

mSMART

Mayo Stratification for Myeloma And Risk-adapted Therapy

Relapsed Myeloma

mSMART

- Multiple myeloma is increasingly recognized as a heterogeneous disease, characterized by marked cytogenetic, molecular, and proliferative variability.
- Availability of novel agents is rapidly redefining the treatment paradigm for patients with myeloma.
- 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 comorbidities such as renal failure, diabetes and presence or absence of coexisting amyloidosis.

mSMART 4.0: Classification of Relapsed MM

High-Risk Myeloma

- Relapse <12 months from transplant or progression within first year of diagnosis
- High Risk Cytogenetic Abnormalities
 1. Del 17p^a and/or *TP53* mutation
 2. Bi-allelic del 1p
 3. t(4;14), (14;16), or t(14;20) *plus* either Gain/Amp 1q or Del 1p
 4. Gain/Amp 1q *plus* Del 1p
- High Plasma Cell S-phase
- Primary plasma cell leukemia
- Extramedullary disease

Standard-Risk Myeloma

- MM with no high risk abnormalities including isolated:
 - Trisomies
 - t(11;14)
 - t(6;14)

^a del(17p) threshold to consider high risk is if the abnormality is detected in $\geq 20\%$ of clonal plasma cells

Abbreviations for Major Drug Classes and Regimens

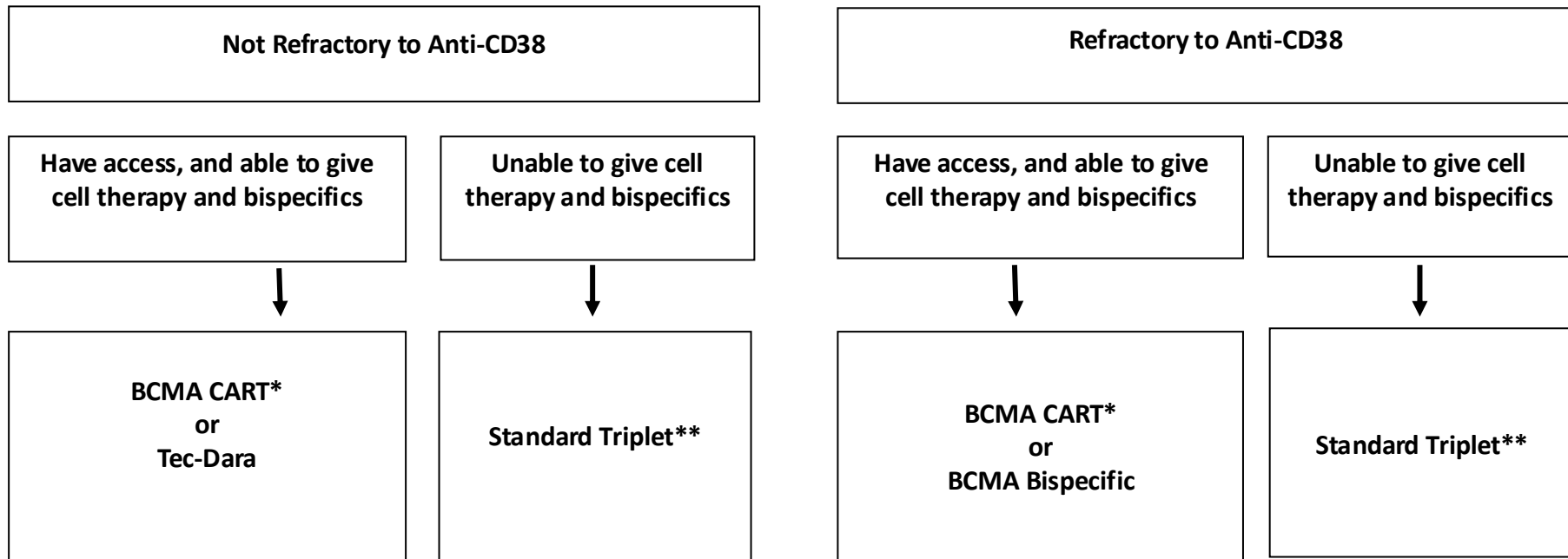
- KRd, carfilzomib, lenalidomide, dexamethasone
- KPd, carfilzomib, pomalidomide, dexamethasone
- PI-Cd, Bortezomib or carfilzomib, plus cyclophosphamide, dexamethasone
- IRd, ixazomib, lenalidomide, dexamethasone
- ICd, ixazomib, cyclophosphamide, dexamethasone
- EPd, elotuzumab, pomalidomide, dexamethasone
- 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
- Anti CD38, daratumumab or isatuximab
- Anti CD38-Kd, daratumumab or isatuximab plus carfilzomib-dexamethasone
- Anti CD38-Pd, daratumumab or isatuximab plus pomalidomide-dexamethasone
- BCMA bispecifics, Teclistamab, elranatamab, linvoseltamab
- CART, chimeric antigen receptor T cell
- BCMA, B cell maturation antigen
- Tec, Teclistamab
- Talq, talquetamab
- Tec-Dara, teclistamab plus daratumumab
- Tec-Talq, teclistamab plus talquetamab



