Multiple Myeloma (MM):

Diagnosis, Treatment, and Side Effect Management

LEUKEMIA & LYMPHOMA SOCIETY®

1

LEARNING OBJECTIVES

- Describe an overview of multiple myeloma (MM)
- Identify tests used to diagnose disease and monitor treatment of MM
- Explain the overarching goals of treatment for MM
- Explain approved and emerging treatment options for MM, including stem cell transplantation, and the role of clinical trials
- Describe strategies to manage treatment side effects as well as potential long-term and late effects of treatments for MM
- Describe the roles of the pharmacist, the nurse and the social worker in treating patients with MM

LEUKEMIA & LYMPHOMA SOCIETY®

2

FACULTY

Sagar Lonial, MD
Chair and Professor
Department of Hematology and Medical Oncology
Anne & Bernard Gray Family Chair in Cancer
Chief Medical Officer
Winship Cancer Institute, Emory University
Atlanta, GA

Sara Scott, PharmD, BCOP
Clinical Pharmacy Specialist
Multiple Myeloma
Winship Cancer Institute, Emory University
Atlanta, GA

LEUKEMIA & LYMPHOMA SOCIETY®

3

MULTIPLE MYELOMA (MM): DIAGNOSIS, TREATMENT AND SIDE EFFECTS MANAGEMENT

Sagar Lonial, MD
Chair and Professor
Department of Hematology and Medical Oncology
Anne & Bernard Gray Family Chair in Cancer
Chief Medical Officer, Winship Cancer Institute
Emory University School of Medicine
Atlanta, GA

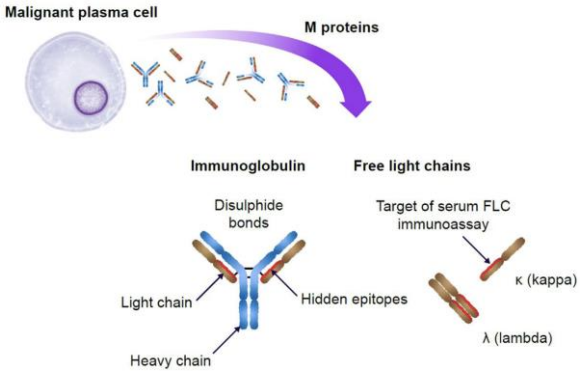
Sara Scott, PharmD, BCOP
Clinical Pharmacy Specialist
Multiple Myeloma
Winship Cancer Institute
Emory Healthcare
Atlanta, GA

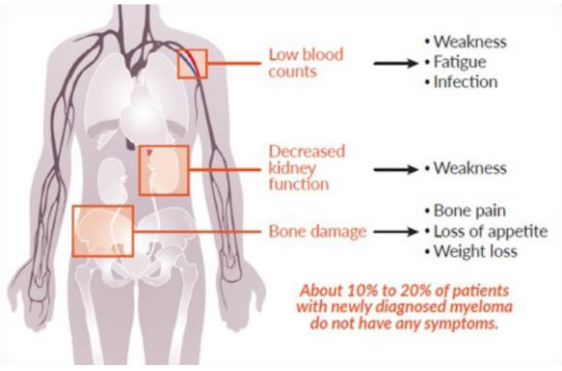
EMORY WINSHIP CANCER INSTITUTE

NCI Designated Comprehensive Cancer Center

4

Multiple Myeloma: Pathophysiology





EMORY WINSHIP CANCER INSTITUTE

Mikhael, Bhutani, and Cole, AJM. 2023; https://themmrf.org/multiple-myeloma/

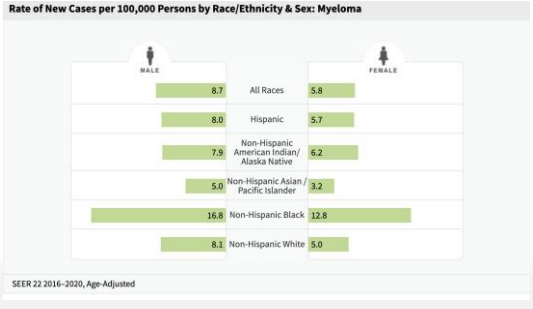
5

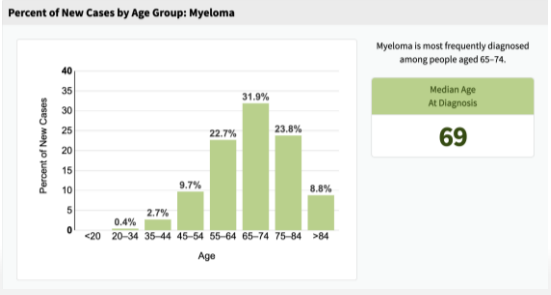
Multiple Myeloma: Epidemiology

Estimated New Cases in 2023	35,730
% of All New Cancer Cases	1.8%

Estimated Deaths in 2023	12,590
% of All Cancer Deaths	2.1%

5-Year Relative Survival
59.8%
2013–2019





EMORY WINSHIP CANCER INSTITUTE

SEER Database, Accessed Jan 2024

6

Diagnostic Workup

- Chemistry panel, CBC + differential
- Albumin and beta-2 microglobulin
- Monoclonal protein in serum and urine
  - UPEP – evaluates total protein in urine
  - SPEP – quantitative immunoglobulin levels
  - UIFE and SIFE – specific M protein present
- Bone marrow biopsy
  - Plasma cells in bone marrow
  - Chromosomal analysis
- Bone imaging, now with MRI or CT or PET

EMORY WINSHIP CANCER INSTITUTE

UPEP, urine protein electrophoresis; UIFE, urine immunofixation electrophoresis
SPEP, serum protein electrophoresis; SIFE, serum immunofixation electrophoresis

NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma (Version 2.2024).

7

Updated IMWG Criteria for Diagnosis of Multiple Myeloma

MGUS	Smoldering Myeloma	Multiple Myeloma
• M-protein < 3 g/dL • Clonal plasma cells in BM < 10% • No myeloma defining events	• M-protein ≥ 3 g/dL (serum) or ≥ 500 mg/24 hrs (urine) • Clonal plasma cells in BM ≥ 10% - 60% • No myeloma defining events	• Underlying plasma cell proliferative disorder AND • 1 or more myeloma defining events including either: ✓≥ 1 CRAB feature(s) OR ✓≥ 1 Biomarker Driven

C: Calcium elevation (> 11 mg/dL or > 1 mg/dL higher than ULN)
R: Renal insufficiency (creatinine clearance < 40 mL/min or serum creatinine > 2 mg/dL)
A: Anemia (Hb < 10 g/dL or 2 g/dL < normal)
B: Bone disease (≥ 1 lytic lesions on skeletal radiography, CT, or PET-CT)

Biomarker driven (1) Sixty-percent (≥60%) clonal PCs by BM; (2) serum free Light chain ratio involved:uninvolved ≥100; (3) >1 focal lesion detected by MRI

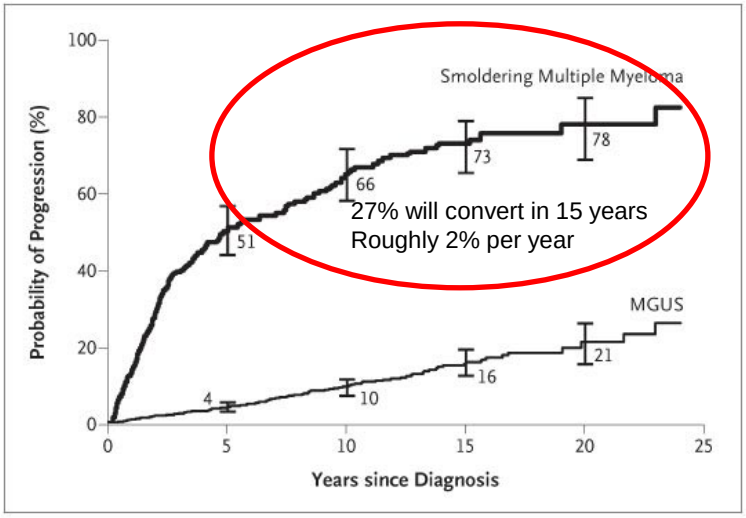
EMORY WINSHIP CANCER INSTITUTE

IMWG, International Myeloma Working Group

Rajkumar SV, et al. *Lancet Oncol*. 2014;15:e538-e548.

8

Probability of Progression to Active Multiple Myeloma or Primary Amyloidosis in Patients with Smoldering Multiple Myeloma

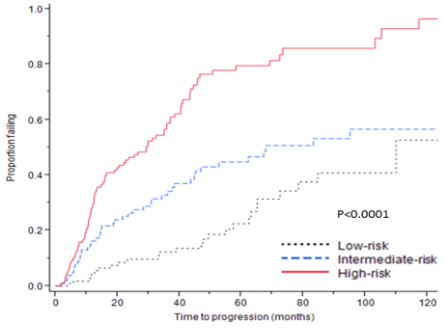


EMORY WINSHIP CANCER INSTITUTE

Kyle R et al. N Engl J Med 2007;356:2582-2590.

9

Revised Risk Stratification (20/20/20)



Factors

- BMPC >20%
- M Spike >20g/L
- FLC ratio >20

Stratification

Low-risk: 0 Intermediate-risk: 1 high-risk: >=2

Time from diagnosis (years)	Low risk ($n = 143$)	Intermediate risk ($n = 121$)		High risk ($n = 153$)	
	Estimated rate of progression (%)	Rate of progression, % (CI)	OR for progression relative to low-risk group (CI)	Rate of progression, % (CI)	OR for progression relative to low-risk group (CI)
2	9.7 (5.3–17.1)	26.3 (18.4–36.2)	2.71 (1.08–6.83)	47.4 (38.6–56.4)	4.89 (2.25–10.69)
5	22.5 (14.2–33.6)	46.7 (35.8–57.9)	2.08 (1.07–4.08)	81.5 (71.3–88.6)	3.63 (2.12–6.22)
10	52.7 (30.1–74.2)	65.3 (45.5–80.9)	1.24 (0.61–2.69)	96.5 (80.9–99.4)	1.83 (1.09–3.30)

BMPC % bone marrow-plasma cell percentage, *CI* 95% confidence intervals, *FLCr* involved to uninvolved free light chain ratio, *OR* odds ratio

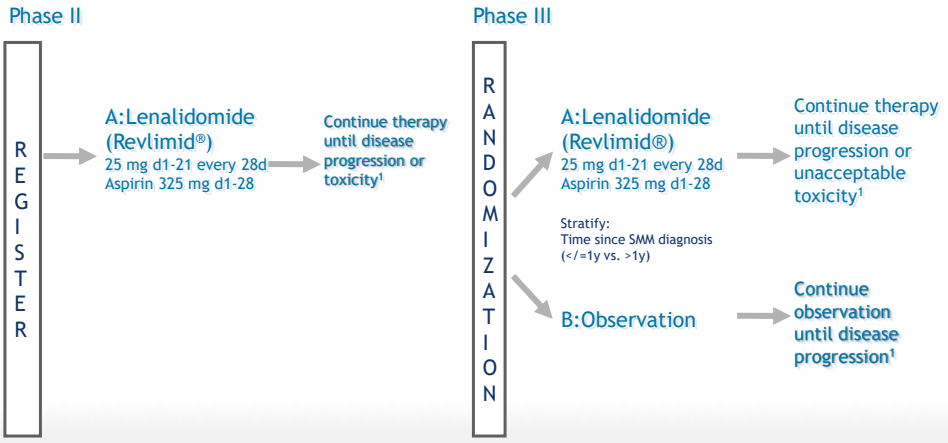
EMORY WINSHIP CANCER INSTITUTE

Lakshman et al, BCJ, 2018.

10

Schema

E3A06: Phase II/III Study
A: Lenalidomide (Revlimid®) vs B: Observation

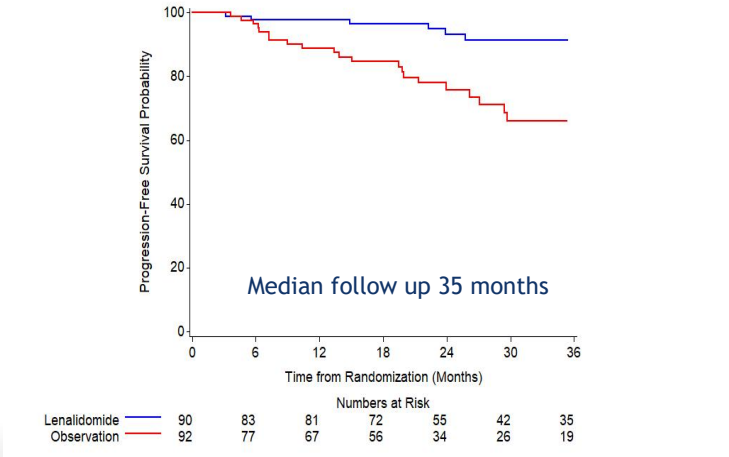


[1]Mobilize stem cells following 4-6 cycles of therapy. While stem cell collection is suggested strongly, it is not required

Lonial et al, ASCO 2019.

11

Phase III PFS ITT^



Treatment Hazard Ratio = 0.28 [95% CI: (0.12-0.63)]

one-sided stratified log-rank test p-value = 0.0005

Phase 3 PFS	Len	Obs
1 yr	0.98	0.89
2 yr	0.93	0.76
3 yr	0.91	0.66

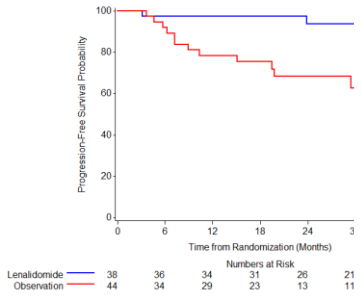
^The DSMC advised release of data in fall 2018 when at the 2nd planned interim analysis (39% full information), the observed p-value from the one-sided stratified log-rank test crossed the related boundary of nominal significance.

Lenalidomide=(Revlimid®)

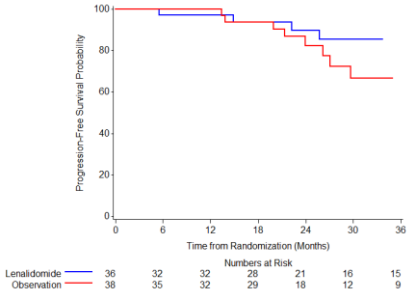
Lonial et al, ASCO 2019.

12

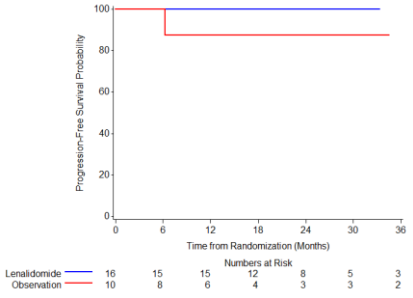
Phase III PFS by Mayo 2018 Risk Criteria



High Risk



Intermediate Risk



Low Risk

EMORY WINSHIP CANCER INSTITUTE

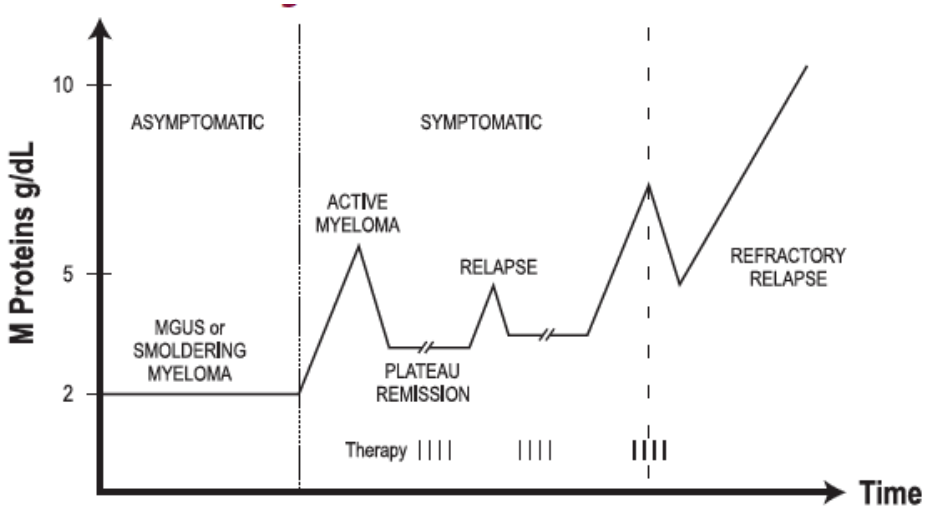
ECOG-ACRIN cancer research group

Lenalidomide=(Revlimid®)

Lonial et al, ASCO 2019.

