Treatment of Relapsed Myeloma
Mayo Consensus

Scottsdale, Arizona

Rochester, Minnesota

Jacksonville, Florida

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mSMART

Mayo Stratification for Myeloma And Risk-adapted Therapy

Relapsed Myeloma

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- Multiple myeloma is increasingly recognized as a heterogenous disease, characterized by marked cytogenetic, molecular, and proliferative variability.
- Availability of novel agents are rapidly redefining the treatment paradigm for patients with myeloma and with multiple available treatment options.
- This is a consensus opinion that takes into account the various risk factors and the treatment strategies currently available.
- The general approach is presented below. However, clinical trials must be considered and are preferred at every level.
- Management decisions should take into account the age as well as other co-morbidities such as renal failure, diabetes and presence or absence of coexisting amyloidosis.

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mSMART 2.0: Classification of Relapsed MM

High-Risk

- Relapse <12 months from transplant or progression within first year of diagnosis
- FISH
  - Del 17p
  - t(14;16)
  - t(14;20)
- High risk GEP

Intermediate-Risk

- FISH
  - t(4;14)
  - 1q gain
- Complex karyotype
- Metaphase Deletion 13 or hypodiploidy
- High PC S-phase

Standard-Risk

All others including:

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

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.

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First Relapse Off-Study

Relapsing after Auto Transplant

On Maintenance

CyBorD if Rev maintenance*; Rd, or KRd if Vel maintenance*

Off-therapy/ Unmaintained

Rd or CyBorD if standard-risk*; CyBorD or VRd if high risk*

Relapsing after Non-Transplant Therapy

On Therapy/ Maintenance

Not Eligible for ASCT

CyBorD if Rev maintenance; Rd, or KRd if Vel maintenance

Transplant Eligible

Auto SCT

Off-therapy/ Unmaintained

Not Eligible for ASCT

Repeat first-line Rx if remission off therapy is >12months; If not, CyBorD if relapsing after ImiD based Rx; otherwise Pom/dex or KRd

*Consider 2nd auto if eligible and >18 months unmaintained or >36 months maintained response to first auto

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Second or later Relapse* Off-Study

Not Plasma Cell Leukemia (PCL) or Similar extramedullary disease (EMD)

Dual-Refractory (Bortezomib and Lenalidomide)**	Triple-Refractory (Bortezomib, Lenalidomide and Carfilzomib)**	Triple-Refractory (Bortezomib, Len, and Pomalidomide)**
↓	↓	↓
KRd or Pom/dex to maximum response or 18 months, then Rd	PCD, PVD or Car-Pom-Dex to maximum response or 18 months, then Pom/dex	KRd or Car-Pom-Dex to maximum response or 18 months, then Rd or Pom/dex

*** If single refractory, refer to First Relapse algorithm; **Auto transplant is an option, if transplant candidate and feasible; Doublets such as Cylco-Pred, Pd or Kd could be considered in patients with indolent disease**

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Second or Higher Relapse – Off-Study

Secondary PCL or extensive EMD

↓

**VDT-PACE x 2 cycles;*
Auto transplant if transplant candidate; if not maintain with one of the regimens listed that the patient is not known to be refractory to (VRd, VCd, KRd, PVd, or Car-Pom-Dex)**

Quadruple-refractory (Lenalidomide, Pomalidomide, Bortezomib, and Carfilzomib)

↓

VDT-PACE* x 2 cycles if possible.* Auto transplant if transplant candidate; if not, consider alkylator-containing combination if not alkylator refractory or treat with anthracycline containing regimen such as RAD, VDD, PAD, or CHOP**

***CVAD or similar regimen can be used in place of VDT-PACE in older patients or patients with poor functional status**
**** Other options to consider in fit patients: bendamustine or panobinostat containing regimens**