



Opening Remarks

Mary DeRome, MS
MMRF

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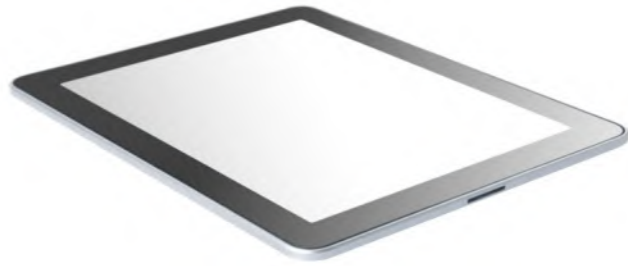
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Program Faculty

Hearn Jay Cho, MD, PhD

MMRF
Norwalk, Connecticut
Icahn School of Medicine at Mount Sinai
New York, New York

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Icahn School of Medicine at Mount Sinai
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Santiago Thibaud, MD

Icahn School of Medicine at Mount Sinai
New York, New York

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Summit Agenda

Time (ET)	Topic	Speakers
9:00 – 9:15 AM	Introduction to MMRF	Mary DeRome, MS
9:15 – 9:30 AM	Welcome	Hearn Jay Cho, MD, PhD Sundar Jagannath, MD
9:30 – 9:45 AM	Multiple Myeloma Biology	Cesar Rodriguez, MD
9:45 – 10:00 AM	Treatment for Newly Diagnosed Multiple Myeloma	Joshua Richter, MD
10:00 – 10:15 AM	Autologous Stem Cell Transplant	Shambavi Richard, MD
10:15 – 10:30 AM	Town Hall Q&A	Speaker panel
10:30 – 10:45 AM	Break	
10:45 – 11:00 AM	Treatment for Relapsed/Refractory Multiple Myeloma	Santiago Thibaud, MD
11:00 – 11:15 AM	Personalized Medicine	Samir S. Parekh, MD
11:15 – 11:30 AM	Supportive Care	Leora A. Giacoia, MS, FNP-BC, ACHPN
11:30 – 11:45 AM	Town Hall Q&A	Speaker panel
11:45 AM – 12:15 PM	Lunch and Patient Speaker	Roger Rawlings
12:15 – 12:30 PM	Closing Remarks	Mary DeRome, MS, and Sundar Jagannath, MD

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MMRF Introduction

Mary DeRome, MS and Hearn Jay Cho, MD, PhD
MMRF

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The Work of the MMRF

The MMRF does three things in relentless pursuit of its mission to accelerate a cure for each and every myeloma patient.

1

We accelerate new treatments

Bringing next-generation therapies to patients faster

2

We drive precision medicine

Using data to deliver better answers and more precise treatments for patients

3

We empower patients

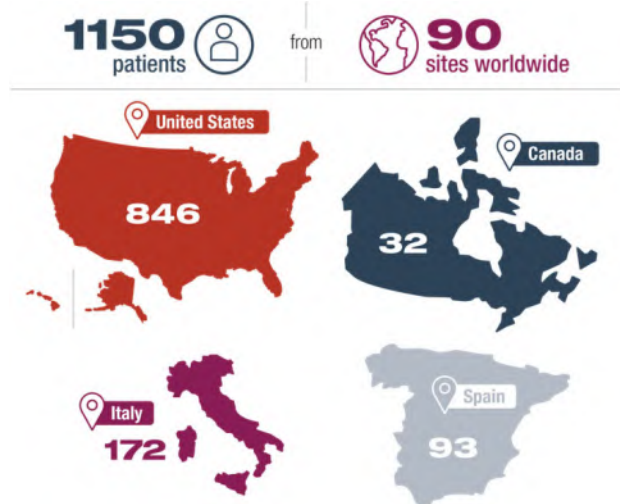
Putting them on The Right Track and guiding them to the right team, tests, and treatments to extend their lives

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MMRF CoMMpass Study: Advancing Personalized Medicine Research

- Landmark study focusing on the genomics of myeloma
- Goals
 - Learn which patients respond best to which therapies
 - Identify new targets and new hypotheses
- Newly diagnosed patients are followed for at least 8 years

All participants undergo a type of detailed DNA testing called genomic sequencing at diagnosis and each relapse.



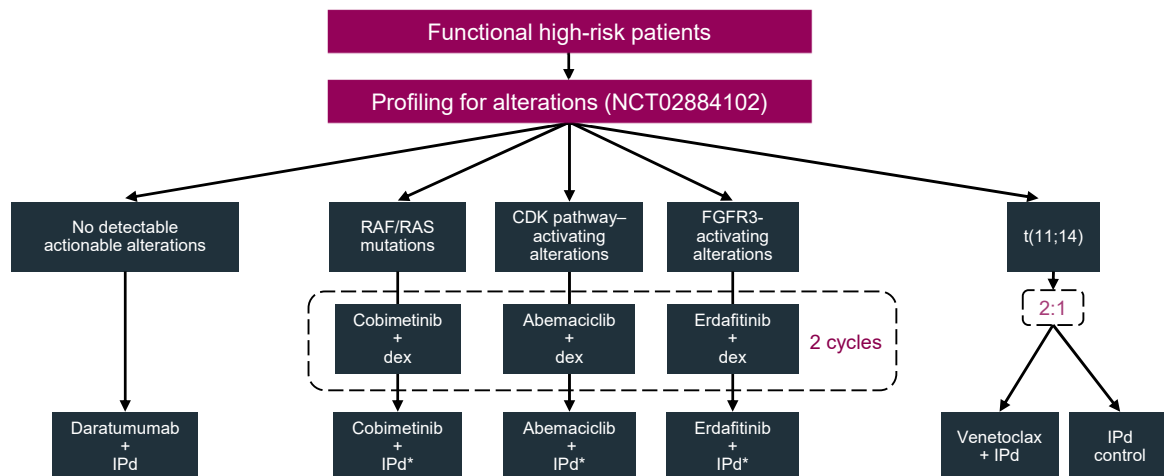
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CoMMpass Is a Trial of Discovery

- CoMMpass data has
 - Provided the myeloma community with information on
 - Frequency of genetic abnormalities
 - How genetic abnormalities play a role in myeloma
 - Drive multiple myeloma cell growth and survival
 - Contribute to drug resistance
 - May predict which patients respond to which therapy
 - Genetic abnormalities that help refine risk assessment
 - Led to conception of the MyDRUG trial

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MyDRUG Trial



*Assess single-agent activity after 2 cycles; after cycle 2, add backbone to single agent

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MMRF Research Initiatives

1. MMRF Myeloma Accelerator Challenge (MAC) Grants

- Broad, multi-institutional research grants designed to advance clinical trial concepts in the areas of
 - High-risk newly diagnosed multiple myeloma (NDMM)
 - High-risk smoldering myeloma (SMM)
- Each research network will be funded up to \$7M over 3 years

2. MMRF Horizon Adaptive Platform Trials

- Paired with MAC grants
- Done in collaboration with 13 MMRC sites
- Trials in relapsed/refractory myeloma, high-risk NDMM, high-risk SMM

For more information, visit themmrf.org

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2023 Myeloma Accelerator Challenge Program Grant Recipients



Samir Parekh, MD

Transforming Treatment of High-Risk Myeloma

Network includes Tisch Cancer Center at Mt Sinai, Albert Einstein Medical College, Hackensack University Medical Center, Stanford University Medical Center, UCSF, Washington University of Saint Louis



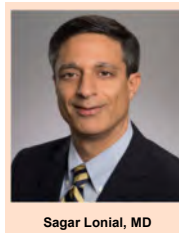
Pieter Sonneveld, MD, PhD

A Systems Biology Approach to High-Risk Myeloma

Network includes Erasmus Medical Center, Rotterdam; Amsterdam University Medical Centers; Julius Maximilian University of Wurzburg; University of Turin; University of Salamanca



Each network will receive \$7M over 3 years for a total \$21M investment by the MMRF, meant to foster collaboration and advance compelling hypotheses that are ready for rapid testing in clinical trials.



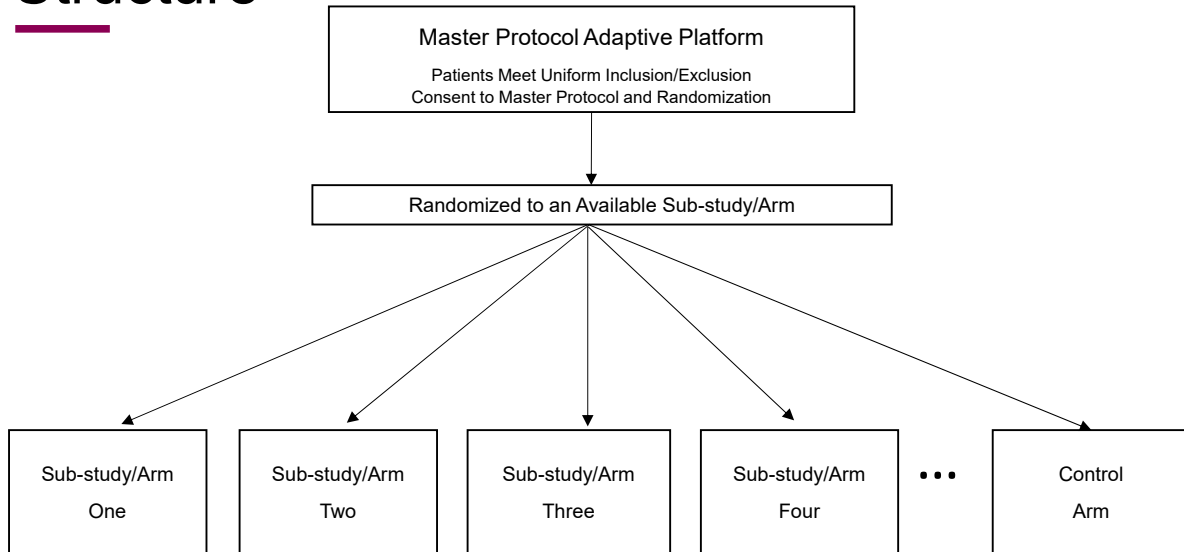
Sagar Lonial, MD

Clinical and Multi-Omics Platforms to Define High-Risk Smoldering Myeloma

Network includes Emory University, Atrium Health Levine Cancer Institute, Icahn School of Medicine at Mt. Sinai, Mass General Hospital, Mayo Clinic, MSKC Institute, Dana-Farber Cancer Institute

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MMRC Horizon Adaptive Platform Trial Structure



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MMRF 2023 Scholars Grant Awardees

Eden Biltibo Vanderbilt University Medical Center



Grant Proposal:
Identifying Effective and Cost-Conscious Maintenance Daratumumab Dosing
Frequent hospital visits cost money and increases exposure to bad bugs. If we prove every 8-week daratumumab works as good, patients won't have to come to the hospital on a monthly basis.

Eden Biltibo, MD, MS is a Hematology/Oncology clinical fellow at Vanderbilt University Medical Center., who is passionate about developing strategies to bridge health care disparities in Multiple Myeloma care. She particularly focuses on the equitable utilization of immunotherapeutics in multiple myeloma and improving racial diversity of clinical trial participants in those trials.

Joselle Cook Mayo Clinic, Rochester



Grant Proposal:
Prevalence Of MGUS Among Unique Populations Of Black People
For people who test positive for MGUS, we will perform DNA testing which will inform us about ancestral origins and will give information on genetic variations that we know are associated with MGUS and MM.

Joselle Cook, MBBS is an assistant professor and Hematology/Oncology Fellow at Mayo Rochester. Dr. Cook received her medical degree from University of the West Indies Faculty of Medical Sciences. She completed her residency and fellowship training in 2022.

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Welcome!

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Question

Are you a...

1. Patient
2. Caregiver (family member or friend who helps patient manage his or her disease)
3. Other

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Question

At what stage is your myeloma? (If you are a caregiver, what is the stage of the patient's myeloma?)

1. Newly diagnosed
2. Relapsed/refractory
3. Remission: still on therapy
4. Remission: not on therapy
5. MGUS or smoldering myeloma not currently requiring treatment
6. Other
7. I don't know.

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Question

Have you had a stem cell transplant?

1. No, but I will soon!
2. No, but I am considering one (or my doctor is discussing with me).
3. No, my doctor tells me I am not a candidate.
4. Yes
5. Not applicable

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Question

Do you know if you had any molecular characterization performed on your tumor, such as FISH, cytogenetics, or sequencing?

1. No
2. Yes, I had FISH.
3. Yes, I had cytogenetics.
4. Yes, I had sequencing.
5. Yes, I had more than one of these tests performed.
6. I don't know.

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Question

Have you and your care team ever discussed the possibility of you joining a clinical trial that you are eligible for? (If you are a caregiver, do you know if joining a clinical trial has ever been discussed?)

1. Yes
2. No
3. I don't know.

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Multiple Myeloma Biology

Cesar Rodriguez, MD

Icahn School of Medicine at Mount Sinai
New York, New York

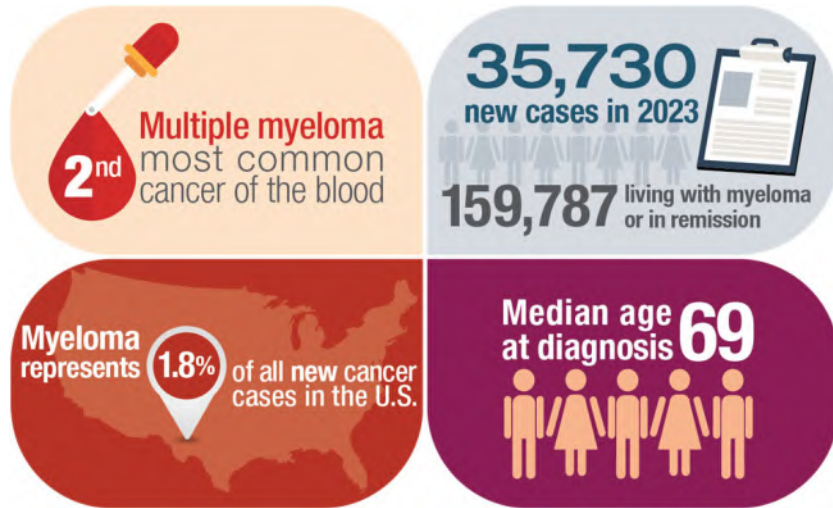
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Disclosures

- *Research Support/PI:* Amgen, Celgene, ORIC, Janssen, BMS, Teneobio
- *Employee:* N/A
- *Consultant:* Amgen, Bristol Myers Squibb, Janssen, Karyopharm, Sanofi, Abbvie, Artiva
- *Major Stockholder:* N/A
- *Speakers Bureau:* BMS, Takeda
- *Honoraria:* N/A
- *Scientific Advisory Board:* BMS, Janssen, Sanofi, Abbvie, Artiva

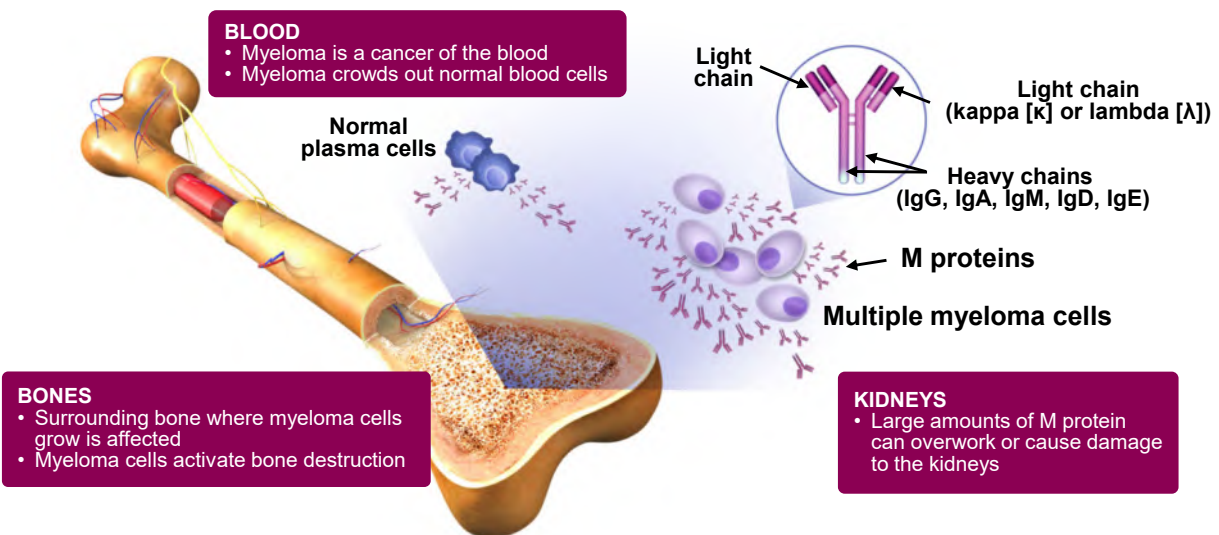
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How common is multiple myeloma?



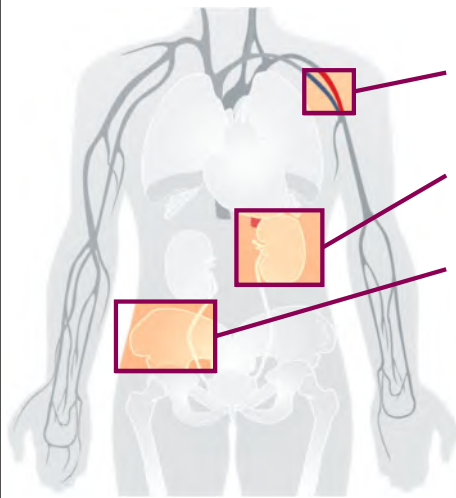
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Multiple Myeloma Affects Your Bones, Blood, and Kidneys



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Effects of Myeloma and Common Symptoms



Low blood counts

-
- Weakness
- Fatigue
- Infection

Decreased kidney function

→ Weakness

Bone damage

→ Bone pain

About 10% to 20% of patients with newly diagnosed myeloma do not have any symptoms.

Disease presentation and myeloma-related complications after myeloma diagnosis are different in patients by race

More common in Black patients

- Hypercalcemia
- Kidney dysfunction
 - Hemodialysis
- Anemia

Less common in Black patients

- Bone fractures

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Demographic Risk Factors: Multiple Myeloma

Older age

Male sex

Obesity

Race: 2× incidence in African Americans

Family history

- One first-degree relative with multiple myeloma
- Relatives of multiple myeloma patients have more monoclonal gammopathy of undetermined significance (MGUS)
- Current recommendation is to not screen families

Schinasi LH et al. *Br J Haematol.* 2016;175:87. Thordardottir M et al. *Blood Adv.* 2017;1:2186.

