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HIGHLIGHTS IN THERAPY: MULTIPLE MYELOMA

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WELCOMING REMARKS

HIGHLIGHTS IN THERAPY: MULTIPLE MYELOMA

Lizette Figueroa-Rivera, MA
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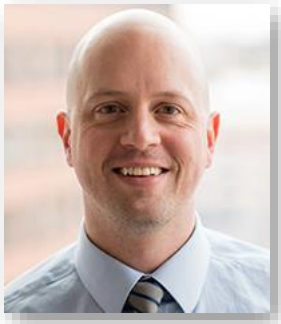
PRESENTATION

HIGHLIGHTS IN THERAPY: MULTIPLE MYELOMA



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DISCLOSURES

HIGHLIGHTS IN THERAPY: MULTIPLE MYELOMA

Andrew J. Cowan, MD

Research Funding: AbbVie, Adaptive Biotechnologies, BMS, Harpoon, IGM Biosciences, Janssen, Nektar, Regeneron, Sanofi

Consultancy, advisory board, or steering committee: AbbVie, Adaptive Biotechnologies, BMS, Sanofi, Janssen

HIGHLIGHTS IN THERAPY - OVERVIEW

1. Introduction
2. Understanding Multiple Myeloma
3. Current Treatments for Multiple Myeloma
4. Emerging Approved Immunotherapies
5. Managing Side Effects
6. Quality-of-Life Considerations
7. Patient and Caregiver Resources
8. Conclusion

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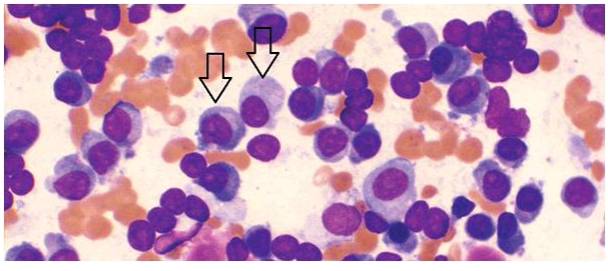
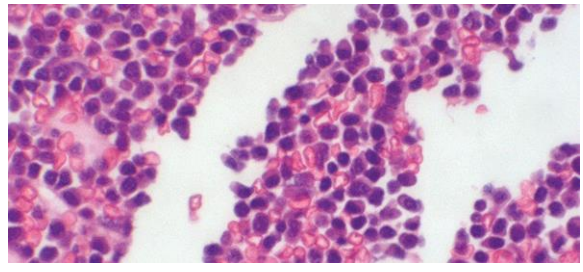
WHAT IS MULTIPLE MYELOMA?

Plasma cell neoplasm

- Characterized by malignant plasma cells infiltrating the bone marrow, and sometimes other organs and tissues
- Symptoms depend on tumor burden and complications by plasma cell clones
- The clones produce monoclonal immunoglobulin, cytokines, and other factors that interfere with bone metabolism, kidney function, hematopoiesis, immune mechanisms, and other organ systems





Eslick R, Talaulikar D. Multiple myeloma: from diagnosis to treatment. *Aust Fam Physician*. 2013 Oct;42(10):684-8.

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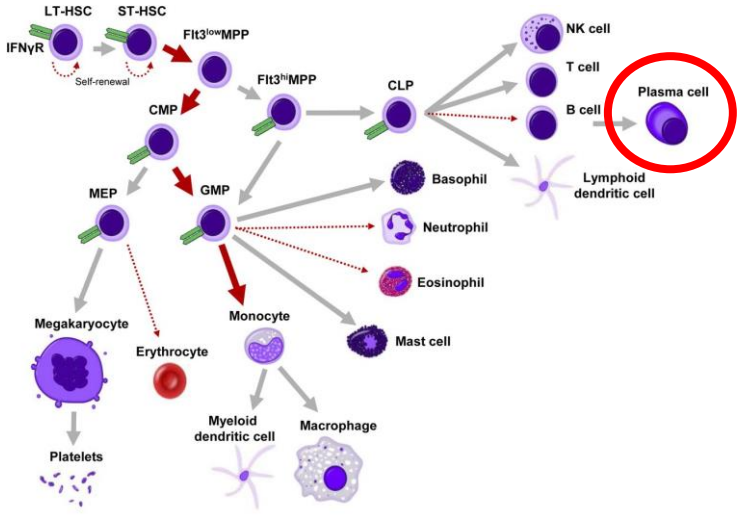
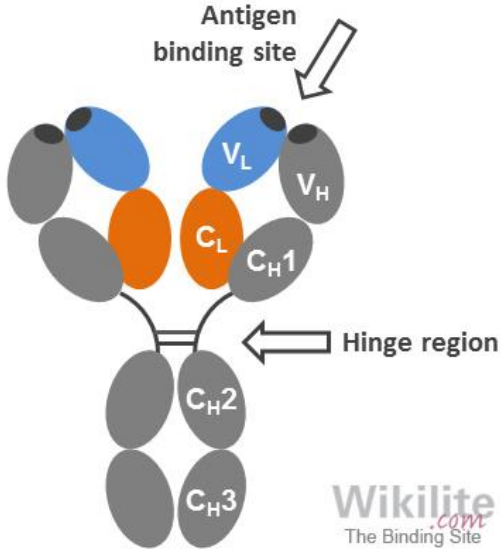
HEMATOPOIESIS

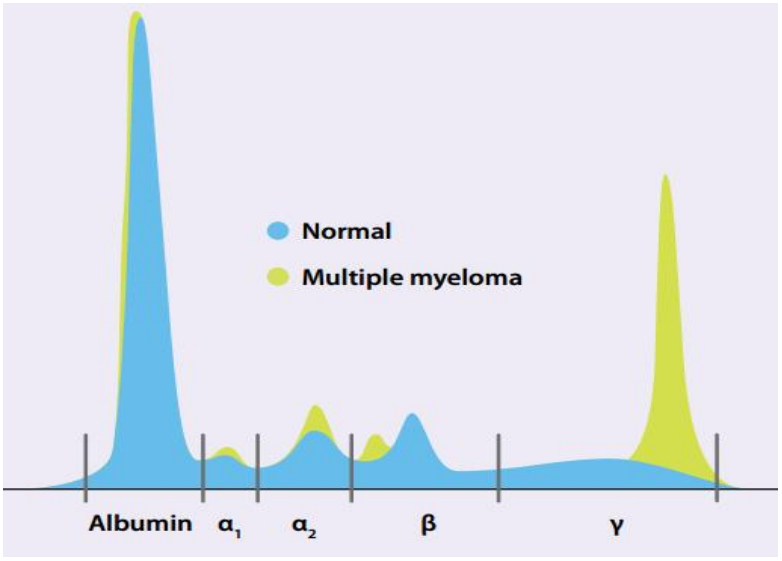


THE IMMUNOGLOBULIN MOLECULE

- V_L: light chain variable domain;
- C_L: light chain constant domain;
- V_H: heavy chain variable domain;
- C_H1–C_H3: heavy chain constant domains 1–3.



SERUM PROTEIN ELECTROPHORESIS (SPEP)



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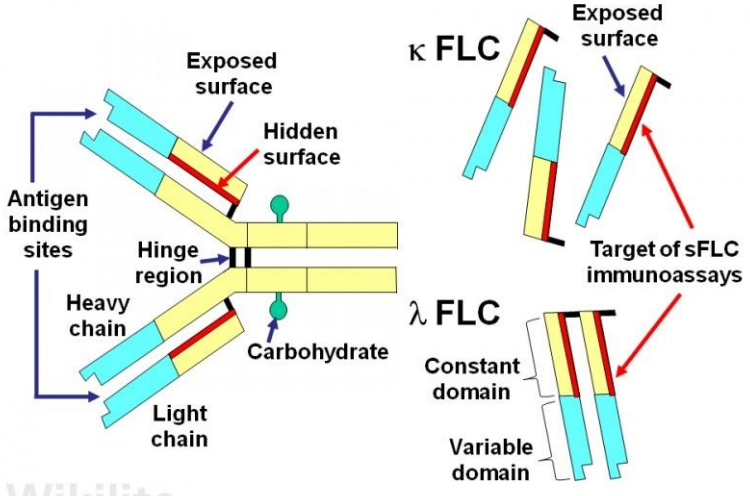
WHAT ARE SERUM FREE LIGHT CHAINS (FLC)?



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EPIDEMIOLOGY OF MULTIPLE MYELOMA - USA

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%
Prevalence (2020)	170,405 people with myeloma in the USA

11 SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/statfacts/html/mulmy.html.

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CLINICAL PRESENTATION OF MULTIPLE MYELOMA

Signs or symptoms related to the infiltration of plasma cells into the bone or other organs or to kidney damage from excess light chains:

- Anemia – 73%
- Bone pain – 58%
- Elevated creatinine – 48%
- Fatigue/generalized weakness – 32%
- Hypercalcemia – 28%
- Weight loss – 24%, one-half of whom had lost ≥9 kg

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MULTIPLE MYELOMA - DIAGNOSTIC CRITERIA SINCE 2014

Clonal bone marrow plasma cells >10% OR biopsy proven plasmacytoma + "CRAB" Criteria (Classic):

Hyper**C**alcemia
Renal failure
Anemia
Bone lesions

New additions with 2014 IMWG (Biomarker driven):

- Serum free light chain ratio (involved/uninvolved) ≥100
- 1 or more focal bone lesions on MRI (>5 mm in size)
- >60% clonal plasma cells on bone marrow examination

IMWG, International Myeloma Working Group; MRI, magnetic resonance imaging.
13 Rajkumar et al *Lancet* 2014.

