

# **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



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- The general approach is presented below (mSMART off-study). However, <u>clinical trials must be considered and are preferred</u> 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<sup>c</sup>
- •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<sup>a</sup>

All others including:

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

<sup>&</sup>lt;sup>a</sup>Trisomies 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



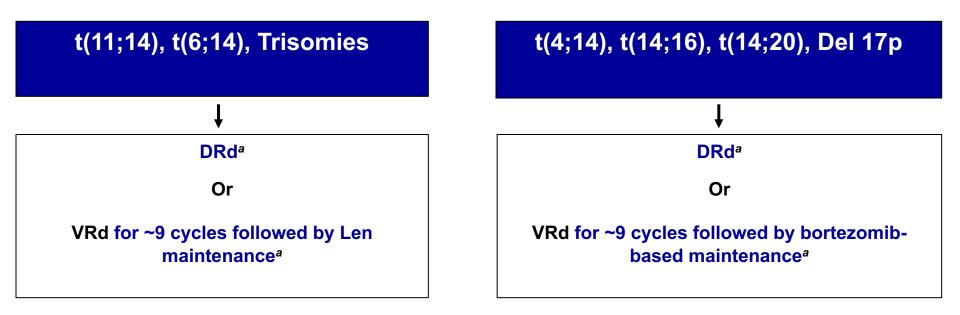
## **Dosing for Major Regimens**

Please refer to: <a href="https://onlinelibrary.wiley.com/doi/full/10.1002/ajh.25791">https://onlinelibrary.wiley.com/doi/full/10.1002/ajh.25791</a>



### mSMART — Off-Study

#### Transplant Ineligible

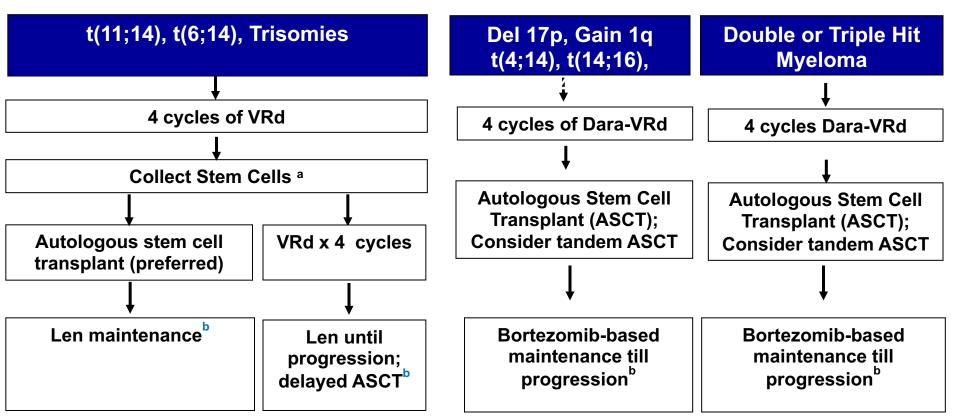


VRd, Bortezomib, lenalidomide, dexamethasone; DRd, daratumumab, lenalidomide, dexamethasone

<sup>&</sup>lt;sup>a</sup> Duration is usually until progression, based on tolerance



#### mSMART — Off-Study Transplant Eligible



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

VRd, Bortezomib, lenalidomide, dexamethasone; Dara, daratumumab

Dispenzieri et al. Mayo Clin Proc 2007;82:323-341; Kumar et al. Mayo Clin Proc 2009 84:1095-1110; Mikhael et al. Mayo Clin Proc 2013;88:360-376. v19 //last reviewed Feb 2021