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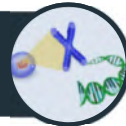
The Right Tests: Common Tests Conducted in Myeloma Patients

Blood tests Urine tests



- Confirms the type of myeloma or precursor condition

Bone marrow biopsy



- Confirms diagnosis of myeloma
- Determines how advanced the myeloma or precursor condition is

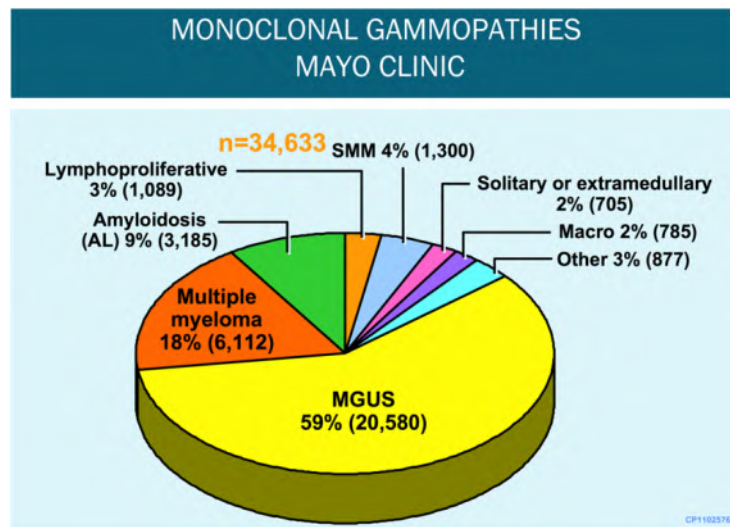
Imaging tests



- Detects the presence and extent of bone disease and the presence of myeloma outside of the bone marrow

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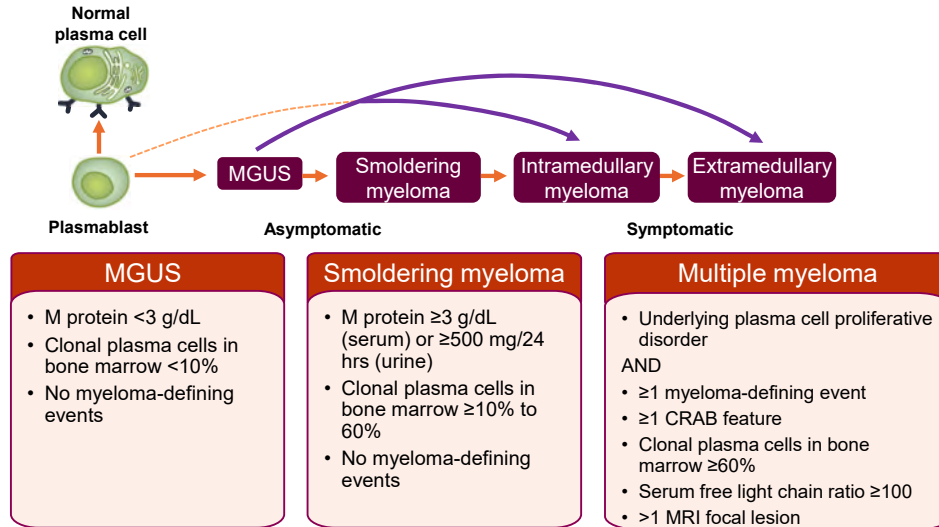
Not All M Spikes Are Myeloma!



Medical oncology best practices. 2012.

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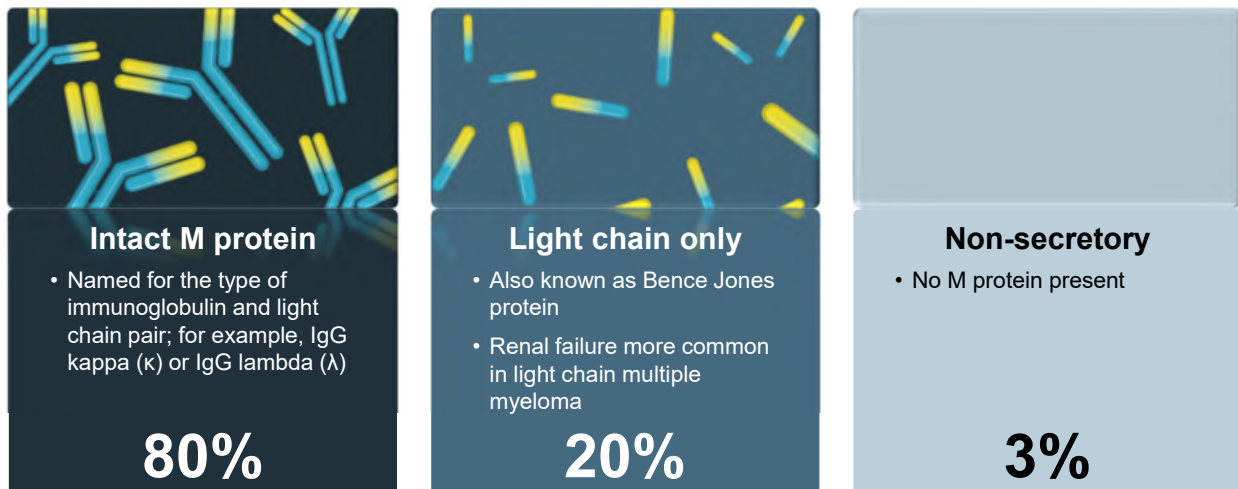
Type of Disorder Has the Potential to Evolve



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

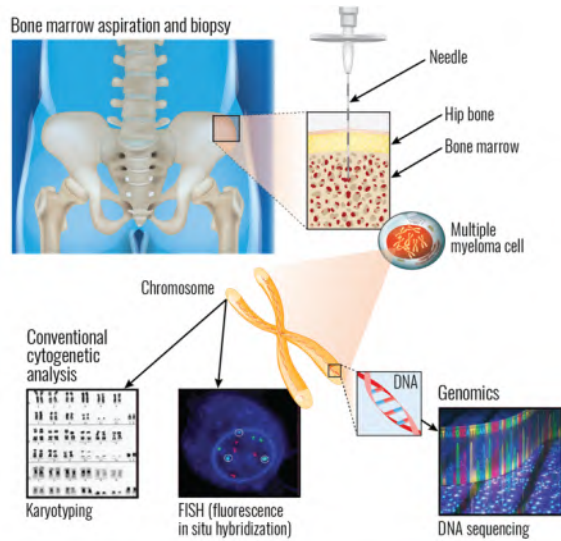
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Types of Multiple Myeloma Based on Blood or Urine Tests

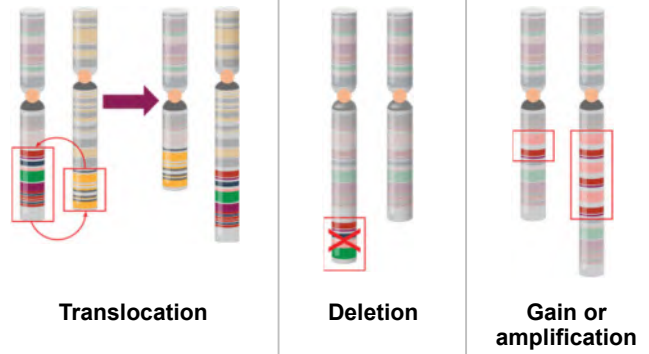


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Know Your Bone Marrow Tests!



Types of chromosomal abnormalities



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Multiple Myeloma Prognosis and Risk

Revised International Staging System (R-ISS)

R-ISS stage	Laboratory measurements
I	<ul style="list-style-type: none"> Serum β2M level <3.5 mg/L Serum albumin level \geq3.5 g/dL No high-risk CA* Normal LDH level
II	All other possible combinations
III	<ul style="list-style-type: none"> Serum β2M level \geq5.5 mg/L High-risk CA* or high LDH level

*High-risk chromosomal abnormality (CA) by FISH: del(17p) and/or t(4;14) and/or t(14;16)

Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Guidelines

- High risk**
- High-risk genetic abnormalities
 - t(4;14)
 - t(14;16)
 - t(14;20)
 - del 17p
 - p53 mutation
 - gain 1q
 - R-ISS Stage 3
 - High plasma cell S phase
 - GEP: high-risk signature
- Double-hit myeloma:** any two high-risk genetic abnormalities
- Triple-hit myeloma:** three or more high-risk genetic abnormalities

- Standard risk**
- All others including:
 - Trisomies
 - t(11;14)
 - t(6;14)

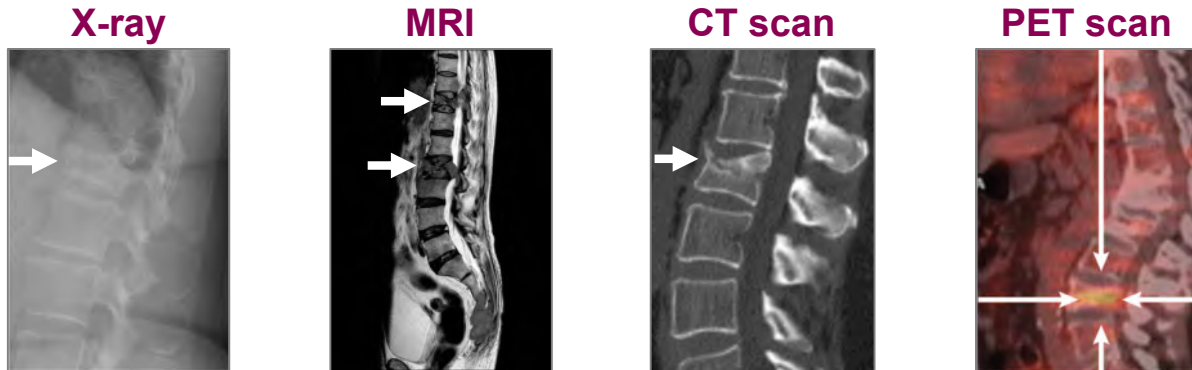
β 2M; beta-2 microglobulin; LDH, lactate dehydrogenase; GEP, gene-expression profiling
Greipp PR et al. *J Clin Oncol.* 2005;23:3412; Palumbo A et al. *J Clin Oncol.* 2015;33:2863;
Mikhael JR et al. *Mayo Clin Proc.* 2013;88:360.

Currently cannot identify with great certainty all high-risk patients.

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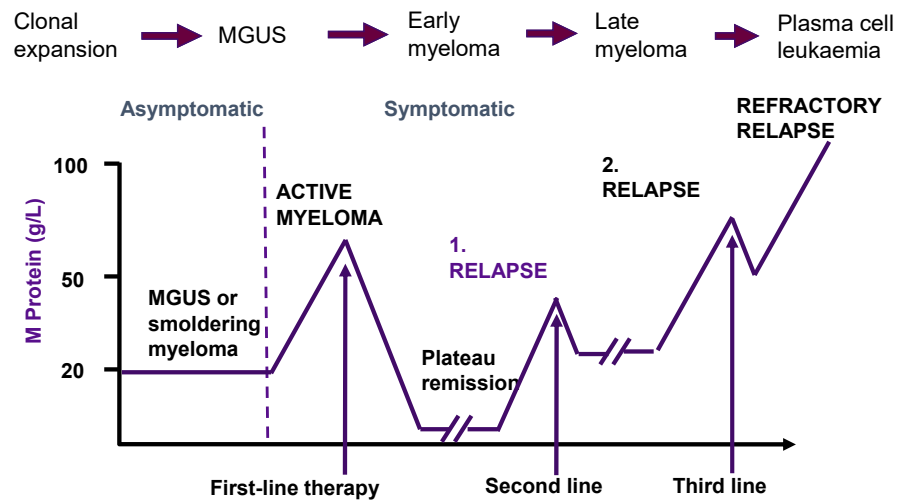
Know Your Imaging Tests!

Assess changes in the bone structure and determine the number and size of tumors in the bone



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Natural History of MM After Treatment



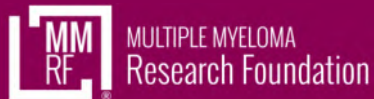
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Summary

- Multiple myeloma is a rare blood cancer that can negatively affect the bones, kidneys, and bone marrow, leading to lowered blood counts.
- The prognosis of multiple myeloma depends on the genetic makeup of the myeloma cell and its chromosomes; R-ISS is used for staging in multiple myeloma.
- Knowledge is power: right team, right test, right treatment.

Be an informed and empowered part of your health care team!

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Please take a moment to answer two questions about this presentation.

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Treatment for Newly Diagnosed Multiple Myeloma

Joshua Richter, MD, FACP

Icahn School of Medicine at Mount Sinai
New York, New York






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Disclosures

- *Consultant/advisor:* Janssen, BMS, Pfizer, Karyopharm, Sanofi, Takeda, Genentech, AbbVie, Regeneron, Forus, Menarini/Stemline, Antengene
- *Speakers Bureau:* Janssen, BMS, Sanofi, Adaptive Biotechnologies

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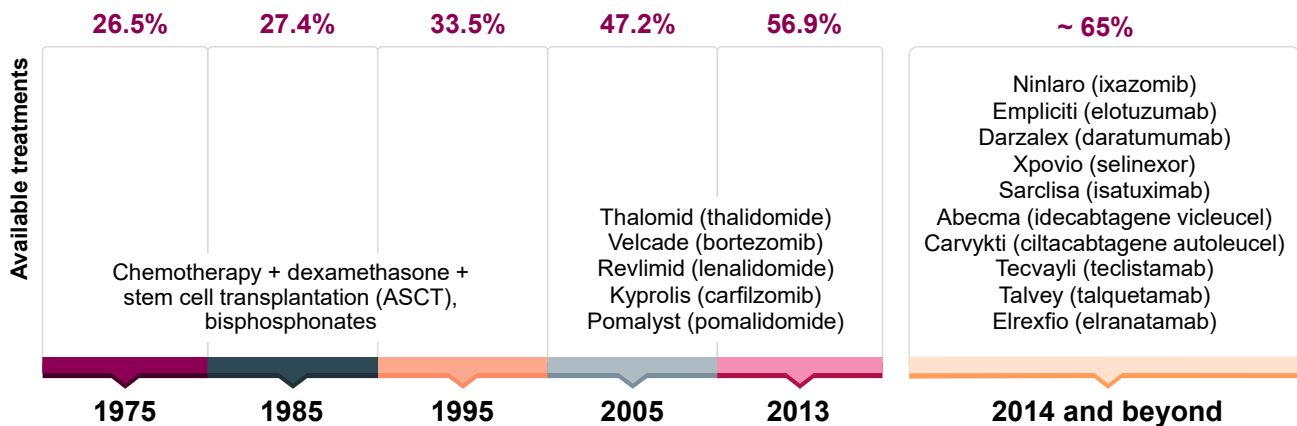
Getting the Right Treatment: Goals of Multiple Myeloma Therapy

- 
 Reduce the amount of M protein (as measured by serum protein electrophoresis) or light chains (as measured via the free light chain test) to the lowest level possible.
- 
 Eliminate myeloma cells from the bone marrow, as measured via minimal residual disease (MRD) testing.
- 
 Improve quality of life with as few treatment side effects as possible.
- 
 Provide the longest possible period of response before first relapse.
- 
 Prolong overall survival.

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Myeloma Survival Has Improved Over Time, Mainly Due to Novel Agents and Immune Therapies (including mAbs)

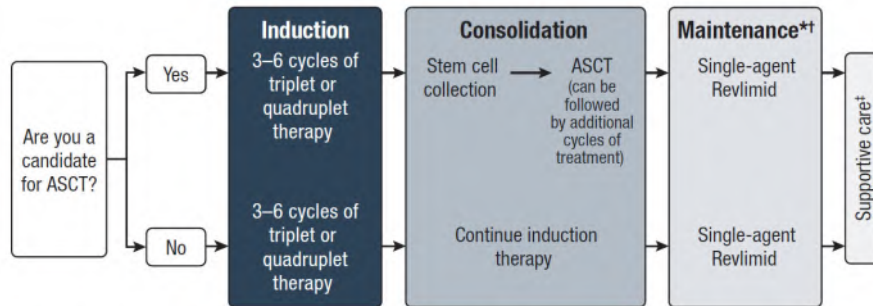
The percentage of people expected to survive 5 years or more after being diagnosed with myeloma has dramatically improved in the last 20 years



mAbs, monoclonal antibodies

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Overview of Treatment Approach for Active Multiple Myeloma



*If you have high-risk markers, additional agents may be given with Revlimid; if you cannot tolerate Revlimid, another treatment (for example, a proteasome inhibitor) may be given.

**In the U.S., maintenance is typically given until progression, but studies are evaluating stopping treatments for patients with deep responses. If you have little or no evidence of disease but are experiencing side effects, discuss with your doctor whether to continue until progression. Dose adjustments are also options.

*Supportive care is given throughout treatment.

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Induction Therapy Regimens

	Preferred	Recommended	Certain circumstances
Transplant eligible	<ul style="list-style-type: none"> • Revlimid-Velcade-dex (RVd)* • Kyprolis-Revlimid-dex (KRd) 	<ul style="list-style-type: none"> • Darzalex-Revlimid-Velcade-dex (D-RVd) 	<ul style="list-style-type: none"> • Velcade-Cytoxan-dex (VCd) • Velcade-Doxil-dex (VDd) • Kyprolis-Cytoxan-dex (KCd) • Darzalex-Velcade-Thalomid-dex (D-VTd) • Darzalex-Kyprolis-Revlimid-dex (D-KRd) • Darzalex-Cytoxan-Velcade-dex (D-VCd) • Sarclisa-Revlimid-Velcade-dex • VTD-PACE
Transplant ineligible	<ul style="list-style-type: none"> • Revlimid-Velcade-dex (RVd)* • Darzalex-Revlimid-dex (DRd)* 	<ul style="list-style-type: none"> • Kyprolis-Revlimid-dex (KRd) • Darzalex-Velcade-melphalan-prednisone (D-VMP)* • Darzalex-Cytoxan-Velcade-dex (D-VCd) 	<ul style="list-style-type: none"> • Velcade-dex (Vd) • Revlimid-dex (Rd)* • Velcade-Cytoxan-dex (VCd) • Revlimid-Cytoxan-dex (RCd) • Kyprolis-Cytoxan-dex (KCd) • Revlimid-Velcade-dex (RVd)-lite

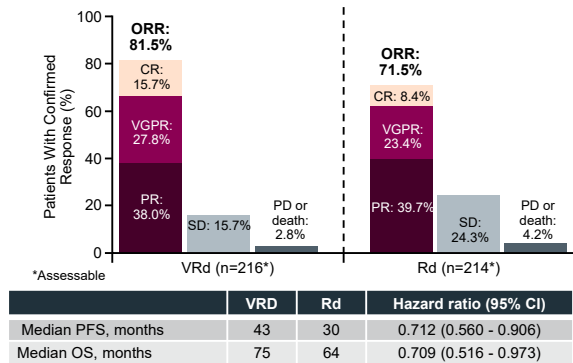
*Category 1 recommendation. Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2024. Multiple Myeloma.