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CURRENT TREATMENT OF NEWLY DIAGNOSED MM IN 2023

Transplant Eligible

4 drug combinations
Dara-RVd or Dara KRd
3 drug combinations**:**
RVd, KRd,
VCd (renal failure)

→ Autologous stem cell transplantation →

Maintenance
Standard:
Lenalidomide
High risk:
PI/IMiD, CD38/IMID

Not Transplant Eligible

Dara Rd
RVd

→ **Maintenance**

Supportive Care →

Dara, daratumumab; Dara KRd, carfilzomib, lenalidomide, dexamethasone; IMiD, immunomodulatory drugs; PI, proteasome inhibitor; RVd,
14 lenalidomide, bortezomib, dexamethasone.

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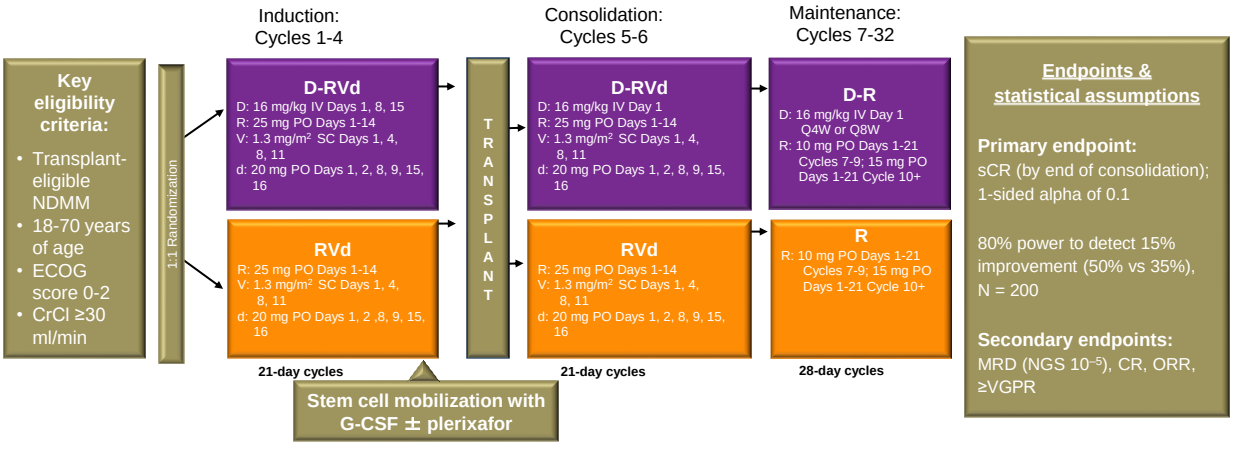
GRIFFIN (NCT02874742): RANDOMIZED PHASE 2

Phase 2 study of D-RVd vs RVd in transplant-eligible NDMM, 35 sites in US with enrollment from 12/2016 and 4/2018



NDMM, newly diagnosed multiple myeloma.

15 Voorhees P et al. ASH Annual Meeting, Orlando, 2019.

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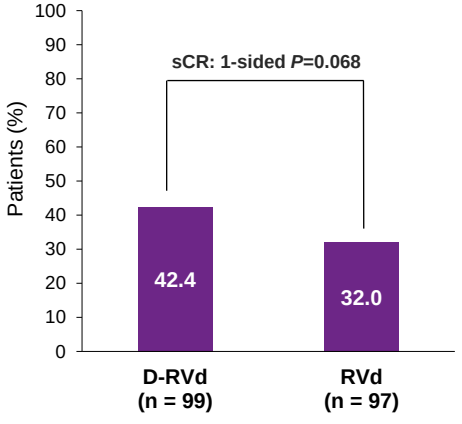
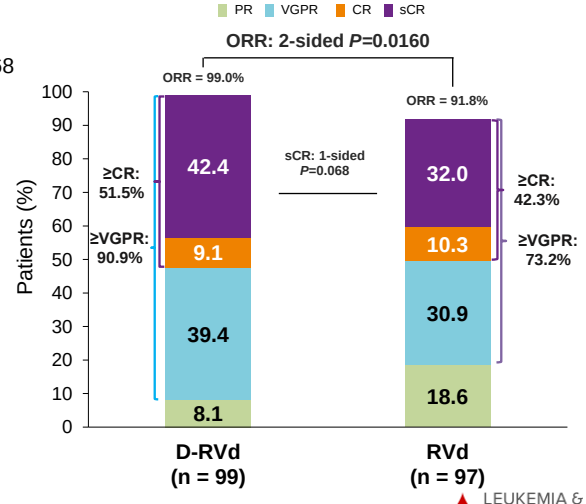
PRIMARY ENDPOINT: sCR BY THE END OF CONSOLIDATION

Primary endpoint met at pre-set 1-sided alpha of 0.1

- sCR by end of consolidation
  - 42.4% D-RVd vs 32.0% RVd
  - Odds ratio, 1.57; 95% CI, 0.87-2.82; 1-sided *P*=0.068



Post-consolidation depth of response



CI, confidence interval; sCR, stringent complete response.

16 Voorhees P et al. ASH Annual Meeting, Orlando, 2019.

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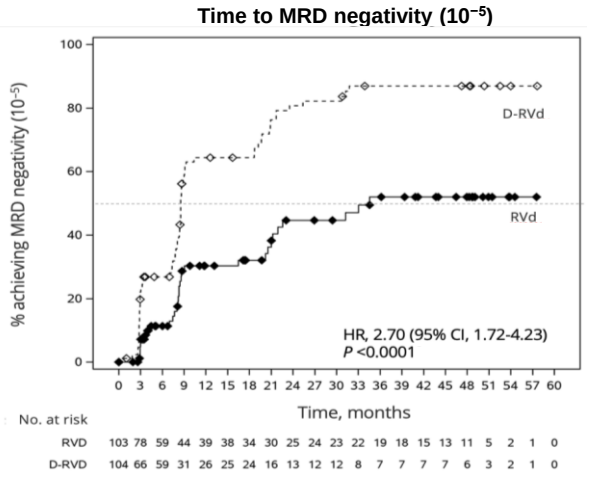
GRIFFIN: TIME TO MRD NEGATIVITY

- **Median time to MRD negativity (10^{-5})**
  - D-RVd: 8.5 months
  - RVd: 34.6 months for RVd
- **At the 10^{-6} threshold, time to MRD negativity**
  - D-RVd: 33.9 months
  - RVd: not reached
- **Time to MRD negativity was shorter for D-RVd versus RVd; however, as a caveat, MRD was not assessed as frequently as response**



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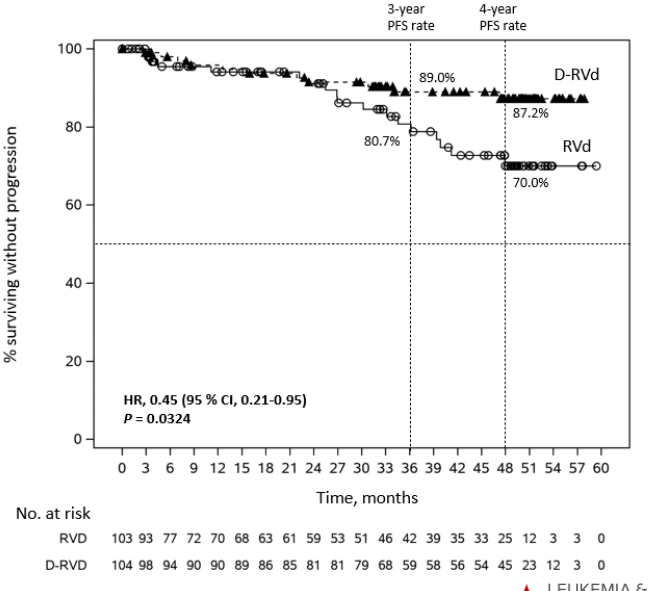
GRIFFIN: PFS IN THE ITT POPULATION

- Median follow-up: 49.6 months
- Median PFS was not reached in either group
- PFS was longer for D-RVd/D-R versus RVd/R, with a clinically meaningful 55% reduction in the risk of disease progression or death
- The separation of the PFS curves occurred beyond 1 year of maintenance and suggests a benefit of prolonged D-R maintenance therapy



ITT, intent to treat; PFS, progression-free survival.
Sborov D et al IMS Meeting, LA, 2022.