13

Myeloma Progression



EMORY WINSHIP CANCER INSTITUTE

Concise review of the disease and treatment options: multiple myeloma. International Myeloma Foundation 2015.

14

Revised ISS staging

Table 1. Standard Risk Factors for MM and the R-ISS

Prognostic Factor	Criteria
ISS stage	
I	Serum β_2-microglobulin < 3.5 mg/L, serum albumin ≥ 3.5 g/dL
II	Not ISS stage I or III
III	Serum β_2-microglobulin ≥ 5.5 mg/L
CA by iFISH	
High risk	Presence of del(17p) and/or translocation t(4;14) and/or translocation t(14;16)
Standard risk	No high-risk CA
LDH	
Normal	Serum LDH < the upper limit of normal
High	Serum LDH > the upper limit of normal
A new model for risk stratification for MM	
R-ISS stage	
I	ISS stage I and standard-risk CA by iFISH and normal LDH
II	Not R-ISS stage I or III
III	ISS stage III and either high-risk CA by iFISH or high LDH

Abbreviations: CA, chromosomal abnormalities; iFISH, interphase fluorescent in situ hybridization; ISS, International Staging System; LDH, lactate dehydrogenase; MM, multiple myeloma; R-ISS, revised International Staging System.

EMORY WINSHIP CANCER INSTITUTE

Palumbo et al, *JCO* 2015.

15

Risk Stratification

- High risk
  - Deletion 17p ≥20%
  - Deletion 1p and +1q
  - High risk 14q32 trans and (+1q or deletion 1p)
- Standard risk
  - Hyperdiploidy
  - t(11;14)

EMORY WINSHIP CANCER INSTITUTE

NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma (Version 1.2020).
Palumbo A. *N Engl J Med.* 2011;364:1046-1060.

16

MM Related Diagnosis

- Monoclonal gammopathy
- Waldenstrom's macroglobulinemia
- Primary AL amyloidosis
- Heavy chain disease
- Light chain deposition disease
- Plasma cell leukemia
- POEMS syndrome

EMORY WINSHIP CANCER INSTITUTE

17

MM Treatment

- Induction
- Autologous Stem Cell Transplant (ASCT)
- Maintenance Therapy
- Relapsed/Refractory Disease
- Supportive Care

EMORY WINSHIP CANCER INSTITUTE

18

Induction

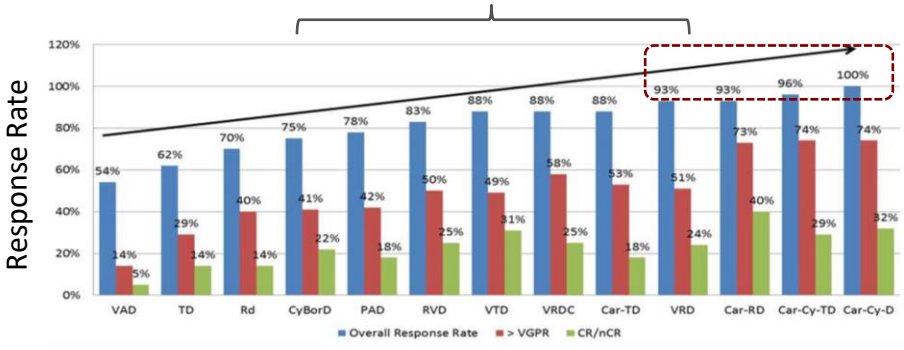
- Initiate therapy
  - Symptomatic myeloma (SLiM-CRAB criteria)
- Select induction regimen
  - ASCT candidate?
    - Age – no specific age cut off for ASCT
    - Co-morbidities
  - Risk stratification

EMORY WINSHIP CANCER INSTITUTE

ASCT, autologous stem cell transplant

19

More Is Better, Especially When Adding a New Drug



Marked improvement in response in MM patients with novel 3 drug combinations

What about the addition of monoclonal antibodies?

EMORY WINSHIP CANCER INSTITUTE

Image adapted from Mailankody et al Nat Rev Clin Onc 2015.

20

NCCN Preferred Induction Regimens	
Proteasome inhibitor (PI) + Immunomodulatory drug (IMiD) + dexamethasone (Decadron®)	Bortezomib + lenalidomide + dexamethasone (Category 1) (Velcade®+ Revlimid®+ Decadron®) Carfilzomib + lenalidomide + dexamethasone (Category 2A) (Kyprolis®+ Revlimid®+ Decadron®)
Other Induction Regimens	
Anti-CD38 monoclonal antibody + Proteasome inhibitor (PI) + Immunomodulatory drug (IMiD) + dexamethasone (Decadron®)	Daratumumab + bortezomib + lenalidomide + dexamethasone (Category 2A) (Darzalex® + Velcade®+ Revlimid®+ Decadron®)
For patients with acute renal insufficiency	PI + cyclophosphamide + dexamethasone (Category 2A) (Velcade® or Kyprolis® + Cytoxan® + Decadron®)
Combination chemotherapy	Dexamethasone + thalidomide + cisplatin + doxorubicin + cyclophosphamide + etoposide + bortezomib (VTD-PACE)

EMORY WINSHIP CANCER INSTITUTE

PI, proteasome inhibitor

NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma (Version 2.2024).

21

Monoclonal Antibodies with Induction

	ALCYONE	MAIA
Design	Bortezomib (Velcade®), melphalan, (Alkeran®) and prednisone (Deltasone®) given with daratumumab (Darzalex®) (n=350) or alone (n=356)	Lenalidomide (Revlimid®) and dexamethasone (Decadron®) with daratumumab (Darzalex®) (n=368) or alone (n=369)
Medium follow-up	16.5 months	28 months
Outcomes	18-month PFS rate was 71.6% (daratumumab) (Darzalex®) versus 50.2% (control) ORR was 90.9% (daratumumab) (Darzalex®) versus 73.9% (control) MRD negativity achieved ($1x10^{-5}$) in 22.3% (daratumumab) (Darzalex®) versus 6.2% (control)	Disease progression or death was 26.4% (daratumumab) (Darzalex®) versus 38.8% (Control) ORR was 92.9% (daratumumab) (Darzalex®) versus 81.3% (control) MRD negativity achieved ($1x10^{-5}$) in 24.2% (daratumumab) (Darzalex®) versus 7.3% (control)

EMORY WINSHIP CANCER INSTITUTE

PFS, progression free survival; MRD, minimal residual disease

Mateos MV, et al. N Engl J Med. 2018;378:518-28.
Facon T , et al. N Engl J Med. 2019;380:2104-15.

22

Four Drug Induction Transplant Eligible

	CASSIOPEIA	GRIFFIN
Design	Dara(Darzalex®)-VTD versus VTD (Total n=1085)	Dara (Darzalex®)-RVD versus RVD (Total n=207)
Outcomes	At day 100 post-ASCT, sCR achieved in 29% of dara [Darzalex®]-VTD versus 20% of VTD (p=0.0010) Rate of VGPR or better was 83% (dara [Darzalex®] -VTD) versus 78% (VTD) MRD negativity (10^{-5}) 64% (dara [Darzalex®]-VTD) versus 44% (VTD)	After cycle 6, 42.4% Dara-RVD achieved sCR versus 32.0% of RVD alone Dara (Darzalex®)-RVD produced a higher ORR (99% versus 92) and higher rate of VGPR or better (91% versus 73%) versus RVD alone Rate of MRD negativity (10^{-5}) in patients achieving a CR or better was higher with dara (Darzalex®)-VRD (59% versus 24%)

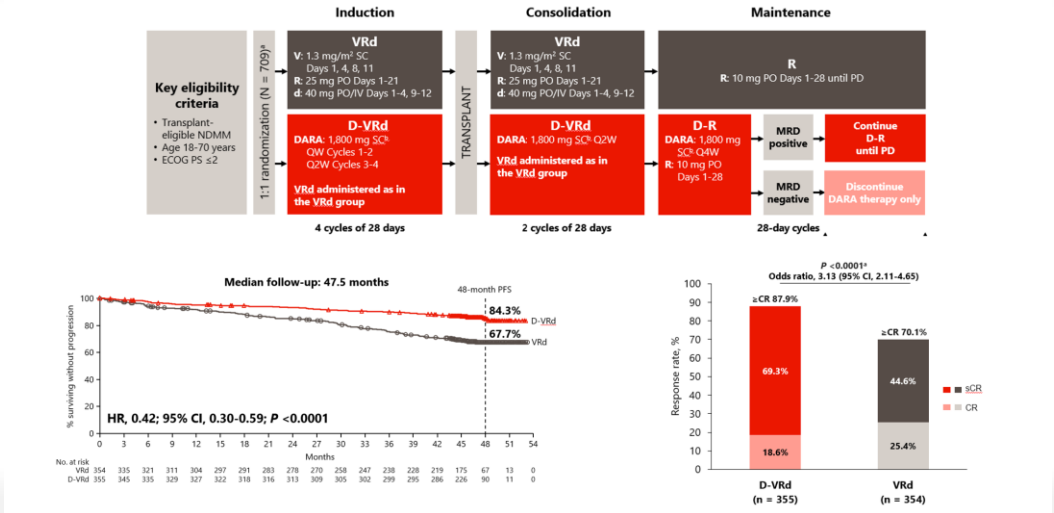
EMORY WINSHIP CANCER INSTITUTE

Dara: daratumumab ; VTD = Velcade® (bortezomib), Thalomid ® (thalidomide) , and Decadron® (dexamethasone);
RVD = Revlimid® (lenalidomide), Velcade® (bortezomib), and Decadron® (dexamethasone)
VGPR: very good partial response; MRD: minimal residual disease

Moreau P, et al. Lancet; 2019;394:29-38.
Voorhees PM, et al. IMW 2019:OAB-87.

23

ASH 2023 Updates: PERSEUS

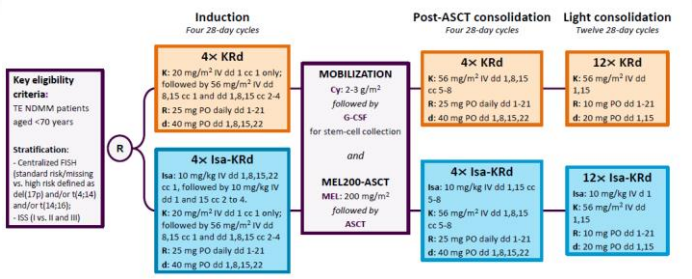


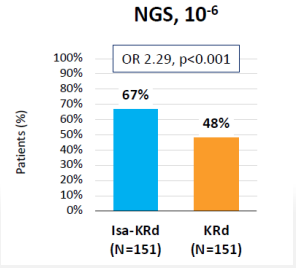
EMORY WINSHIP CANCER INSTITUTE

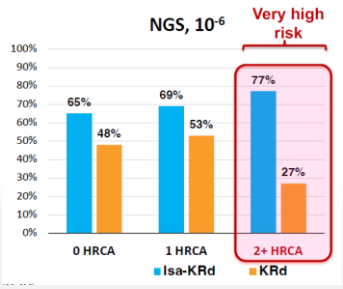
Sonneveld P, et al. *N Engl J Med*. 2024;390(4):301-313.

24

ASH 2023 Updates: IsKia EMN24





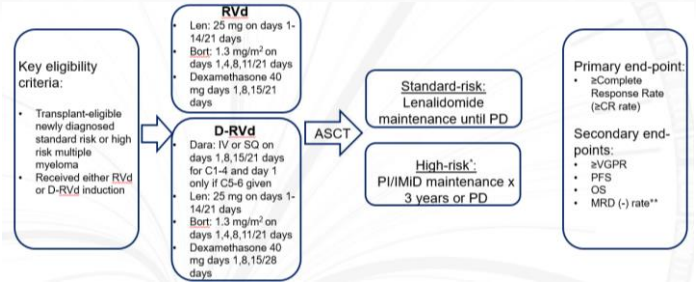


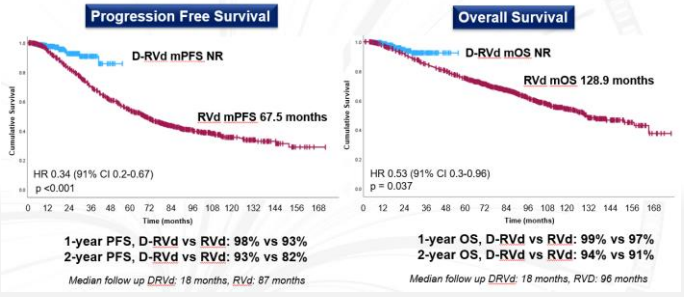
EMORY WINSHIP CANCER INSTITUTE

Sonneveld P, et al. *N Engl J Med*. 2024;390(4):301-313.

25

ASH 2023 Updates: Emory Real World Analysis





EMORY WINSHIP CANCER INSTITUTE

Joseph NS, et al. Presented at 65th ASH Annual Meeting. December 10, 2023.

26

Improving Induction Can Improve High Dose Therapy (HDT)

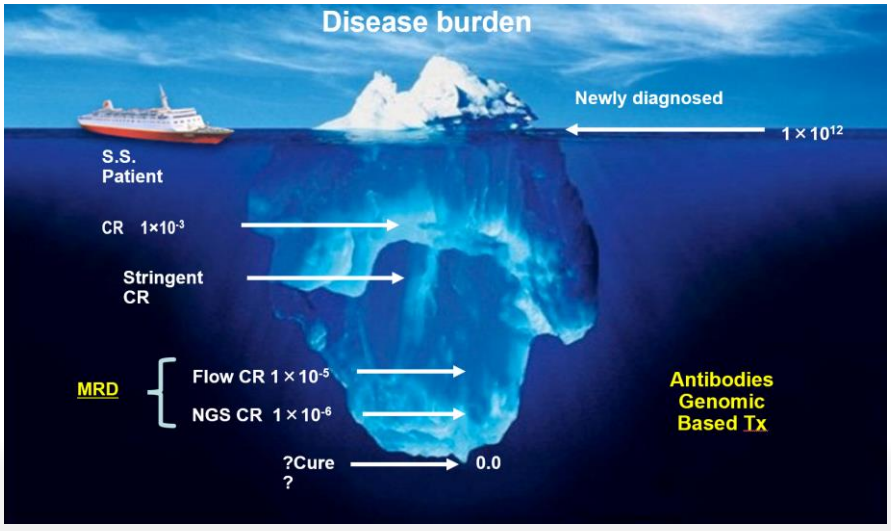
- Needs to use modern drugs
- New evidence that 4 drugs over 3 drugs is better
- While it can improve the outcomes for high risk, may lead to higher cure rate among standard risk
- Need to be cautious about presuming complete responses are all the same (induction vs HDT related)

EMORY WINSHIP CANCER INSTITUTE

Kazmi et al (2015). *Clin Lymphoma Myeloma Leuk, 15:687-693; Rajkumar S. (2016). Am J Hematol*, 91:719-34; Rosinol et al. (2014), *Expert Rev Hematol*,7:43-53.

