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mSMART

Mayo Stratification for Myeloma And Risk-adapted Therapy

Relapsed Myeloma

Version 7. Last reviewed Feb 2023

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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 or 1q amp
  - t(14;16)
  - t(14;20)
  - 1p del
  - p53 mutation
- 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 Drug Classes and Regimens

- Anti CD38 moAB, daratumumab or isatuximab
- KRd, carfilzomib, lenalidomide, dexamethasone
- KPd, carfilzomib, pomalidomide, dexamethasone
- PI-Cd, Bortezomib or carfilzomib, plus cyclophosphamide, dexamethasone
- IRd, ixazomib, lenalidomide, dexamethasone
- ICd, ixazomib, cyclophosphamide, dexamethasone
- EPd, elotuzumab, pomalidomide, dexamethasone
- PI plus Pd, Bortezomib or carfilzomib plus pomalidomide, dexamethasone
- PVd, pomalidomide, bortezomib, dexamethasone
- DRd, daratumumab, lenalidomide, dexamethasone
- DVd, daratumumab, bortezomib, dexamethasone
- DPd, daratumumab, pomalidomide, dexamethasone
- Isa-Pd, Isatuximab, pomalidomide, dexamethasone
- Isa-Kd, Isatuximab, carfilzomib, dexamethasone

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Dosing for Major Regimens

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

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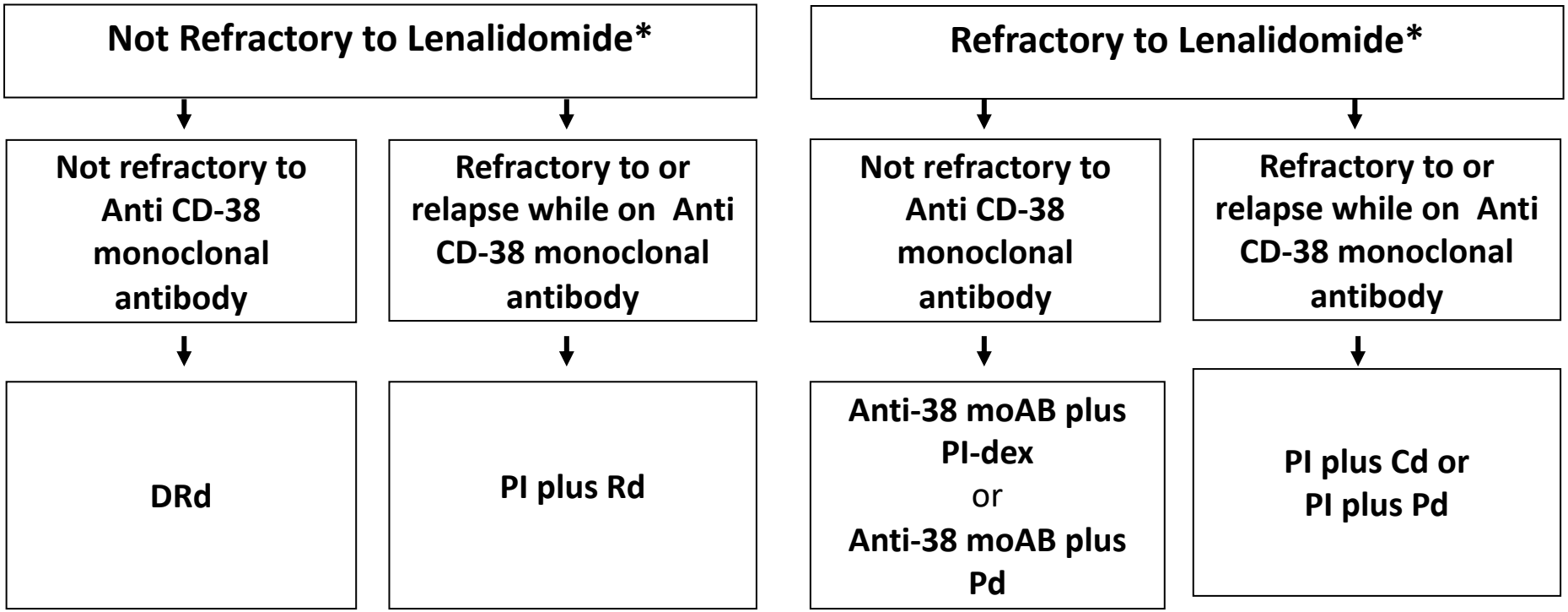
First Relapse
Off-Study



***Consider salvage ASCT in patients eligible for ASCT who have not had transplant before**

PI, proteasome inhibitor; Preferred PI is bortezomib or carfilzomib
moAB, monoclonal antibody: daratumumab or isatuximab

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Second or later Relapse

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

Off-Study Treatment Options

Triple Class Refractory, Type 1*

Refractory to:

- Bortezomib
- Lenalidomide
- Anti CD38 moAB

↓

KPd

KCd

Venetoclax -based therapy if t(11;14)

Triple Class Refractory, Type 2*

Refractory to:

- Bortezomib and Carfilzomib
- Lenalidomide
- Anti CD38 moAB

↓

PCd

EPd

Venetoclax-based therapy if t(11;14)

Triple Class Refractory, Type 3*

Refractory to:

- Bortezomib & Carfilzomib
- Lenalidomide & Pomalidomide
- Anti CD38 moAB

↓

Anti BCMA CAR-T or Bispecific

Venetoclax-based therapy if t(11;14)

*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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Refractory MM

Refractory to IMIDs (Lenalidomide and Pomalidomide), PIs Bortezomib and Carfilzomib), Alkylators, CD38, and BCMA

Options

- Another anti-BCMA treatment approach
- Non-BCMA immunotherapy (eg., cevostamab, talquetamab on clinical trial)
- Selinexor-based regimen
- VDT-PACE
- Alkylator or Bendamustine-based regimens

*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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Secondary PCL or extensive EMD

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VDT-PACE or similar to debulk x 1-2 cycles;*
Then: Auto transplant if transplant candidate, or BCMA approach, or Venetoclax-based therapy for t(11;14)

*CVAD or similar regimen can be used in place of VDT-PACE in older patients or patients with poor functional status