MULTIPLE MYELOMA Research Foundation

From Diagnosis to Prognosis: Understanding Multiple Myeloma (A Guide for Newly Diagnosed Patients)

January 24, 2023

1

Tech Support

1-719-234-7952

2

3

Resources

- Resource tab includes
  - Speaker bios
  - Copy of the slide presentation
  - Exhibit Hall

Submit your questions throughout the program!

4

MMRF Research Initiatives

MM RC MULTIPLE MYELOMA Research Consortium

CoMMpass Study℠

MMRF CureCloud™

For more information, visit themmrf.org

5

Speakers

Craig Emmitt Cole, MD
Michigan State University
Karmanos Cancer Institute at
McLaren Greater Lansing
Lansing, Michigan

Joshua R. Richter, MD
Tisch Cancer Institute/Icahn School
of Medicine at Mount Sinai
New York, New York

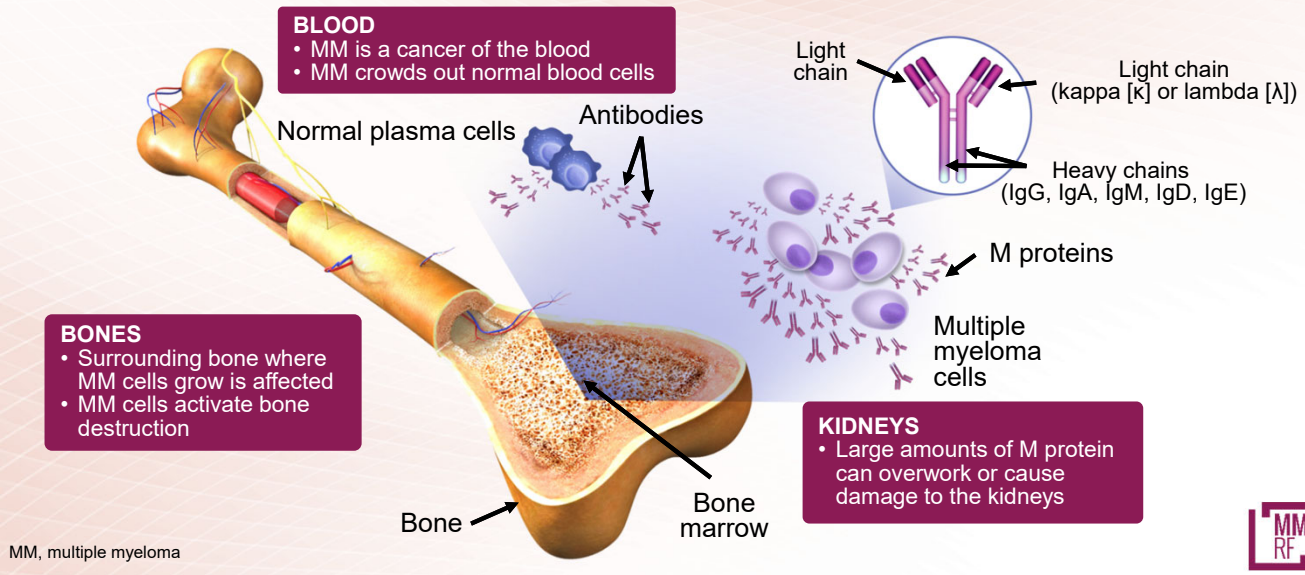
6

Multiple Myeloma Diagnosis and Prognosis

Joshua R. Richter, MD
Associate Professor of Medicine
Hematology and Oncology in the Myeloma Division
Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai
Director of Myeloma
Blavatnik Family Chelsea Medical Center at Mount Sinai
New York, New York