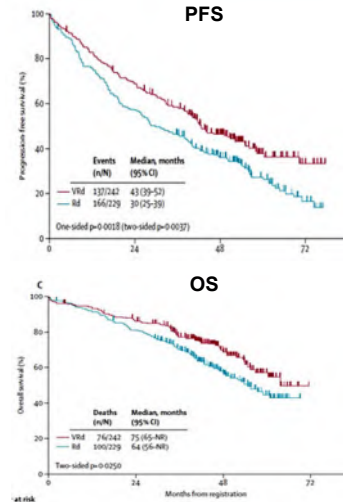
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Phase 3 SWOG S0777 Trial Bortezomib + Lenalidomide + dex (VRd) vs Lenalidomide + dex (Rd) and Rd Maintenance

Newly diagnosed myeloma (transplant eligible and non-eligible patients)



ORR, overall response rate; CR, complete response; VGPR, very good partial response; PR, partial response; SD, stable disease; PD progressive disease; CI, confidence interval; PFS, progression-free survival; OS, overall survival
Durie B et al. ASH 2015. Abstract 25. Durie B et al. *Lancet*. 2017;389:519.



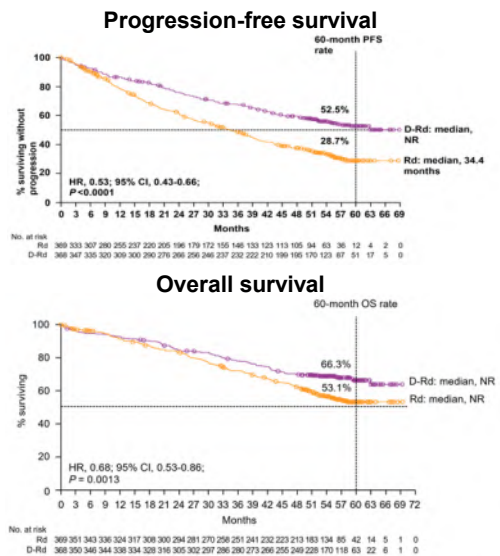
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MAIA: Updated Efficacy Results

- Phase 3 Study of lenalidomide and dex ± daratumumab
- Median duration of follow-up: 56.2 mos

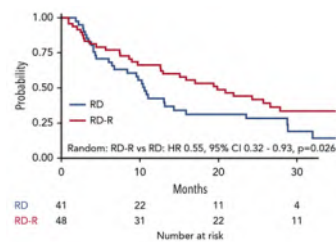
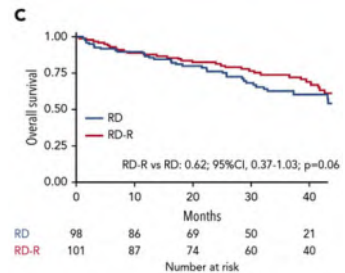
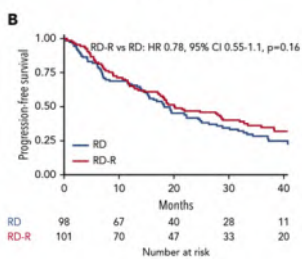
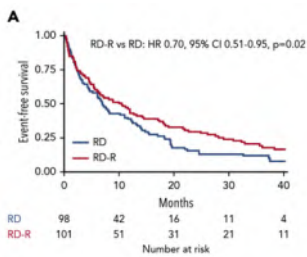
Response	DRd	Rd
ORR	92.9%	81.3%
PR	13.6%	28.2%
VGPR	31.8%	28.2%
CR	17.1%	12.5%
sCR	30.4%	12.5%
≥VGPR	79.3%	53.1%
MRD- (10 ⁻⁵)	31%	10%

Facon T et al. *Lancet Oncol*. 2021;22:1582. Facon T et al. *N Engl J Med*. 2019;380:2104.



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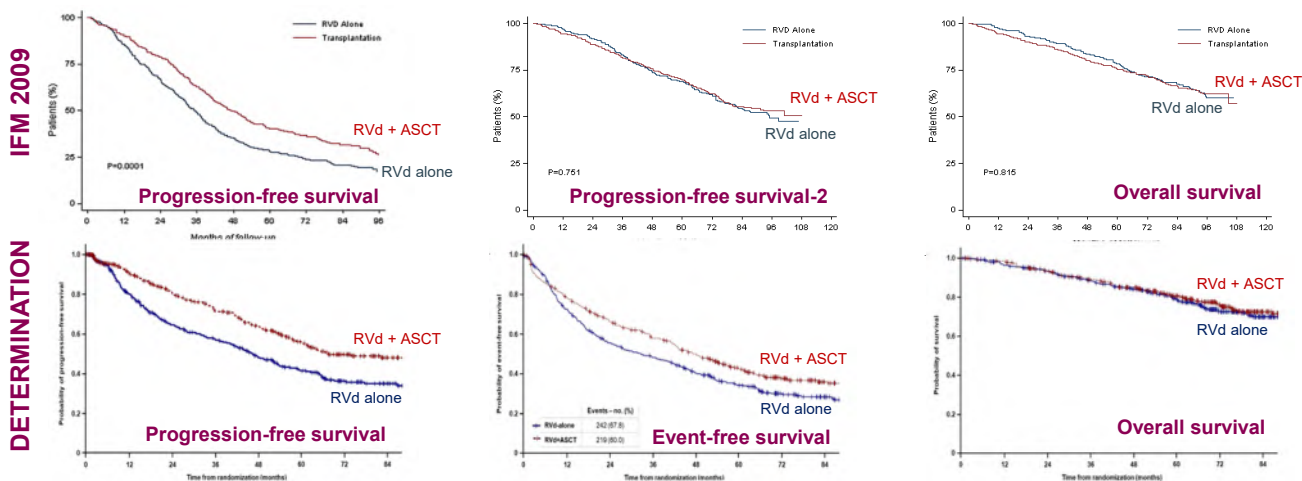
Drop the Dex



Larocca A et al. *Blood*. 2021;137:3027.

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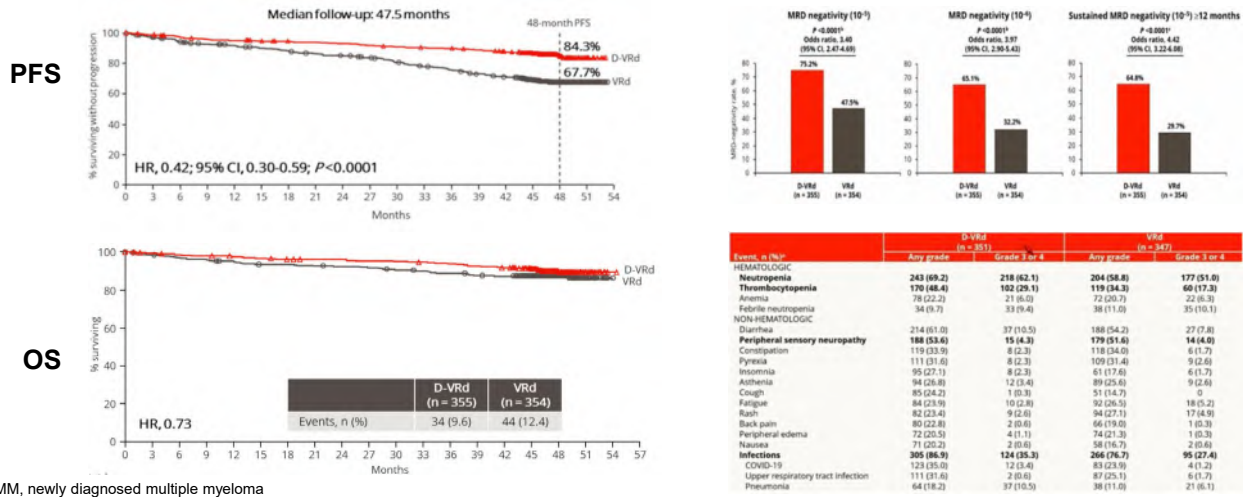
What is the role of ASCT in the current age of modern induction regimens?



Perrot A et al. *Blood*. 2020. Abstract 143.
 Richardson et al. *N Engl J Med*. 2022;387:132.

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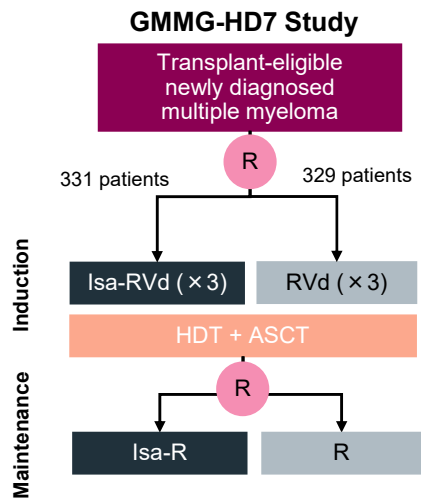
Phase 3 Study of Darzalex + Velcade + Revlimid + Dex vs Velcade + Revlimid + Dex in NDMM



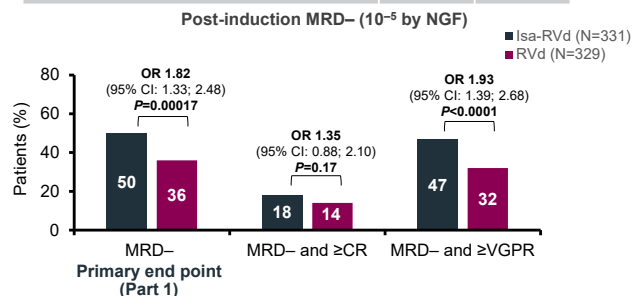
NDMM, newly diagnosed multiple myeloma
PERSEUS Study. Sonneveld P et al. *N Engl J Med*. December 12, 2023 [Online ahead of print].

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Investigational Phase 3 With RVd Backbone



Baseline characteristics	Isa-RVd (n=331)	RVd (n=329)
Median (IQR) age, years	59 (54-64)	60 (54-65)
R-ISS Stage I/II/III, %	23/66/8	30/56/8
HRCAs: ≥1 of: del(17p), t(4;14), or t(14;16) (%)	18	20

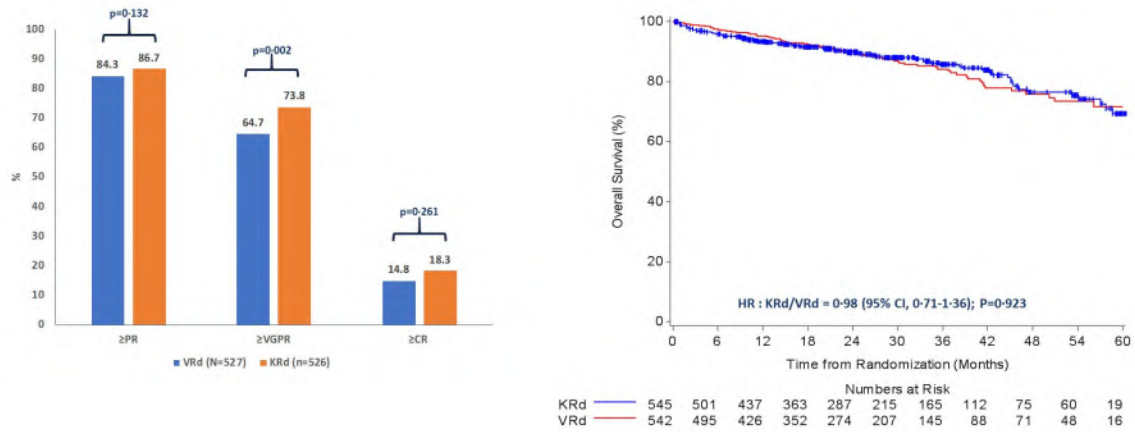


There was no impact on SC mobilization with the addition of Isa to RVd.

HDT, high-dose therapy; HRCA, high-risk chromosomal abnormalities; R-ISS, Revised International Staging System; OR, odds ratio
Goldschmidt H et al. *Lancet Haematol*. 2022;9:e810.

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KRd vs VRd Superior >VGPR But Comparable PFS and OS

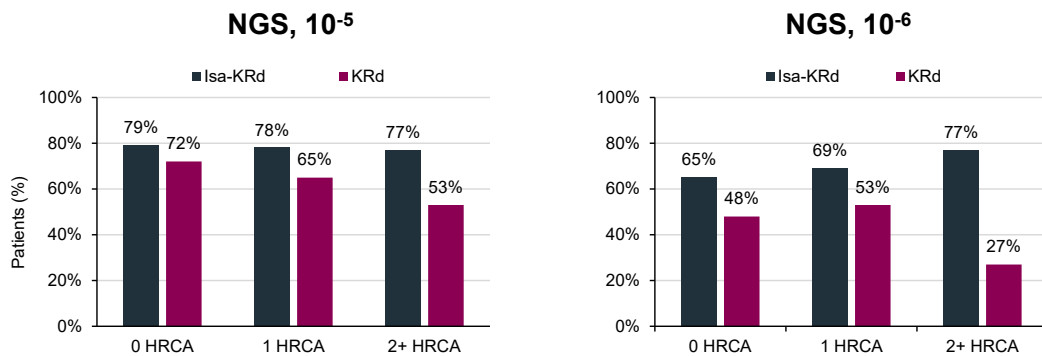


Kumar SK et al. *Lancet Oncol.* 2020;21(10):1317.

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Investigational Phase 3 Study of Isatuximab + KRd vs KRd in Transplant-Eligible NDMM

Post-consolidation MRD negativity by NGS Subgroup analysis by cytogenetic risk



1 HRCA was defined as the presence of one of the following high-risk cytogenetic abnormalities: *del(17p13.1)*, *t(4;14) (p16.3;q32.3)*, *t(14;16) (q32.3;q23)*, *gain(1q21)*, or *amp(1q21)*; 2+ HRCA was defined as the presence of at least two high-risk cytogenetic abnormalities.

NGS, next-generation sequencing

IsKia/EMN24 Study. Gay F et al. *Blood.* 2023;142. Abstract 4.

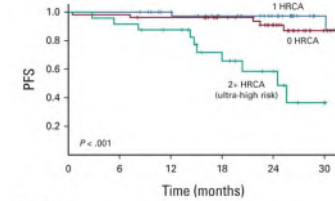
50

MASTER: MRD Response-Adapted Therapy Using a Dara-KRd Platform

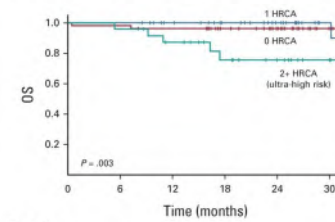
- 4 cycles of Dara-KRd → ASCT → 4 cycles of Dara-KRd → 4 cycles of Dara-KRd → Len maintenance
- MRD assessment after completion of each cassette of therapy
- Transition to observation with 2 consecutive MRD-negative readouts at 10^{-5}

Treatment phase	All patients		0 HRCA* abnormality		1 HRCA abnormality		≥2 HRCA abnormalities	
	MRD- 10^{-5}	MRD- 10^{-6}	MRD- 10^{-5}	MRD- 10^{-6}	MRD- 10^{-5}	MRD- 10^{-6}	MRD- 10^{-5}	MRD- 10^{-6}
Post induction	38%	24%	40%	30%	41%	25%	29%	8%
Post SCT	65%	48%	60%	44%	73%	59%	63%	38%
Post MRD-directed consolidation	80%	66%	78%	64%	82%	73%	79%	58%

*HRCAs: gain or amp 1q21, del(17p), t(4;14), t(14;16), t(14;20)



No. at risk:	0 HRCA	1 HRCA	2+ HRCA
0	50	44	24
6	49	44	22
12	46	36	19
18	36	30	12
24	27	23	7
30	10	9	2



No. at risk:	0 HRCA	1 HRCA	2+ HRCA
0	50	44	24
6	49	44	23
12	46	36	19
18	36	30	13
24	29	23	9
30	11	9	3

Costa L et al. *J Clin Oncol.* 2022;40:2901.

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Continuous or Maintenance Therapy

Successful maintenance therapy must...

Be convenient

Be safe and well tolerated long term

Not interfere with the use of other future treatments

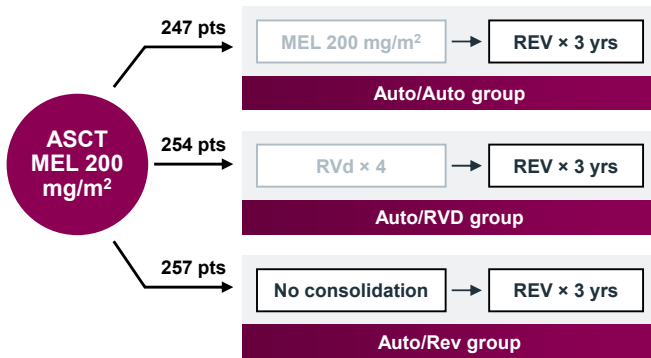
	Preferred	Recommended	Certain circumstances
Transplant eligible	• Revlimid*	• Velcade	• Velcade-Revlimid • Kyprolis-Revlimid • Darzalex ± Revlimid • Ninlaro
Transplant ineligible	• Revlimid*	• Velcade	• Velcade-Revlimid • Ninlaro

*Category 1 recommendation. Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. National Comprehensive Cancer Network Guidelines Version 4.2023. Multiple Myeloma.