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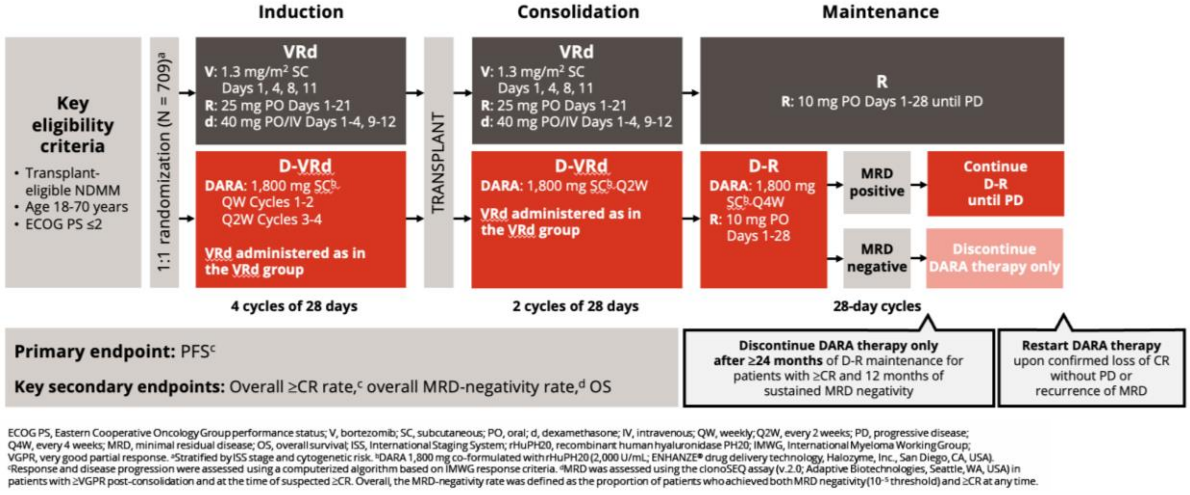
PERSEUS TRIAL: LBA-1: RANDOMIZED PHASE 3 TRIAL



ECOG PS, Eastern Cooperative Oncology Group performance status; V, bortezomib; SC, subcutaneous; PO, oral; d, dexamethasone; IV, intravenous; QW, weekly; Q2W, every 2 weeks; PD, progressive disease; Q4W, every 4 weeks; MRD, minimal residual disease; OS, overall survival; ISS, International Staging System; rHuPH20, recombinant human hyaluronidase PH20; IMWG, International Myeloma Working Group; VGPR, very good partial response. [a]Stratified by ISS stage and cytogenetic risk. [b]DARA 1,800 mg co-formulated with rHuPH20 (2,000 U/mL; ENHANZE® drug delivery technology, Halozyme, Inc., San Diego, CA, USA). [c]Response and disease progression were assessed using a computerized algorithm based on IMWG response criteria. [d]MRD was assessed using the clonoSEQ assay (v.2.0; Adaptive Biotechnologies, Seattle, WA, USA) in patients with ≥VGPR post-consolidation and at the time of suspected ≥CR. Overall, the MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity (10^{-5} threshold) and ≥CR at any time.

19 Sonneveld et al. *NEJM*. 2024;390:301-13. https://www.nejm.org/doi/full/10.1056/NEJMoa2312054.

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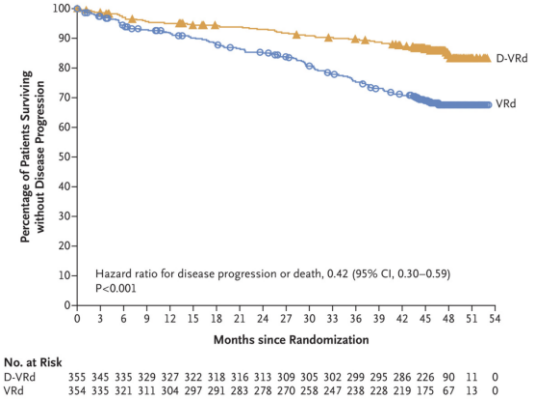
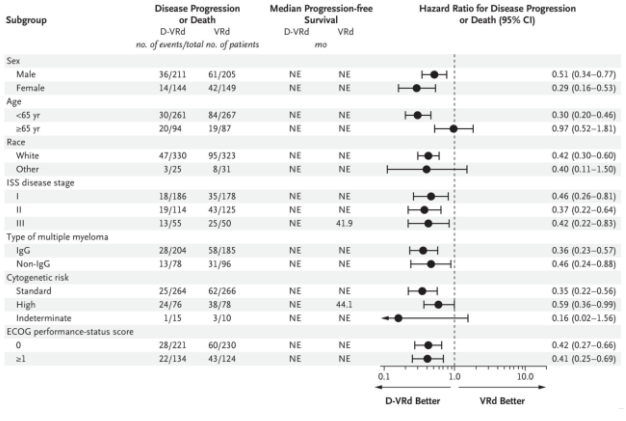
PERSEUS OUTCOMES: DARA-RVD VS RVD





20 Sonneveld et al. *NEJM*. 2024;390:301-13. https://www.nejm.org/doi/full/10.1056/NEJMoa2312054.

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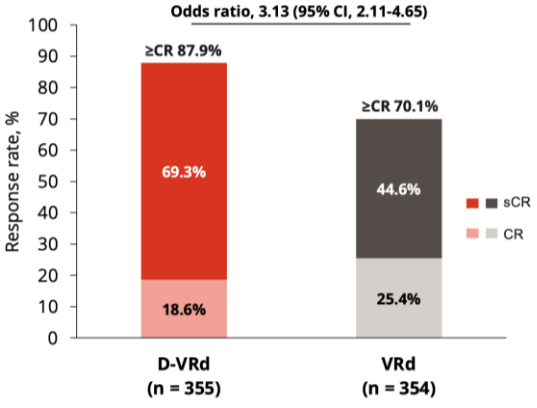
PERSEUS: OVERALL ≥CR RATES



Subgroup	VRd (no. of patients with ≥CR/total no. (%))	D-VRd (no. of patients with ≥CR/total no. (%))	Odds ratio (95% CI)
Sex			
Male	143/205 (69.8)	185/211 (87.7)	3.08 (1.86-5.12)
Female	105/149 (70.5)	127/144 (88.2)	3.13 (1.69-5.80)
Age			
<65 y	186/267 (69.7)	235/261 (90.0)	3.94 (2.43-6.37)
≥65 y	62/87 (71.3)	77/94 (81.9)	1.83 (0.91-3.68)
Race			
White	226/323 (70.0)	289/330 (87.6)	3.03 (2.02-4.53)
Other	22/31 (71.0)	23/25 (92.0)	4.70 (0.91-24.25)
ISS stage			
I	129/178 (72.5)	167/186 (89.8)	3.34 (1.87-5.95)
II	84/125 (67.2)	101/114 (88.6)	3.79 (1.91-7.54)
III	34/50 (68.0)	44/55 (80.0)	1.88 (0.77-4.58)
Type of MM			
IgG	122/185 (65.9)	178/204 (87.3)	3.54 (2.12-5.90)
Non-IgG	73/96 (76.0)	72/78 (92.3)	3.78 (1.45-9.83)
Cytogenetic risk			
Standard risk	182/266 (68.4)	234/264 (88.6)	3.60 (2.27-5.70)
High risk	59/78 (75.6)	63/76 (82.9)	1.56 (0.71-3.44)
Indeterminate	7/10 (70.0)	15/15 (100)	NE (NE-NE)
ECOG PS			
0	160/230 (69.6)	195/221 (88.2)	3.28 (2.00-5.39)
≥1	88/124 (71.0)	117/134 (87.3)	2.82 (1.49-5.34)

[a] *P* value (2 sided) was calculated with the use of the Stratified Cochran-Mantel-Haenszel chi-squared test

CR, complete response.

21 Sonneveld et al. *NEJM*. 2024;390:301-13. https://www.nejm.org/doi/full/10.1056/NEJMoa2312054.

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Table 2. Summary of Tumor Response and MRD Status (Intention-to-Treat Population).

Variable	D-VRd (N=355)	VRd (N=354)	P Value*
Tumor response†			
Overall response — no. (% [95% CI])	343 (96.6 [94.2–98.2])	332 (93.8 [90.7–96.1])	—
Response — no. (%)			
Stringent complete response	246 (69.3)	158 (44.6)	—
Complete response	66 (18.6)	90 (25.4)	—
Very good partial response	26 (7.3)	68 (19.2)	—
Partial response	5 (1.4)	16 (4.5)	—
Complete response or better — no. (%)	312 (87.9)	248 (70.1)	<0.001
Very good partial response or better — no. (%)	338 (95.2)	316 (89.3)	—
Stable disease — no. (%)	4 (1.1)	9 (2.5)	—
Progressive disease — no. (%)	2 (0.6)	1 (0.3)	—
Response could not be evaluated — no. (%)	6 (1.7)	12 (3.4)	—
MRD status‡			
MRD-negative status — no. (%)			
10^{-5} sensitivity threshold	267 (75.2)	168 (47.5)	<0.001
10^{-6} sensitivity threshold	231 (65.1)	114 (32.2)	—
Sustained MRD-negative status, assessed at 10^{-5} sensitivity threshold, for ≥12 mo — no. (%)	230 (64.8)	105 (29.7)	—

MRD, minimal residual disease.