7

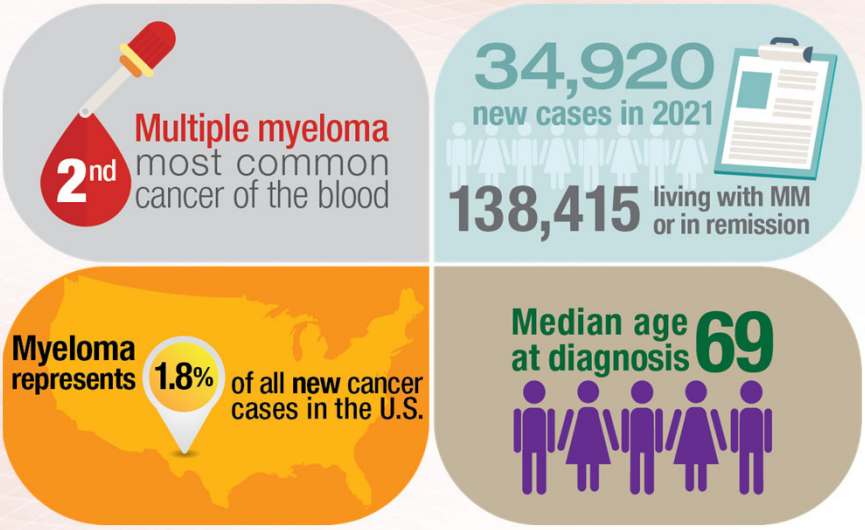
Multiple Myeloma Affects Your Bones, Blood, and Kidneys



MM, multiple myeloma

8

How common is multiple myeloma?

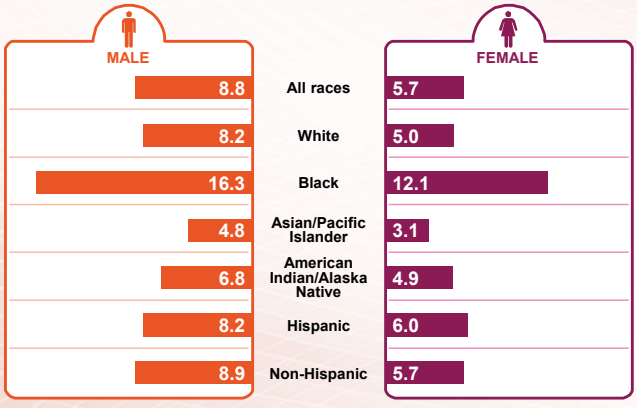


SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/statfacts/html/mulmy.html

9

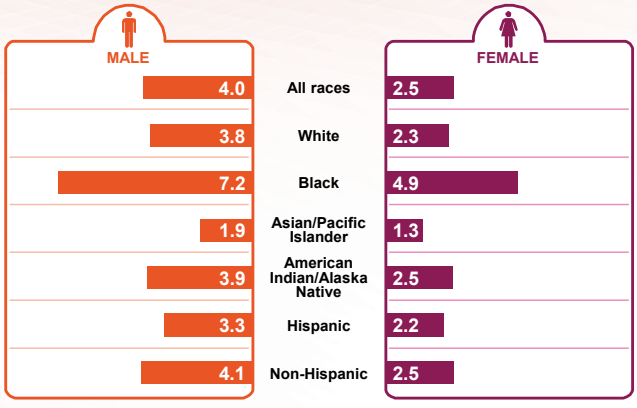
Multiple Myeloma Is Twice as Common—and Twice as Deadly—in Black Patients

Rate of new cases per 100,000 persons by race/ethnicity and sex



SEER 21 20144-2018, age-adjusted

Death rate per 100,000 persons by race/ethnicity and sex



U.S. 2015-2019, age-adjusted

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

10

Demographic Risk Factors: Multiple Myeloma

- Older age
- Male sex
- Race
  - ↑ Blacks (2× Whites)
  - Ashkenazi Jews
  - Europe: Ireland
  - ↓ Asian

Family history risks

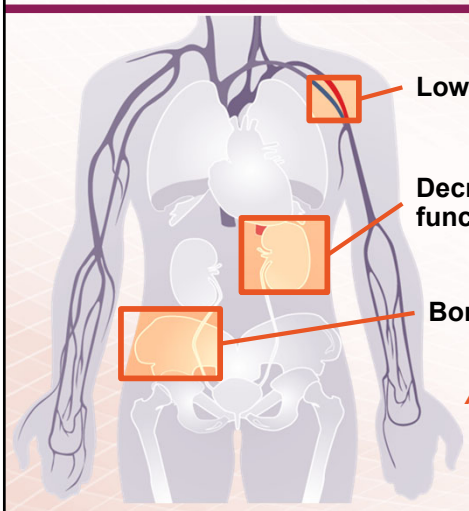
One first-degree relative with multiple myeloma

Relatives of multiple myeloma patients have more monoclonal gammopathy of undetermined significance (MGUS)

Schinasi LH et al. *Br J Haematol*. 2016;175:87.