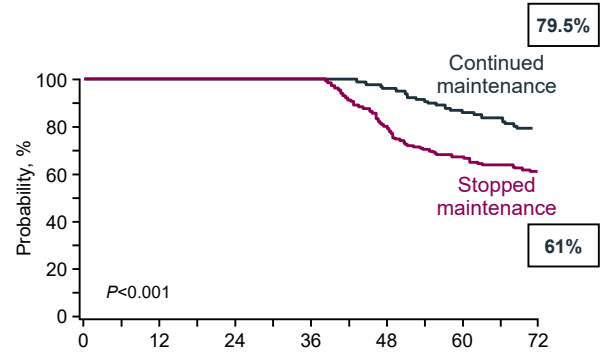
52

Revlimid Maintenance Duration

STAMINA Trial (BMT-CTN0702)



There was no difference in PFS or OS between the 3 groups



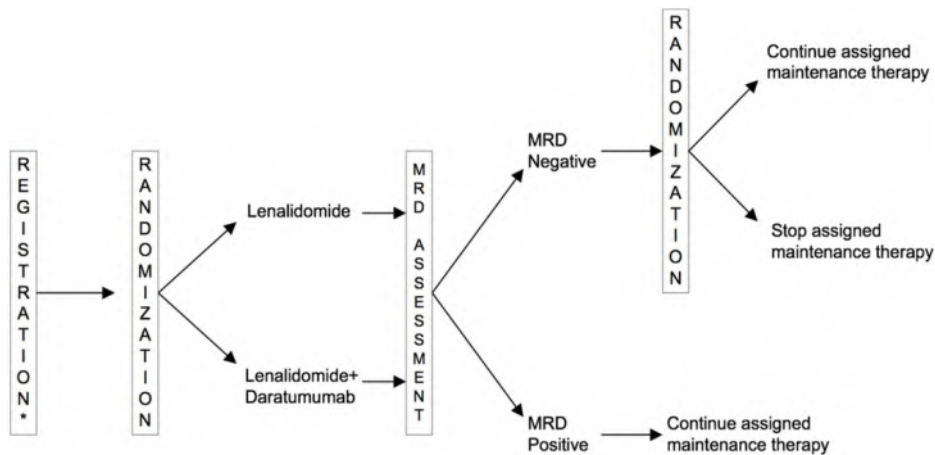
Discontinuation of Revlimid maintenance at 3 years is not recommended because of the increased risk of disease progression.

MEL, melphalan; RVD, Revlimid-Velcade-dex; REV, Revlimid

STAMINA Trial. Stadtmauer EA et al. *J Clin Oncol*. 2019;37:589; Hari P et al. *J Clin Oncol*. 2020;38. Abstract 8506.

53

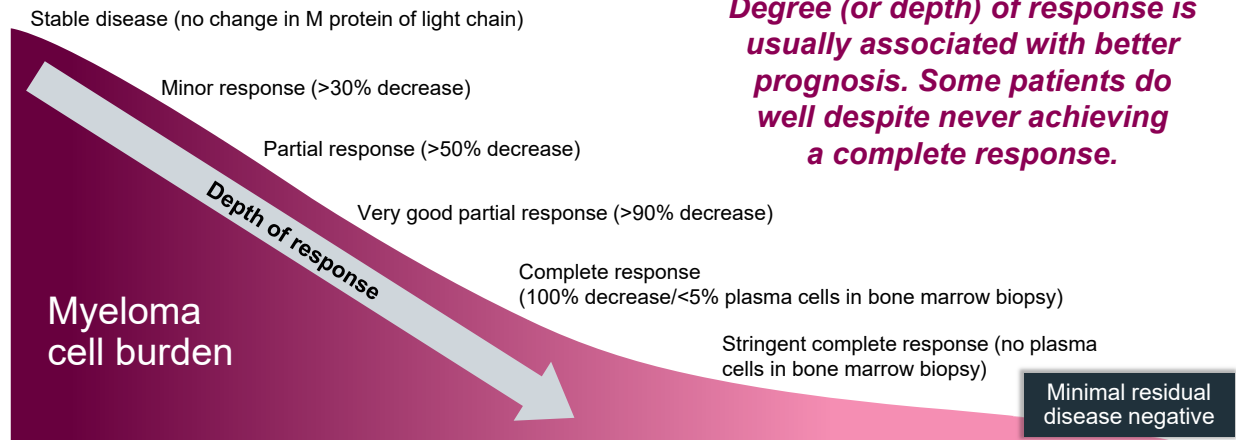
Phase III Study of Daratumumab/rhuph20 (nsc- 810307) + Lenalidomide or Lenalidomide as Post-Autologous Stem Cell Transplant Maintenance Therapy in Patients With Multiple Myeloma (mm) Using Minimal Residual Disease To Direct Therapy Duration (DRAMMATIC study): SWOG s1803



Krishnan A et al. *Blood*. 2020;136 (Supplement 1):21.

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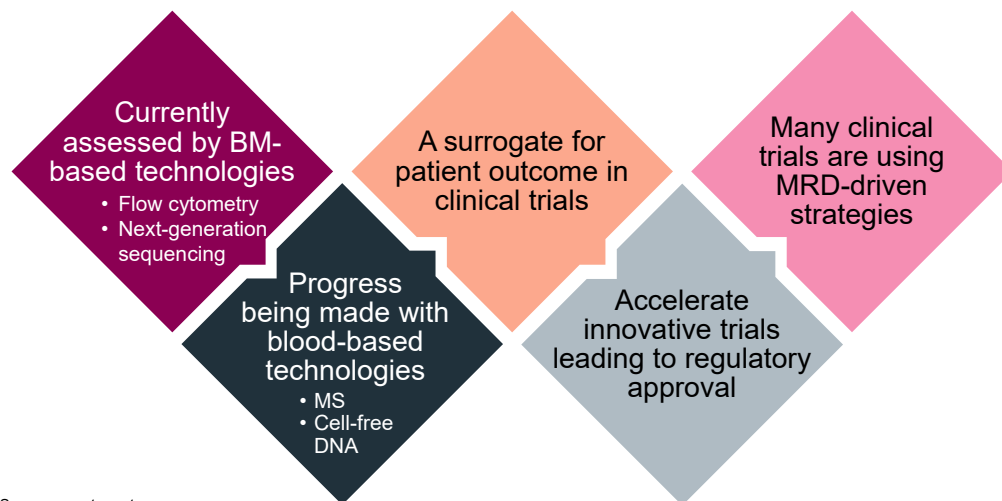
Measuring Response to Therapy



ClonoSEQ is an FDA-approved next-generation sequencing (NGS) test to measure MRD in myeloma patients.
 Palumbo A et al. *J Clin Oncol.* 2014;32:587. Kumar S et al. *Lancet Oncol.* 2016;17:e328.

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MRD Is Important for Clinical Care and New Drug Registration



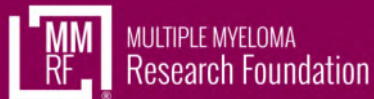
BM, bone marrow; MS, mass spectrometry
 Anderson KC et al. *Clin Cancer Res.* 2021;27:5195. Costa LJ et al. *Leukemia.* 2021;35:18.

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Summary

- Survival rates are improving because of new drugs and new combinations of drugs, including immune therapies and especially monoclonal antibodies.
- The body of evidence from phase 3 trials indicates that maintenance therapy improves PFS and likely OS.
- MRD is the deepest response after myeloma treatment, including bone marrow MRD and imaging MRD. NGF and NGS are the two most commonly used marrow MRD tests. Blood-based MRD is in exploration.
- MRD is also useful as an end point in clinical trials helping to expedite new drug approval in myeloma.
- The treatment paradigm will continue to change with the approval of additional novel agents.

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Please take a moment to answer two questions about this presentation.

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Autologous Stem Cell Transplantation

Shambavi Richard, MD

Icahn School of Medicine at Mount Sinai
New York, New York

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Disclosures

- Honoraria received – Janssen, BMS
- Steering Committee– Gracell Biotechnologies
- Research support – Janssen, BMS, C4 Therapeutics, Gracell Biotechnologies, Heidelberg Pharma

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What does transplant mean?

Understanding the basics of autologous stem cell transplantation

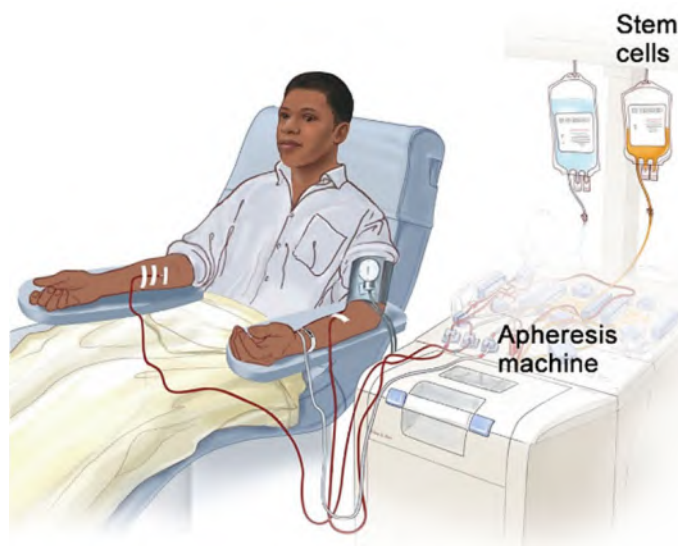
Blood-forming stem cells are collected from the patient's own blood. Stem cells are frozen and stored.

Patient gets high-dose chemotherapy (melphalan). Most myeloma cells are destroyed; some normal cells (hair follicles, taste buds, and blood cells) are also temporarily destroyed.

The previously collected stem cells are given back by IV infusion. Stem cells restore blood cells with fewer myeloma cells. Other cells (hair follicles and taste buds) recover.

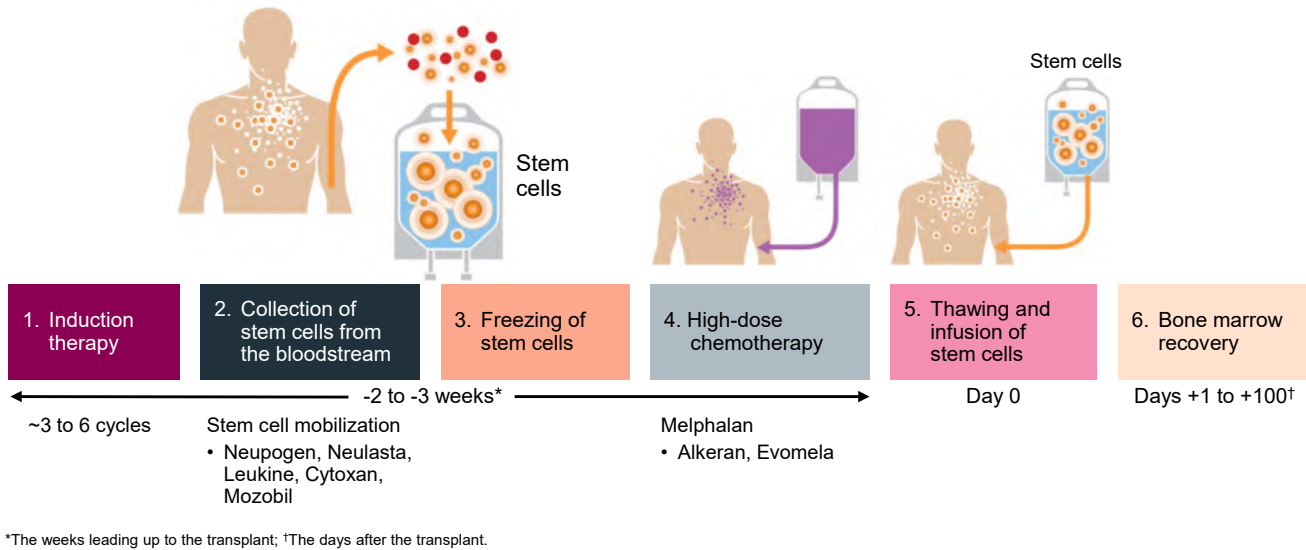
61

Stem Cell Harvest



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Autologous Stem Cell Transplantation (ASCT)



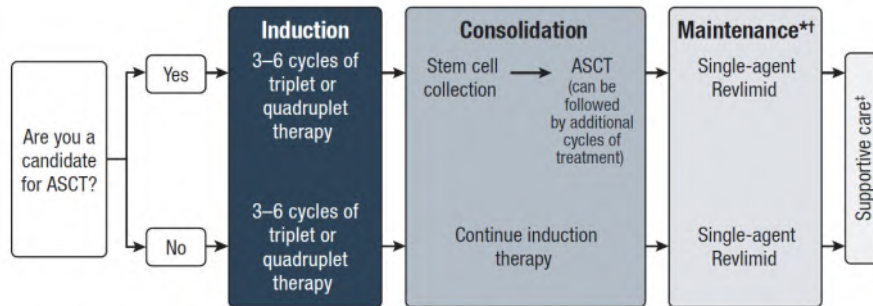
63

Side Effects of High-Dose Chemotherapy

<p>Fatigue</p> <ul style="list-style-type: none"> • Expected • May last 1–3 months 	<p>Nausea, vomiting, and diarrhea</p> <ul style="list-style-type: none"> • Symptoms much more manageable with newer anti-emetics • Try to prevent nausea • May include stomach cramping • Encourage small amounts of food, more often • Avoid milk, milk products, high-fiber foods 	<p>Mucositis</p> <ul style="list-style-type: none"> • Pain, sores in mouth; sore throat • Pain meds, mouth swishes • Avoid tart, acidic, salty, spicy foods • Soft food better tolerated 	<p>Low blood counts</p> <ul style="list-style-type: none"> • Low white blood cell count (risk for infection) • Hemoglobin drop (fatigue) • Platelet count drop (bleeding risk) • Blood transfusion • Platelet transfusion • Antibiotics • White blood cells and platelets recover in 2 weeks 	<p>Hair loss</p>
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Current Treatment Paradigm for Newly Diagnosed Multiple Myeloma



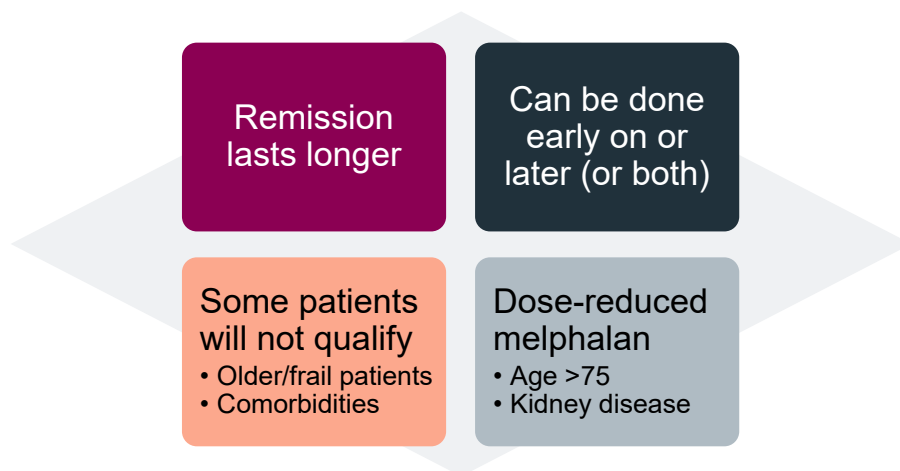
*If you have high-risk markers, additional agents may be given with Revlimid; if you cannot tolerate Revlimid, another treatment (for example, a proteasome inhibitor) may be given.

†In the U.S., maintenance is typically given until progression, but studies are evaluating stopping treatments for patients with deep responses. If you have little or no evidence of disease but are experiencing side effects, discuss with your doctor whether to continue until progression. Dose adjustments are also options.

‡Supportive care is given throughout treatment.

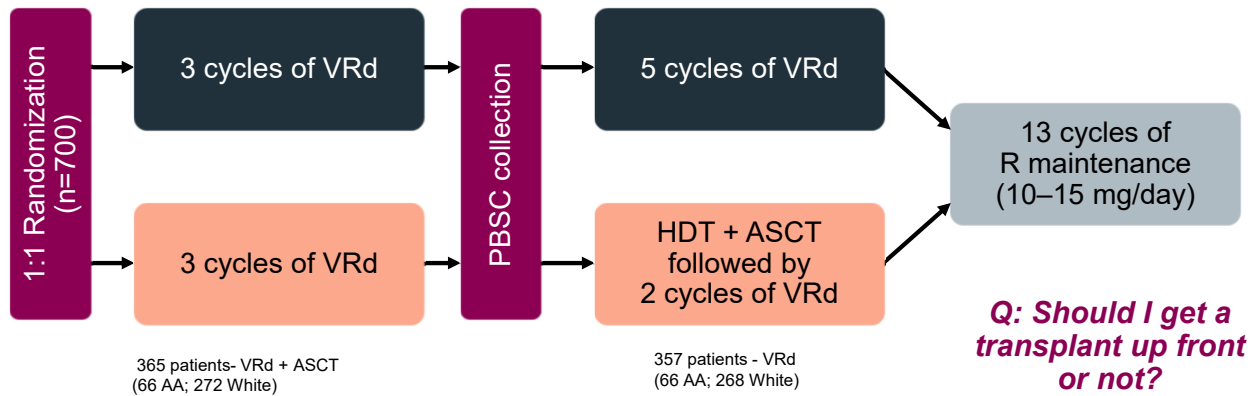
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High-Dose Chemotherapy and Stem Cell Transplantation



66

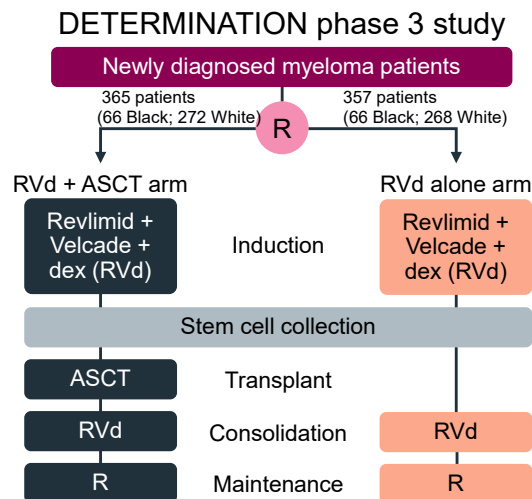
IFM 2009/DETERMINATION Phase 3 Study



VRd, Velcade (bortezomib) + Revlimid (lenalidomide) + dexamethasone; PBSC, peripheral blood stem cells; HDT, high-dose therapy; ASCT, autologous stem cell transplant; R, Revlimid

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Is transplant still required in newly diagnosed myeloma?



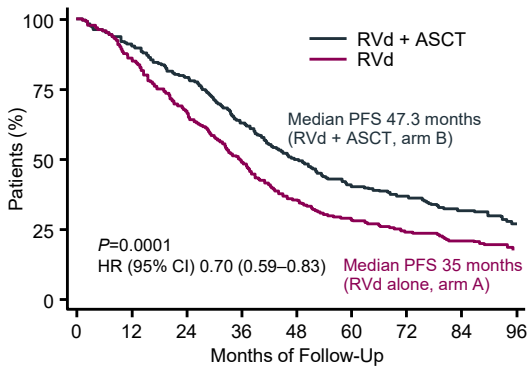
Q: Should I get a transplant up front or not?

