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mSMART

Mayo Stratification for Myeloma And Risk-adapted Therapy

Newly Diagnosed Myeloma

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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. v20 //last reviewed March 2022

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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
  - 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)

[a] Trisomies may ameliorate
[b] By FISH or equivalent method
[c] Cut-offs vary
[d] 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

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

Rajkumar SV. Am J Hematol 2020;95:548-567. Last reviewed March 2022

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mSMART – Off-Study

Transplant Ineligible

t(11;14), t(6;14), Trisomies	t(4;14), t(14;16), t(14;20), Del 17p, Gain 1q
↓	↓
DRd[a] Or VRd or ~9 cycles followed by Len maintenance[a]	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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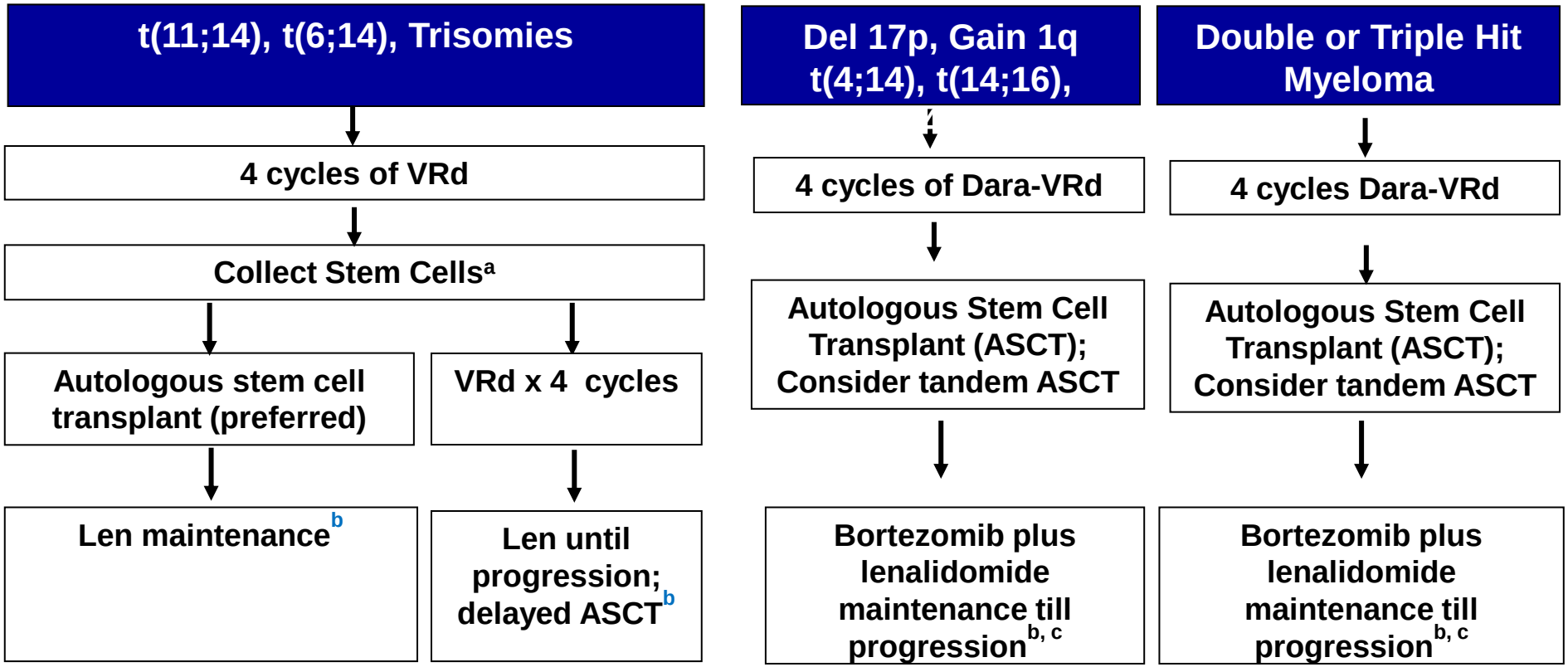
mSMART – Off-Study

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. v20 //last reviewed March 2022