Dosing for Major Regimens

- Refer to: <https://onlinelibrary.wiley.com/doi/10.1002/ajh.27422>

Treatment of Myeloma: First Relapse

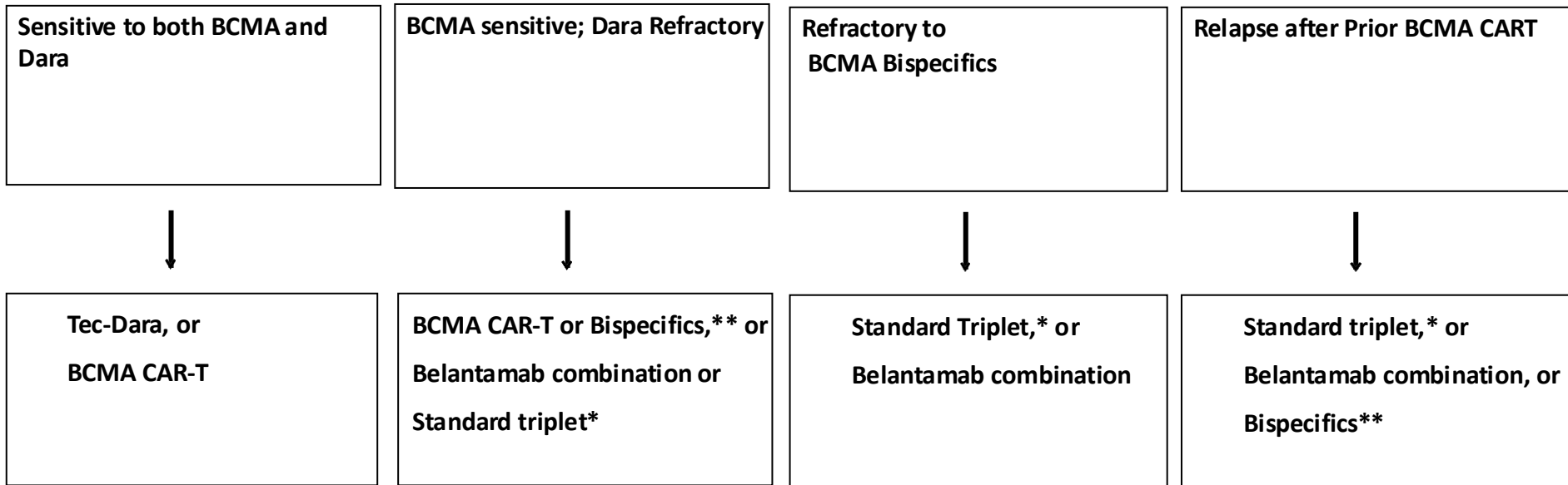


*Cilta-cel should be discussed with eligible patients, and patients should have a discussion on pros and cons of a one-time CART approach vs prolonged therapy

** Choice of standard triplet is based on refractoriness to Len, anti-CD38, and other drugs. Key options are DRd, KRd, KPd, Anti CD38-Pd, Anti CD38-Kd, EloPd, Dara-KPd, PI-Cd and choose a triplet with at least two drugs the patient is not refractory to.

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

Second Relapse



*Choice of standard triplet is based on refractoriness to Len, anti-CD38, and other drugs. Key options are DRd, KRd, KPd, Anti CD38-Pd, Anti CD38-Kd, EloPd, Dara-KPd, PI-Cd and choose a triplet with at least two drugs the patient is not refractory to. If t11;14 myeloma, Dara-Venetoclax-dex and Carfilzomib-Venetoclax-Dex are additional triplet options to consider.

**BCMA Bispecifics can be Teclistamab, Elranatamab, Linvoseltamab, or the Tec-Dara combination

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

Refractory MM

Refractory to Imid, PI, anti CD38, and BCMA approaches



- Venetoclax if t(11;14)
- Talquetamab or Tec-Talq combination*
- Other non-BCMA immunotherapy
- Alkylator-based regimens (VCd, KCd, IV melphalan)
- Selinexor-based regimen
- High dose cyclophosphamide (eg., 1000-1500mg/m² 2 doses over 2 days)
- Combination chemo (DCEP, VDT-PACE, CVAD, DPACE)
- Bendamustine-based regimens
- Alternative BCMA based therapy (CART if BCMA Bispecific refractory, and vice-versa)

***Tec-Talq combination has shown efficacy in patients with relapsed MM plus EMD**