Richardson PG et al. *N Engl J Med.* 2022;387:132.

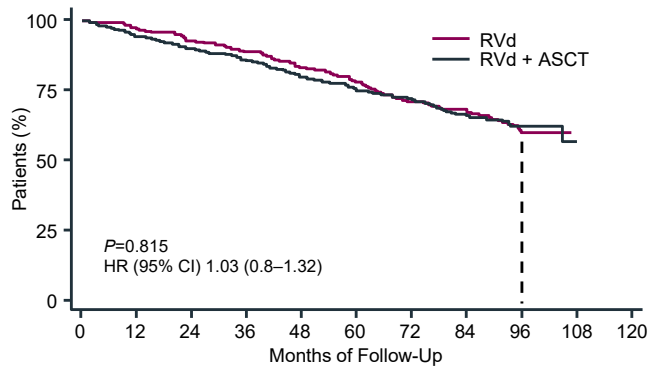
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IFM 2009: ASH 2020 Updated Results

Updated PFS (primary end point)



Median follow-up: 93 months



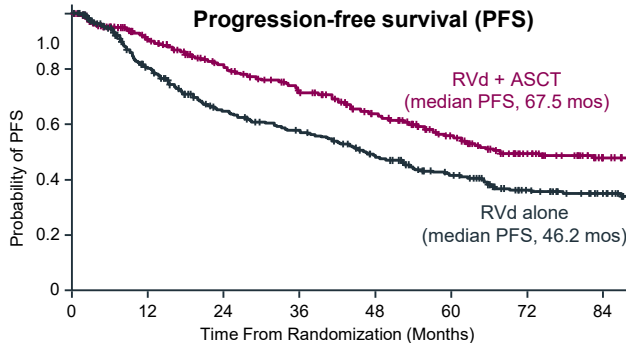
30% reduction in the risk of progression or death in patients receiving transplant

- 8-year OS 62.2% for RVd-ASCT and 60.2% for RVd alone (60% alive in both arms after 8 years)

PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval
Perrot A et al. *Blood*. 2020. 136. Abstract 39.

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Phase 3 Study of ASCT for NDMM: Survival Analysis



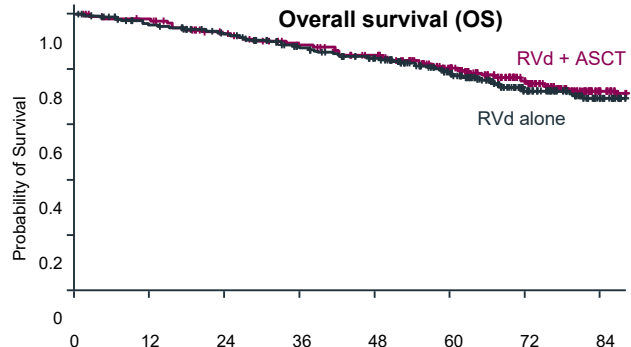
Primary end point

- PFS for RVd + ASCT: approximately 5.5 years
- PFS for RVd alone: approximately 4 years

Transplant extended time to progression by 20 months

Risk of progression or death 53% higher in RVd alone group

NDMM, newly diagnosed multiple myeloma
Richardson PG et al. *N Engl J Med*. 2022;387:132.

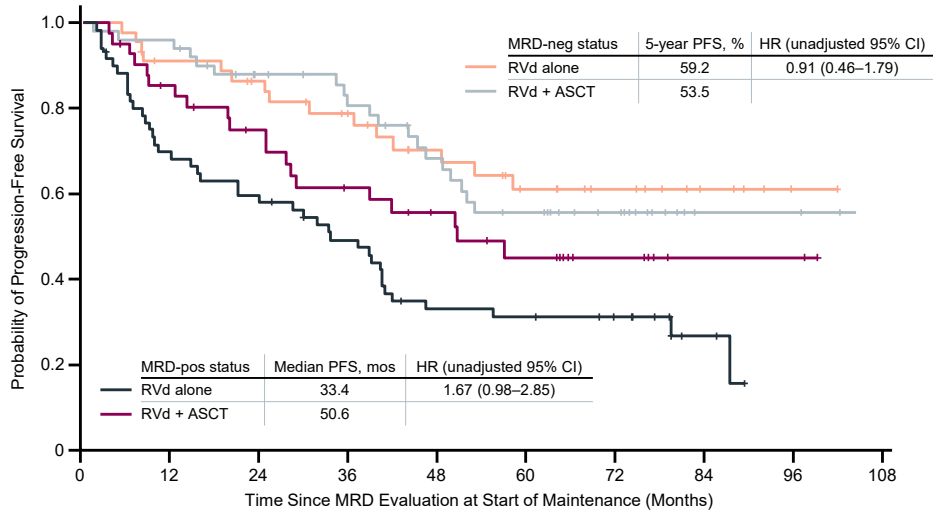


Length of OS: no difference (with a median follow-up time of 76 months).

- High risk PFS 17.1 vs 55.5 mo PFS (n=66 vs 66); HR 1.99

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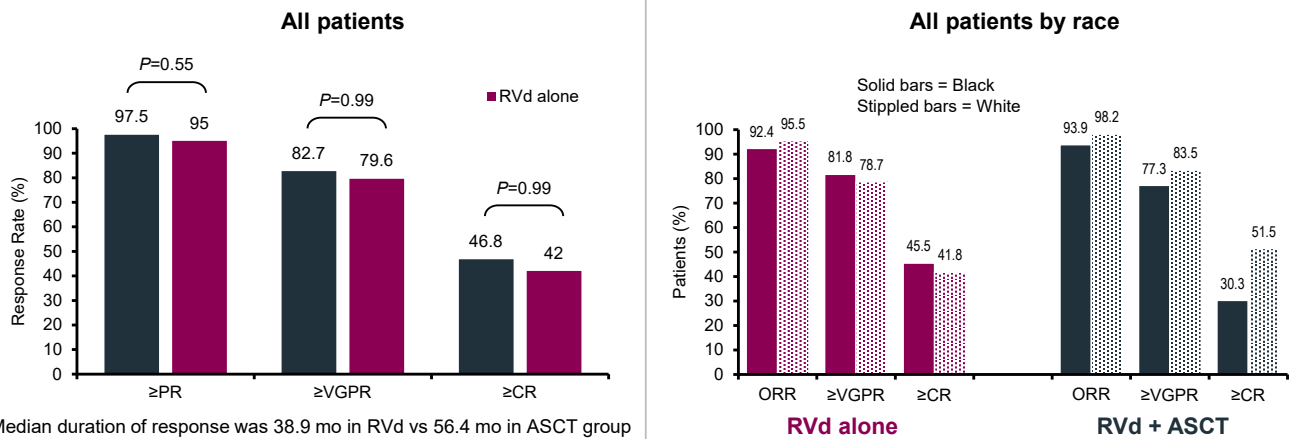
Phase 3 Study of ASCT for NDMM: Survival Analysis by MRD Status



Richardson PG et al. *N Engl J Med.* 2022;387:132.

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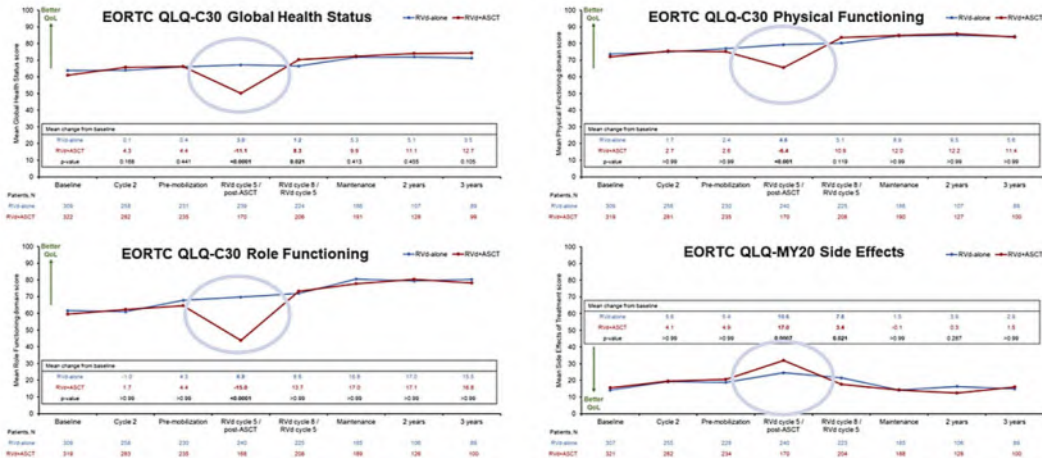
Phase 3 Study of ASCT for NDMM: Best Response to Treatment and Duration of Response



Richardson PG et al. *N Engl J Med.* 2022;387:132.
 Houde CA et al. *Blood.* 2023;142. Abstract 4762.

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Phase 3 Study of ASCT for NDMM: Quality of Life



Richardson PG et al. *J Clin Oncol*. 2022;40. Abstract LBA4.
Richardson PG et al. *N Engl J Med*. 2022;387:132.

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Phase 3 Study of ASCT for NDMM: Subsequent Therapy and Rate of ASCT in RVD-Alone Arm (Late ASCT)

Subsequent therapy in patients off protocol therapy (%)	Rvd alone (N=279) late transplant	Rvd + ASCT (N=276) early transplant
Any treatment*	79.6	69.6
Subsequent therapy	n=222	n=192
Any immunomodulatory drug	55.9	58.3
Pomalyst (pomalidomide)	30.2	29.2
Revlimid (lenalidomide)	25.7	29.2
Any proteasome inhibitor	55.9	50.0
Velcade (bortezomib)	27.5	25.5
Kyprolis (carfilzomib)	21.2	16.7
Ixazomib	8.1	7.8
Marizomib	0	0.5
Any monoclonal antibody	16.2	27.6
Darzalex (daratumumab)	11.3	21.4
Empliciti (elotuzumab)	4.5	6.3
Sarclisa (isatuximab)	0.5	0

*Including immunomodulatory drugs (IMiDs), protease inhibitors (PIs), monoclonal antibodies (mAbs), HDACi (panobinostat), ASCT, chemotherapy, radiation therapy (RT), steroids, other

Richardson PG et al. *J Clin Oncol*. 2022;40. Abstract LBA4. Richardson PG et al. *N Engl J Med*. 2022;387:132.

Only 28.0% of RVD alone (late transplant) patients had received ASCT at any time following end of study treatment.

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Early vs Late Transplant

Pros and Cons



Pros

Early ASCT

- Deeper and more durable response
- Youngest/healthiest you are going to be
- Allows for fewer cycles of induction treatment

Late ASCT

- PFS may be shorter, but currently appears OS is the same
- Fewer side effects without high-dose chemotherapy
- Conserve quality of life in the early part of disease journey



Cons

Early ASCT

- No proven impact on overall survival
- 20% of patients still relapse within 2 years
- More side effects, including a small risk of serious life-threatening complications
- 3 months to full clinical recovery

Late ASCT

- Need more cycles of induction
- May need next treatment sooner, including (late) transplant
- Not all patients relapsing are able to undergo salvage ASCT

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Early vs Late ASCT Summary

- ASCT is a standard of care for frontline therapy of myeloma.
- ASCT safety has been established, and it induces long progression-free survival.
- Decision of ASCT should be individualized in every patient and deserves a thorough discussion between the patient and provider.
Emerging data suggests patients with an extremely good response (that is, complete response and ideally minimal residual disease negative) to induction therapy may have a long PFS. Studies are ongoing to determine whether these patients require ASCT.

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Please take a moment to answer two questions about this presentation.

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Questions?

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Treatment for Relapsed/Refractory Multiple Myeloma

Santiago Thibaud, MD

Icahn School of Medicine at Mount Sinai
New York, New York

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Disclosures

- Santiago Thibaud, MD, has no relevant financial information to disclose.

80

Definitions: What is relapsed/refractory disease and a line of therapy?

- **Relapsed:** recurrence (reappearance of disease) after a response to therapy
- **Refractory:** progression despite ongoing therapy
- **Progression:** increase in M protein/light chain values
- **Line of therapy:** change in treatment due to either progression of disease or unmanageable side effects
 - **Note:** initial (or induction) therapy + stem cell transplant + consolidation/maintenance therapy = 1 line of therapy

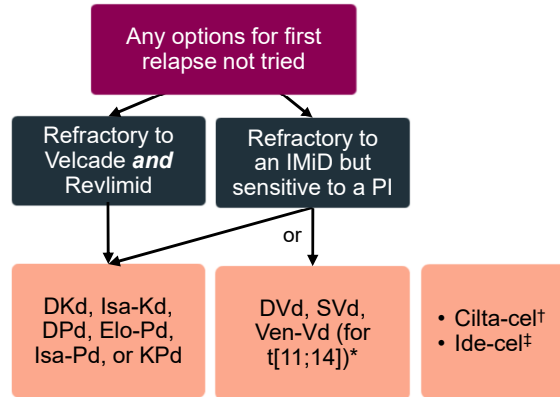


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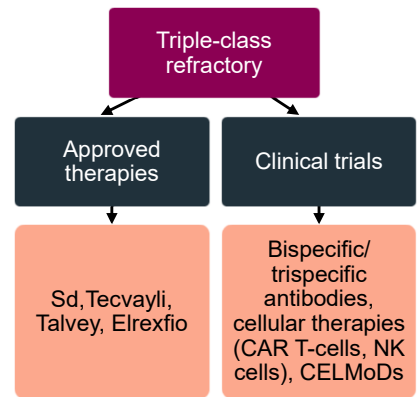
Treatment Approach

First relapse

Proteasome inhibitor/
immunomodulatory drug/
antibody-based therapy



>1 Relapse






D, daratumumab (Darzalex); K, carfilzomib (Kyprolis); d, dexamethasone; Isa, isatuximab (Sarclisa); P, pomalidomide (Pomalyst); Elo, elotuzumab (Empliciti); V, bortezomib (Velcade); S, selinexor (Xpovio); Ven, venetoclax (Venclexta); ide-cel, idecabtagene vicleucef (Abecma); cilta-cel, ciltacabtagene autoleucef (Carvykti)

*Not approved for use in myeloma patients; †At least 1 prior line of therapy, including a PI and an IMiD, and are refractory to Revlimid; ‡After two or more prior lines of therapy including an IMiD, a PI, and an anti-CD38 monoclonal antibody.

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Currently Available Monoclonal Antibodies for One to Three Prior Lines of Therapy

Drug	Formulation	Approval
Darzalex (daratumumab)	 SC once a week for first 8 weeks, then every 2 weeks for 4 months, then monthly	<ul style="list-style-type: none"> For relapsed/refractory myeloma as a single agent and as a triplet with Revlimid or Velcade or Kyprolis or Pomalyst plus dexamethasone
Empliciti (elotuzumab)	 IV once a week for first 8 weeks, then every 2 weeks (or every 4 weeks with pom)	<ul style="list-style-type: none"> For relapsed/refractory myeloma as a triplet with Revlimid or Pomalyst and dexamethasone
Sarclisa (isatuximab)	 IV once a week for first 4 weeks, then every 2 weeks	<ul style="list-style-type: none"> For relapsed/refractory myeloma as a triplet with Pomalyst or Kyprolis and dexamethasone

IV, intravenous; SC, subcutaneous

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Currently Available Agents for One to Three Prior Lines of Therapy

Drug	Formulation	Approval
Velcade (bortezomib)	 • IV infusion  • SC injection	<ul style="list-style-type: none"> For relapsed/refractory myeloma
Kyprolis (carfilzomib)	 • IV infusion • Weekly dosing	<ul style="list-style-type: none"> For relapsed/refractory myeloma as a single agent, as a doublet with dexamethasone, and as a triplet with Revlimid or Darzalex plus dexamethasone
Ninlaro (ixazomib)	 Once-weekly pill	<ul style="list-style-type: none"> For relapsed/refractory myeloma as a triplet with Revlimid and dexamethasone
Revlimid (lenalidomide)*	 Once-daily pill	<ul style="list-style-type: none"> For relapsed/refractory myeloma in combination with dexamethasone
Pomalyst (pomalidomide)*	 Once-daily pill	<ul style="list-style-type: none"> For relapsed/refractory myeloma in combination with dexamethasone
XPOVIO (selinexor)	 Once-weekly pill	<ul style="list-style-type: none"> For relapsed/refractory myeloma as a triplet with Velcade and dexamethasone

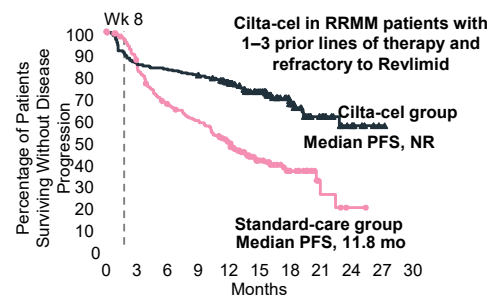
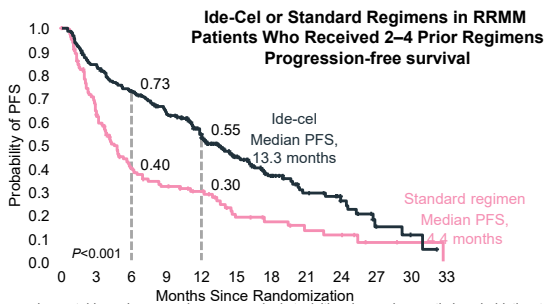
*Black box warnings: embryo-fetal toxicity; hematologic toxicity (Revlimid); venous and arterial thromboembolism

IV, intravenous; SC, subcutaneous

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Currently Available Agents for One to Three Prior Lines of Therapy

Class	Drug	Formulation
Chimeric antigen receptor (CAR) T cell	Abecma (idecabtagene vicleucel)*	300 to 510 × 10 ⁶ genetically modified autologous CAR T cells in one or more infusion bags
CAR T cell	Carvykti (ciltacabtagene autoleucel)†	0.5 to 1.0 × 10 ⁶ genetically modified autologous CAR T cells/kg of body weight



*Black box warning: cytokine release syndrome; neurologic toxicities; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia
 †Black box warning: cytokine release syndrome; neurologic toxicities; Parkinsonism and Guillain-Barré syndrome; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia
 Abecma, Carvykti, Tecvyli, Talvey, and Elexxio are available only through a restricted distribution program.