11

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

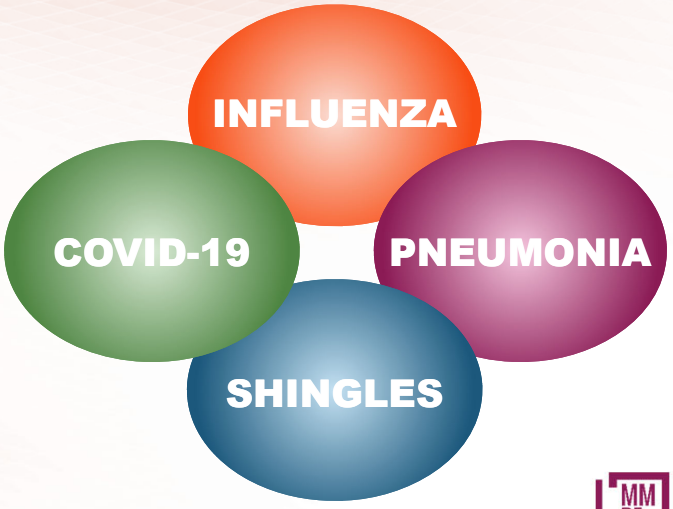
- Bone fractures

MMRF. Multiple myeloma symptoms, side effects, and complications. https://themmrf.org/multiple-myeloma/symptoms-side-effects-and-complications/. Campbell K. *Nurs Times*. 2014;110:12; Kyle R et al. *Mayo Clin Proc*. 2003;78:21; Ailawadhi S et al. *Cancer*. 2018;124:1710.

12

Infections and Vaccinations in Multiple Myeloma

- Risk of infection higher for myeloma patients
- Types of infections include
  - Urinary tract infections
  - Pneumonia (an infection of the lungs)
  - Septicemia (blood infection)
  - Fungal infections
  - Viral infections such as influenza and varicella zoster (shingles)
- Preventive strategies (prophylaxis) are recommended
  - Intravenous immunoglobulin (IVIG)
  - Antibiotics
  - Growth factors
  - Vaccines
  - Other precautions: hand-washing, avoiding sick contacts
- COVID-19
  - Know your vulnerability to COVID-19 infection due to weakened immune system
  - Important to adhere to recommendations to prevent infection (social distancing, wearing a mask, cleaning surfaces, washing hands frequently, avoiding travel except for treatment, and limiting contacts)



13

The Right Team

Available resources

Connect with a myeloma specialist—a doctor who diagnoses and treats a high number of myeloma patients

MMRF's online myeloma treatment locator: **themmrf.org/resources/find-a-treatment-center**

Seek a second opinion at any point in your journey

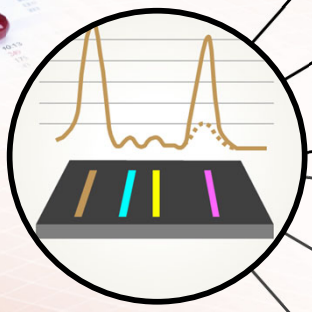
Contact the MMRF Patient Navigation Center: **themmrf.org/resources/patient-navigation-center**

1-888-841-MMRF (6673)

14

Learn Your Labs!

Blood tests



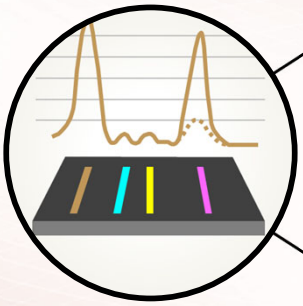
- **CBC** — Number of red blood cells, white blood cells, and platelets
- **CMP** — Measure levels of albumin, calcium, lactate dehydrogenase (LDH), blood urea nitrogen (BUN), and creatinine. Assess function of kidney, liver, and bone status and the extent of disease
- **B2M** — Determine the level of a protein that indicates the presence/extent of MM and kidney function
- **SPEP** — Detect the presence and level of M protein
- **IFE** — Identify the type of abnormal antibody proteins
- **SFLC** — Freelite® test measures light chains (kappa or lambda)

CBC, complete blood count; CMP, complete metabolic panel; B2M; beta-2 microglobulin; SPEP, serum protein electrophoresis; IFE, immunofixation electrophoresis; SFLC, serum free light chain assay

15

Learn Your Labs!