27

Combinations can Achieve Better Depth and Duration of Response



EMORY WINSHIP CANCER INSTITUTE

Kazmi et al (2015). *Clin Lymphoma Myeloma Leuk, 15:687-693; Rajkumar S. (2016). Am J Hematol*, 91:719-34; Rosinol et al. (2014), *Expert Rev Hematol*,7:43-53.

28

Maintenance Therapy

- Lenalidomide (Revlimid®) post ASCT
- Two phase III clinical trials

	CALGB 100104	IFM 2005-02
Design	Lenalidomide (Revlimid®) (n=231) vs. placebo (n=229) post ASCT	Lenalidomide (Revlimid®) (n=307) vs. placebo (n=307) post ASCT
Medium follow-up	34 months	30 months
Outcomes	Disease progression or death: 37% (lenalidomide [Revlimid®]) vs. 58% (placebo) Median time to progression: 46 months (lenalidomide [Revlimid®]) vs. 27 months (placebo)	Median PFS: 41 months (lenalidomide [Revlimid®]) vs. 23 months (placebo)

EMORY WINSHIP CANCER INSTITUTE

PFS, progression free survival

McCarthy PL. *N Engl J Med.* 2010;366:1770-1781.
Attal M. *N Engl J Med.* 2012;366:1782-1791.

29

Maintenance Therapy

- Ixazomib (Ninlaro®)[a second-generation proteasome inhibitor] was evaluated versus placebo in phase 3 Tourmaline-MM3 trial
- PFS was superior with ixazomib (Ninlaro®) versus placebo (median 26.5 mo versus 21.3 mo, p=0.002)
- Conversion from MRD positive at study entry to MRD negativity was higher with ixazomib (Ninlaro®) versus placebo (12% versus 7%)

EMORY WINSHIP CANCER INSTITUTE

PFS, progression free survival; MRD, minimal residual disease

Dimopoulos MA, et al. Blood; 2018:132:301.

30

Maintenance Therapy: Combination Regimens

- Aim to improve outcomes in high-risk patients
- Carfilzomib + IMiD + dexamethasone

Study	Treatment	Outcomes
FORTE	Carfilzomib + lenalidomide vs lenalidomide	• 3-year PFS: 75% vs 65% (HR 0.64, p=0.023) • Vascular events: 7% vs 1%
Nooka, et al.	Carfilzomib + pomalidomide + dexamethasone	• 36-month PFS: 63.2% • 36-month OS: 72.4% • Responses post-transplant deepened with maintenance

- Should anti-CD38 monoclonal antibody be added?
- Can MRD be used to determine duration of maintenance?

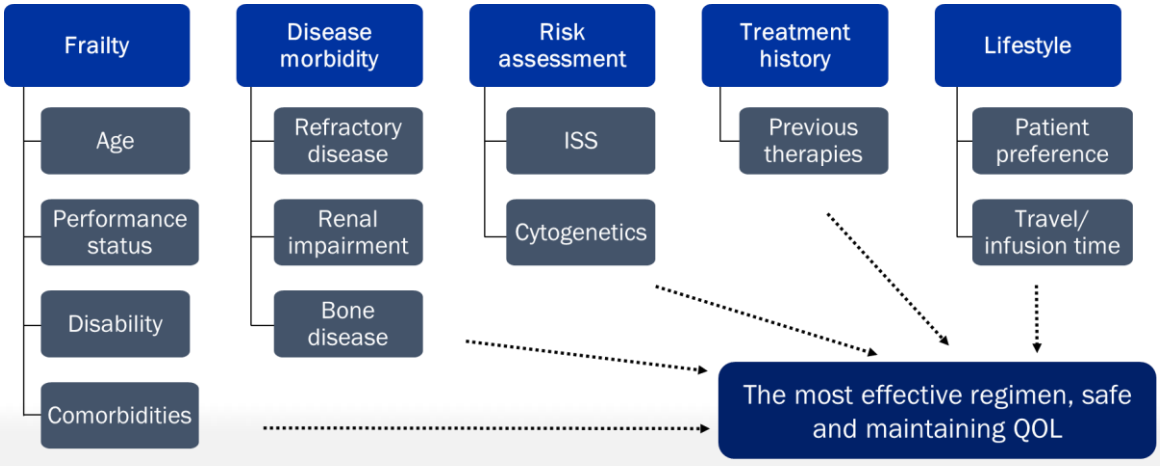
EMORY WINSHIP CANCER INSTITUTE

IMiD, immunomodulatory drug

Mina R, et al. *The Lancet Oncology*. 2023;24(1):64-76.
Nooka AK, et al. *JCO*. 2023;41(16_suppl)8001.

31

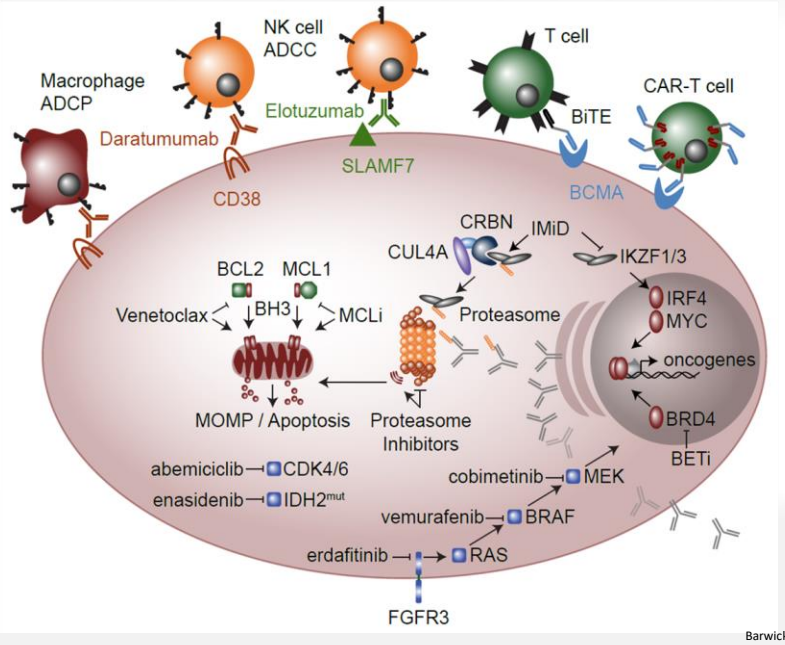
Disease and Patient Factors Influence Treatment Choices in RELAPSED/REFRACTORY MM



EMORY WINSHIP CANCER INSTITUTE

32

Therapeutic Modalities in Multiple Myeloma



EMORY WINSHIP CANCER INSTITUTE

Barwick et al. *Frontiers Immunology*. 2019.

33

Treatment Algorithms, No One Size Fits All R/R MM

		Subsequent relapse
Lenalidomide sensitive	DRd	KPd, PCyd or KCyd, IsaKd
	Alternative: KRd	PCyd, DVd, DPd, or IsaPd
	Frail: IRd, ERd, Rd	DPd or IsaPd
Lenalidomide refractory	DVd, DKd, DPd, or IsaPd, IsaKd	KPd, PCyd or KCyd, IsaKd
	Alternative: KPd, VCd, DKd, XVd, PCyd, KCyd	PCyd, IsaKd
	Frail: IPd EPd, Pd	XVd
	*After exposure to both PI and IMiD	Consider eligible patients for clinical trial

Key: consider either 2 new agents that patient is not refractory to or novel agents

4+ prior lines

- Idecabtagene vicleucel†
- Ciltacabtagene autoleucel†
- Teclistamab
- Elranatamab
- Talquetamab

†After exposure to ≥1 PI, IMiD, and anti-CD38 mAb;‡4+ prior therapies

EMORY WINSHIP CANCER INSTITUTE

Cy = cyclophosphamide; D = daratumumab; d = dexamethasone; E = elotuzumab; I = ixazomib; Isa = isatuximab; K = carfilzomib; P = pomalidomide; R = lenalidomide; V = bortezomib; X = selinexor;
PI = proteasome inhibitor; IMiD = immunomodulatory drug; CD = cluster of differentiation; mAb = monoclonal antibody.

Modified from Rajkumar SV, Kumar S. *Blood Cancer J*. 2020;10:94.

34

Lenalidomide (Revlimid®) + Dexamethasone (Decadron®) vs Triplet Regimens

Relapsed/Refractory Myeloma After 1-3 Prior Regimens

Proteasome inhibitors

- **ASPIRE[1]**
  - Len + dex vs **Len + dex + carfilzomib**
- **TOURMALINE-MM1[2]**
  - Len + dex vs **Len + dex + ixazomib**

Immunotherapy

- **ELOQUENT-2[3]**
  - Len + dex vs **Len + dex + elotuzumab**
- **POLLUX (1-11 prior regimens)[4a]**
  - Len + dex vs **Len + dex + daratumumab**

EMORY WINSHIP CANCER INSTITUTE

[a]Eligibility required at least one prior line of therapy
Len = Lenalidomide (Revlimid®); Dex = dexamethasone (Decadron®); carfilzomib (Kyprolis®); ixazomib (Ninlaro®) elotuzumab (Empliciti®); daratumumab (Darzalex®)

1.Stewart AK, et al. *N Engl J Med*. 2015;372(2):142-152. 2. Moreau P, et al. *N Engl J Med*. 2016;374(17):1621-1634. 3. Lonial S, et al. N *Engl J Med*. 2015;373(7):621-631. 4. Dimopoulos MA, et al. *N Engl J Med*. 2016;375(14):1319-1331.

35

Bortezomib (Velcade®) + Dexamethasone (Decadron®) vs Triplet Regimens

Relapsed/Refractory Myeloma After 1-3 Prior Regimens

Proteasome inhibitors (head-to-head comparison)

- **ENDEAVOR[1]**
  - BTZ + dex vs **carfilzomib + dex**

Histone deacetylase inhibitor

- **PANORAMA-2[2]**
  - BTZ+ dex vs BTZ **+ dex + panobinostat**

Immunotherapy

- **BORTEZOMIB + DEX +/- ELOTUZUMAB[3a]**
  - BTZ + dex vs **BTZ + dex + elotuzumab**
- **CASTOR (1-10 prior regimens)[4b]**
  - BTZ+ dex **vs BTZ + dex + daratumumab**

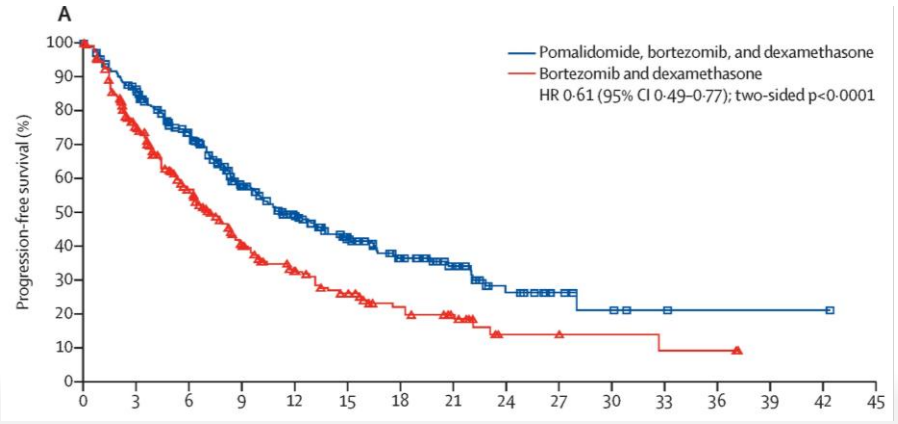
EMORY WINSHIP CANCER INSTITUTE

[a]Randomized phase II study/
[b]Eligibility required at least one prior line of therapy
BTZ = Bortezomib (Velcade®); dex = (Decadron®); carfilzomib (Kyprolis®); panobinostat (Farydak®); elotuzumab (Empliciti®); daratumumab (Darzalex®)

1. Dimopoulos MA, et al. *Lancet Oncol*. 2016;17(1):27-38. 2. San-Miguel SF, et al. *Lancet Oncol*. 2014;15(11):1195-1206. 3. Jakubowiak A, et al. *Blood*. 2016;127(23):2833-2840. 4. Palumbo A, et al. *N Engl J Med*. 2016;375(8):754-766.

36

OPTIMISSM: Pomalidomide-Bortezomib-Dex
(Pomalyst®- Velcade®-Decadron®)

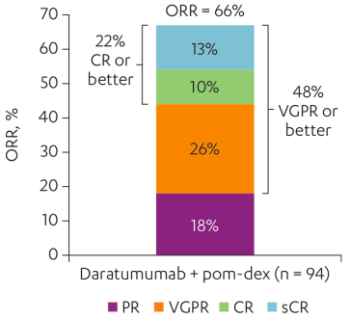


EMORY WINSHIP CANCER INSTITUTE

The Lancet Oncology 2019 20, 781-794.

37

Daratumumab (Darzalex®), Pomalidomide (Pomalyst®) Dexamethasone (Decadron®): Phase 1b



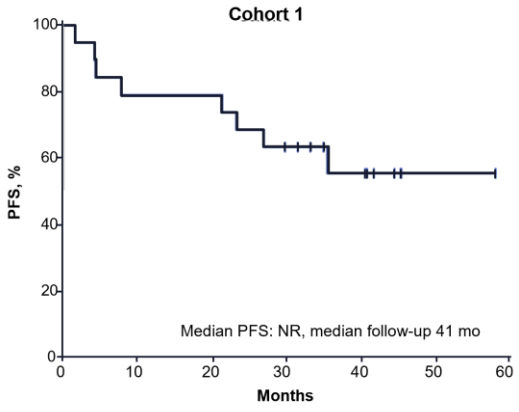
- DARA (16 mg/kg) + POM-D induced responses, including MRD negativity, in a heavily pretreated patient population
  - Median of 4 prior lines of therapy
  - 71% double refractory to a PI and an IMiD
  - High ORR maintained in double-refractory & high-risk patients
- Median PFS 9.9 months
  - Median DOR 21.5 months
- Median OS 25.1 months
- DARA can be combined with POM-D
  - 77% Gr 3/4 neutropenia in population with 44% baseline neutropenia
  - FN rates consistent with POM-D alone

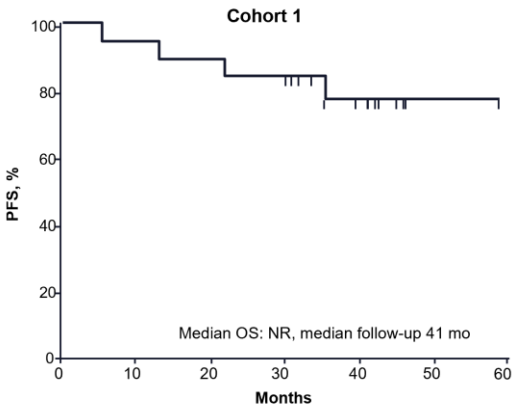
EMORY WINSHIP CANCER INSTITUTE

Chari A, et al. Blood. 2017.
Facon T, et al. ASH 2017. Poster.