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CAR T: Expected Toxicities



Cytokine release syndrome (CRS)



Neurotoxicity (ICANS)



Cytopenias



Infections

	CRS	ICANS
Onset	1-9 days after CAR T-cell infusion	2-9 days after CAR T-cell infusion
Duration	5-11 days	3-17 days
Symptoms	<ul style="list-style-type: none"> Fever Difficulty breathing Dizziness Nausea Headache Rapid heartbeat Low blood pressure 	<ul style="list-style-type: none"> Headache Confusion Language disturbance Seizures Delirium Cerebral edema
Management	<ul style="list-style-type: none"> Actemra (tocilizumab) Corticosteroids Supportive care 	<ul style="list-style-type: none"> Antiseizure medications Corticosteroids

*Based on the ASTCT consensus; †Based on vasopressor; ‡For adults and children >12 years; §For children ≤12 years; ¶Only when concurrent with CRS

ICANS, immune effector cell-associated neurotoxicity syndrome

Xiao X et al. *J Exp Clin Cancer Res.* 2021;40(1):367; Lee DW et al. *Biol Blood Marrow Transplant.* 2019;25:625; Shah N et al. *J Immunother Cancer.* 2020;8:e000734.

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Ongoing Clinical Studies With Ide-Cel and Cilta-Cel

Ide-Cel Studies

- KarMMa-2
 - Phase 2 study in RRMM and high-risk myeloma (relapse early after induction)
- KarMMa-4
 - Phase 1 study in newly diagnosed high-risk myeloma

Cilta-Cel Studies

- CARTITUDE-2
 - Phase 2 study in RRMM and high-risk myeloma (relapse early after induction)
 - Arm D: len/dex after CAR
 - Arm E: dara-RVd induction, CAR then dara-R consolidation
- CARTITUDE-6
 - Phase 3 study in NDMM
 - Replaces transplant with CAR-T

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Triple-Class Refractory

- Patients with relapsed or refractory multiple myeloma who have received treatment with—and did not respond satisfactorily to, or progressed while on treatment with—the **three main classes** of drugs currently used to treat myeloma

Proteasome inhibitors

- Velcade (bortezomib)
- Kyprolis (carfilzomib)
- Ninlaro (ixazomib)

Immunomodulatory drugs


- Revlimid (lenalidomide)
- Pomalyst (pomalidomide)

Anti-CD38 monoclonal antibodies

- Darzalex (daratumumab)
- Sarclisa (isatuximab)

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Currently Available Drugs for Triple-Class Refractory Myeloma



Class	Drug	Formulation	Approval
Nuclear export inhibitor	XPOVIO (selinexor)	 Twice-weekly pill	• For relapsed/refractory myeloma in combination with dexamethasone (after at least 4 prior therapies and whose disease is refractory to at least 2 PIs, at least 2 IMiDs, and an anti-CD38 mAb)

XPOVIO + dexamethasone in relapsed/refractory myeloma	No. patients with ≥PR (%) ¹
Total	32 (26)
Previous therapies to which the disease was refractory, n (%)	
Velcade, Kyprolis, Revlimid, Pomalyst, and Darzalex	21 (25)
Kyprolis, Revlimid, Pomalyst, and Darzalex	26 (26)
Velcade, Kyprolis, Pomalyst, and Darzalex	25 (27)
Kyprolis, Pomalyst, and Darzalex	31 (26)

Additional analyses showed clinical benefit with XPOVIO regardless of patient age and kidney function.^{2,3}

1. STORM Trial. Chari A et al. *N Engl J Med*. 2019;381:727. 2. Gavriatopoulou M et al. Presented at the 17th International Myeloma Workshop; September 12-15, 2019. Abstract FP-110. 3. Vogl DT et al. Presented at the 17th International Myeloma Workshop; September 12-15, 2019. Abstract FP-111.

Currently Available Drugs for Triple-Class Refractory Myeloma

Class	Drug	Formulation
Bispecific antibody	Tecvayli (teclistamab)* [‡]	 Step-up dosing [†] the first week then once weekly thereafter by subcutaneous injection
Bispecific antibody	Talvey (talquetamab)* [‡]	 Step-up dosing [†] the first week then once weekly thereafter by subcutaneous injection
Bispecific antibody	Elrexfio (elranatamab)*	 Step-up dosing [‡] the first week then once weekly thereafter by subcutaneous injection

And, CAR T-cell therapies: Abecma, Carvykti

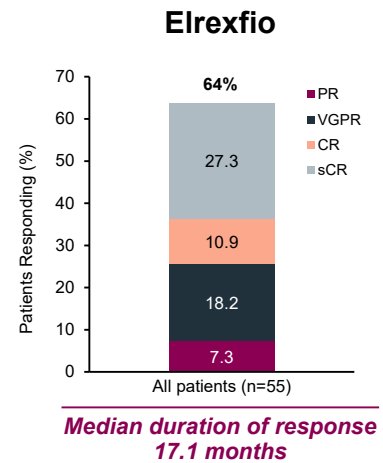
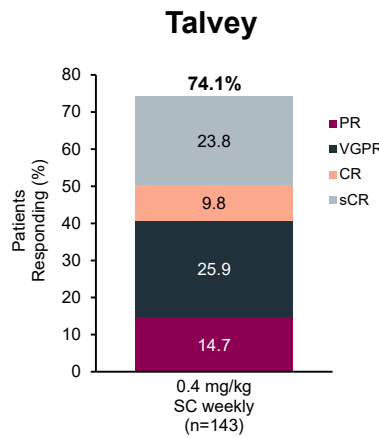
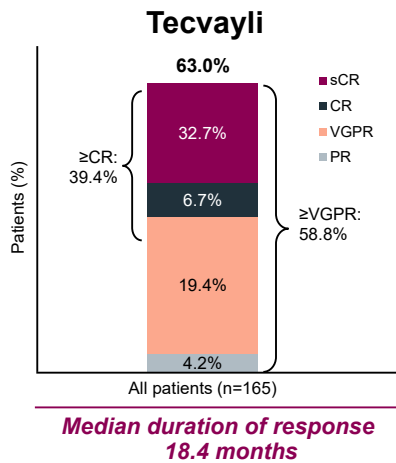
*Black box warning: cytokine release syndrome; neurologic toxicities

[†]Patients are hospitalized for 48 hours after administration of all step-up doses.

[‡]Patients are hospitalized for 48 hours after administration first step-up dose and for 24 hours after second step-up dose.

Abecma, Carvykti, Tecvayli, Talvey, and Elrexfio are available only through a restricted distribution program.

Now Approved: Three Bispecific Antibodies!



MajesTEC-1 Study. Moreau P et al. *N Engl J Med.* 2022;387:495.
 Chari A et al. *N Engl J Med.* 2022;387:2232.
 Schinke CD et al. *J Clin Oncol.* 2023;41. Abstract 8036.

91

Expected Toxicities With T Cell–Activating Therapies (CAR T and Bispecific Antibodies)



Cytokine release syndrome (CRS)



Infections



Cytopenias



Neurotoxicity (ICANS)

Off-target effects (with GPRC5D-targeted agents)



Cytokeratin changes/rash
Dysgeusia

ICANS, immune effector cell-associated neurotoxicity syndrome

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GPRC5D-Associated Side Effects

Affected area	Symptoms and effects	Management
Skin	Rash, skin peeling	Relatively benign, not painful, self-limiting, and manageable with emollients
Nails	Nail thinning and loss	Mostly aesthetic but take time to resolve
Oral	Difficulty swallowing, dry mouth, taste changes	Can lead to weight loss; have longer duration and can affect quality of life. Most successfully managed with dose modification. Supportive measures may be used (eg, NaCl mouth rinse, artificial saliva spray, diet modification)

Myeloma patients respond well to treatment, and GPRC5D-associated side effects improve over time, becoming more tolerable; notable reduction in side effects is seen with dose modification

Catamero D et al. *Clin Lymphoma Myeloma Leuk.* 2023;23. Abstract NSP-03.

93

Bispecific Antibodies Under Investigation

Bispecific antibody	Target (on MM cell × T cell)	Status
Tecvayli (teclistamab)	BCMA × CD3	Approved for use in myeloma patients
Elrexio (elranatamab)	BCMA × CD3	Approved for use in myeloma patients
Linvoseltamab	BCMA × CD3	Clinical studies
Alnuctamab	BCMA × CD3	Clinical studies
ABBV-383	BCMA × CD3	Clinical studies
Talvey (talquetamab)	GPRC5D × CD3	Approved for use in myeloma patients
Forimtamig (RG6234)	GPRC5D × CD3	Clinical studies
Cevostamab	FcRH5 × CD3	Clinical studies

BCMA

- Highly expressed only on the surface of plasma cells
- Myeloma patients have significantly higher serum BCMA levels than healthy individuals

GPRC5D

- Highly expressed on myeloma cells in the bone marrow
- Lowly expressed on hair follicles but not on other healthy cells
- Expression on myeloma cells is independent of BCMA

FcRH5

- Selectively expressed on B cells and plasma cells

CD3: a T-cell receptor

GPRC5D, G protein-coupled receptor family C group 5 member D

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Summary

- We now have many different options for relapsed myeloma depending on patient and myeloma factors at relapse.
- Therapy choices will depend on teamwork between physician, patient, and caregivers and are based on many decision points.
- Combinations of proteasome inhibitors with either immunomodulatory drugs or selinexor improve PFS.
- We have three different monoclonal antibodies that improve PFS when added to other standard therapies without significantly increasing side effects.
- CAR T and bispecific antibodies are very active even in heavily pre-treated patients with unprecedented response rates and durations of response.

95



Please take a moment to answer two questions about this presentation.

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Personalized Medicine

Samir S. Parekh, MD

Icahn School of Medicine at Mount Sinai
New York, New York

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Disclosures

- Dr. Parekh discloses consulting relationships with Grail and research support from Amgen, Celgene/BMS Corporation, and Caribou

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Multiple Myeloma Is Not Just One Disease!

Multiple myeloma is a heterogeneous disease even within cytogenetically defined molecular subtypes.

In the future, the goal is to go beyond a one-size-fits-all approach.

How do we customize treatment?
Personalized medicine

99

Treatment of Multiple Myeloma

Where are we now?

- Standard induction with proteasome inhibitors and IMiDs, consolidation with ASCT, and maintenance therapy have benefited the majority of multiple myeloma patients
- A subset of myeloma patients still have poor outcome with standard therapy
- Personalized medicine approaches are needed to address high-risk patients



What we need

- Evolving definitions of high-risk beyond historic markers such as translocation 4;14 and deletion of chromosome 17p
- Advanced molecular diagnostics are key to revealing individual targets and therapies
- Immunotherapies are emerging as promising new weapons in the fight against multiple myeloma

IMiDs, immunomodulatory drugs; ASCT, autologous stem cell transplantation



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An Example of the Importance of Personalized Medicine

	CoMMpassMMRF2172 	CoMMpassMMRF2250 
Age	72	71
Ethnicity	Caucasian	Caucasian
ISS stage	II	II
Baseline treatment	VRD	VRD
Cytogenetics	t(4;14), del13	t(4;14), del13
Time of progression	11 months	36 months
Overall survival	1.6 years	6.3 years

101

An Example of the Importance of Personalized Medicine

	CoMMpassMMRF2172 	CoMMpassMMRF2250 
Age	72	71
Ethnicity	Caucasian	Caucasian
ISS stage	II	II
Baseline treatment	VRD	VRD
Cytogenetics	t(4;14), del13	t(4;14), del13
Time of progression	11 months	36 months
Overall survival	1.6 years	6.3 years
Other genetic events	1q21, del17p + TP53 mut	No 1q21, no 17p or TP53 mut

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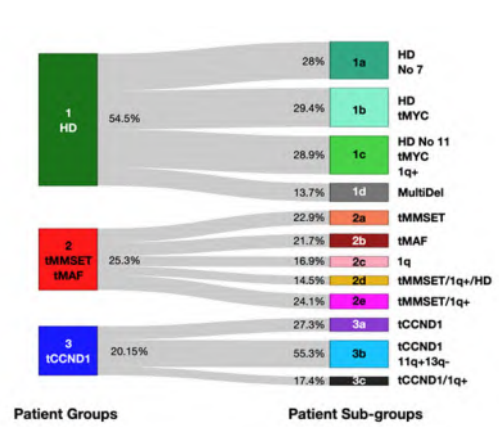
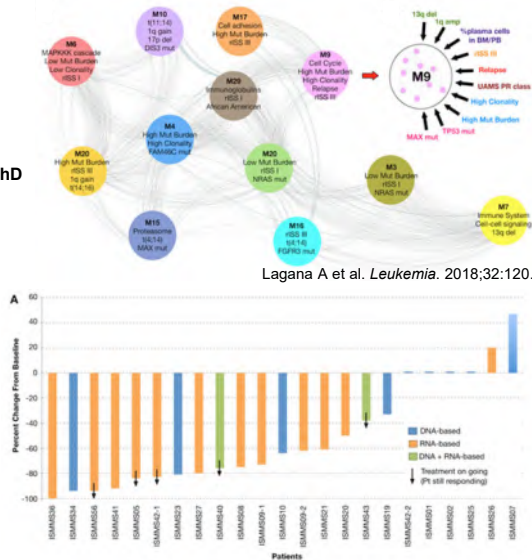
Multiple Myeloma Genomics/Precision Medicine at Sinai



Alessandro Lagana, PhD



Joel Dudley, PhD



Lagana A et al. *JCO Precis Oncol*. 2018;2018:PO.18.00019.

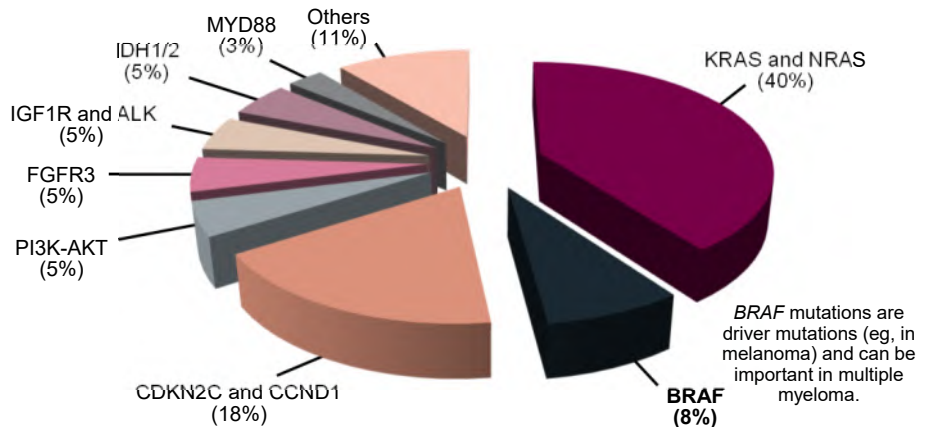
103

Actionable Alterations in Multiple Myeloma



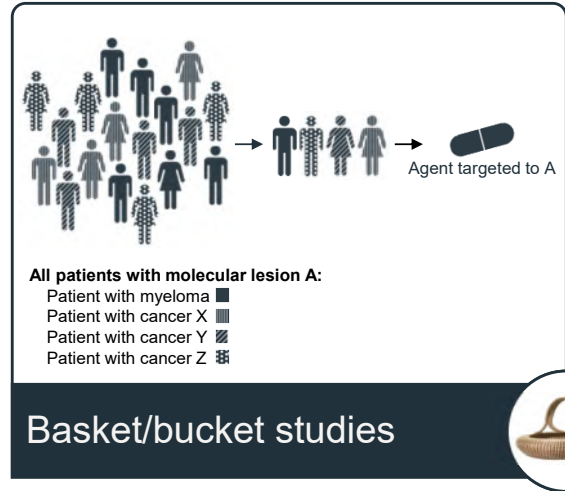
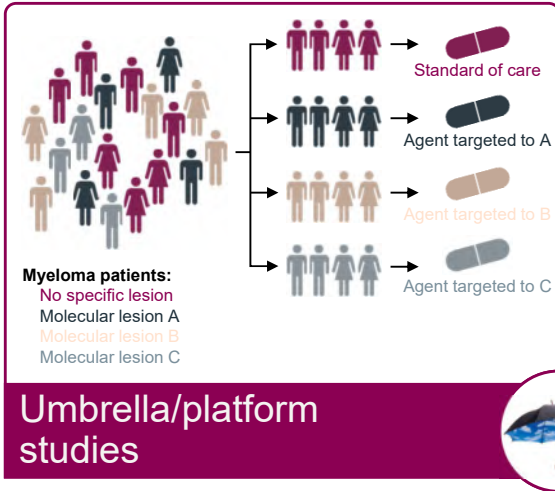
These alterations may be the Achilles' heel of myeloma cells.

Precision medicine efforts have identified molecular alterations for which there are drugs in the clinic.



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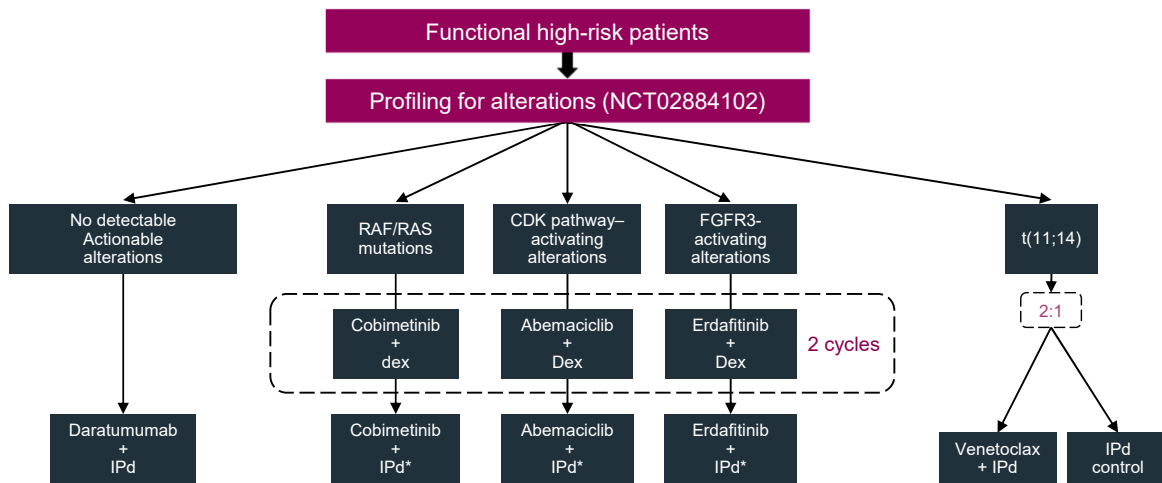
Innovative Study Designs: Shaping the Future of Cancer Research Toward Personalized Medicine



Pawlyn C, Davies F. *Blood*. 2019;133:660.