22 Sonneveld et al. *NEJM*. 2024;390:301-13. https://www.nejm.org/doi/full/10.1056/NEJMoa2312054.

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PERSEUS: COMMON ADVERSE EVENTS

- **Neutropenia**
  - Any grade: 69% DRVD, 58% RVD
  - Grade 3 or 4: DRVD 29%, RVD 17%
- **Thrombocytopenia**
  - Any grade: DRVD 48%, RVD 34%
  - Grade 3 or 4: DRVD 29%, RVD 17%
- **Peripheral neuropathy**
  - Any grade: DRVD 53%, RVD 51%
  - Grade 3 or 4: DRVD 4.3%, RVD 4%
- **Infections**
  - Any grade: DRVD 86%, RVD 76%
  - Grade 3 or 4: DRVD 35%, RVD 27%

23 Sonneveld et al. *NEJM*. 2024;390:301-13. https://www.nejm.org/doi/full/10.1056/NEJMoa2312054.

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PERSEUS: SUMMARY

- GRIFFIN phase 2 trial – increased rates of sCR, MRD (-), and improved PFS with Dara RVD
- Large global phase 3 trial – confirms benefit of upfront treatment with CD38/IMID/PI/Dexamethasone in conjunction with autologous HCT
- Daratumumab and lenalidomide maintenance a reasonable option based on GRIFFIN, PERSEUS
- Benefit of quad even in high-risk subgroups

24 MRD, minimal residual disease; PFS, progression-free survival; sCR, stringent compete response.

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DARA RVD ADMINISTRATION: THE FRED HUTCH APPROACH

- **28-day cycles (plan for 4-6 before ASCT, or until deepest response):**
  - Daratumumab subQ per package insert
  - Bortezomib 1.3 mg/m^2 on Days 1, 8, 15 (2x weekly okay if acute cast nephropathy)
  - Lenalidomide 25 mg Days 1-21 out of 28
  - Dex 20 mg weekly for first 1-2 cycles, then plan to stop

- **No post-ASCT consolidation!**
  - At Day +80, move to lenalidomide maintenance. For high-risk cytogenetics, add q14day proteasome inhibitor
  - We do not give daratumumab + lenalidomide maintenance
  - **No dex during maintenance.** Zero benefit and very real risk of long-term toxicities, e.g., visually significant cataracts (Banerjee 2023)

ASCT, autologous stem cell transplant.

25 Banerjee R et al. *AJH*. 2023. Online ahead of print. doi: 10.1002/ajh.27133.

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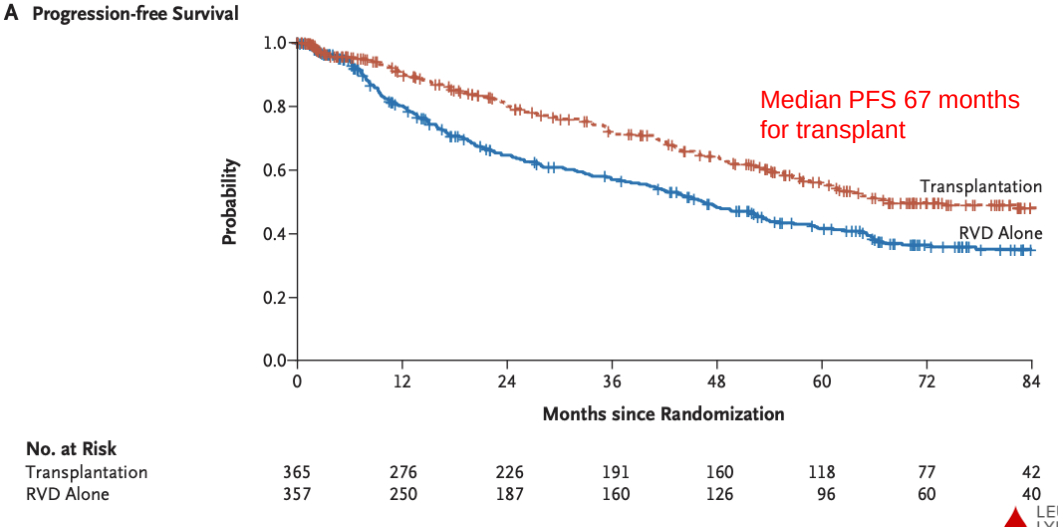
DETERMINATION RVD + R VS RVD/AUTO HCT/R RANDOMIZED TRIAL FOR NDMM



26 Richardson PG et al *NEJM* 2022.

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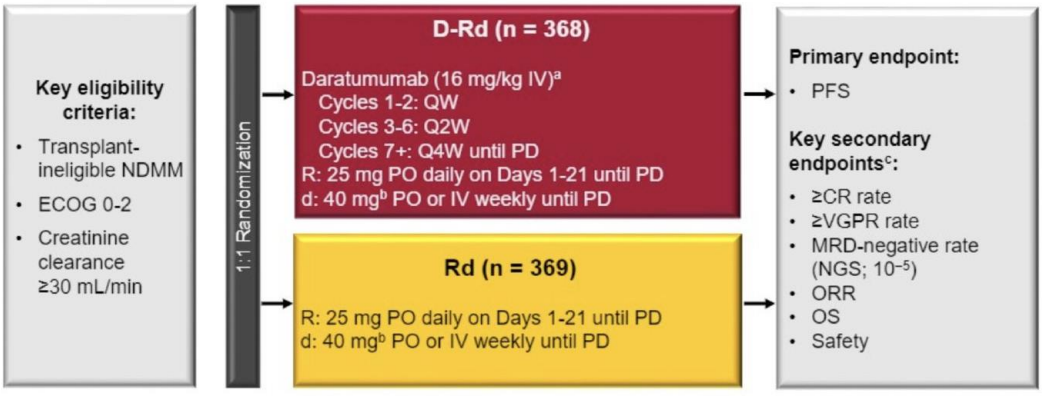
DARA-RD VS RD: MAIA TRIAL – STUDY DESIGN

- Phase 3 study of D-Rd vs Rd in transplant-ineligible NDMM (N = 737)



Facon T, Kumar SK, Plesner T, et al. Phase 3 randomized study of daratumumab plus lenalidomide and dexamethasone (D-Rd) versus lenalidomide and dexamethasone (Rd) in patients with newly diagnosed multiple myeloma (NDMM) ineligible for transplant (MAIA). Abstract #LBA-2. Presented at the 2018 ASH Annual Meeting, December 4, 2018; San Diego, CA.

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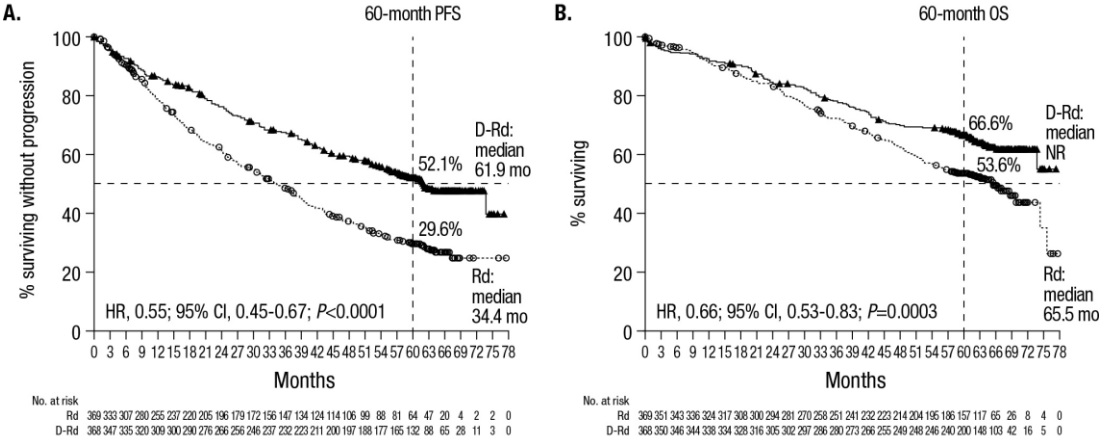
MAIA TRIAL: DARA-RD VS RD UPFRONT TREATMENT FOR ASCT-INELIGIBLE NDMM PATIENTS

Figure: Progression-free survival (A) and overall survival (B) with D-Rd and Rd in the intent-to-treat population.



D-Rd, daratumumab plus lenalidomide/dexamethasone; Rd, lenalidomide/dexamethasone; PFS, progression-free survival; HR, hazard ratio; CI, confidence interval; OS, overall survival; NR, not reached.