38

PFS and OS for Daratumumab (Darzalex®), Pomalidomide (Pomalyst®), and Dexamethasone (Decadron®) in First Relapse[1]



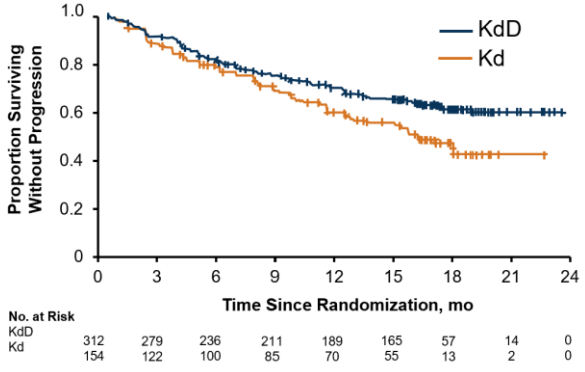


EMORY WINSHIP CANCER INSTITUTE

1. Nooka A et al. *Cancer*. In press

39

CANDOR: KdD Significantly Prolongs PFS Versus Doublet in RRMM[1]



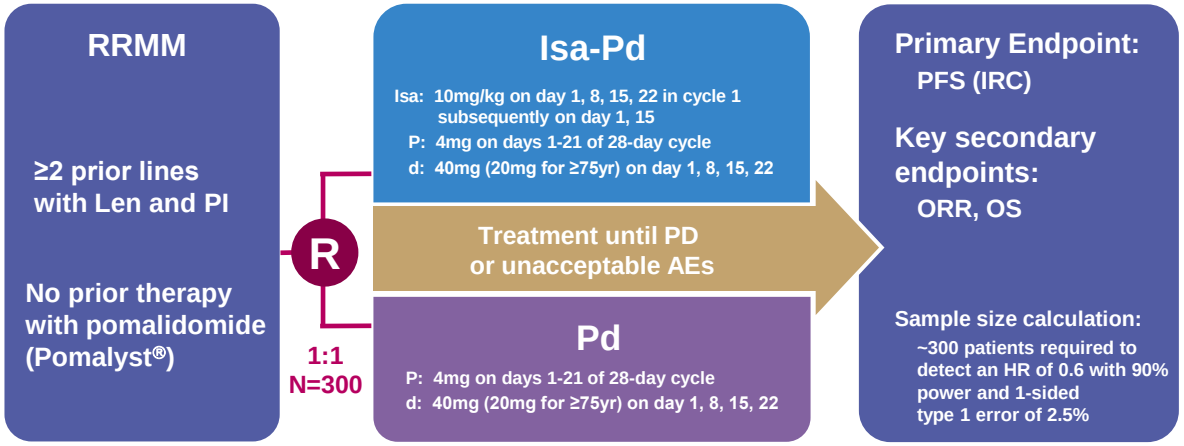
	KdD (n = 312)	Kd (n = 154)
Median follow-up time, mo	16.9	16.3
Progression/death, n (%)	110 (35%)	65 (44%)
Median PFS, mo	NE	15.8
HR (KdD/Kd) (95% CI)	0.63 (0.46-0.85)	
P (1 sided)	.0014	

EMORY WINSHIP CANCER INSTITUTE

1. Usmani SZ et al. ASH 2019. Abstract LBA-6.

40

Global phase 3 Pivotal Study of Isatuximab* with Pd in RRMM - Study Design



ICARIA-MM is the 1st randomized phase 3 trial adding a CD38 antibody to the Pd backbone

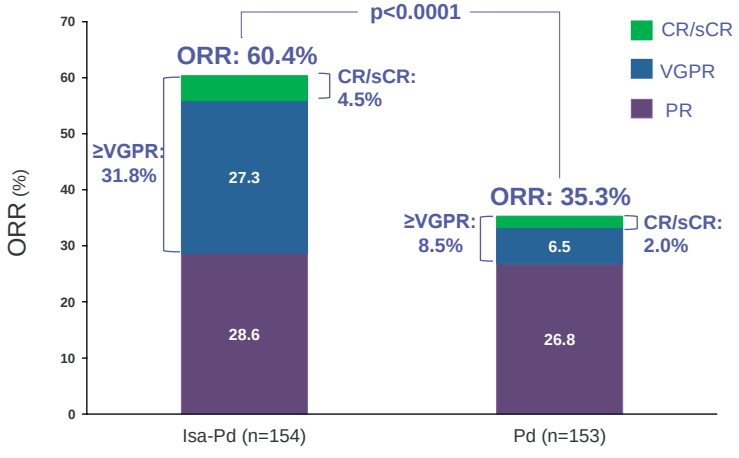
EMORY WINSHIP CANCER INSTITUTE

ICARIA-MM study: EFC14335; NCT02990338
AE, adverse event; d, dexamethasone; HR, hazard ratio; IRC, independent review committee; Isa, isatuximab; ORR, overall response rate; OS, overall survival; P, pomalidomide; PD, progressive disease; PFS , progression-free survival; R, randomization
*Isa: Not yet FDA approved.

Richardson PG, et al. *Future Oncol* 2018;14:1035–47

41

Response Summary – IRC Assessment



Median time to 1st response: Isa-Pd 35 days vs Pd 58 days

True CR rate in Isa-Pd underestimated because of isatuximab interference with M-protein measurement

	Isa-Pd (n=154)	Pd (n=153)
nCR*, %	15.6	3.3

MRD negativity at 10^{-5} (ITT): 5.2% for Isa-Pd vs 0% for Pd

Addition of Isa to Pd resulted in significant improvement in overall and depth of response

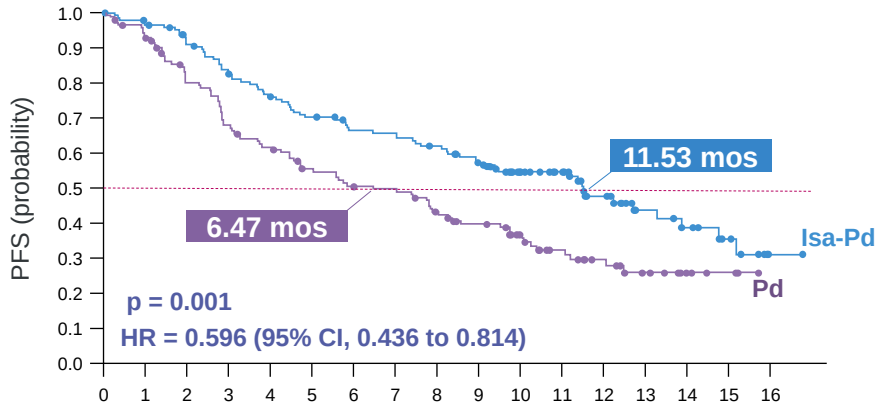
EMORY WINSHIP CANCER INSTITUTE

Data cut-off 11 Oct, 2018
CR complete response; d, dexamethasone; IRC, Independent Review Committee; Isa, isatuximab; ITT, intent-to-treat; MRD, minimal residual disease; nCR, near complete response; ORR, overall response rate; P, pomalidomide; PR, partial response; sCR, stringent complete response; VGPR, very good partial response
*All criteria for a complete response were met except that immunofixation remained positive [Richardson PG, et al. *N Engl J Med*. 2003;348(26):2609-2617]

Richardson PG, et al. *Future Oncol* 2018;14:1035–47

42

PFS Primary Endpoint – IRC Assessment



No. at risk									
Isa-Pd	154	129	106	89	81	52	30	14	1
Pd	153	105	80	63	51	33	17	5	0

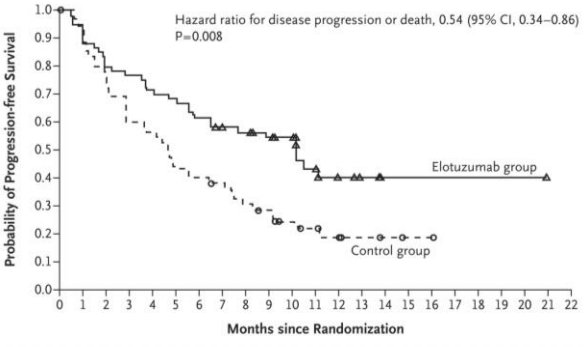
Statistically significant and clinically meaningful improvement in PFS

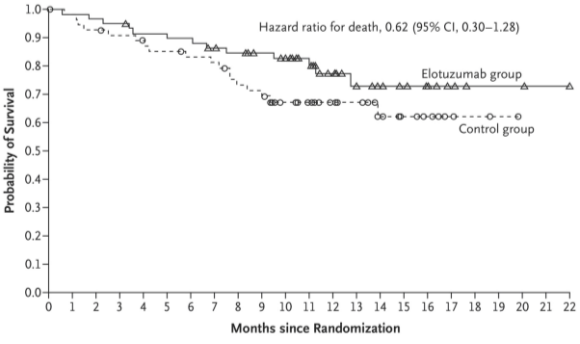
EMORY WINSHIP CANCER INSTITUTE

Data cut-off 11 Oct,,2018 .
CI, confidence interval; d, dexamethasone; HR, Hazard ratio; IRC, Independent Review Committee; Isa, isatuximab; mos, months; PFS, progression-free survival; P, pomalidomide

43

Elotuzumab-Pomalidomide-Dex (Empliciti®- Pomalyst®-Decadron®)





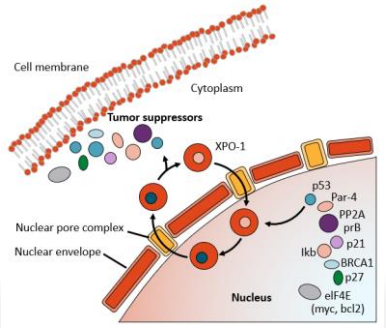
EMORY WINSHIP CANCER INSTITUTE

N Engl J Med 2018; 379:1811-1822.

44

Selinexor (Xpovio®)

- **Selinexor**: an XPO1 inhibitor that induces nuclear retention and activation of TSPs and the GRPs in the presence of steroids and suppresses oncoprotein expression



- FDA approved:
  - In combination with Vd after ≥1 previous therapy
  - In combination with dex after ≥4 previous therapies and refractory to ≥2 PIs, ≥2 IMiDs, and an anti-CD38 mAb

Dosing With Vd	**100 mg PO (five 20-mg tablets) once weekly**
Dosing With Dex	**80 mg PO (four 20-mg tablets) on Days 1 and 3 of each wk**

Patients should take 5-HT3 antagonists and/or other antinausea agents (eg, olanzapine) prior to and during treatment with selinexor

Counsel patients on what to expect when receiving selinexor; advise patients to maintain adequate fluid and caloric intake; help patients with tools to ensure compliance with oral therapy

EMORY WINSHIP CANCER INSTITUTE

Selinexor PI. Gravina. J Hematol Oncol. 2014;7:85. Culjkovic-Kraljacic. Cell Rep. 2012;2:207. Gasparetto. EJHaem. 2020;2(1): 56-65.

45

Selinexor Clinical Trials

Trial	Line of Therapy	Regimen	Efficacy/Safety Endpoints
STORM (Phase IIb; n=122)	3+	Selinexor PO + dexamethasone • Selinexor 80 mg twice weekly	• ORR: 26% • PFS: 3.7 months • All-grade thrombocytopenia (73%), anemia (67%), neutropenia (40%), nausea (72%)
BOSTON (Phase III; n=402)	1-3	Selinexor PO + bortezomib + dexamethasone (vs bortezomib + dexamethasone) • Selinexor 100 mg once weekly	• ORR: 76.4% (vs 62.3%) • PFS: 13.9 months (vs 9.5 months) • All-grade thrombocytopenia (60%), anemia (36%), neutropenia (15%), nausea (50%)
STOMP XKD (Phase Ib/II; n=33)	1+	Selinexor PO + carfilzomib + dexamethasone • Selinexor 60 – 100 mg once weekly	• 66.7% • PFS: 13.8 months • All-grade thrombocytopenia (82%), anemia (58%), neutropenia (30%), nausea (76%)

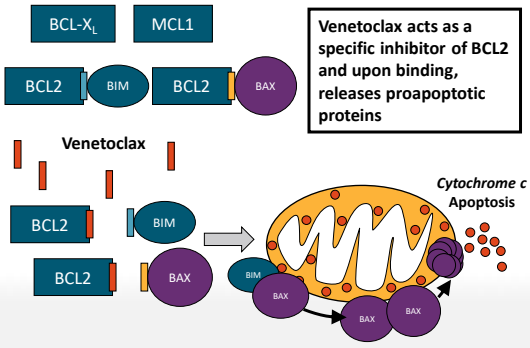
EMORY WINSHIP CANCER INSTITUTE

Chari A et al. *N Engl J Med*. 2019;381(8):727-38. Grosicki S et al. *Lancet*. 2020;396:1563-73. Schiller GJ et al. *Blood*. 2022; 140(Supplement 1): 10050-10053.

46

Venetoclax

- **Venetoclax**: a selective oral inhibitor of BCL-2



Venetoclax acts as a specific inhibitor of BCL2 and upon binding, releases proapoptotic proteins

- **Not currently FDA approved for myeloma** but can be considered for off-label use in some circumstances
  - **Has been most effective in patients with t(11;14) translocation**

Dosing	400-800 mg QD + Dexamethasone weekly
Dosing	800 mg QD + bortezomib 1.3 mg/m^2 + dexamethasone 20 mg
Dosing	400 mg QD (with daratumumab + dexamethasone)

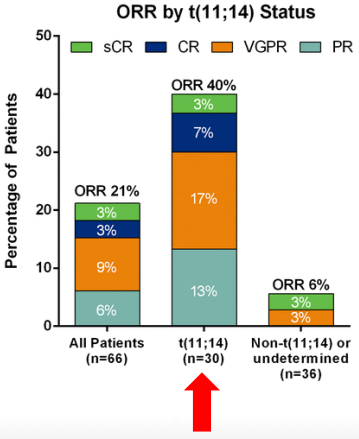
Consider dose escalation strategy for venetoclax (400 mg QD for first wk, then escalate to 800 mg/day) and counsel patients on need for close monitoring when beginning therapy with venetoclax

EMORY WINSHIP CANCER INSTITUTE

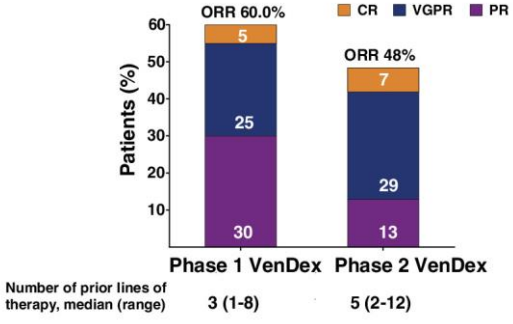
Souers. Nat Med 2013;19:202. Touzeau. Leukemia. 2018;32:1899. Kumar. Lancet Oncol. 2020;21:1630. Kumar. Blood. 2017. Bahlis. J Clin Oncol. 2021;39(32):3602-3612.