105

MyDRUG Study



*Assess single-agent activity after 2 cycles; after cycle 2, add backbone to single agent

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Personalized Medicine in Myeloma: MyDRUG (NCT03732703)

Case study: man, age 59

Treatments

1st Line

- VRd/KRd induction, ASCT, Rev maintenance
- Best response: CR
- Progressed in 30 months (22 months post-ASCT/maint.)

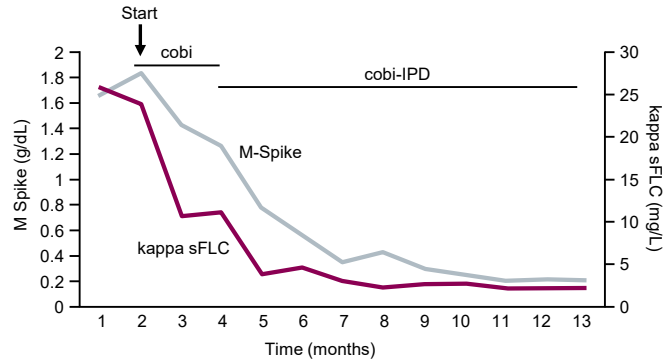
2nd Line

- EPd
- Best response: MR
- Progressed in 4 months

3rd Line

- MyDRUG

Response on MyDRUG



Genomics

- Hyperdiploid, del13q, del1p, Myc ampl.
- NRAS Q61H, 56% allelic fraction

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Personalized Medicine Agents Under Clinical Investigation

Clinical phase	Novel agents
	Personalized medicine
Phase 3	Venetoclax*
Phase 1, 2	Abemaciclib* Cobimetinib* Dabrafenib Enasidenib Erdafitinib* Idasanutlin Trametinib Vemurafenib

*Being studied in the MyDRUG trial

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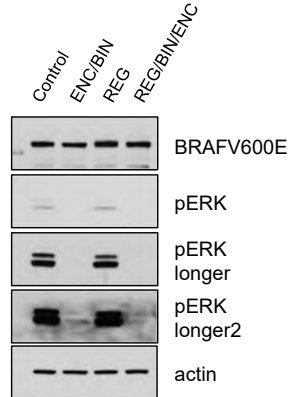
64-Year-Old With Relapsed Myeloma After CAR T With BRAF V600E



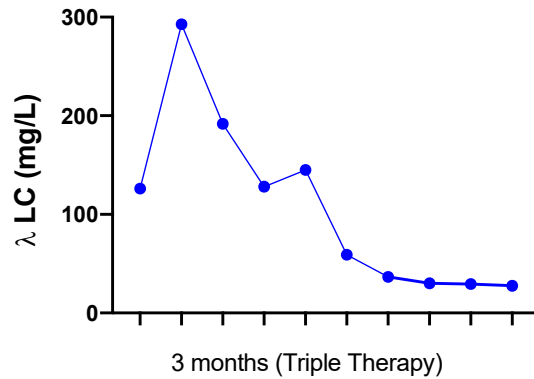
Muhammad Elnaggar, MD, PhD



Sarita Agte, MD



48-hour treatment
 Encorafenib: 50 nM
 Binimetinib: 250 nM
 Regorafenib: 1 μ M



Phase 2 clinical trial (R01 funded) in 2022 to include other genomic guided drugs (for example, Selinexor).

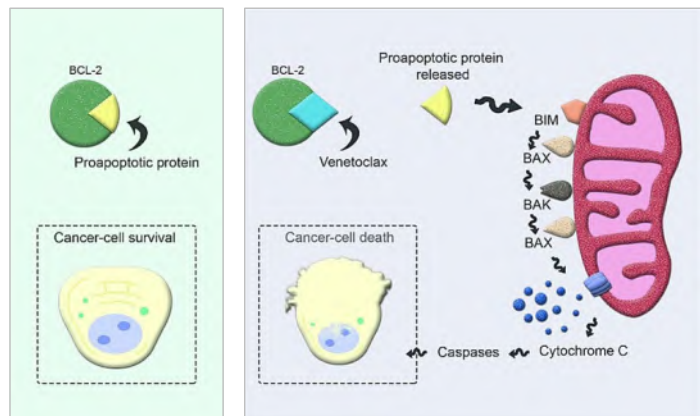
Elnaggar M et al. *J Hematol Oncol.* 2022;15:109.

109

Venetoclax and t(11;14)

Venetoclax is a Bcl-2 inhibitor

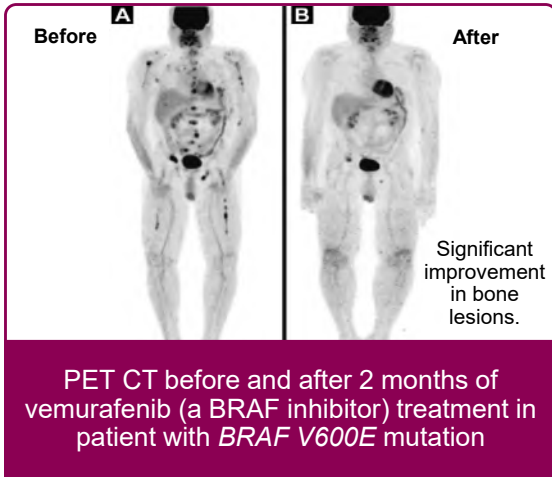
- BCL2 inhibitor
- Induces cancer cell death
- t(11;14) multiple myeloma \rightarrow \uparrow BCL2 and \downarrow MCL1
- t(11;14): first predictive marker in multiple myeloma, indicating susceptibility to BCL2 inhibition



Ehsan H et al. *J Hematol.* 2021;10:89.

110

BRAF and MEK



- 12 patients treated with
 - BRAF TOVI (encorafenib)
 - MEK TOVI (binimetinib)
- 83% of patients responded to treatment
- Common side effects included blurred vision, macular edema, cramps, arthralgia, diarrhea, rash, and decreased left ventricular function
- Serious side effects included low blood counts and hypertension

A phase 2 study evaluating combined BRAF and MEK inhibition in relapsed/refractory multiple myeloma patients with activating BRAF V600E mutations

Sharman JP et al. *Clin Lymphoma Myeloma Leuk.* 2014;14:e161.

GMMG-Birma Trial. Raab MS et al. *Blood.* 2020;136. Abstract 294.

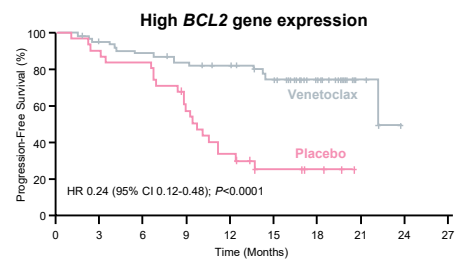
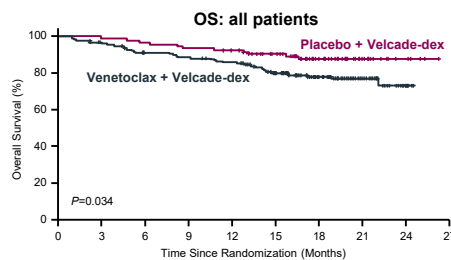
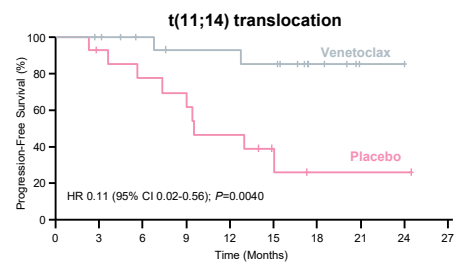
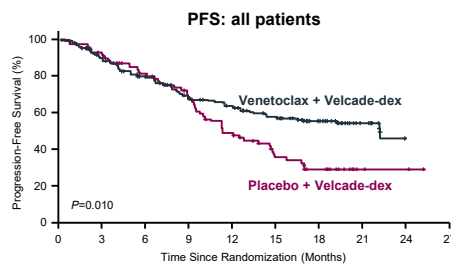
111

Venetoclax and t(11;14)

Venetoclax bortezomib dex vs placebo bortezomib dex; 1-3 prior lines

Median follow up 18.7 m mPFS
22.4 m venetoclax
11.5 m placebo

Venetoclax especially active in t(11;14) or BCL2^{high} MM



The BELLINI Trial. Kumar SK et al. *Lancet Oncol.* 2020;21:1630.

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Next-Generation BCL-2 Inhibitors

Lisaftoclax¹

30 patients

- 22 RRMM, lisaftoclax + pom-dex
- 3 RRMM, lisaftoclax + dara-Rd
- 5 RR AL, lisaftoclax + pom-dex
- Median 4 prior lines of therapy
- 18 patients triple-class exposed

Safety

- TRAEs: neutropenia 16.7%, nausea 16.7%
- Grade ≥ 3 TRAEs: neutropenia 10%

ORR, lisaftoclax + pom-dex in RRMM: 67%

RRMM, relapsed/refractory multiple myeloma; RR AL, relapsed/refractory amyloid light chain amyloidosis; TRAE, treatment-related adverse event; ORR, overall response rate; AE, adverse event; SAE, serious adverse event

1. Ailawadhi S et al. *Blood*. 2023;142. Abstract 2016. 2. Quach H et al. *Blood*. 2023;142. Abstract 1011.

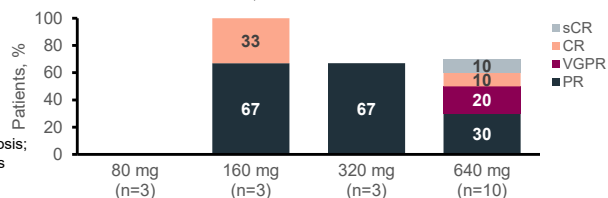
Sonrotoclax²

19 patients

- Median age 68 years
- 21% R-ISS III; 16% high-risk cytogenetics
- Median 4 prior lines of therapy
- All patients received prior IMiD and prior PI

Safety

- Hematologic AEs 21%, infections 32%
- Grade ≥ 3 AEs 26%, SAEs 11%



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The Road Ahead

- Comprehensive translational and clinical research to find the best combinations of targeted and immune therapies for each group of myeloma patient
- Deliver on the promise of personalized medicine for every patient



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Personalized Medicine Summary

- Efforts are under way to better understand the nature of the disease and to provide patients with a more personalized approach to treatment.
- Genomic sequencing and data from myeloma patients are key to identifying subtype: our goal is to help individualize treatment for better outcomes.
- Participation in clinical studies to provide bone marrow and peripheral blood is paramount.
- Personalized medicine provides the right treatment at the right time for each myeloma patient.

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Supportive Care

Leora A. Giacoia, MS, FNP-BC, ACHPN
Mount Sinai Hospital
New York, NY

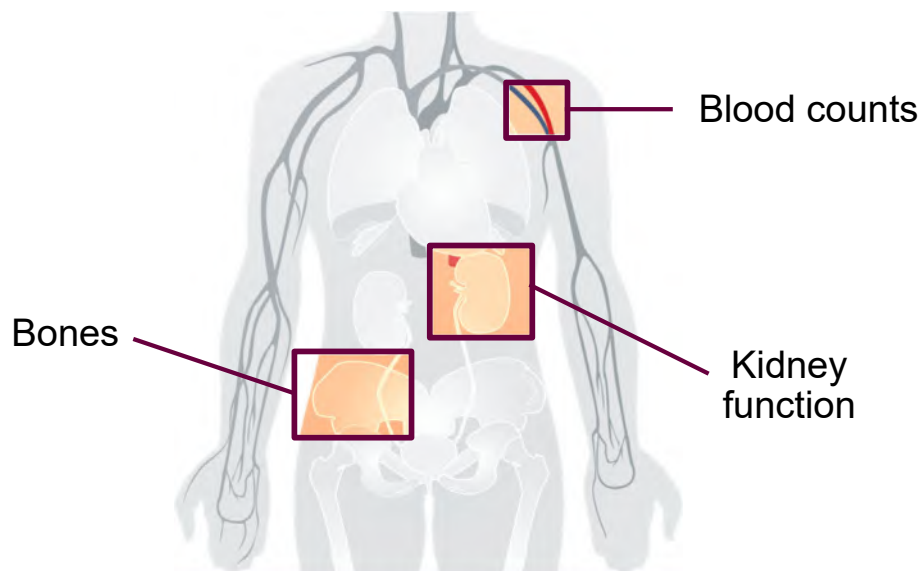
116

Disclosures

- Leora A. Giacoia, MS, FNP-BC, ACHPN, has no relevant financial information to disclose.

117

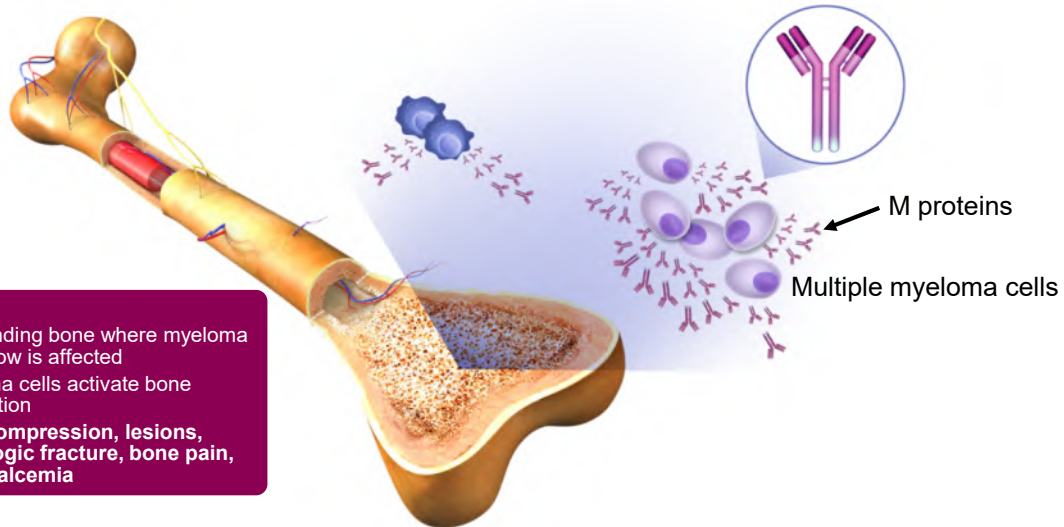
Myeloma Affects Your...



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Multiple Myeloma Affects Your...

Bones



BONES

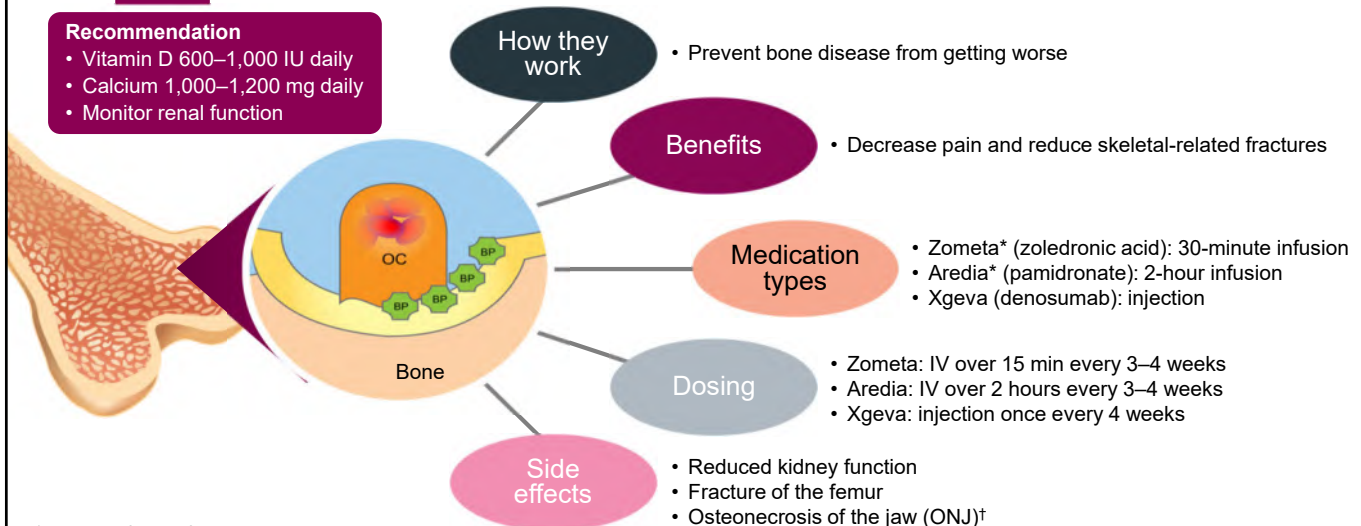
- Surrounding bone where myeloma cells grow is affected
- Myeloma cells activate bone destruction
- Cord compression, lesions, pathologic fracture, bone pain, hypercalcemia

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Medications for Myeloma Bone Disease

Recommendation

- Vitamin D 600–1,000 IU daily
- Calcium 1,000–1,200 mg daily
- Monitor renal function



*Dose adjust for renal function

OC, osteoclast (inhibited, halting bone breakdown); BP, bisphosphonate

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Recommendations for Reducing the Risk of ONJ and Infection

- Complete major dental work before beginning treatment for bone disease
- Practice good oral hygiene
- Schedule regular dental visits/antibiotic prophylaxis
- Let your dentist know that you are receiving treatment for bone disease
- Keep your doctor informed of dental issues/need for dental work
- Be attentive! ONJ seems to be related to the length of time patients are on treatment for bone disease



ONJ, osteonecrosis of the jaw

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Procedures for Bone Pain Radiation and Surgical Intervention

- Minimally invasive procedures
- Can be performed without hospitalization
- Small incision
- Cement filler stabilizes bone
- Potential for relatively rapid symptom relief (approximately 1 month with kyphoplasty)

Vertebroplasty



Kyphoplasty



- Destroys myeloma cells
- Stops bone destruction
- Pain control
- Targeted and localized therapy
- Can affect bone marrow function
- Can affect adjacent tissues

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Pain Management Medications

Acetaminophen (Tylenol)

High dosage can hurt your liver; caution with elevated liver function tests (LFTs)

NSAIDs (nonsteroidal anti-inflammatory drugs)

Prefer to avoid with multiple myeloma due to increased risk of kidney injury
Topical NSAIDs may be acceptable on case by case basis

Opioids

Potential for constipation, sedation, confusion, physiologic dependence

Corticosteroids (dexamethasone, prednisone)

Has myeloma-fighting effects. Can raise blood sugar and cause insomnia; short- and long-term effects

GABA analogues (gabapentin and Lyrica)

For use of neuropathic pain. Potential for drowsiness and dizziness

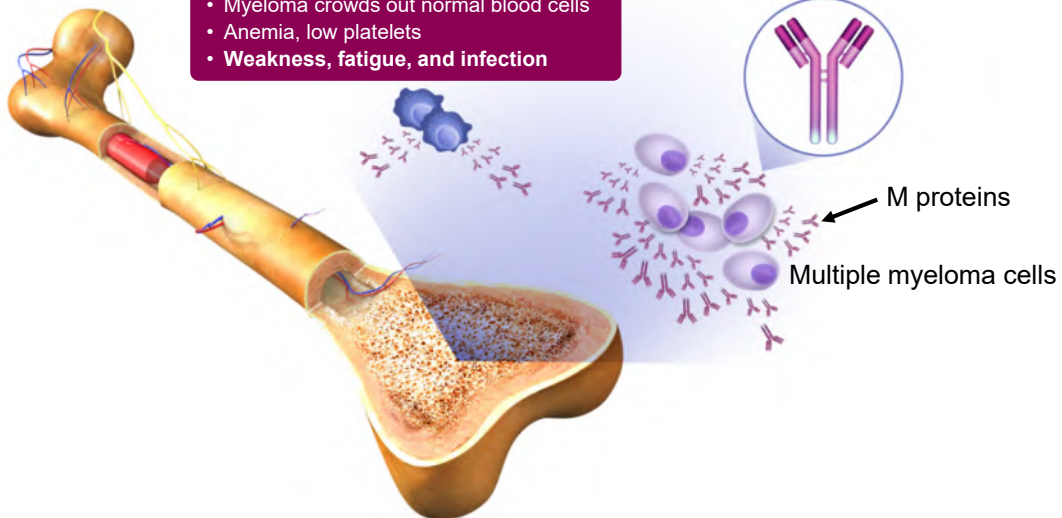
123

Multiple Myeloma Affects Your...