ASCT, autologous stem-cell transplant.
Kumar S et al ASH 2022

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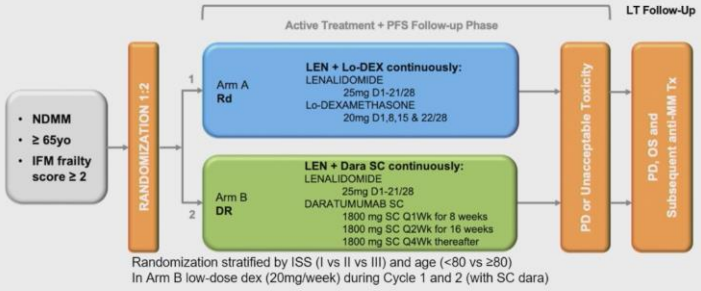
A DEXAMETHASONE SPARING-REGIMEN WITH DARATUMUMAB AND LENALIDOMIDE IN FRAIL PATIENTS WITH NEWLY-DIAGNOSED MULTIPLE MYELOMA: EFFICACY AND SAFETY ANALYSIS OF THE PHASE 3 IFM2017-03 TRIAL

IFM 2017-03 – Study design



Randomization stratified by ISS (I vs II vs III) and age (<80 vs ≥80)
In Arm B low-dose dex (20mg/week) during Cycle 1 and 2 (with SC dara)

Primary endpoint: PFS

Interim analysis endpoints: 12-months-therapy data cut:

- Overall response rate,
- VGPR or better rate,
- MRD rate,
- Occurrence of grade 3 or more side effects

NCT03993912

29 Manier S et al ASH 2022.

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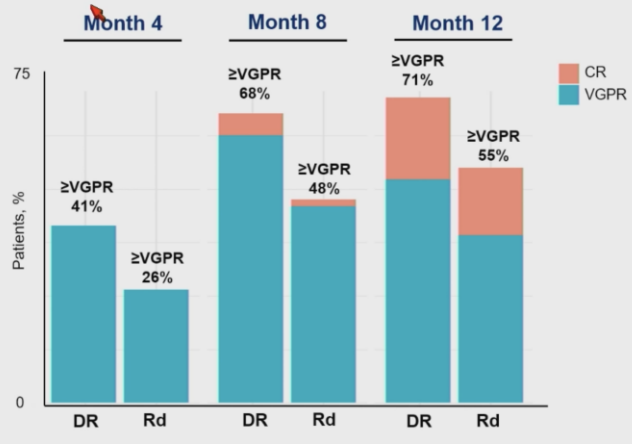
IFM 2017-03 – Rates of VGPR or better over time



Deeper responses were obtained with DR at all time points, including at early time points

30 Manier S et al ASH 2022.

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MANAGEMENT OF RELAPSED MULTIPLE MYELOMA IN 1+ LINE OF THERAPY IN 2024

Most patients:

RVD or Dara RVD → autologous HCT → Lenalidomide maintenance

OR

Dara RD / RVD → lenalidomide maintenance

Progression of Disease

1-3 Lines of therapy

- CD38 + IMID: Carfilzomib, pomalidomide, dexamethasone
- CD38 + PI:Carfilzomib + either Daratumumab/Isatuximab and dexamethasone

4+ Lines of therapy

- BCMA CAR T cells:Cilta-cel, or Ide-cel
- BCMA Bispecific: Teclistamab, elrantabamab
- GPRC5D Bispecific: Talquetamab

Post-BCMA relapse

- Clinical trials
- GPRC5D bispecific: Talquetamab (if not already given)

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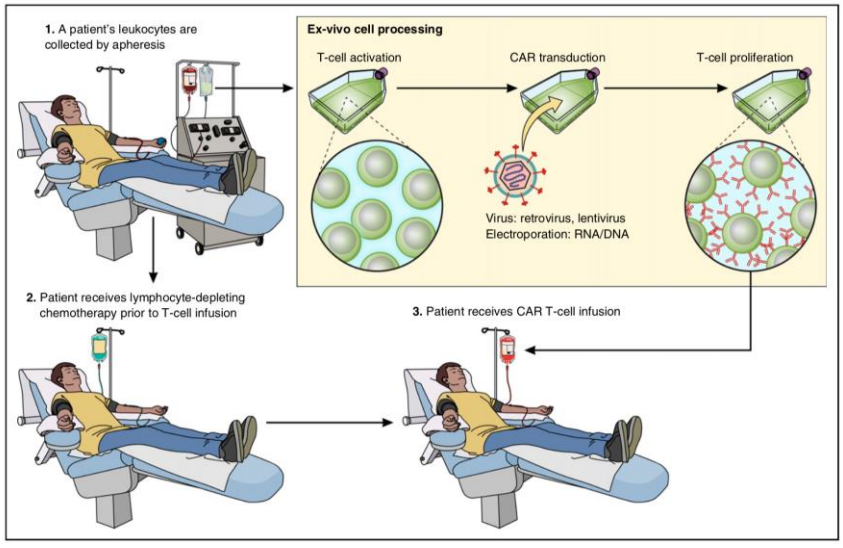
CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY (CAR T CELLS)



32 Mikkilineni L, Kochenderfer J, *Blood* 2017.

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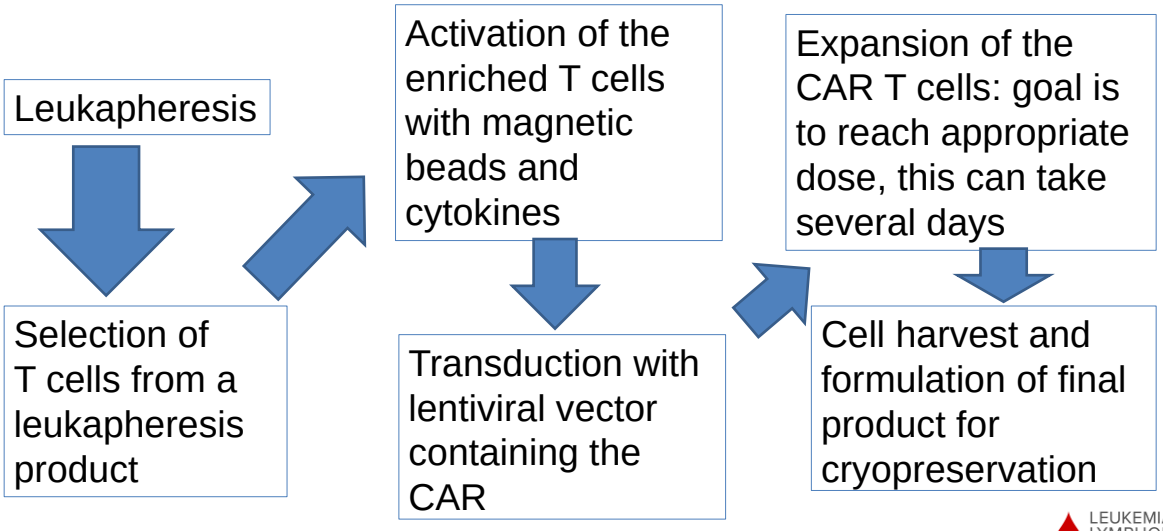
CAR T-CELL MANUFACTURING



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TOXICITIES FROM CAR T-CELL THERAPY

- Cytokine release syndrome
- ICANS – aka neurotoxicity
- Prolonged cytopenias
- B-cell aplasia and hypogammaglobulinemia
- Secondary malignancy

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WHAT IS CYTOKINE RELEASE SYNDROME (CRS)?

- Pro-inflammatory syndrome caused by excessive immune activation from CAR T cell therapy
- If not recognized and treated early, results in substantial morbidity and mortality
- Hallmark of this syndrome is fever, hypotension, hypoxia

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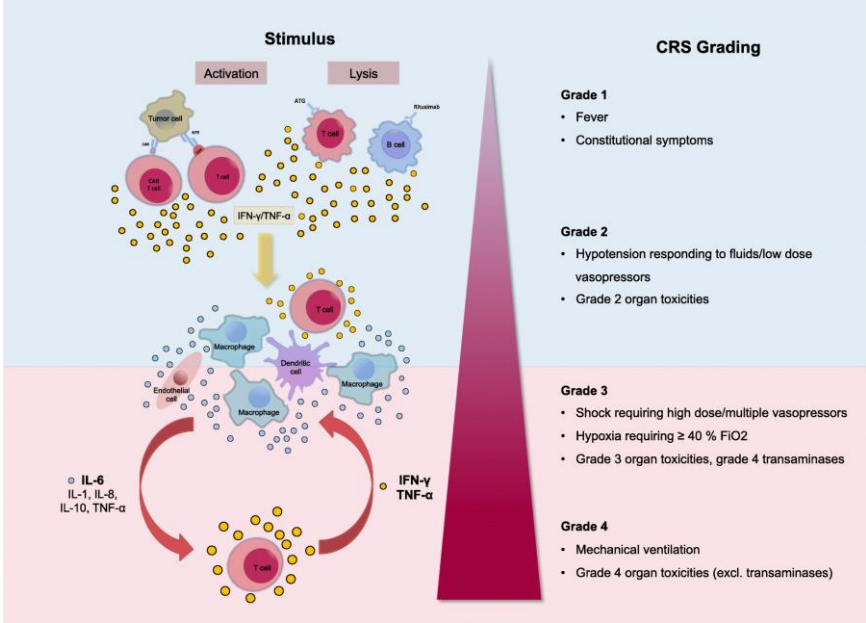

36 Shimabukuro-Vornhagen, et al. *Journal for Immunotherapy of Cancer*; 2018;6:56.

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WHAT IS NEUROTOXICITY ASSOCIATED WITH CAR T-CELL THERAPY?

- Neurotoxicity – also more recently known as “Immune Effectory Cell-Associated Neurotoxicity Syndrome” – ICANS
- Predominant symptoms: Ranges from mild confusion, lethargy, word finding difficulties, to more severe states such involving global encelphalopathy such as coma, persistent vegetative states
- Important – has resulted in deaths in some patients receiving CAR T-cell therapy
- Dexamethasone – mainstay of treatment – treat early, don’t delay!

