Treatment of Relapsed Myeloma
Mayo Consensus

Scottsdale, Arizona

Rochester, Minnesota

Jacksonville, Florida

MAYO CLINIC

mSMART

Mayo Stratification for Myeloma And Risk-adapted Therapy

Relapsed Myeloma

v6 //last reviewed May 2020; Dingli et al. Mayo Clin Proc 2017;92(4):578-59

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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: Classification of Relapsed MM

High-Risk

- Relapse <12 months from transplant or progression within first year of diagnosis
- FISH
  - Del 17p
  - t(4;14)
  - 1q gain
  - t(14;16)
  - t(14;20)
- High risk GEP
- High PC S-phase

Standard-Risk

All others including:

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

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Abbreviations for Major Regimens

- KRd, carfilzomib, lenalidomide, dexamethasone
- KPd, carfilzomib, pomalidomide, dexamethasone
- CyBord, cyclophosphamide, bortezomib, dexamethasone
- IRd, ixazomib, lenalidomide, dexamethasone
- ICd, ixazomib, cyclophosphamide, dexamethasone
- Rd-Elo, lenalidomide, dexamethasone, elotuzumab
- Pom-dex, pomalidomide, dexamethasone
- PVd, pomalidomide, bortezomib, dexamethasone
- Dara, daratumumab
- DVd, daratumumab, bortezomib, dexamethasone
- DRd, daratumumab, lenalidomide, dexamethasone
- Isa-Pd, Isatuximab, pomalidomide, dexamethasone

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Dosing for Major Regimens

- Refer to: https://onlinelibrary.wiley.com/doi/epdf/10.1002/ajh.25791

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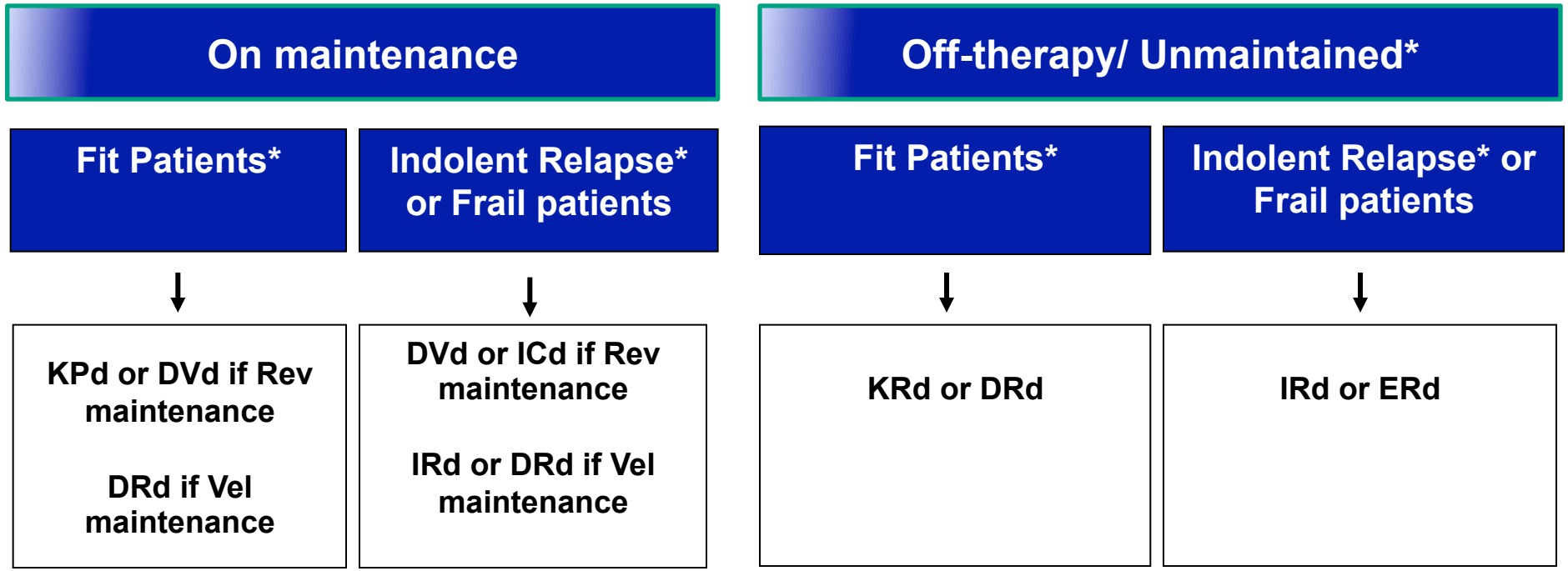
First Relapse Off-Study



*Consider salvage auto SCT in patients eligible for ASCT who have not had transplant before; Consider 2nd auto SCT 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)

Single Refractory*	Dual Refractory*	Triple Refractory*	Triple Refractory*
• Refractory to Imid or PI but not both	• Bortezomib and/or Ixazomib • Lenalidomide	• Bortezomib and/or Ixazomib • Lenalidomide • Carfilzomib	• Bortezomib and/or Ixazomib • Lenalidomide • Pomalidomide
↓	↓	↓	↓
DVd if refractory to Imid DRd if refractory to PI**	Pom-Dex *plus* daratumumab or isatuximab ** Or KPd/KRd	Pom-Dex *plus* daratumumab/ isatuximab** or Pom-Cyclo-Dex	Dara-based regimen;** or Alkylator-based regimen if alkylator naïve; or Proteasome inhibitor plus panobinostat

*Auto transplant is an option, if transplant candidate and feasible; **If known to be refractory to Daratumumab as single agent, use elotuzumab instead

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Second or later Relapse – Off-Study

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

VDT-PACE* x 2 cycles if possible.*
Auto transplant if transplant candidate; if not, treat with regimens that the patient is not known to be refractory to (eg., daratumumab-containing regimen; selinexor-pomalidomide-dexamethasone; panobinostat-containing regimen; bendamustine; alkylator-containing combination if not alkylator refractory; or 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**

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Second or later 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 (eg., daratumumab-containing regimen; alkylator-containing combination if not alkylator refractory; or 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**