Blood

BLOOD

- Myeloma is a cancer of the blood
- Myeloma crowds out normal blood cells
- Anemia, low platelets
- **Weakness, fatigue, and infection**



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Effects of Myeloma: Low Blood Counts

- Symptoms
 - Fatigue; depression/mood changes; difficulty breathing; rapid heartbeat; dizziness
- Other causes
 - Low levels of iron, folate, and vitamin B12

- Symptoms
 - Easy or excessive bruising; superficial bleeding into the skin; prolonged bleeding from cuts; bleeding from the gums or nose; blood in urine or stool
- Other causes
 - Viral infection (hep B or C); immune thrombocytopenia; medications

- Symptoms
 - Fatigue; frequent infections
- Other causes
 - Radiotherapy
 - Infection

Low red blood cells (anemia)



Treatment: Identify and treat causes other than myeloma; supplements; medications to increase number of red blood cells; blood transfusions

Low platelets (thrombocytopenia)



Treatment: Identify and treat causes other than myeloma; platelet transfusion; hold anticoagulation

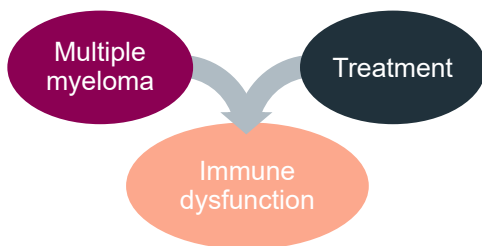
Low white blood cells (leukopenia)



Treatment: Medications to stimulate production of white blood cells; antibiotics; infection prevention

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Infection Can be Serious for Patients With Myeloma



7-10-fold increased risk of bacterial and viral infections for people with myeloma

Report fever of more than 100.4°F, shaking chills even without fever, dizziness, shortness of breath, low blood pressure to HCP as directed.

General infection-prevention tips

- Good personal hygiene (skin, oral)
- Environmental control (wash hands, avoid crowds and sick people, etc)
- Growth factor (Neupogen, Neulasta)
- IV gamma globulin infusion (Gamunex)
 - 4-hour infusion every 4 weeks IV
- Immunizations
 - COVID-19 vaccination + booster(s)
 - Pneumococcal 20-valent conjugate vaccine
 - Seasonal inactivated influenza vaccine
 - Shingles vaccine: zoster vaccine recombinant, adjuvanted
- Prophylactic medications (antibacterial, antiviral)
 - Valacyclovir/acyclovir
 - Hepatitis B virus nucleoside reverse transcriptase inhibitors
 - Bactrim, Mepron, or dapsone

Brigle K et al. *Clin J Oncol Nurs.* 2017;21(5)suppl:60. Faiman B et al; IMF Nurse Leadership Board. *Clin J Oncol Nurs.* 2011;15(Suppl):66. Miceli TS et al. *Clin J Oncol Nursing.* 2011;15(4):9. ASH Website. COVID-19 Resources. <https://www.hematology.org/covid-19/covid-19-and-multiple-myeloma>

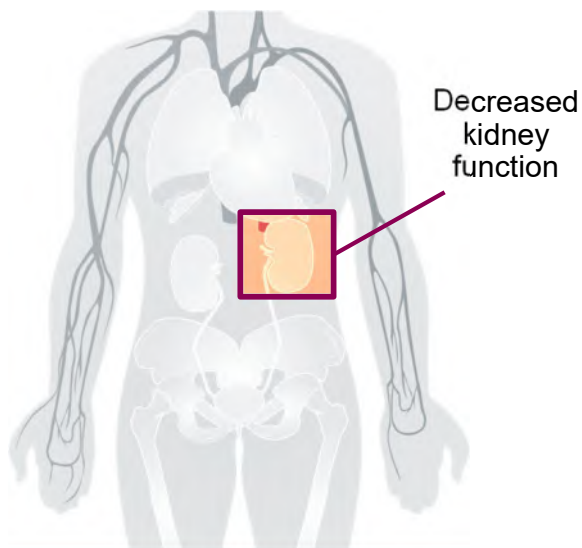
126

Multiple Myeloma Affects Your... Kidneys



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Effects of Myeloma: Decreased Kidney Function



- Detection
 - Decreased amount of urine
 - Increase in creatinine and other proteins
- Other causes beside myeloma
 - Hypertension
 - Diabetes
 - Some medications
- Treatment
 - Fluids
 - Avoid nephrotoxic substances
 - Nonsteroidal anti-inflammatory drugs (NSAIDs) such as Aleve, Advil/Motrin
 - CT contrast
 - Plasmapheresis
 - Treat other causes
 - Dialysis (severe)

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Side Effects and Management of Myeloma Therapies

Immunomodulatory medications

Revlimid, Pomalyst

- Fatigue and weakness
- Blood clots
- GI effects: diarrhea
- Muscle cramping and back pain
- Drug rash
- Shortness of breath
- Upper respiratory infections
- Mental foginess
- Birth defects

Management

Blood thinners for potential clots; tonic water/hydration for cramps; avoid dairy; fiber Imodium; cholestyramine for GI toxicities; sleep hygiene, regular exercise, dose reduction for fatigue

Proteasome inhibitors

Velcade, Kyprolis, Ninlaro

- **Peripheral neuropathy**
- Low platelets
- GI problems
- Styes
- Fatigue
- Rash
- Hypertension
- Cardiac toxicity
- Shortness of breath
- Back pain

Management

Dose or frequency decrease, vitamins and supplements, gabapentin, pregabalin, duloxetine, opioids, acupuncture, anticoagulants, antivirals, stop meds if needed

Monoclonal antibodies

Darzalex/Sarclisa, Emluciti

- Infusion reactions
- Fatigue
- Low platelets
- Hepatitis B reactivation
- Upper respiratory tract infections

Management

Premedication in anticipation of infusion reactions, post-infusion medications (dex), antivirals

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Side Effects of Steroids (Dexamethasone)

Insomnia



- Healthy sleep habits
- Timing
- Medication to assist with sleeping as needed

Fluid retention



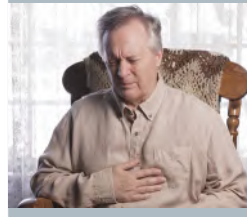
- Monitor for swelling of extremities and "puffy" face
- Monitor weight changes/gain
- Reduce dose

Mood changes



- Irritable, anxiety, difficulty concentrating
- Severe cases → depression, euphoria

Dyspepsia-heartburn



- Dietary modifications (avoid spicy, acidic foods)
- Avoid NSAIDs
- Acid-blocking medications
- Take steroid with food; use enteric-coated aspirin with food

Elevation in glucose



- Monitor glucose and refer/treat as needed

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Bispecific Antibodies

Tecvayli, Talvey, Elrexfio

- Tecvayli (teclistamab) and Elrexfio (elranatamab)
 - BCMA target: CRS, neurotoxicities/ICANS, infections, decreased blood counts, injection-related reactions
- Talvey (talquetamab)
 - GPRC5D target: CRS, neurotoxicities/ICANS, neutropenia, hypogammaglobulinemia, taste changes, oral and skin effects, nail changes



Management

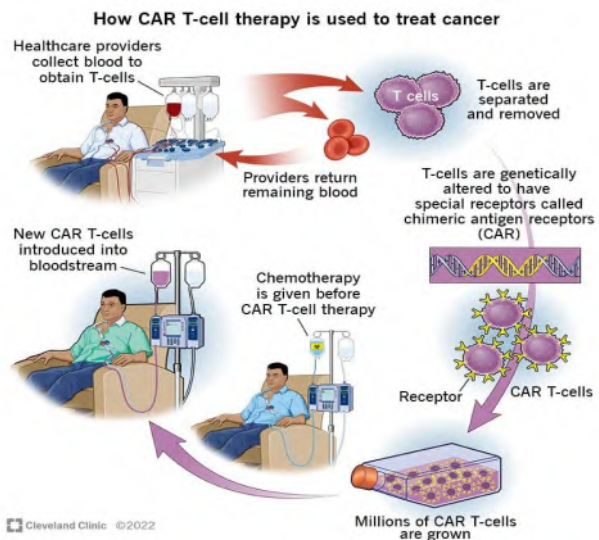
- Patients receive step-up dosing and are monitored in an inpatient setting
- CRS is managed with tocilizumab
- Neurological toxicities managed with anakinra and/or steroids
- Supportive care (oral, skin, and nail care)
- Injection reactions are managed with oral antihistamines and topical steroids
- Infection prevention!



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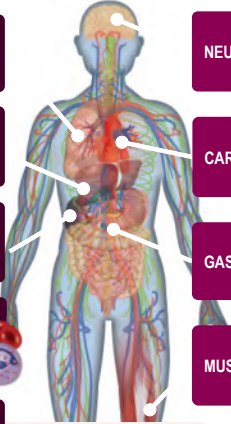
Chimeric Antigen Receptor T Cell (CAR T)

- Cytokine release syndrome (CRS)
- Neurotoxicity/ICANS
 - Caregiver role
- Low blood counts
- Infection risk
 - Prophylactic medications
 - Levaquin
 - Mepron
 - Bactrim



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CRS With Bispecifics and CAR T: Early Recognition and Treatment Is Key



RESPIRATORY	<ul style="list-style-type: none"> • Difficulty breathing • Shortness of breath 	NEUROLOGIC	<ul style="list-style-type: none"> • Tremors • Altered wakefulness • Difficulty speaking
HEPATIC	<ul style="list-style-type: none"> • Altered liver function tests in the blood 	CARDIOVASCULAR	<ul style="list-style-type: none"> • Rapid heart rate • Low blood pressure • Arrhythmias
RENAL	<ul style="list-style-type: none"> • ↑ Serum creatinine • Renal insufficiency 	GASTROINTESTINAL	<ul style="list-style-type: none"> • Nausea • Vomiting • Diarrhea
HEMATOLOGIC	<ul style="list-style-type: none"> • Anemia • Thrombocytopenia • Neutropenia 	MUSCULOSKELETAL	<ul style="list-style-type: none"> • Weakness
CONSTITUTIONAL	<ul style="list-style-type: none"> • Fever • Fatigue • Headache 		





Mitigation and monitoring for CRS

- Step-up dosing with hospitalization for monitoring
- Frequent vital signs
- Rule out infection
- Laboratory monitoring
- Early intervention with **tocilizumab**

Oluwole OO, Davila ML. *J Leukoc Biol.* 2016;100:1265. June CH et al. *Science.* 2018;359:1361. Brudno JN, Kochenderfer JN. *Blood.* 2016;127(26):3321. Brudno JN, Kochenderfer JN. *Blood Rev.* 2019;34:45. Shimabukuro-Vornhagen A et al. *J Immunother Cancer.* 2018;6:56. Lee DW et al. *Biol Blood Marrow Transplant.* 2019;25:625.

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Taking Care of Yourself

-  Talk to your provider about side effects... there is usually a way to make treatment tolerable.
-  Pay attention to your own needs and don't be afraid to ask for help.
-  Learn more about multiple myeloma.
-  Look for the positive.

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Please take a moment to answer two questions about this presentation.

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Questions?

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Patient Experience

Roger Rawlings

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Thank you!

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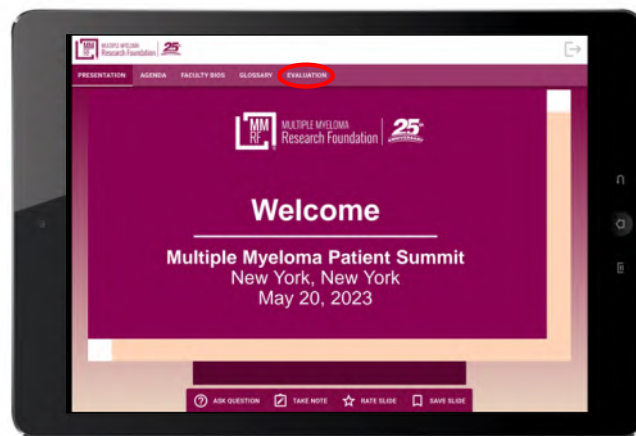
REGENERON
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sanofi

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Don't Forget!

Complete your evaluation
Leave the iPad at your seat



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Upcoming Patient Education Events

Save the Date

Topic	Date and Time (ET)	Speakers
Autologous Stem Cell Transplantation FAQs <i>Livestream</i>	Monday, May 6, 2024 4:00 PM	Amrita Krishnan, MD Cherry Lou Rudge, NP-C Todd Kennedy
Understanding Your Lab Report <i>Webinar</i>	Monday, May 13, 2024 3:30 PM	Craig Emmitt Cole, MD Amy Blake, NP-C
Understanding Lab Report FAQs <i>Livestream</i>	Friday, June 7, 2024 3:00 PM	Joshua Richter, MD Michelle Lyn, NP
Patient Summit <i>Hybrid</i>	Saturday, August 17, 2024 Los Angeles, California	Amrita Krishnan, MD—Host

For more information or to register, visit themmrf.org/educational-resources

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MMRF Patient Resources

EXPECT GUIDANCE.

MMRF Patient Navigation Center

- Information & Resources
- Expert Advice
- Support

MMRF MULTIPLE MYELOMA Research Foundation

MMRF Patient Navigation Center

You and your care team will have many decisions to make along your treatment journey. The Patient Navigation Center is a space for multiple myeloma patients and their caregivers to connect with patient navigators – who are professionals specializing in oncology – for guidance, information, and support. You can connect with a patient navigator via phone, or email. Whatever questions you may have, our patient navigators are here to help.

MMRF Patient Navigators include:

- Grace Allison, RN, BSN, OCN, RN-BC
- Brittany Hartmann, RN-BSN
- Erin Mensing, RN-BSN, OCN

THE RIGHT TRACK

Get on the right track for you

The MMRF's Right Track program puts you on the path to the best results for you.

Right Team

Access experts and centers that have extensive experience treating multiple myeloma.

Right Tests

Get the information, tests, and precise diagnoses to make the right treatment decisions.

Right Treatment

Work with your team to consider the best treatment plan and identify clinical trials that are right for you.

Contact the Patient Navigation Center Today

Looking for guidance? We're here to help.

Monday – Friday | 9:00am – 7:00pm ET

Phone: 1-888-841-MMBF (6673) | Online: [TheMMRF.org/PatientNavigationCenter](https://themmrf.org/PatientNavigationCenter)

Email: patientnavigator@themmrf.org

Supported By

Adaptive Genentech | AMGEN | Bristol Myers Squibb | Cure | Janssen | sanofi | Takeda | ONCOLOGY

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Myeloma Mentors® allows patients and caregivers the opportunity to connect with trained mentors. This is a phone-based program offering an opportunity for a patient and/or caregiver to connect one-on-one with a trained patient and/or caregiver mentor to share his or her patient journeys and experiences.

No matter what your disease state—smoldering, newly diagnosed, or relapsed/refractory—our mentors have insights and information that can be beneficial to both patients and their caregivers.

Contact the Patient Navigation Center at 888-841-6673 to be connected to a Myeloma Mentor or to learn more.

Join the MMRF Community!

National Walk/Run Program

- | | |
|-----------------------------|----------------------------|
| Atlanta 10.26.24 | Philadelphia 10.19.24 |
| Boston 10.12.24 | San Francisco 8.24.24 |
| Chicago 9.8.24 | Scottsdale 12.7.24 |
| Dallas 11.16.24 | Southeast Michigan TBD |
| Houston 11.23.24 | Tampa TBD |
| Los Angeles 8.17.24 | Twin Cities 9.14.24 |
| National Virtual 12.14.24 | Washington, D.C. 9.28.24 |
| New York City 10.5.24 | |



Other MMRF Event Programs



Moving Mountains for Multiple Myeloma



Half and Full Marathons



Bike/Road to Victories



Create Your Own Fundraiser



Need help with travel to a clinical study?

- The MMRF has partnered with the Lazarex Cancer Foundation to help provide more equitable access to clinical studies for multiple myeloma patients
- This partnership is one facet of the MMRF's commitment to improve diversity and representation in myeloma clinical trials
- MMRF has provided \$100,000 over 2 years to Lazarex to fund travel, lodging, and food for patients (and a travel companion) so that they can participate in clinical studies that are appropriate for them
- Patients are funded according to income guidelines and will be reimbursed for allowed expenses
- For more information on this program and to be connected with Lazarex, call our Patient Navigation Center at 1-888-841-6673



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**Multiple Myeloma Patient
and Caregiver Summit
New York, New York
May 4, 2024**

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