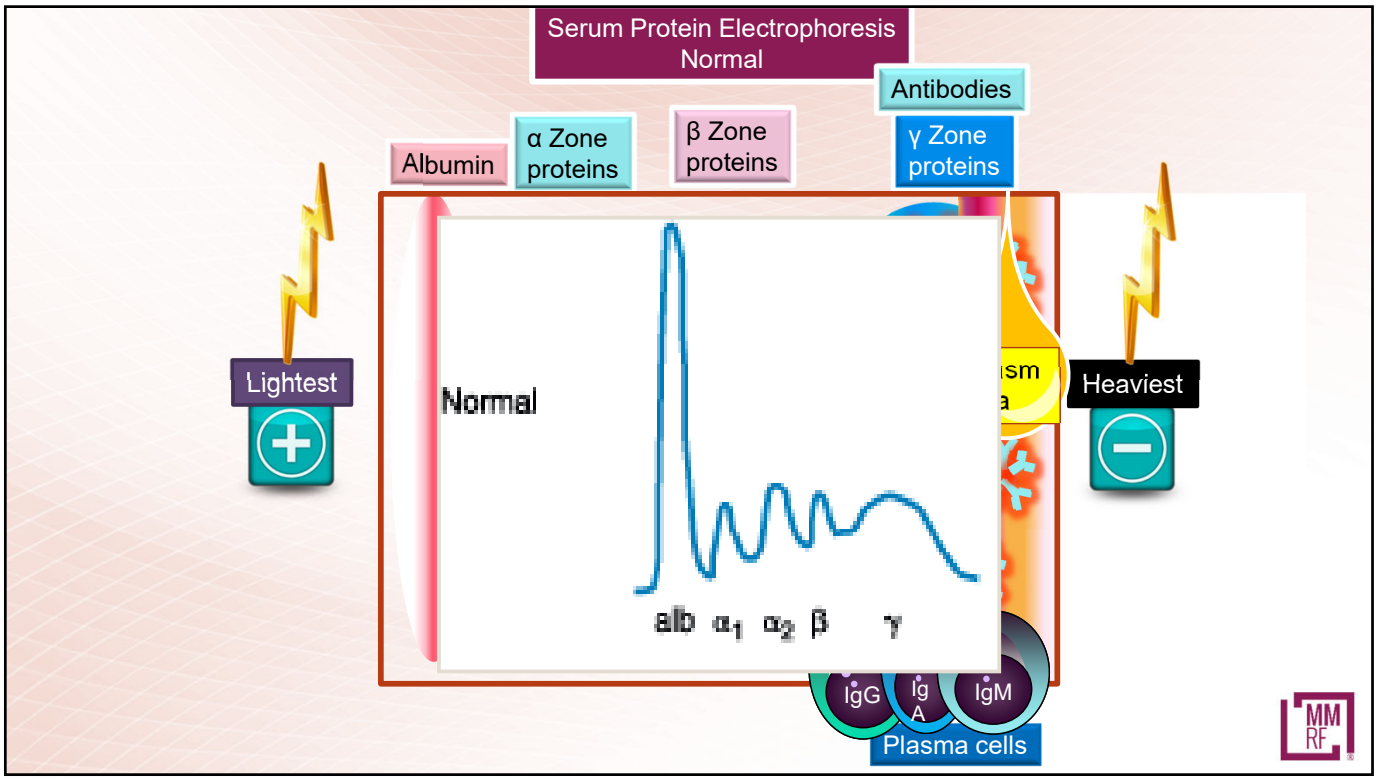
Urine tests



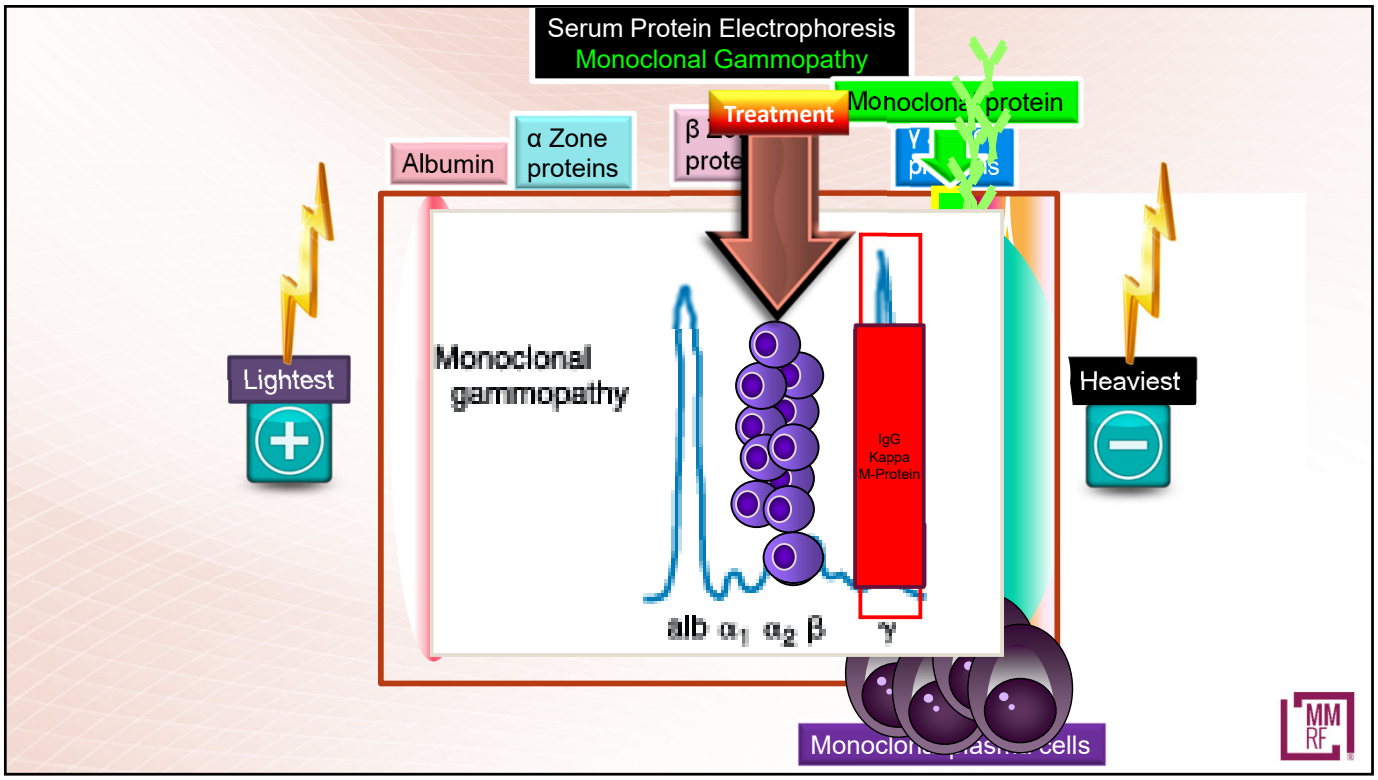
- **UPEP** — Detect Bence Jones proteins (otherwise known as myeloma light chains)
- **24-hr urine analysis** — Determine the presence and levels of M protein and Bence Jones protein

UPEP, urine protein electrophoresis

16

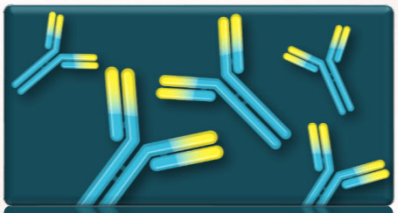

Serum Protein Electrophoresis
Normal
Antibodies
Albumin
α Zone proteins
β Zone proteins
γ Zone proteins
Lightest
Heaviest
Normal
alb α1 α2 β γ
IgG
IgA
IgM
Plasma cells

17


Serum Protein Electrophoresis
Monoclonal Gammopathy
Treatment
Albumin
α Zone proteins
Lightest
Heaviest
Monoclonal gammopathy
IgG Kappa M-Protein
alb α1 α2 β γ

18

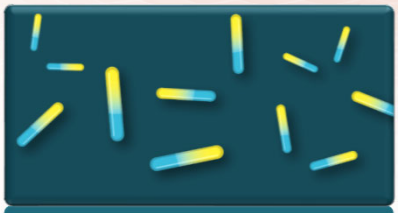
Types of Multiple Myeloma Based on Blood or Urine Tests



Intact M protein

- Named for the type of immunoglobulin and light chain pair; for example, IgG kappa (κ) or IgG lambda (λ)

80%



Light chain only

- Also known as Bence Jones protein
- Renal failure more common in light chain multiple myeloma

20%

Non-secretory

- No M protein present

3%

19

Know Your Imaging Tests!