47

Targeting BCL2 is Effective in Patients with t(11;14) Myeloma



Kumar *et al., Blood* , 2018



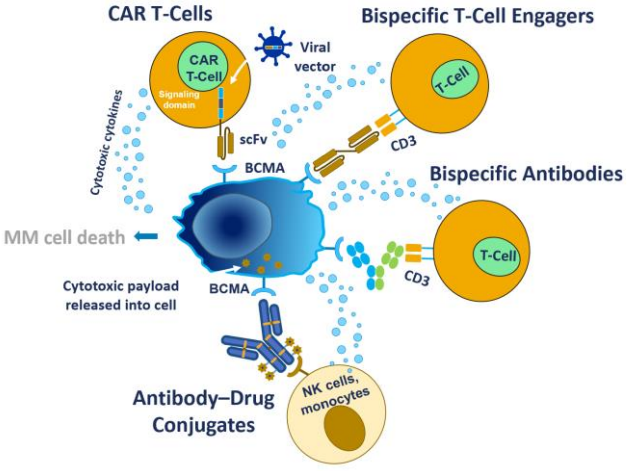
Kaufman *et al., Am. J. Hematol*., 2021

EMORY WINSHIP CANCER INSTITUTE

48

BCMA in Multiple Myeloma

- Expressed on late memory B-cells committed to PC differentiation and PCs
- BCMA plays a role in survival of long-lived PCs
- γ-secretase cleaves BCMA from the cell surface, yielding soluble BCMA

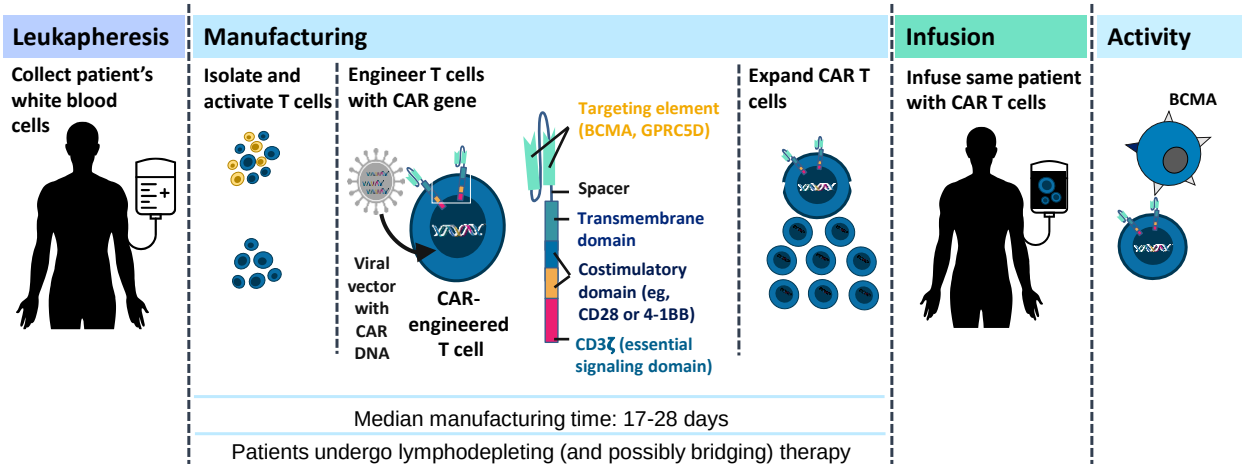


EMORY WINSHIP CANCER INSTITUTE

Cho. Front Immunol. 2018;10:1821.

49

Autologous CAR T-Cell Therapy: Underlying Principles

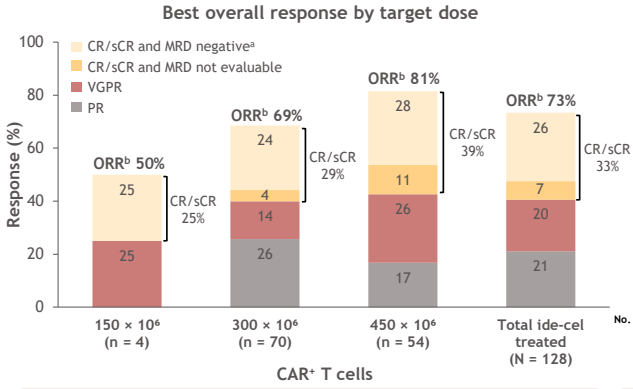


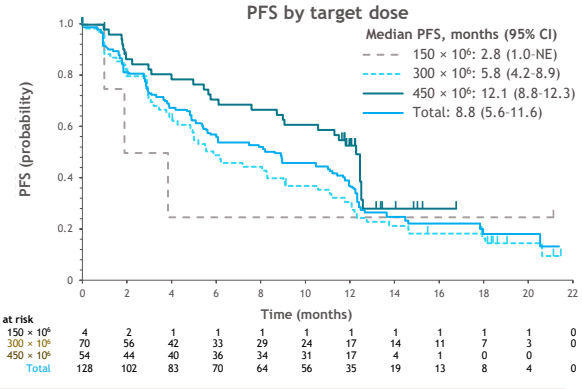
EMORY WINSHIP CANCER INSTITUTE

Majors. EHA 2018. Abstr PS1156. Lim. Cell. 2017;168:724. Sadelain. Nat Rev Cancer. 2003;3:35. Brentjens. Nat Med. 2003;9:279. Park. ASH 2015. Abstr 682. Axicabtagene ciloleucel PI. Tisagenlecleucel PI.

50

Ide-cel Delivers High Response Rates and PFS in RRMM





Median follow-up: 13.3 months across target dose levels

PFS increased with higher target dose

EMORY WINSHIP CANCER INSTITUTE

Data cut-off date: 14 January 2020. Values may not add up due to rounding.
[a] MRD negative defined as < 10^{-5} nucleated cells by next-generation sequencing; only MRD values within 3 months of achieving CR/sCR until PD/death (exclusive) were considered. [b] Defined as ≥ PR.

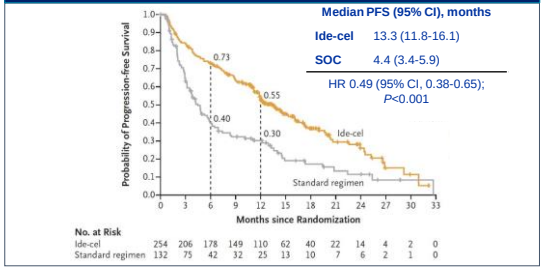
CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
Munshi NC, et al. N Eng J Med. 2021;384:705-16.

51

KARMMA-3: IDE-CEL IN EARLIER LINES OF THERAPY IN RRMM

EFFICACY AND SAFETY[1,2]

PFS



Response, n (%)	Ide-Cel (n=254)	SOC (n=132)
ORR[a]	181 (71)	55 (42)
CR/sCR	98 (39)	7 (5)
VGPR	55 (22)	13 (10)
PR	28 (11)	35 (27)
SD	31 (12)	48 (36)
PD	24 (9)	10 (8)

AEs (≥25% Any Grade)	Ide-Cel (n=250)		SOC (n=126)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Nonhematologic				
CRS[b]	197 (88)	9 (4)	0	0
Infection[c]	146 (58)	61 (24)	68 (54)	23 (18)
Nausea	112 (45)	4 (2)	34 (27)	0
Diarrhea	85 (34)	4 (2)	30 (24)	4 (3)
Hypophosphatemia	78 (31)	50 (20)	10 (8)	3 (2)
Hypokalemia	78 (31)	12 (5)	14 (11)	1 (1)
Fatigue	69 (28)	4 (2)	44 (35)	3 (2)
Pyrexia	69 (28)	2 (1)	22 (17)	1 (1)
Constipation	67 (27)	0	9 (7)	0
Hematologic				
Neutropenia	195 (78)	189 (76)	55 (44)	50 (40)
Anemia	165 (66)	127 (51)	45 (36)	23 (18)
Thrombocytopenia	136 (54)	106 (42)	36 (29)	22 (17)
Lymphopenia	73 (29)	70 (28)	25 (20)	23 (18)
Leukopenia	72 (29)	71 (28)	15 (12)	11 (9)

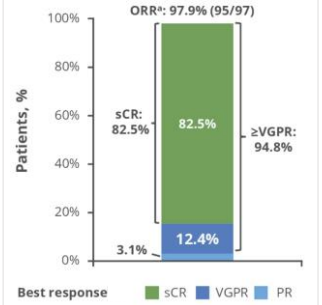
EMORY WINSHIP CANCER INSTITUTE

Data cutoff date: April 18, 2022.
[a] PR or better. [b] Assessed in N=225 (Ide-cel group) and N=126 (standard regimen group); 2 (1%) grade 5 CRS events occurred in the Ide-cel group. [c] 11 (4%) and 3 (2%) grade 5 infection events occurred in the Ide-cel and standard regimen group, respectively.
1. Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388(11):1002-1014. **2.** ClinicalTrials.gov Identifier: NCT03651128. Accessed June 15, 2023. https://clinicaltrials.gov/ct2/show/NCT03651128

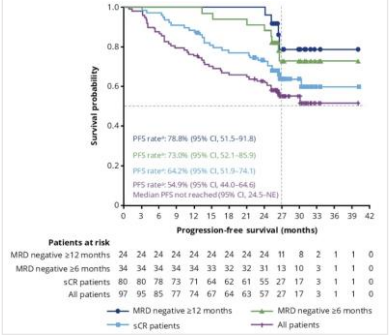
52

Landmark 2 Years Post-Last Patient-in Results of the CARTITUDE-1 Phase 1/2 Study of Cilta-Cel in Patients With RRMM: Efficacy[1,2]

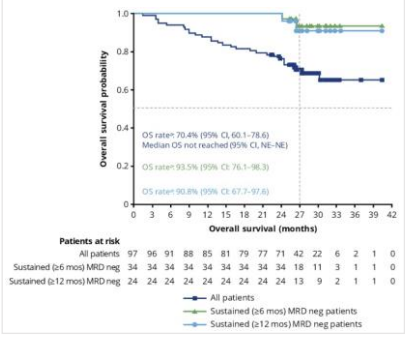
ORR BY IRC



PFS BY MRD AND RESPONSE STATUS



OS BY MRD STATUS



- Median DOR: NE (95% CI, 23.3 months-NE)
- Of 61 patients evaluable, 91.8% were MRD neg (10^{-5})
- DOR, PFS, and/or OS were shorter in subgroups with high-risk cytogenetics, ISS stage III, and high tumor burden, as well as presence of plasmacytomas

EMORY WINSHIP CANCER INSTITUTE

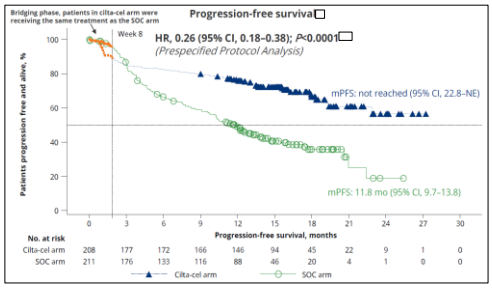
Data cutoff: January 11, 2022. Median follow-up: 27.7 months.
[a] 27-month PFS and OS rates.
1. Usmani SZ, et al. ASCO 2022. Abstract 8028. 2. Lin Y, et al. EHA 2022. Abstract P961.

53

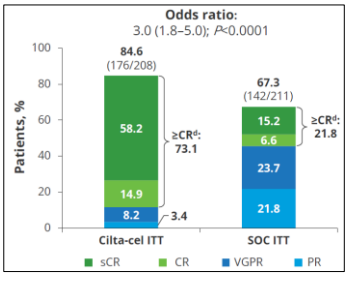
CARTITUDE-4: Cilta-Cel vs SOC in Len-Refractory RRMM

Efficacy[1,2]

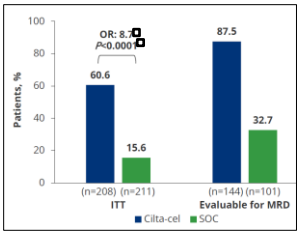
PFS



ORR



MRD Negativity at 10^{-5}



- **Median follow-up: 15.9 mo (range, 0.1-27)**
- **12-month PFS rate: 76% Cilta-cel vs 49% SOC**
- **OS data were immature**
  - **39 deaths in Cilta-cel arm vs 47 deaths in SOC arm**
  - **HR=0.78 (95% CI, 0.5-1.2); *P*=0.26**

DOR

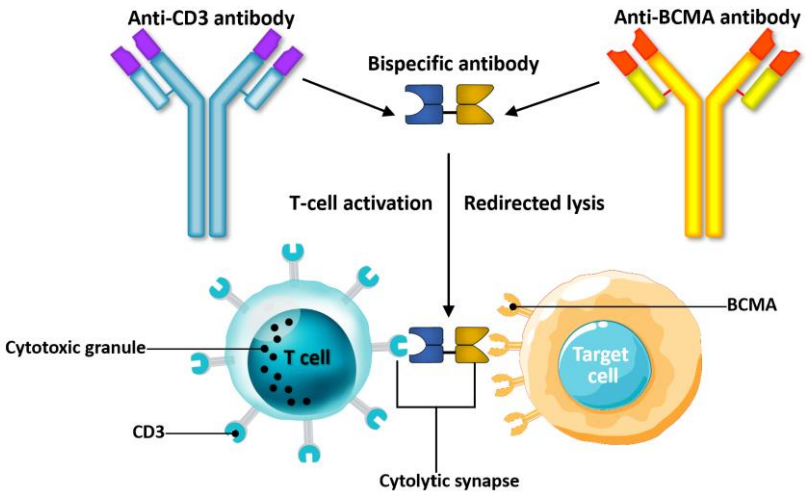
	Cilta-Cel (n=208)	SOC (n=211)
Median DOR, mo (95% CI)	NR	16.6 (12.9-NE)
12-month DOR rate, % (95% CI)	84.7 (78.1-89.4)	63.0 (54.2-70.6)

EMORY WINSHIP CANCER INSTITUTE

•Data cutoff: November 1, 2022.
•**1.** Dhakal B, et al. ASCO 2023. Abstract LBA106. **2.** Einsele H, et al. EHA 2023. Abstract S100.

54

Bispecific T Cell Engagers



EMORY WINSHIP CANCER INSTITUTE

Baeuerle PA, et al. *Cancer Res.* 2009;69:4941-4944.

55

BCMAxCD3 Bispecifics

Bispecific Antibody	Teclistamab[1-2] (JNJ-64007957)	Elranatamab[3] (PF-06863135)	Linvoseltamab[4] (REGN5458)	ABBV-383[5-6]	Alnuctamab[7] BMS-93269	HPN217[8]
Structure/Function	Humanized antibody	Humanized antibody	*Veloci-Bi*® platform fully human antibody	Low CD3 affinity fully human antibody	Humanize antibody 2 BCMA + 1 CD3	Trispecific 50kDa (albumin)
Treatment	Weekly SC	Weekly SC	Weekly IV	IV q3w	Qwk -> Q4wk SQ	Q2wk IV
Patients	n= 165	n= 123	n= 252	n= 174	n= 68	n= 62
Median prior lines	5	5	5	5	4	6
Triple-class refractory	78%	97%	81%	80%	63%	76%
ORR at RP2d	63%	61%	64%	58-61%	65%	73%
RP2D (n)	1.5 mg/kg SC **(n=165)**	76 mg SQ **(n=123)**	200 mg IV (n=58)	40 to 60 mg IV (n=52 n=59)	30 mg SQ (n=26)	?12 or 24 mg (n=13)
PFS	11.3 mos (8.8-17.1)	NE @ 12 mos	NR	13.7 or 11.2 mos	NR	NR
DOR	18.4 mos (14.9-NE)	NE @12 mos	89% @ 6 mos	NE	NE	NR
Median f/u	14.1 mos /23 mos	10.4 mos	3.2 mos	6.8	4.6 mos	
AEs, (All/(Gr 3+);						
CRS	72% (0.6%)	58% (0%)	44% (1%)	60% (1%)	53% (0%)	27 (0%)
Infections	80% (55%)	67% (35%)	54% (29%)	(22%)	34% (9%)	45% (16%)
Neutropenia	72% (66%)	48% (48%)	25% (23%)	34% (26%)	37%(32%)	16% (13%)
Anemia	52% (37%)	48% (37%)	36% (31%)	37% (16%)	38%(25%)	44% (34%)
Thrombocytopenia	40% (21%)	26% (24%)	18% (6%)	29% (11%)	24%(9%)	NR
Neuro	Neurotoxicity 15% (0.1)	NR/ PN?	ICANS 2% (1%)	5% (0.1%)	ICANS 3 (0%)	16% (0%)
# Deaths	68/(41 due to PD)	21 (/11 due to PD)	NR	46	1	NR
Hypogamma/IVIg	72%//46%	75%/40%	NR	NR		

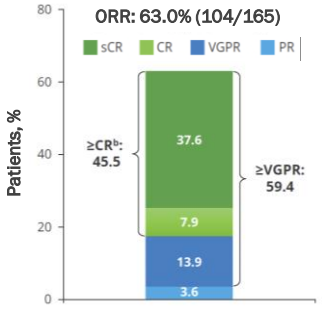
1. Moreau P, et al. *N Engl J Med.* 2022;387:495-505. 2. Van de Donk N, IMS 2023; Abstract OA-51. 3. Lesohkin AM, et al. *Nature Med.* 2023;29:2259-2267. 4. Bumma N, et al. *Blood.* 2022;140(Suppl 1):10140-10141. 5. Voorhees PM, et al. *Blood.* 2022;140(Suppl 1):4401-4404. 6. D'Souza A, et al. J Clin Oncol. 2022;40(31):3576-3586. 7. Wong SW, et al. *Blood.* 2022;140(Suppl. 1):400-402. 8. Abdallah AO, et al. *Blood.* 2022;140(Suppl 1):7284-7285.
Courtesy of A. Chiari.