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EARLIER USE OF BCMA CAR T

KarMMA-3 – Otero P et al, *NEJM* 2023

Ide-cel/Abecma: BCMA targeted chimeric antigen receptor T-cell therapy, approved by FDA in 2020

Multiple myeloma

2-4 prior lines of therapy

Triple class exposed

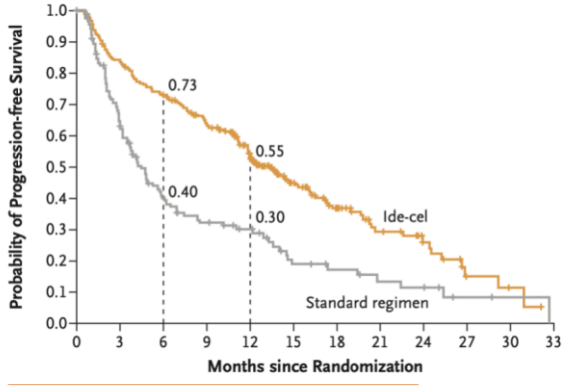
2:1 Randomization

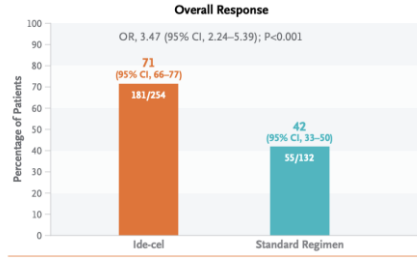
- Ide-cel, N=254
- SOC therapy, n=132

n.b. KdDara or IsaKD not permitted as SOC; 5 approved regimens

Primary endpoint: PFS

Crossover ALLOWED





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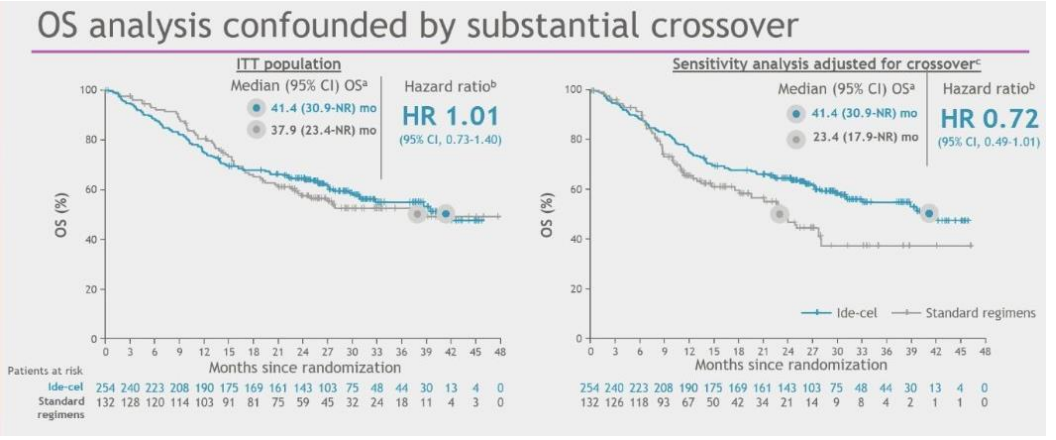
KARMMA-3: UPDATED ANALYSIS

Otero P et al, ASH 2023



[a] Based on Kaplan-Meier approach.
[b] Stratified HR is based on the univariate Cox proportional hazards model. CI is two sided and calculated by bootstrap method.
[c] Two-stage Weibull model without recensoring (prespecified analysis).

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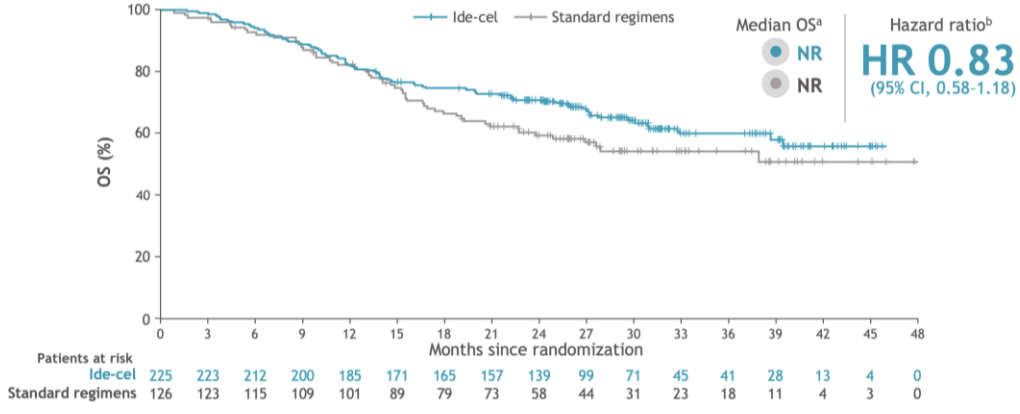
TREND OF OS BENEFIT WITH IDE-CEL AMONG TREATED PATIENTS



- This is an exploratory analysis of the treated population without adjusting for crossover

[a] Based on Kaplan–Meier approach.
[b] Stratified HR based on the univariate Cox proportional hazards model. CI is 2-sided.
OS, overall survival.
Otero P et al, ASH 2023.

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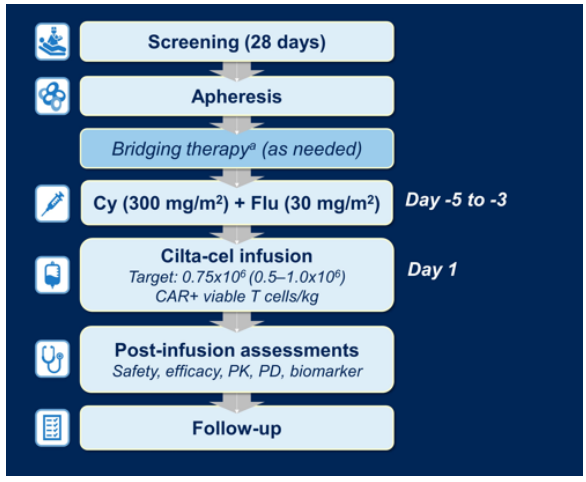
CARTITUDE 1 STUDY DESIGN

- **Primary Objectives**
  - Phase 1b: Determine safety and RP2D
  - Phase 2: Efficacy
- **Eligibility criteria, in brief**
  - PD per IMWG
  - 3 or more prior therapies
  - Prior exposure to IMiD, PI, CD38
  - Measurable disease



[a] Treatment with previously used agent resulting in at least stable disease.

41 Usmani Z et al, ASCO Annual Meeting 2021.

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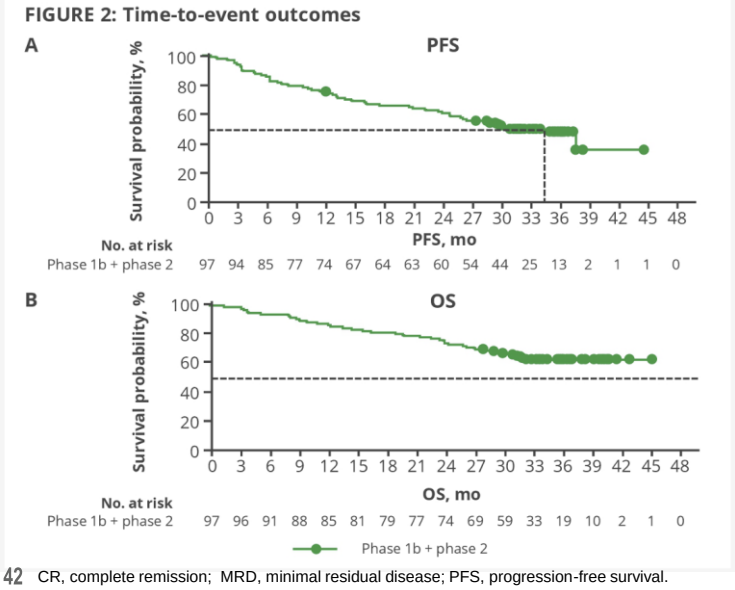
CARTITUDE-1: FINAL RESULTS



42 CR, complete remission; MRD, minimal residual disease; PFS, progression-free survival.

PFS by CR and sustained MRD neg:

- All pts: median PFS 34.9 months
- > CR, median PFS 38.2 months
- 12 mo sustained MRD neg: 30 mo PFS 74.9%
- 12 mo sustained MRD neg, > CR: 30 mo PFS 78.5%

Lin Y et al, ASCO 2023

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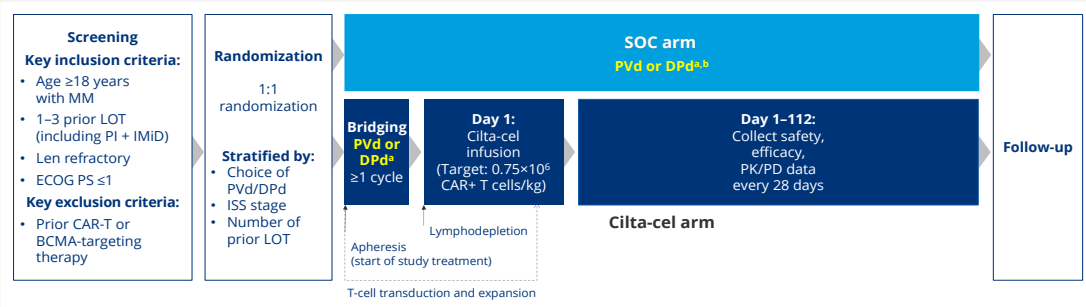
CARTITUDE-4: STUDY DESIGN AND ENDPOINTS



Primary endpoint
- PFS[c]

Secondary endpoints
- Efficacy: ≥CR, ORR, MRD negativity, OS
- Safety
- PROs

[a]Physicians' choice. [b]Administered until disease progression. [c]Time from randomization to disease progression/death.
BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; cilta-cel, ciltacabtagene autoleucel; CR, complete response; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; Len, lenalidomide; LOT, line of therapy; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; SOC, standard of care.

