MAYO CLINIC

mSMART

Mayo Stratification for Myeloma And Risk-adapted Therapy

Newly Diagnosed Myeloma

Version 21 //last reviewed Jan2024

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- 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

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. v21 //last reviewed Jan 2024

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- 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, peripheral neuropathy, and presence or absence of coexisting amyloidosis.

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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
  - Chromosome 1 abnormalities (Gain or Amp 1q; or Del 1p)[c]
- RISS Stage 3
- High Plasma Cell S-phase[d]
- 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

All others including:

- Trisomies
- t(11;14)[e]
- t(6;14)

[a] Presence of concurrent trisomies may ameliorate the high risk effect
[b] By FISH or equivalent method
[c] Lower impact with isolated gain 1q without other concurrent high risk abnormalities on prognosis
[d] Cut-offs vary
[e] t(11;14) may be associated with plasma cell leukemia

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Abbreviations for Major Regimens

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

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Dosing for Major Regimens

Refer to: https://onlinelibrary.wiley.com/doi/10.1002/ajh.26590

v21 //last reviewed Jan 2024; Rajkumar SV. Am J Hematol 2022; 97:1086-1107

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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, Gain/Amp 1q, Del 1p

↓

DRd[a]

Or

VRd for ~9 cycles followed by bortezomib plus lenalidomide maintenance[a]

[a] Duration is usually until progression, based on tolerance

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

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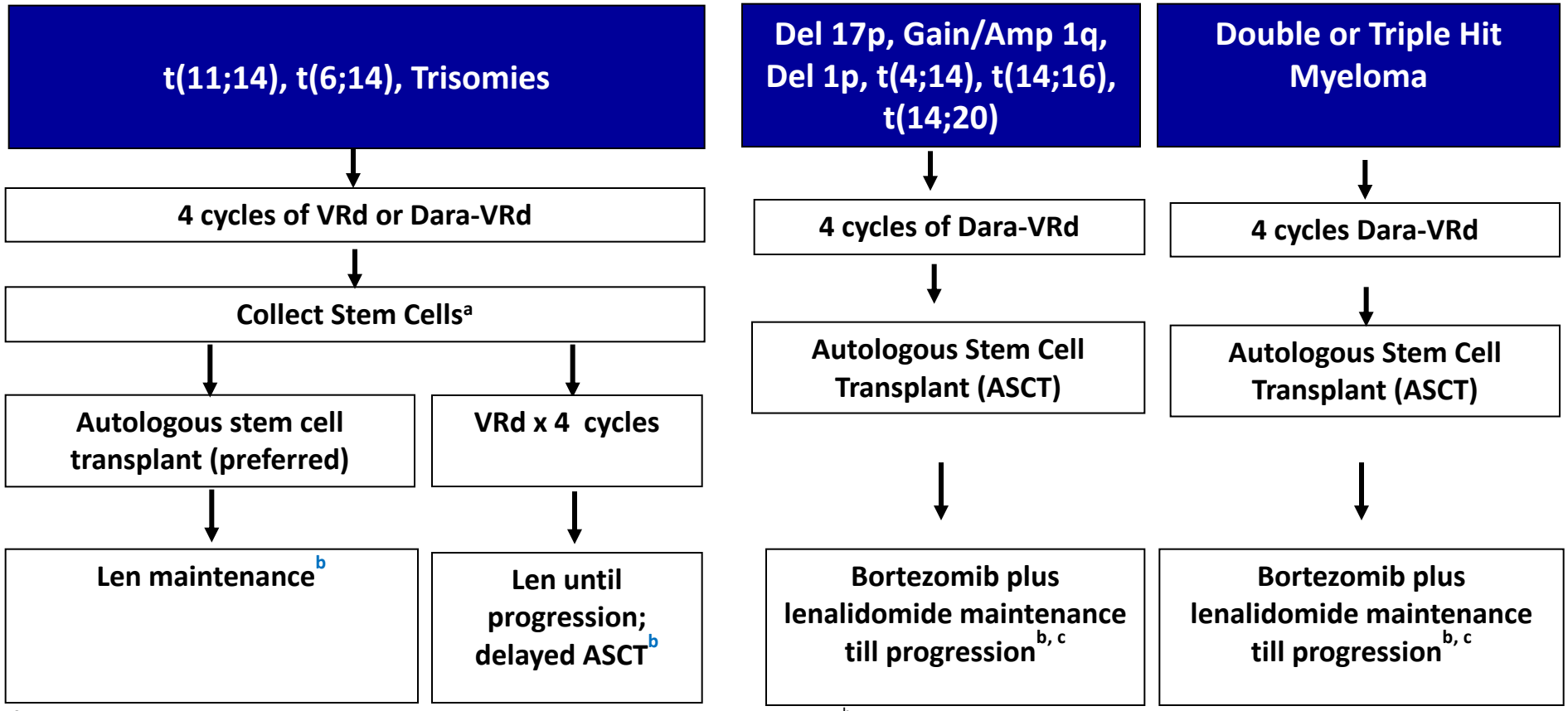
mSMART – Off-Study

Transplant Eligible



[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; [c] In patients with grade 2 or higher neuropathy at baseline, and for patients in whom bortezomib needs to be dose reduced or discontinued due to neuropathy, consider carfilzomib instead.

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. v21 //last reviewed Jan 2024