Accelerated approval

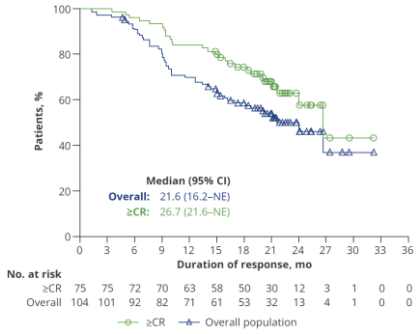
56

Long-Term Follow-Up Results From the MajesTEC-1 Phase 1/2 Study of Teclistamab in Patients With RRMM: Treatment and Response

Best Response



DOR



Additional Response Data

- ORR was consistent across clinically relevant subgroups
  - ≤3 prior LOT: 74.4% (32/43)
  - >3 prior LOT: 59.0% (72/122)
  - High-risk cytogenetics and/or EMD: 53.3% (32/60)
- Median time to first response: 1.2 months (range, 0.2-5.5)
- Median time to ≥CR: 4.6 months (range, 1.6-18.5)
- Median DOR increased since the previous report
- 34/42 (81.0%) MRD-evaluable patients (at day 100) were MRD negative (10^{-5})
  - 44/54 (81.5%) MRD-evaluable patients (as of March 2022) were MRD negative at any point

- At median follow-up of 23 months (data cutoff: January 4, 2023)
  - 165 patients had received RP2D of teclistamab
  - 47 patients remained on treatment; 42 had switched to q2w dosing (9 on q4w)
    - 41 of these patients maintained a deep response

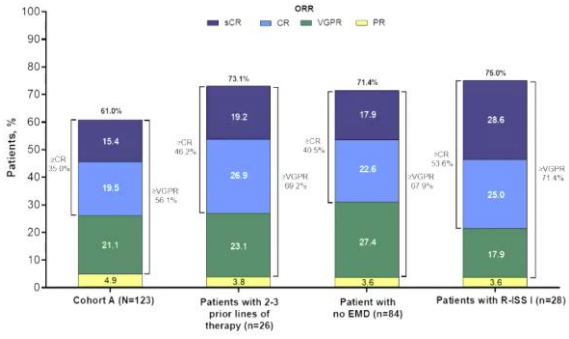
EMORY WINSHIP CANCER INSTITUTE

van de Donk NWCJ, et al. ASCO 2023. Abstract 8011.

57

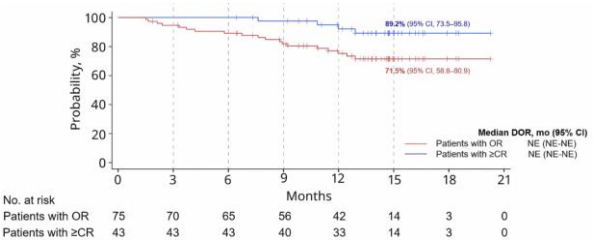
Updated Cohort A Results From the MagnetisMM-3 Phase 2 Study of Elranatamab in BCMA-Naive Patients With RRMM: Response

ORR by BICR



- Confirmed ORR by BICR: 61.0% (95% CI, 51.8-69.6)
  Median time to response: 1.2 months (range, 0.9-7.4)
- MRD negativity (10^{-5}): 89.7% of evaluable patients who achieved CR/sCR (n=29)

DOR by BICR (Responders Only)



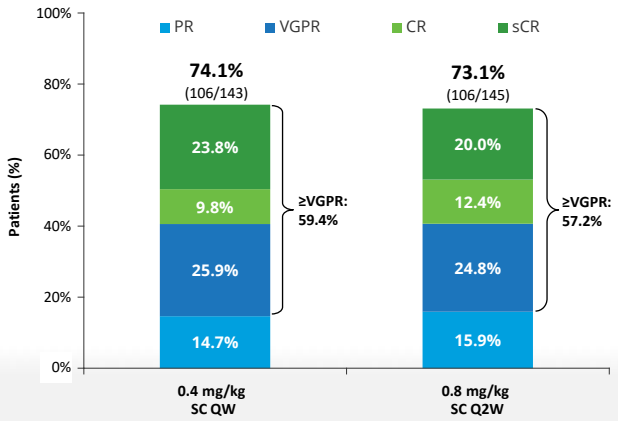
- 50 patients had a response per BICR and switched to q2w dosing
  - 40 of these patients (80%) maintained or improved their response ≥6 months after the switch
- 66.7% (50/75) objective responses were ongoing

EMORY WINSHIP CANCER INSTITUTE

Mohty M, et al. EHA 2023. Abstract S196.

58

MonumenTAL-1: *ORR was similar for QW and Q2W schedules, and in triple and penta-refractory patients*



- **Triple-class refractory: 72.6%** (95% CI, 63.1–80.9) and **71.0%** (95% CI, 61.1–79.6)
- **Penta-drug refractory: 71.4%** (95% CI, 55.4–84.3) and **70.6%** (95% CI, 52.5–84.9)
- ORR was consistent across subgroups including baseline ISS stage III disease, baseline cytogenetic risk, number of prior therapies, refractoriness to prior therapy, and belantamab exposure, except among patients with baseline plasmacytomas

Timing, months	0.4 mg/kg SC QW n=143	0.8 mg/kg SC Q2W n=145
Median (range) follow-up, efficacy	14.9 (0.5[b]–29.0)	8.6 (0.2[b]–22.5)
Median (range) time to first response[c]	1.2 (0.2–10.9)	1.3 (0.2–9.2)
Median (range) time to best response[c]	2.2 (0.8–12.7)	2.7 (0.3–12.5)

EMORY WINSHIP CANCER INSTITUTE

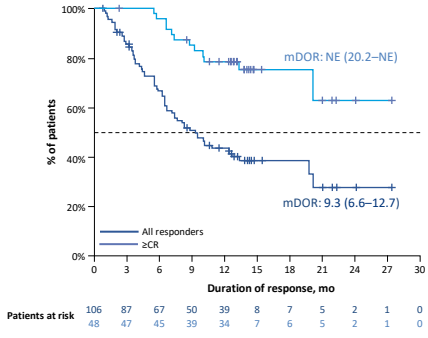
Chari et al., ASH 2022

59

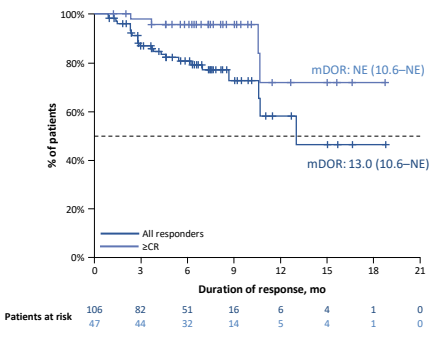
MonumenTAL-1: *Treatment at Both Doses led to Durable Responses*

Median DOR not reached for those patients who achieved ≥CR

DOR, 0.4 mg/kg SC QW[a]



DOR, 0.8 mg/kg SC Q2W[b]



mPFS: 7.5 months (95% CI: 5.7–9.4; 33% censored)

11.9 months (95% CI: 8.4–NE; 61% censored)

EMORY WINSHIP CANCER INSTITUTE

Chari et al., ASH 2022

60

Looking Forward: Additional Novel Agents and New Targets in Myeloma Treatment

- Novel IMiDs: E3 ligase modulators
  - Iberdomide (CC220)
  - Mezigdomide (CC92480)
- Novel oral directed therapies
- CD38-targeted monoclonal antibodies
  - Mezagitamab (TAK-079; anti-CD38), Modakafusp alfa (TAK-573; anti-CD38), TAK-169 (anti-CD38), felzartamab (MOR202)
- Non-BCMA bispecific antibodies
  - Cevostamab (BFCR4350A): targets FcRH5 and CD3
- GPRC5D directed CAR T-cell

EMORY WINSHIP CANCER INSTITUTE

61

Adverse Effects/Supportive Care

- Fatigue
- Infections
- Pain
- Renal dysfunction
- Myelosuppression
- Peripheral neuropathy
- Thrombosis
- Bone health

EMORY WINSHIP CANCER INSTITUTE

62

Therapy Related Adverse Effects

Immunomodulatory Drugs

Class effects: thrombosis, pregnancy risk, REMS

	Thalidomide (Thalomid®)	Lenalidomide (Revlimid®)	Pomalidomide (Pomalyst®)
Adverse Effects	Peripheral neuropathy, constipation, drowsiness	Neutropenia, thrombocytopenia, rash, fatigue, diarrhea	Myelosuppression, fatigue, diarrhea/constipation
DLT	Neuropathy	Neutropenia and thrombocytopenia	Neutropenia
Notes	No dose adjustment needed for renal or hepatic function	Secondary malignancies	Peripheral neuropathy <5%

EMORY WINSHIP CANCER INSTITUTE

DLT, dose-limiting toxicity

N Engl J Med. 2011 Mar 17;364(11):1046-60.
Thalomid (thalidomide) [prescribing information]. Summit, NJ: Celgene Corporation; June 2014.
Revlimid (lenalidomide) [prescribing information]. Summit, NJ: Celgene Corporation; February 2015.
Pomalyst (pomalidomide) [prescribing information]. Summit, NJ: Celgene Corporation; April 2015.

63

Therapy Related Adverse Effects

Proteasome Inhibitors

	Bortezomib (Velcade®)	Carfilzomib (Kyprolis®)	Ixazomib (Ninlaro®)
Adverse Effects	**Peripheral neuropathy, constipation/diarrhea**, myelosuppression, N/V, fatigue	**Myelosuppression**, TTP/HUS, N/V, diarrhea, infusion reactions, heart failure, edema, SOB	Diarrhea/constipation, thrombocytopenia, peripheral neuropathy, N/V, edema, and eye irritation
DLT	Peripheral neuropathy (IV > subQ); myelosuppression	Neutropenia, thrombocytopenia	Neutropenia, thrombocytopenia
Notes	VZV prophylaxis CYP2C19 and 3A4 substrate	VZV prophylaxis Less peripheral neuropathy than bortezomib (Velcade®)	VZV prophylaxis Less peripheral neuropathy than bortezomib (Velcade®)

EMORY WINSHIP CANCER INSTITUTE

VZV, Varicella-zoster virus

N Engl J Med. 2011 Mar 17;364(11):1046-60.
Velcade (bortezomib) [prescribing information]. Cambridge, MA: Millennium Pharmaceuticals Inc; Oct 2014.
Kyprolis (carfilzomib) [prescribing information]. Thousand Oaks, CA: Onyx Pharmaceuticals Inc; March 2015.
Ninlaro (ixazomib) [prescribing information]. Cambridge, MA: Takeda Pharmaceutical Company Limited; Nov 2015.

64

Therapy Related Adverse Effects
Monoclonal Antibodies

	Daratumumab (Darzalex®)	Elotuzumab (Empliciti®)
Adverse Effects	Infusion reactions, fatigue, back pain, headache, pyrexia, cough, upper respiratory tract infection	Infusion reactions, fatigue, diarrhea/constipation, pyrexia, cough, peripheral neuropathy, nasopharyngitis, upper respiratory tract infection, electrolyte changes
Notes	Pre-infusion medication (all cycles) Post-infusion medication (cycle 1 and high risk patients) VZV prophylaxis	Pre-infusion medication (all cycles) Used in combination with IMiD and dexamethasone VZV prophylaxis

EMORY WINSHIP CANCER INSTITUTE

Darzalex (daratumumab) [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; Nov 2015.
Empliciti (elotuzumab) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company. Nov 2015.

65

Therapy Related Adverse Effects
Selinexor (Xpovio™)

	Selinexor (Xpovio™)
MOA	First-in-class nuclear export inhibitor; reversibly inhibits nuclear export of tumor suppressor proteins, growth regulators, and mRNAs of oncogenic proteins by blocking exportin 1
Adverse Effects	Myelosuppression, fatigue, N/V, diarrhea, decreased appetite, weight loss, hyponatremia, hypokalemia, dyspnea, URTI
Notes	• Crosses the BBB • Anti-emetic regimen recommended

EMORY WINSHIP CANCER INSTITUTE

Xpovio™ (selinexor) [prescribing information]. Newton, MA: Karyopharm Therapeutics Inc; July 2019.

66

Therapy Related Adverse Effects
Venetoclax (Venclexta®)

	Venetoclax (Venclexta®)
MOA	BCL-2 inhibitor; selectively inhibits the anti-apoptotic protein BCL-2, which is overexpressed in a subset of myeloma cells
Adverse Effects	Tumor lysis syndrome, neutropenia, diarrhea, and nausea
Notes	• Major CYP3A4 substrate • Considering initiating TLS prophylaxis • Most effective in patients with translocation 11;14 (t(11;14))

EMORY WINSHIP CANCER INSTITUTE

Venclexta (venetoclax) [prescribing information]. North Chicago, IL: AbbVie Inc; July, 2019.
Kumar S, et al. EHA Library 2019;273241: LB2601.

67

Therapy Related Adverse Effects
Cellular Therapies: CRS

Grade	Tocilizumab
1	Tocilizumab: Onset ≥72 hr after infusion, treat symptomatically; onset <72 hr after infusion, consider tocilizumab 8 mg/kg IV over 1 hr (to maximum of 800 mg) Corticosteroids: Consider dexamethasone 10 mg IV every 24 hr
2-3	Tocilizumab 8 mg/kg IV over 1 hr (to maximum of 800 mg), repeat every 8 hr as needed if not responsive to IV fluids or supplemental O_2 Corticosteroids: Dexamethasone 10 mg IV every 12-24 hr If no improvement in 24 hr or rapid progression, repeat tocilizumab and escalate to dexamethasone 20 mg IV every 6-12 hr If no improvement in 24 hr or continued rapid progression, repeat tocilizumab and switch to methylprednisolone 2 mg/kg followed by 2 mg/kg divided 4 times/day
4 (ICU/critical care required)	Tocilizumab 8 mg/kg IV over 1 hr (to maximum of 800 mg), repeat every 8 hr as needed if not responsive to IV fluids or supplemental O_2 Corticosteroids: Dexamethasone 20 mg IV every 6 hr If no improvement in 24 hr, consider methylprednisolone (1-2 g, repeat every 24 hr if needed; taper as clinically indicated) or other anti–T-cell therapies

- After 2 doses of tocilizumab, consider alternative anticytokine agents; do not exceed 3 doses of tocilizumab in 24 hr, or 4 doses total

EMORY WINSHIP CANCER INSTITUTE

CRS, cytokine release syndrome

Idecabtagene vicleucel PI. Ciltacabtagene autoleucel PI.