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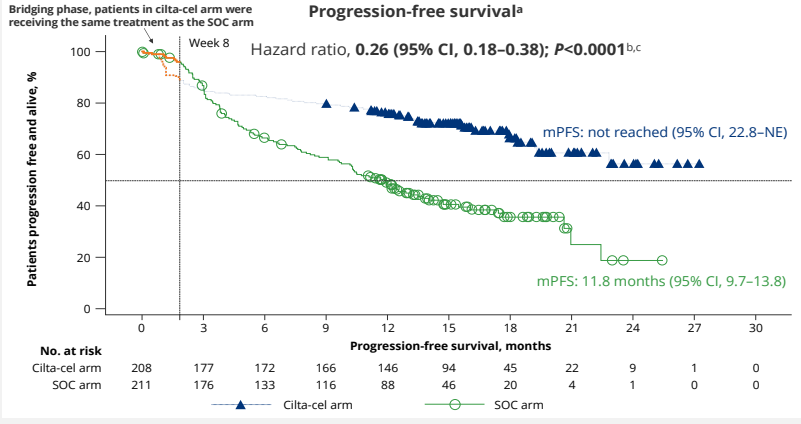
CARTITUDE-4: PRIMARY ENDPOINT – PFS (ITT POPULATION)

Cilta-cel vs SOC
- 12-month PFS rate: 76% vs 49%
- SOC performed as expected



[a]Median follow-up, 15.9 months. [b]Constant piecewise weighted log-rank test. [c]Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable, including only progression-free survival events that occurred >8 weeks post randomization.
cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ITT, intent-to-treat; mPFS, median progression-free survival; NE, not estimable; SOC, standard of care.

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BSABS FOR MM: APPROVED AND IN DEVELOPMENT

BCMAxCD3						
Agent name	**ORR**	**MRD (-)****	**PFS**	**CRS**	**Infections**	**Hospitalization**
Teclistamab[1]*	63%	26.7%	mPFS 11.3 mos	72%	G3-4, 44%	Y – 11 days
Elranatamab[2]*	61%	90%	12 mos PFS 58%	57%	G3-4 35%	Y – 3 days
ABBV-383b[3]	57%	73%	mPFS 10.4 mos	57%	41% all G	Y – 48 hrs D1
Linvoseltamab (REGN5458)[4]	51%	4/10 pts	NA	38%	Not reported	Y
Alnuctamab	43%	Not reported	NA	77%	Not reported	Y
GPRC5DxCD3						
Talquetamab[5]*	68%	69%	mDOR 10.2 mos	80% at 800 ug	G3-4 7%	Y, 11 days
FcRH5xCD3						
Cevostamab[6]	56.7%	7/10 pts	mDOR 11.5 mos	80%	~20%	Y

*FDA Approvals 10/2022, 8/23.
** In Evaluable patients.
1. Moreau P et al, *NEJM* 2022; 2. Bahlis N et al ASH 2022; 3. D Souza A et al, *JCO* 2022; 4. Zonder JA ASH 2021; 5. Chari A et al *NEJM* 2022; 6. Trudel S et al ASH 2021.

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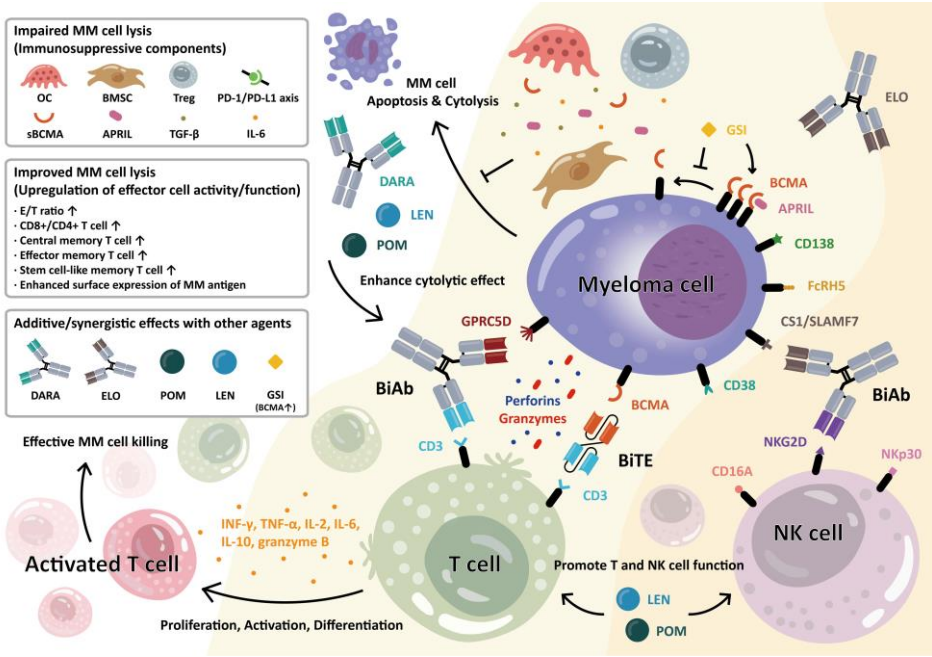

46 Cho SF et al *Frontiers Oncology* 2022.

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QUALITY-OF-LIFE CONSIDERATIONS/MANAGING SIDE EFFECTS

- Treatment-related side effects
  - Peripheral neuropathy
  - Lenalidomide side effects
  - Fatigue
- Mobility and strength
  - Sarcopenia
- Diet and multiple myeloma

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TREATMENT-RELATED SIDE EFFECTS

- Peripheral neuropathy
  - What is it? General dysfunction of nerves.
    - Autonomic, sensory, motor
  - Sensory – pain, tingling, coldness, burning, and numbness
  - Motor – weakness, atrophy of muscles
  - Autonomic – lightheadedness when standing, dry mouth, diarrhea, erectile dysfunction

48 Ref: Weisman J "Healthy Nerves."

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ADVICE FOR PERIPHERAL NEUROPATHY

- Decrease alcohol intake – alcohol has direct toxicity to nerves
- Stop smoking – causes constriction of blood vessels that nourish nerves
- Eat a diet rich in fruits, vegetables, especially dark green leafy vegetables that contain B vitamins (need to discuss latter with your physician first if on blood thinners)
- Muscles use nerves to stay healthy – use them!

49 Ref: Weisman J "Healthy Nerves."

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INTERVENTIONS FOR NEUROPATHY

- Vitamins – Multicomplex B vitamins; B6 should NOT exceed 150 mg daily, folic acid, and vitamin E (B6 > 200 mg daily can CAUSE neuropathy)
- Cramping – stretching of calf muscles
- For pain, burning – medications (always discuss with your physician)
  - Gabapentin – can cause drowsiness, fatigue
  - Pregabalin – same as gabapentin
  - Duloxetine
  - Tricyclics (amitryptiline, and others)

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FATIGUE IN MULTIPLE MYELOMA

- Fatigue is COMMON in multiple myeloma – related to both the disease and sequelae, but also related to treatment
- Grade 3 or higher fatigue in DETERMINATION 6%
- PERSEUS Trial:
  - 24% any grade fatigue with DRVD
  - 2.4% grade 3 or higher fatigue
- Interventions:
  - Exercise
  - Dose reductions of treatment

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LENALIDOMIDE TOXICITY MANAGEMENT

- Gastrointestinal: diarrhea, cramping
  - Heather's tummy fiber
  - Colestipol 1-2 G divided daily; discuss with your physician, may impair absorption of other medications
- Neutropenia
  - Growth factor support, neupogen or Neulasta
  - Dose reductions
- Fatigue
  - Dose reductions
  - Changing treatment schedule, frequency
- VTE prevention
  - Anti thrombotic therapy (aspirin or apixaban/similar)

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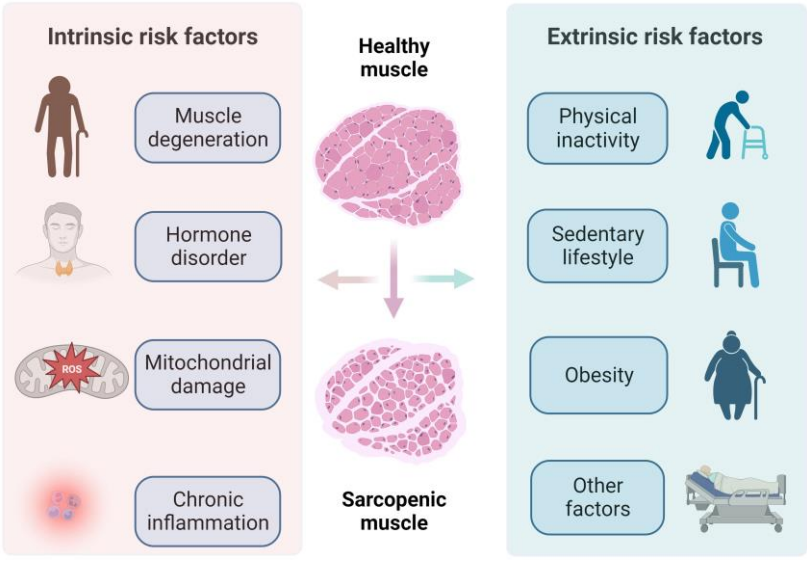
MOBILITY AND STRENGTH - SARCOPENIA