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

X-ray

Conventional x-rays reveal punched-out lytic lesions, osteoporosis, or fractures in 75% of patients.

MRI

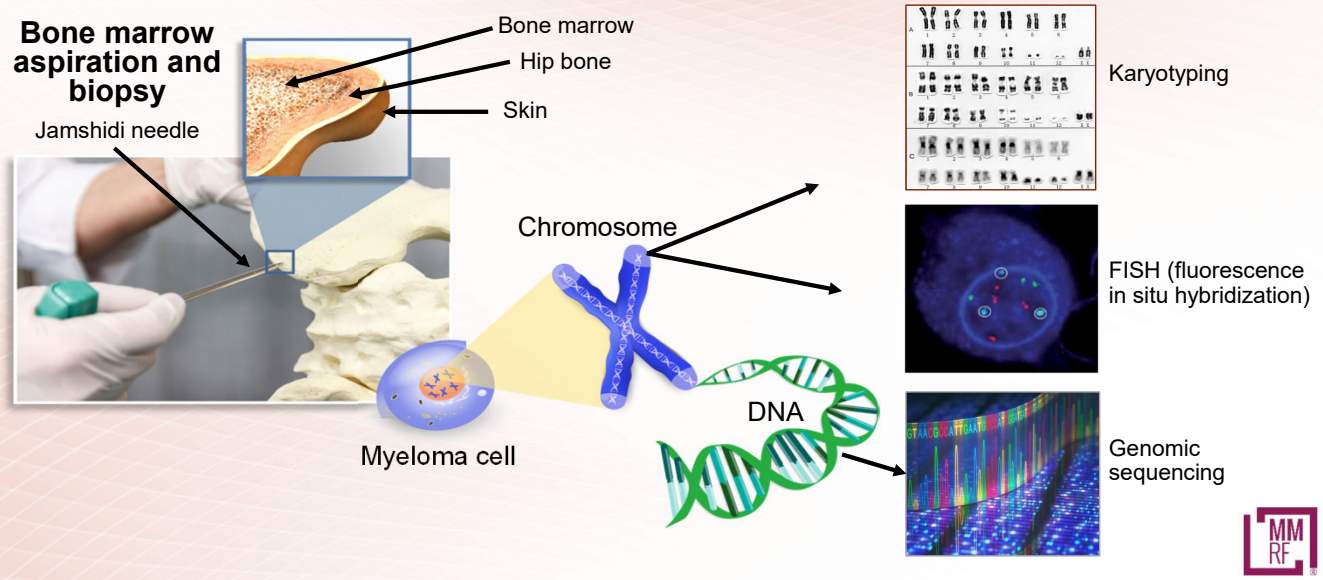
CT scan

PET scan

MRI and PET/CT appear to be more sensitive (85%) than skeletal x-rays for the detection of small lytic bone lesions.

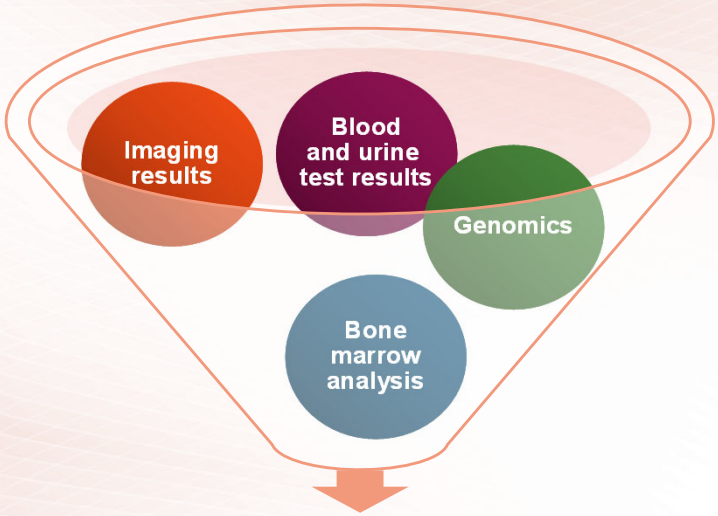
20

Know Your Bone Marrow Tests!