68

Therapy Related Adverse Effects
Cellular Therapies: ICANS

- **Prophylaxis** for seizures with levetiracetam (typically begins during lymphodepleting chemotherapy and is continued until at least 30 days post-CART)
- **Monitor** patients for signs and symptoms of neurologic toxicities
- **Rule out other causes** of neurologic signs or symptoms
- **Provide intensive care supportive therapy** for severe or life-threatening neurologic toxicities
- **Pharmacologic and other interventions** for neurologic toxicities include (depending on nature/severity):
  - Seizure control (eg, benzodiazepines ± phenobarbital and/or lacosamide)
  - Corticosteroids (eg, dexamethasone, methylprednisolone)
  - Hyperventilation and hyperosmolar therapy (eg, for higher grade cerebral edema)

EMORY WINSHIP CANCER INSTITUTE

ICANS, immune effector cell-associated neurotoxicity

Idecabtagene vicleucel PI. Ciltacabtagene autoleucel PI. Brown. Front Oncol. 2021;11:634445. Neelapu. Hematol Oncol. 2019;37 Suppl 1:48. MDACC. IEC therapy toxicity assessment and management (also known as CARTOX) – adult. Approved September 15, 2020.

69

Infections

Infection prophylactic recommendations based on treatment

- Patients receiving a proteasome inhibitor, MoAB, or bispecifics
  - Herpes simplex/Herpes zoster virus prophylaxis
  - Acyclovir or valacyclovir
  - Continue indefinitely
- Patients receiving high-dose steroids or bispecific antibodies
  - PJP prophylaxis
    - Trimethoprim/sulfamethoxazole is the preferred agent
- Patients receiving bispecific antibodies
  - IVIG monthly to maintain IgG > 400
- Consider IVIG for other patients with IgG < 500 and/or recurrent infections

EMORY WINSHIP CANCER INSTITUTE

MoAB, monoclonal antibody; ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T-cell; PJP, pneumocystis jiroveci pneumonia

NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma (Version 2.2024.)

70

Renal Dysfunction

- 20-40% of patients present with renal dysfunction
- Causes include
  - Precipitation of monoclonal light chain in renal tubules
  - Hypercalcemia
- Renal dosing based on CrCl or dialysis
  - Supportive care medications: acyclovir (Zovirax®), levofloxacin (Levaquin®), bisphosphonate therapy
  - Myeloma therapy: cyclophosphamide (Cytoxan or Neosar®) and thalidomide (Thalomid®) do not require adjustments

EMORY WINSHIP CANCER INSTITUTE

CrCl, creatinine clearance

Eleutherakis-Papaiakovou V. *Leuk Lymphoma*. 2007;48:337-341.
Palumbo A. *N Engl J Med*. 2011;364:1046-1060.

71

Myelosuppression

- Supportive care
  - PRBC and platelet transfusions
  - Infectious disease prophylaxis for prolonged ANC < 500
  - Growth factor support
- Consider dose reductions or interruptions of myeloma therapy

EMORY WINSHIP CANCER INSTITUTE

PRBC, packed red blood cells; ANC, absolute neutrophil count

Palumbo A. *N Engl J Med*. 2011;364:1046-1060.

72

Peripheral Neuropathy

- Treatment related
  - Bortezomib > carfilzomib and ixazomib (Velcade®) > (Kyprolis®), and (Ninlaro®)
  - Thalidomide (Thalomid®)
  - Cumulative and dose related
- Prevention
  - Dose reductions
    Twice weekly > weekly
  - Bortezomib (Velcade®) route of administration (SC preferred)
  - MMY-3021 trial evaluated the efficacy of SC vs. IV bortezomib (Velcade®)
    - Efficacy of SC administration non-inferior to IV
    - Significant reduction peripheral neuropathy with SC route

EMORY WINSHIP CANCER INSTITUTE

NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma (Version 1.2020)
Moreau P. *Lancet Oncol*. 2011;12:431-440.

73

Peripheral Neuropathy

Bortezomib (Velcade®) dose reductions

Severity of Peripheral Neuropathy	Recommendation
Grade 1 (no pain or loss of function)	Reduce bortezomib (Velcade®)dose by one level or if receiving twice weekly change to once weekly at the same dose
Grade 1 with pain or Grade 2 with no pain but limiting activities of daily living	Reduce bortezomib (Velcade®) dose by one level or if receiving twice weekly change to once weekly at the same dose
Grade 2 with Pain, Grade 3 or 4	Discontinue bortezomib (Velcade®)

EMORY WINSHIP CANCER INSTITUTE

IMWG guidelines for the management of treatment-emergent peripheral neuropathy in multiple myeloma (MM). http://IMWG.myeloma.org. February 6, 2012. Accessed November 7, 2016.

74

Treatment of Peripheral Neuropathy

- Duloxetine (Cymbalta®, Irenka™)
- Gabapentin or pregabalin (Lyrica®)
- Compounded topical gel (baclofen + amitriptyline + ketamine) (Gablofen®, Lioresal® + Elavil +® Ketalar®)
- Tricyclic antidepressant (nortriptyline [Aventyl®, Pamelor™])
  - Many drug-drug, drug-food interactions and adverse effects

EMORY WINSHIP CANCER INSTITUTE

Hershman DL. *J Clin Oncol.* 2013;32:1941-1967.
IMWG guidelines for the management of treatment-emergent peripheral neuropathy in multiple myeloma (MM). http://IMWG.myeloma.org. February 6, 2012. Accessed November 7, 2016.

75

Thrombosis

- Incidence
  - All cancers: > 7%
  - Myeloma: 3-10%
- Treatment related
  - Thalidomide + dexamethasone (Thalomid® + Decadron®)
    - 14-26% (newly diagnosed)
    - 2-8% (relapsed)
  - Lenalidomide + dexamethasone (Revlimid® + Decadron®)
    - 8-75% (newly diagnosed)
    - 8-16 % (relapsed)
- Risk Factors
  - Obesity
  - Previous VTE
  - Central venous catheter
  - Comorbid conditions: cardiac disease, CKD, DM, acute infection
  - Immobility
  - Surgery
  - Therapy with IMiDs

EMORY WINSHIP CANCER INSTITUTE

VTE, venous thromboembolism;
CKD, chronic kidney disease; DM, diabetes mellitus

Palumbo A. *Leukemia.* 2008;22:414-423.
IMWG guidelines for the prevention of thalidomide- and lenalidomide-associated thrombosis in myeloma. http://imwg.myeloma.org. April 20, 2010. Accessed November 7, 2016.

76

Thrombosis

- Prevention: Patients receiving IMiD + dexamethasone (Decadron®)
  - No risk factor or 1 risk factor
    - Aspirin 81-325 mg daily
  - Two or more risk factors
    - Enoxaparin (Lovenox®) 40 mg SC daily
    - Warfarin (Coumadin®) target INR 2-3
    - Apixaban 2.5 mg twice daily or Rivaroxaban 10 mg daily
    - Fondaparinux 2.5 mg daily
- Treatment
  - Enoxaparin (Lovenox®) 1mg/kg q12h (preferred)
  - Warfarin (Coumadin®) target INR 2-3
  - DOAC (eg. Apixaban, rivaroxaban)
- Continue anticoagulation for duration of therapy

EMORY WINSHIP CANCER INSTITUTE

IMWG guidelines for the prevention of thalidomide- and lenalidomide-associated thrombosis in myeloma. http://imwg.myeloma.org. April 20, 2010. Accessed November 7, 2016

77

Bone Health

- Bisphosphonates should be considered in all patients receiving first-line antimyeloma therapy
  - Pamidronate (Aredia®) 90 mg IV (renal adjustment required)
  - Zoledronic acid (Zometa®) 4mg IV (renal adjustment required)
  - Denosumab (Xgeva®) 120 mg SQ
    - May be preferred for patients with poor renal function
- Duration of therapy: monthly x 2 years, then every 3 months vs. stopping therapy
- Adverse effects
  - Osteonecrosis of the jaw (ONJ)
    - Baseline dental exam and hold for dental procedures

EMORY WINSHIP CANCER INSTITUTE

Anderson K, et al. J Clin Oncol. 2018;36:812-18.

78

Conclusions

- Induction: Four drug therapy with IMiD/PI/dex + anti-CD38 monoclonal antibody is becoming the new standard
- Transplant: continues to play a role for all except frail patients
- Maintenance: Improves OS, needs to be tailored to genetics and risk stratification at diagnosis
- Relapse: Many new targets and immune based treatments
- Supportive care: anticoagulation, infectious disease prophylaxis, bone health

EMORY WINSHIP CANCER INSTITUTE

79

EMORY WINSHIP CANCER INSTITUTE
A Cancer Center Designated by the National Cancer Institute

Nursing Considerations in Multiple Myeloma

Charise Gleason, MSN, NP-BC, AOCNP
VP and Chief APP Officer
Emory Healthcare
NP Myeloma Program
Winship Cancer Institute of Emory University
Atlanta, GA

80

Initial Diagnosis

- Important to provide detailed information about treatment and potential side effects
- Remind patients to report symptoms or side effects early
- Provide handouts
- Financial and Social support
- Local and national support groups
- Shared decision making

EMORY WINSHIP CANCER INSTITUTE

81

Ever-Increasing Factors to Consider

Patient Factors

Clinical
- Age/frailty
- Performance status
- Drug metabolism
- Kidney insufficiency
- Comorbidities

Intangible
- Lifestyle/preferences
- Access to care
- Caregiver support
- Compliance/adherence

Disease

Disease burden
- Stage
- Rate of rise
- Marrow burden
- CRAB symptoms
- Extramedullary involvement

Molecular biology
- Cytogenetic risk status

MM Risk Stratification

Standard risk (~75% of patients)
- Trisomies
- t(11;14)
- t(6;14)

High risk (~25% of patients)
- t(4;14)
- t(14:16)
- t(14;20)
- del(17p)
- gain(1q)
- Double hit: 2 high-risk factors
- Triple hit: ≥ 3 high-risk factors

CRAB, hypercalcemia, renal failure, anemia, and/or lytic bone lesion.

 • Rajkumar SV. Am J Hematol. 2020;95:548-567

82

Select Adverse Events and Prophylaxis by Drug Class

Proteasome Inhibitors	Immunomodulatory Agents	Anti-CD38 Monoclonal Antibodies	Corticosteroids
▪ Herpes zoster prophylaxis ▪ Peripheral neuropathy (bortezomib) ▪ Monitor/manage cardiac conditions carefully (carfilzomib) ▪ Thromboprophylaxis (carfilzomib)	▪ Prophylactic anticoagulation – 81-mg aspirin for patients with no risk factors – Warfarin or LMWH for higher-risk individuals – Possible role for DOACs ▪ 2 birth control methods required ▪ Cytopenias	▪ Premedicate with corticosteroids, antipyretics, and antihistamines prior to daratumumab ▪ Herpes zoster prophylaxis ▪ Consider *Pneumocystis jiroveci* pneumonia prophylaxis per institutional practice ▪ Interference with blood typing and response monitoring ▪ Evaluate hepatitis B viral serologies at baseline	▪ Hyperglycemia ▪ Fatigue ▪ Hyperactivity ▪ Infection risk ▪ Muscle wasting

EMORY WINSHIP CANCER INSTITUTE

Kurtin. J Adv Pract Oncol. 2013;4:307. Raje. J Natl Compr Canc Netw. 2014;12:502.
NCCN. Clinical practice guidelines in oncology: multiple myeloma. v.1.2024. nccn.org. Daratumumab PI.

83

Disease-Related Supportive Care Needs

Bone Disease

Bone-targeting bisphosphonates or denosumab for ≥ 2 years

Infection Risk

HSV and antibacterial prophylaxis; vaccinations against influenza, pneumonia, COVID-19

Thrombosis Risk

VTE prophylaxis with LMWH, warfarin, DOAC, or ASA depending on risk factors

Peripheral Neuropathy

Rule out contributing nutrient deficiencies; trial anticonvulsant or SSRI; non-pharmacologic interventions (ex TENS)

Gastrointestinal Effects

Rule out infection; hydration and electrolytes; antidiarrheals or laxatives

Fatigue

Manage contributing factors (anemia, pain, dehydration, nutrient deficiency); physical activity according to risk

Miceli TS, et al. Cancer Treat Res Commun. 2021;29:10

84

Managing Steroid-Related Side Effects

- Potential Side effects
  - Flushing and sweating
  - Insomnia
  - Fluid retention
  - Mood changes
  - Dyspepsia
  - Vision changes
  - Steroid-induced diabetes
  - Difficulty concentrating
  - Myopathy
  - Muscle cramping
  - Infection
  - Sexual dysfunction
  - Hiccups
  - Diabetes
- Treatment Strategies
  - Take with food
  - Consider taking in early am
  - Know signs and symptoms of infection: fever over 100.5 F or 38 C, shaking chills, dyspnea, hypotension
  - Take OTC or prescription medication to prevent dyspepsia
  - Anti-viral
  - Anti-bacterial when indicated
  - Exercise
  - Signs and symptoms of diabetes

EMORY WINSHIP CANCER INSTITUTE

Renal, GI, and Peripheral Nerves: Evidence-Based Recommendations for the Management of Symptoms and Care for Patients With Multiple Myeloma. Beth Faiman et al. 2017. CJON 2017, 21(5), 19-36 DOI: 10.1188/17.CJON.S5.19-36.

85

Peripheral Neuropathy

- Sensory
  - Numbness, tingling, pain in hands or feet
  - Difficulty hearing, ringing or buzzing in ears
  - Weakness
- Motor
  - Trouble fastening buttons
  - Difficulty opening things or unable to feel small objects
  - Difficulty ambulating
- Treatment Strategies
  - Cocoa butter
  - B-complex vitamins
  - Folic acid supplements
  - Physical therapy
  - Duloxetine (Cymbalta®, Irenka®)
  - Gabapentin (Gralise®, Horizant®, Neurontin®) or pregabalin (Lyrica®)
  - Compounded topical gel
  - Tricyclic antidepressant (nortriptyline [Aventyl®, Pamelor®])

EMORY WINSHIP CANCER INSTITUTE

Tariman JD, Love G, McCullagh E, Sandifer S; IMF Nurse Leadership Board. Tariman JD, et al. Clin J Oncol Nurs. 2008 Jun;12(3 Suppl):29-36. doi: 10.1188/08.CJON.S1.29-35. Clin J Oncol Nurs. 2008. PMID: 18490255.