53 Hou Y et al, Front. *Endocrinol.*, 07 January 2024.

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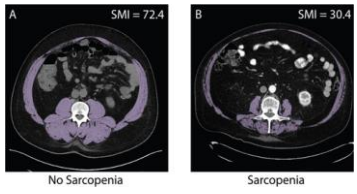
SARCOPENIA IN MULTIPLE MYELOMA

- Sarcopenia is common in multiple myeloma patients:
  - In a single center study of MM pts undergoing auto HCT, sarcopenia (<81% high density muscle) was present in 72/142 pts (51%) and was associated with cardiovascular events[1]
  - Sarcopenia had a negative prognostic impact independent of ISS stage, age, and HR FISH in 322 patients with newly diagnosed MM[2]



  - In an analysis of 61 patients receiving either ide-cel and cilta-cel commercially, 47/61 (77%) met criteria for sarcopenia; sarcopenia associated with higher risk of developing neurotoxicity[3]
  - In a study of 341 patients with newly diagnosed MM, low muscle radiodensity was associated with higher disease stage, anemia, and renal failure, but not with OS[4]

MM, multiple myeloma; HCT, hematopoietic cell transplantation; HR FISH, high-risk fluorescence *in situ* hybridization; OS, overall survival.

54 1. Williams A et al *Bone Marrow Transplant*. 2021 Jan; 56(1): 225–231; 2. Nandakumar B et al, *Cancer* 22 November 2022; 3. Parker N et al ASH Annual Meeting 2022; 4. Abdallah NH et al. *Blood Cancer Journal* volume 13, Article number: 185 (2023).

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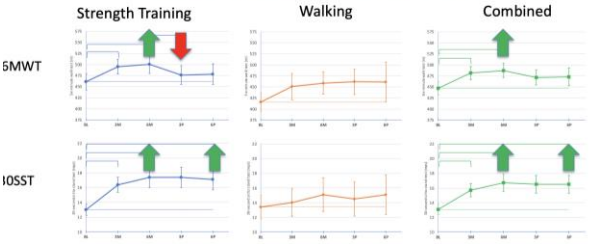
MANAGEMENT OF SARCOPENIA/FRAILTY

- Physical exercise
  - Resistance training – Hillengass et al, IMS 2023: supervised resistance training in a pilot study; no grade 3 or higher AEs, and no new fractures

Intervention

- Cohort 1 (**Resistance Training**): 6 months, twice weekly, supervised resistance training
- Cohort 2 (**Walking**): 6 months, remote prompts to a fitness tracker to reach the recommended 150-300 active minutes per week

Results (6MWT* and 30SST**)



55 Hillengass J et al, IMS Annual Meeting 2023.

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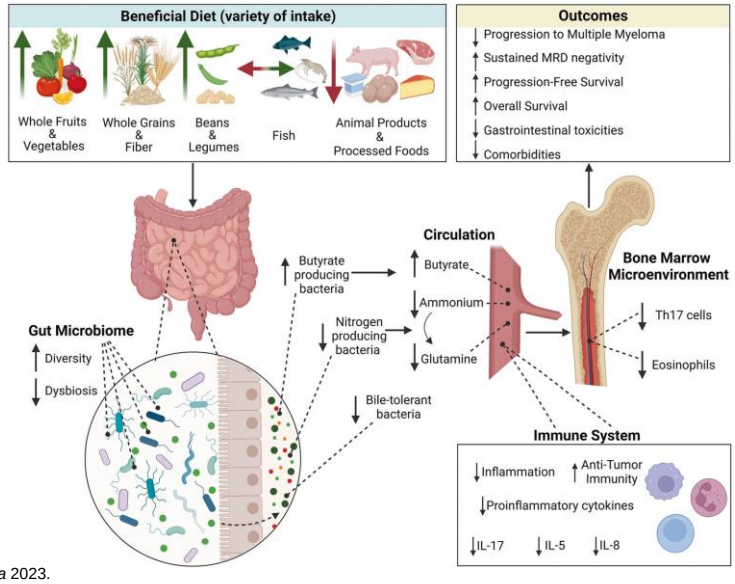
IMPACT OF DIET ON MULTIPLE MYELOMA



56 Shah UA et al *Leukemia* 2023.

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SUMMARY

- Improving outcomes for newly diagnosed MM – with introduction of quad regimens, unprecedented improvements in survival
- Relapsed multiple myeloma seeing gains due to introduction of newer immune based therapies – which would not have been possible without clinical trials!
- Quality of life on treatment still a major issue
  - Neuropathy
  - Fatigue
  - GI issues
  - Strength, energy
- Future research needs to focus not simply on improving survival (and someday finding a cure!) but also on making life more manageable when receiving these treatments.

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ASK A QUESTION

HIGHLIGHTS IN THERAPY: MULTIPLE MYELOMA

Ask a question by phone:

Press star (*) then the number 1 on your keypad.

Ask a question by web:

Click “Ask a question”
Type your question
Click “Submit”

Due to time constraints, we can only take one question per person. Once you’ve asked your question, the operator will transfer you back into the audience line.

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LLS EDUCATION & SUPPORT RESOURCES

HOW TO CONTACT US:

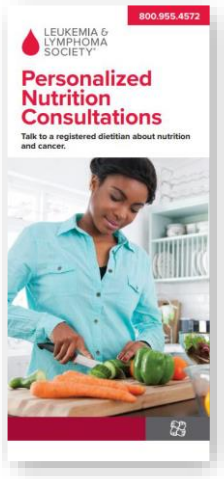
To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:

Call: (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET

Chat live online: www.LLS.org/InformationSpecialist
Monday to Friday, 10 a.m. to 7 p.m. ET

Email: www.LLS.org/ContactUs

CLINICAL TRIAL SUPPORT CENTER
Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.
www.LLS.org/Navigation



NUTRITION CONSULTATIONS
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email.
www.LLSNutrition.org

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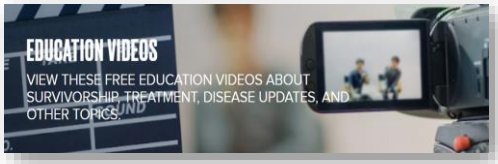
LLS EDUCATION & SUPPORT RESOURCES

Online Chats

Online Chats are free, live sessions, moderated by oncology social workers. To register for one of the chats below, or for more information, please visit **www.LLS.org/Chat**.



Education Videos

View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit **www.LLS.org/EducationVideos**.

Patient Podcast

The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit **www.TheBloodline.org**.

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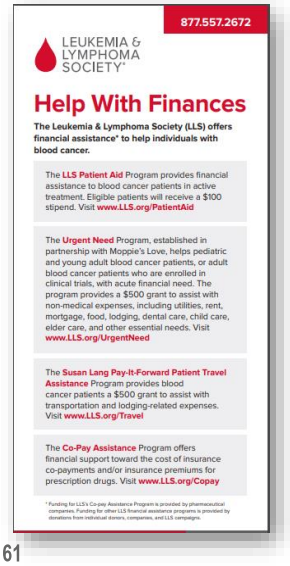
877.557.2672

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Help With Finances

The Leukemia & Lymphoma Society (LLS) offers financial assistance* to help individuals with blood cancer.

The **LLS Patient Aid** Program provides financial assistance to blood cancer patients in active treatment. Eligible patients will receive a $100 stipend. Visit **www.LLS.org/PatientAid**

The **Urgent Need** Program, established in partnership with Moppie's Love, helps pediatric and young adult blood cancer patients, or adult blood cancer patients who are enrolled in clinical trials, with acute financial need. The program provides a $500 grant to assist with non-medical expenses, including utilities, rent, mortgage, food, lodging, dental care, child care, elder care, and other essential needs. Visit **www.LLS.org/UrgentNeed**

The **Susan Lang Pay-It-Forward Patient Travel Assistance** Program provides blood cancer patients a $500 grant to assist with transportation and lodging-related expenses. Visit **www.LLS.org/Travel**

The **Co-Pay Assistance** Program offers financial support toward the cost of insurance co-payments and/or insurance premiums for prescription drugs. Visit **www.LLS.org/Copay**

* Funding for LLS's Co-pay Assistance Program is provided by pharmaceutical companies. Funding for other LLS financial assistance programs is provided by donations from individual donors, companies, and LLS campaigns.

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The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancers:
www.LLS.org/Finances

To order free materials: **www.LLS.org/Booklets**

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THANK YOU

This program is supported by

Genentech A Member of the Roche Group | Biogen | Johnson&Johnson

Please complete our program evaluation

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We have one goal: A world without blood cancers

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