21

Putting the Results Together



Staging, prognosis, and risk assessment

22

Myeloma Staging

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2016
Multiple Myeloma

NCCN Guidelines Index
Multiple Myeloma Table of Contents
Discussion

STAGING SYSTEMS FOR MULTIPLE MYELOMA[1]

Stage	International Staging System (ISS)	Revised-ISS (R-ISS)
I	Serum beta-2 microglobulin <3.5 mg/L, Serum albumin ≥3.5 g/dL	ISS stage I and standard-risk chromosomal abnormalities by iFISH[2] and Serum LDH < the upper limit of normal
II	Not ISS stage I or III	Not R-ISS stage I or III
III	Serum beta-2 microglobulin ≥5.5 mg/L	ISS stage III and either high-risk chromosomal abnormalities by iFISH[2] or Serum LDH > the upper limit of normal

Return to Clinical Presentation (MYEL-1)

[1]Palumbo A, Avet-Loiseau H, Oliva S, et al. Revised international staging system for multiple myeloma: A report from International Myeloma Working Group. J Clin Oncol 2015;33:2863-2869.
[2]Standard-risk: No high-risk chromosomal abnormality. High-risk: Presence of del(17p) and/or translocation t(4;14) and/or translocation t(14;16)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

MYEL-A

TABLE 4: THE DURIE AND SALMON STAGING SYSTEM

STAGE	*CRITERIA*	*MEASURED MYELOMA CELL MASS* *(myeloma cells in billions/m²)**
STAGE I (low cell mass)	*All of the following:* • Hemoglobin value >10g/dL • Serum calcium value normal or <10.5mg/dL • Bone x-ray, normal bone structure (scale 0), or solitary bone plasmacytoma only • Low M-component production rates IgG value <5g/dL; IgA value <3g/dL • Urine light chain M-component on electrophoresis <4g/24h	600 billion*
STAGE II (intermediate cell mass)	*Fitting neither Stage I nor Stage III*	600 to 1,200 billion* **myeloma cells in whole body*
STAGE III (high cell mass)	*One or more of the following:* • Hemoglobin value <8.5g/dL • Serum calcium value >12mg/dL • Advanced lytic bone lesions (scale 3) • High M-component production rates IgG value >7g/dL IgA value >5g/dL • Bence Jones protein >12g/24h	>1,200 billion*
SUBCLASSIFICATION (either A or B)	• A: relatively normal renal function (serum creatinine value) <2.0 mg/dL • B: abnormal renal function (serum creatinine value) >2.0 mg/dL *Examples: Stage IA (low cell mass with normal renal function) Stage IIIB (high cell mass with abnormal renal function)*	

23

Multiple Myeloma Prognosis and Risk

MAYO CLINIC

mSMART 3.0: Classification of Active MM

High-Risk

- High Risk genetic Abnormalities [a,b]
  - t(4;14)
  - t(14;16)
  - t(14;20)
  - Del 17p
  - p53 mutation
  - Gain 1q
- RISS Stage 3
- High Plasma Cell S-phase[c]
- GEP: High risk signature

- Double Hit Myeloma: Any 2 high risk genetic abnormalities
- Triple Hit Myeloma: 3 or more high risk genetic abnormalities

Standard-Risk[a]

All others including:
- Trisomies
- t(11;14)[d]
- t(6;14)

[a]Trisomies may ameliorate
[b] By FISH or equivalent method
[c] Cut-offs vary
[d] t(11;14) may be associated with plasma cell leukemia

Dispenzieri et al. Mayo Clin Proc 2007;82:323-341; Kumar et al. Mayo Clin Proc 2009 84:1095-1110; Mikhael et al. Mayo Clin Proc 2013;88:360-376. v14 //last reviewed August 2018

24

Conclusions

- Myeloma is a complex disease
- Putting it all together requires a whole team as well as a number of different investigative modalities: marrow, blood, urine, scans
- Be open with your care team about everything!

25

Principles of Multiple Myeloma Treatment

Craig Emmitt Cole, MD
Assistant Professor of Medicine
College of Human Medicine
Michigan State University
Karmanos Cancer Institute at McLaren Greater Lansing
Lansing, Michigan

26

The Right Treatment

- