), Trisomies



DRd^a

Or

**VRd for ~9 cycles followed by Len
maintenance^a**

t(4;14), t(14;16), t(14;20), Del 17p



DRd^a

Or

**VRd for ~9 cycles followed by bortezomib-
based maintenance^a**

^a *Duration is usually until progression, based on tolerance*

VRd, Bortezomib, lenalidomide, dexamethasone; DRd, daratumumab, lenalidomide, dexamethasone

mSMART – Off-Study *Transplant Eligible*

t(11;14), t(6;14), Trisomies

4 cycles of VRd

Collect Stem Cells ^a

Autologous stem cell
transplant (preferred)

VRd x 4 cycles

Len maintenance ^b

Len until
progression;
delayed ASCT ^b

**Del 17p, Gain 1q
t(4;14), t(14;16),**

4 cycles of Dara-VRd

Autologous Stem Cell
Transplant (ASCT);
Consider tandem ASCT

Bortezomib-based
maintenance till
progression ^b

**Double or Triple Hit
Myeloma**

4 cycles Dara-VRd

Autologous Stem Cell
Transplant (ASCT);
Consider tandem ASCT

Bortezomib-based
maintenance till
progression ^b

^a If age >65 or > 4 cycles of VRd, consider mobilization with G-CSF plus cytoxan or plerixafor; ^b Duration usually until progression based on tolerance

VRd, Bortezomib, lenalidomide, dexamethasone; Dara, daratumumab