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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. v14 //last reviewed July 2016

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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 and presence or absence of coexisting amyloidosis.

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. v13 v14 //last reviewed July 2016

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mSMART 2.0: Classification of Active MM

High-Risk

- FISH[c]
  - 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

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mSMART – Off-Study

Transplant Ineligible

Standard-Risk	Intermediate-Risk	High-Risk
t(11;14), t(6;14), Trisomies	t(4;14)	Del 17p, t(14;16), t(14;20)
↓	↓	↓
VRd for ~12 months; If age ≥75 or frail: Rd [a]	VRd for ~12 months	VRd[c] for ~12 months
↓	↓	↓
Rd x 1 year [a, b]	Bortezomib-based maintenance for minimum of 1 year	Bortezomib-based maintenance for minimum of 1 year

[a] *In patients treated initially with Rd, continuing treatment until progression is an option for patients responding well with low toxicities;*
[b] *Dex is usually discontinued after first year*
[c] *Clinical trials strongly recommended as the first option*

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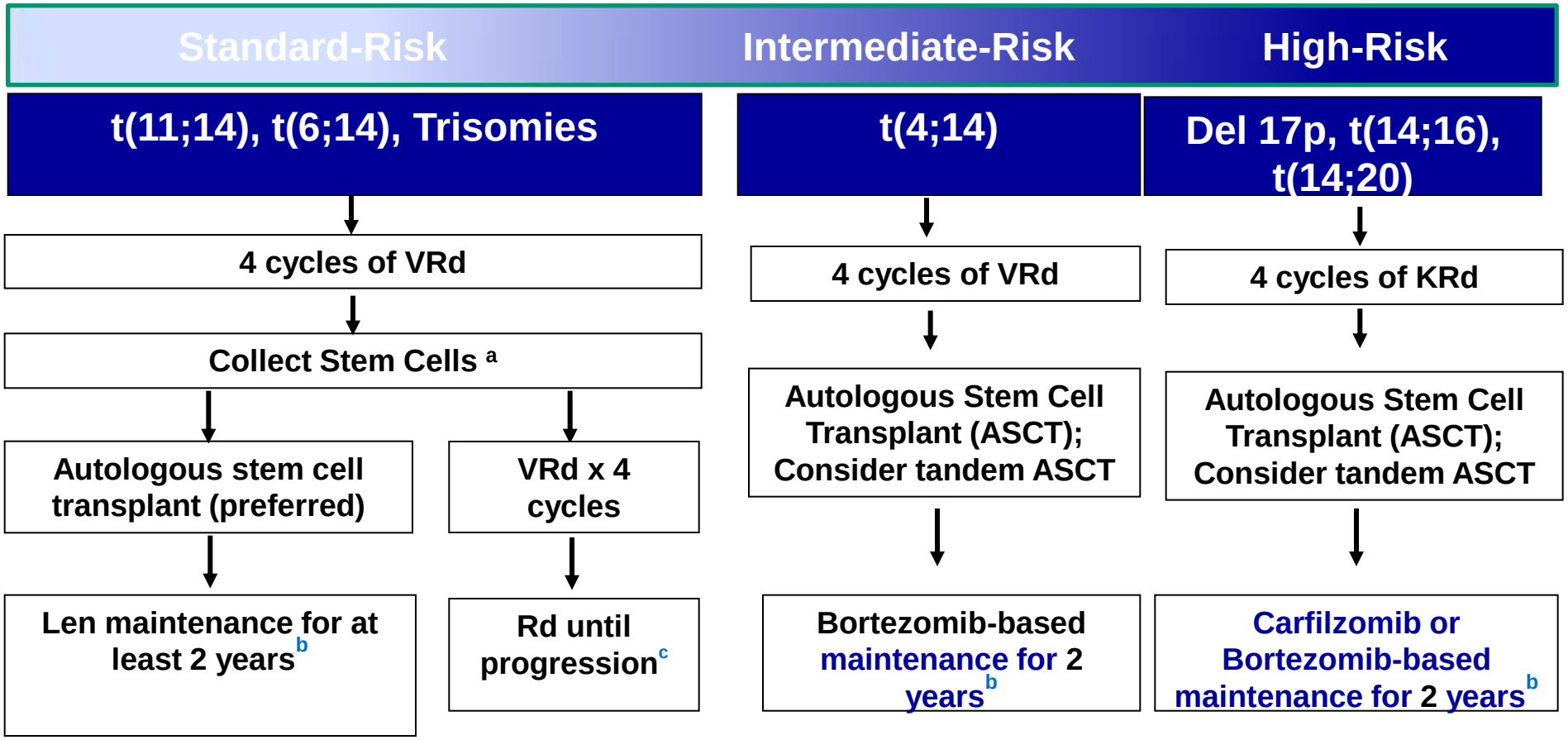
mSMART – Off-Study

Transplant Eligible



a *If age >65 or > 4 cycles of VRd, consider mobilization with G-CSF plus cytoxan or plerixafor*
b *Duration based on tolerance; consider risks and benefits for treatment beyond 2 years*
c *Continuing Rd for patients responding to Rd and with low toxicities*

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