86

Incidence of Peripheral Neuropathy

Proteasome Inhibitors

- Bortezomib (Velcade®)[1]
  - Grade ≥2: 24% (SC); 39% (IV)
  - Grade ≥3: 6% (SC); 15% (IV)
- Carfilzomib (Kyprolis™)[2]
  - Any grade: 11%
  - Grade ≥3: 2%
- Ixazomib (Ninlaro®)[3]
  - Any grade: 28% (with IRd vs 21% with Rd)
  - Grade ≥3: 2%

Immunomodulatory Agents

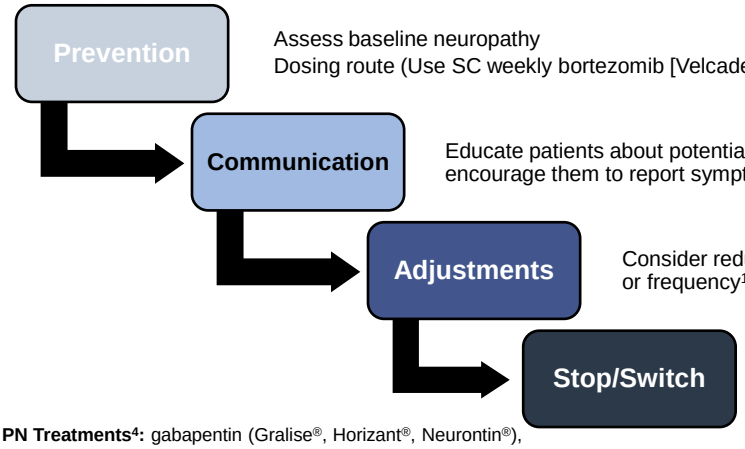
- Lenalidomide (lenalidomide [Revlimid®],[4] pomalidomide [Pomalyst®])[5]
  - Any grade: 10%-15%
  - Grade ≥3: 1%-3%
- Thalidomide (Thalomid®)[6]
  - Any grade: 54%
  - Grade ≥3: 4%

IRd, ixazomib, lenalidomide, dexamethasone; IV, intravenous; Rd, lenalidomide, dexamethasone; SC, subcutaneous

1.bortezomib (Velcade®) [prescribing information] 2017; 2. carfilzomib (Kyprolis™) [prescribing information] 2018; 3. ixazomib (Ninlaro®) [prescribing information] 2016; 4. lenalidomide (Revlimid®) [prescribing information] 2017; 5. pomalidomde (Pomalyst®) [prescribing information] 2018.; 6. thalidomide (Thalomid®)[prescribing information] 2017.

87

Managing Peripheral Neuropathy



PN Treatments[4]: gabapentin (Gralise®, Horizant®, Neurontin®), pregabalin (Lyrica®), amitriptyline (Elavil®), duloxetine (Cymbalta®, Irenka®)

PN, peripheral neuropathy

1. bortezomib (Velcade®)[prescribing information] 2017.; 2. carfilzomib (Kyprolis™) [prescribing information] 2018; 3. ixazomib (Ninlaro®) [prescribing information] 2016; 4. gabapentin (Gralise®, Horizant®, Neurontin®); 5. pregabalin (Lyrica®), amitriptyline (Elavil®); duloxetine (Cymbalta®, Irenka®).6. International Myeloma Working Group (IMWG) website.

88

GI Side Effects

- Nausea/vomiting
  - Anti-emetics
  - Smaller, more frequent meals
  - Avoid fatty or fried foods
  - Avoid strong odors
  - Hydration
  - Dose adjustments as indicated
  - When to notify team

EMORY WINSHIP CANCER INSTITUTE

Renal, GI, and Peripheral Nerves: Evidence-Based Recommendations for the Management of Symptoms and Care for Patients With Multiple Myeloma
Beth Faiman et al. 2017. CJON 2017, 21(5), 19-36 DOI: 10.1188/17.CJON.S5.19-36.

89

GI Side Effects

- Diarrhea
  - Anti-diarrheals
  - Number of episodes
  - Increase fluids
  - Avoid caffeinated, carbonated, heavily sugared beverages
  - Discontinue medications that may contribute

EMORY WINSHIP CANCER INSTITUTE

Renal, GI, and Peripheral Nerves: Evidence-Based Recommendations for the Management of Symptoms and Care for Patients With Multiple Myeloma
Beth Faiman et al. 2017. CJON 2017, 21(5), 19-36 DOI: 10.1188/17.CJON.S5.19-36.

90

GI Side Effects

- Constipation
  - Assess for abdominal pain, bowel sounds, n/v, inability to urinate
  - Increase fluid and fiber intake
  - Laxatives and stool softeners
  - Discuss bowel regimen if on pain medications
- Nutrition support with any GI issue
  - Contact nutritionist

EMORY WINSHIP CANCER INSTITUTE

Renal, GI, and Peripheral Nerves: Evidence-Based Recommendations for the Management of Symptoms and Care for Patients With Multiple Myeloma Beth Faiman et al. 2017. CJON 2017, 21(5), 19-36 DOI: 10.1188/17.CJON.S5.19-36.

91

Thromboembolic Events – DVT/PE

- Risk factors
  - Immobility
  - Obesity
  - Smoking
  - History of blood clots
  - Estrogen
  - Epo
  - Surgery
  - Travel
  - Central venous catheter
  - Comorbid conditions
  - Therapy with IMiDs
- Signs and symptoms
  - Swelling, pain, aching, tightness
  - Tachycardia
  - Veins distended
- Treatment
  - Considered medical emergency
  - Prophylaxis based on risk factors
  - Low dose aspirin if no risk factors
  - Low molecular weight heparin or oral agents
  - Continue anticoagulation for duration of therapy

DVT = deep venous thrombosis; IMiDs = Immunomodulatory drugs;
PE = pulmonary embolism; MM = multiple myeloma; Epo= epoetin alfa.

EMORY WINSHIP CANCER INSTITUTE

Palumbo et al, 2014, International Myeloma Working Group consensus statement for the management, treatment, and supportive care of patients with myeloma not eligible for standard autologous stem-cell transplantation. J. Clin. Oncol. 2014;32:587–600. doi: 10.1200/JCO.2013.48.7934; Palumbo et al, 2008. Leukemia 22(2):414-423.

92

Prevention of Thromboembolism: IMWG Recommendations

Thromboprophylaxis	Risk Factors
Daily aspirin (81-325 mg)	0-1 individual or disease-related
LMWH or therapeutic warfarin	≥ 2 individual or disease-related OR ≥ 1 therapy-related

- Limited data on use of direct oral anticoagulants (DOAC)
- OK to resume immunomodulatory (IMiD) agents after thromboembolic event if fully anticoagulated

IMWG, International Myeloma Working Group; LMWH, low-molecular weight heparin.
Palumbo et al. *Leukemia* 2008;22:414-423;IMWG website.

93

Myelosuppression

- Anemia
  - Increased fatigue
  - Dyspnea
  - Difficulty with ADLs
  - Chest pain with activity
  - Transfusion support
  - Consider erythropoietin
- Neutropenia
  - Monitor for infection
  - Growth factor support (eg, filgrastim [Neupogen®, Zarxio®])
- Thrombocytopenia
  - Increased bruising
  - Petechiae
  - Epistaxis
  - Avoid activities that can cause bleeding
  - Transfusion support

EMORY WINSHIP CANCER INSTITUTE

Kevin Brigle 1 , Amy Pierre 2 , Elizabeth Finley-Oliver 3 , Beth Faiman 4 , Joseph D Tariman 5 , Teresa Miceli 6, 2017 Myelosuppression, Bone Disease, and Acute Renal Failure: Evidence-Based Recommendations for Oncologic Emergencies Affiliations Expand PMID: 28945730 DOI: 10.1188/17.CJON.S5.60-76. .

94

Infection Precautions for Myeloma Patients

- Compromised immunity from MM disease & treatment
  - Good personal hygiene (skin, oral)
  - Environmental control (wash hands, avoid crowds and sick people, etc)
  - Prompt medical attention at signs of infection (eg, fever, chills)
  - Medications (antibacterial, antiviral)
  - Growth factor (eg, filgrastim [Neupogen®, Zarxio®])
  - Intravenous immunoglobulin (IVIG) for hypogammaglobulinemia
    - Post CAR-T, bispecific antibodies
  - Immunizations (NO live vaccines)
    - Pneumovax 20. covid vaccine, seasonal inactivated influenza

EMORY WINSHIP CANCER INSTITUTE

Faiman B, Mangan P, Spong J, Tariman JD, IMF Nurse Leadership Board. *Clin J Oncol Nurs.* 2011;15(Suppl):66-76; Miceli TS, et al. *Clin J Oncol Nursing.* 2011;15(4):9-23.

95

Antiviral Prophylaxis

- Herpes zoster (shingles) resulting from VZV reactivation has a substantial negative effect on quality of life[1]
- MM is associated with more than a 4-fold risk of herpes zoster[1]
- Risk of VZV reactivation increases with
  - PI treatment[2]
  - Post-ASCT[3]
  - Monoclonal antibody treatment[4]
- Acyclovir (Zovirax®) is standard prophylaxis
  - Reduces risk to 1%-2%
- Adjuvanted shingles vaccine for patients with MM[6]
  - More than 90% effective among more than 38,000 individuals
  - High efficacy, no safety signals after ASCT

ASCT, autologous stem cell transplantation; MM, multiple myeloma; PI, proteasome inhibitor; VZV, varicella zoster virus.

1. Hansson et al. *Br J Cancer* 2017;116:1643-1651. 2. Chanan-Khan et al. *J Clin Oncol.* 2008;26:4784-4790. 3. Kamber et al. *Bone Marrow Transplant.* 2015;50:573-578. 4. Kumar et al. NCCN Guidelines. Multiple myeloma. V4.2018. 5. Fukushima et al. *Anticancer Res.* 2012;32:5437-5440. 6. Cunningham et al. *N Engl J Med.* 2016; 375:1019-1032

96

Tools for Management of Fatigue

- Individualized assessment
  - Sleep, nutrition, depression, medications, activity, comorbidities
- Individualized interventions
  - Balance between activity and energy conservation
  - Psychosocial interventions
  - Nutrition consultation
  - Sleep evaluation
  - Pharmacologic interventions
    - Psychostimulants, sleep medications

EMORY WINSHIP CANCER INSTITUTE

NCCN, Guidelines for Fatigue, V1, 2016.

97

Adherence to Therapy

- Provide treatment calendar
- More oral options
- Inform patient and caregiver of possible side effects and symptoms to expect
- The importance of continuing on therapy

EMORY WINSHIP CANCER INSTITUTE

98

Strategies for Staying Well

- Eat a balanced diet
- Get daily activity/exercise
- Avoid infection
- Avoid bleeding or clotting
- Continue to enjoy things you love…
  in other words, LIVE
- Get enough rest
- Take advantage of available resources
- Ask for help when needed

EMORY WINSHIP CANCER INSTITUTE

99

Conclusion

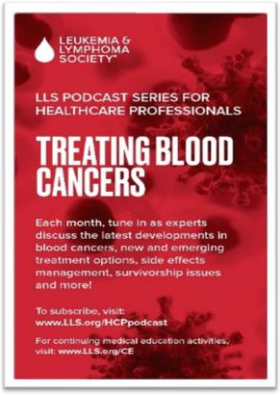
- Nurses contribute to all aspects of care
- Side effect management is essential to keep patients on treatment and improve quality of life
- Encourage patient to be an active participant
- Shared decision making
- Patients living longer and will be exposed to multiple therapies over the course of their disease

EMORY WINSHIP CANCER INSTITUTE

100

FREE LLS RESOURCES FOR HEALTHCARE PROVIDERS

- CME & CE courses: www.LLS.org/CE
- Fact Sheets for HCPs: www.LLS.org/HCPbooklets
- Videos for HCPs: www.LLS.org/HCPvideos
- Podcast series for HCPs: www.LLS.org/HCPpodcast



LEUKEMIA & LYMPHOMA SOCIETY®

101

FREE LLS RESOURCES FOR PATIENTS

- **Information Specialists** – Personalized assistance for managing treatment decisions, side effects, and dealing with financial and psychosocial challenges (IRC).
  - www.LLS.org/IRC
- **Clinical Trial Nurse Navigators** – RNs and NPs provide a personalized service for patients seeking treatment in a clinical trial, sift through the information and provide information to bring back to their HC team (CTSC).
  - www.LLS.org/CTSC
- **Nutrition Education Services Center** – one-on-one consultation with a registered dietician for patients/caregivers of all cancer types (NESC).
  - www.LLS.org/Nutrition
- **Reach out Monday–Friday, 9 am to 9 pm ET**
  - Phone: (800) 955-4572
  - Live chat: www.LLS.org/IRC
  - Email: infocenter@LLS.org
  - HCP Patient Referral Form: www.LLS.org/HCPreferral

LEUKEMIA & LYMPHOMA SOCIETY®

102

HERE TO HELP: LLS COMMITMENT

LLS is committed to providing education and resources to help patients access clinical trials.

CLINICAL TRIAL SUPPORT CENTER

- A team of highly trained nurses and nurse practitioners experienced with hematological malignancies and clinical research.
- Provide education to patients about clinical trials, treatment options, and other disease specific information.
- Provide patients, families, and their caregivers with a professional, detailed, individualized search to discuss with their HCP.
- Provide guidance and serve as advocates throughout the clinical trial process. Help make connections between the patient and the trial site to facilitate enrollment as appropriate.
- Provide a personal connection and develop long term relationships to help better serve our patients.

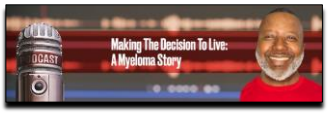
LEUKEMIA & LYMPHOMA SOCIETY®

103

FREE LLS RESOURCES FOR PATIENTS AND CAREGIVERS

❑ **Webcasts, Videos, Podcasts, booklets**:

- www.LLS.org/Webcasts
- www.LLS.org/EducationVideos
- www.LLS.org/Podcast
- www.LLS.org/Booklets
- **www.LLS.org/Myeloma**



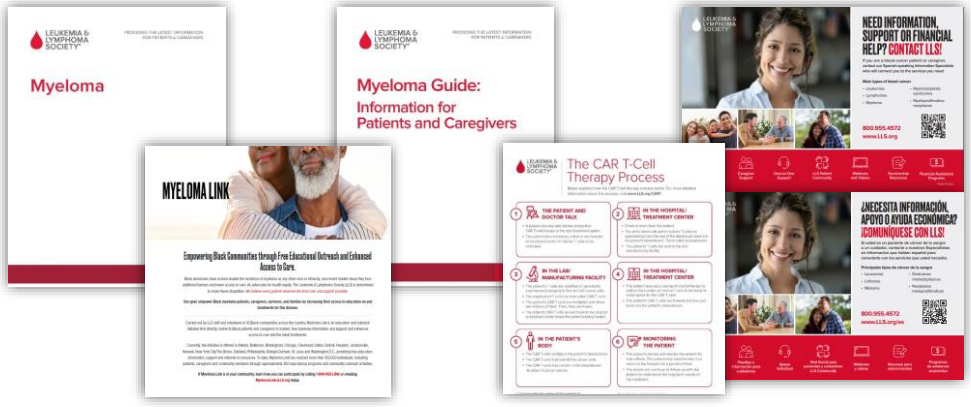
❑ **Support Resources**

- ❑ Financial Assistance: www.LLS.org/Finances
  - Urgent Need
  - Patient Aid
  - Travel Assistance
- ❑ Other Support: www.LLS.org/Support
  - LLS Regions
  - Online Weekly Chats Facilitated by Oncology SW
  - LLS Community Social Media Platform
  - First Connection Peer to Peer Program

LEUKEMIA & LYMPHOMA SOCIETY®

104

FREE LLS RESOURCES FOR YOUR PATIENTS



- www.LLS.org/Myelomalink

BOOKLETS AND FACT SHEETS

English – www.LLS.org/Booklets
Spanish – www.LLS.org/Materiales

LEUKEMIA & LYMPHOMA SOCIETY®

105

THANK YOU

To speak with an Information Specialist or to refer a patient:
Phone (800) 955-4572 Email: Infocenter@LLS.org

For questions about this program, concerns, or assistance for people with disabilities or grievances, please contact us at Profeducation@LLS.org

We have one goal: A world without blood cancers

LEUKEMIA & LYMPHOMA SOCIETY®

106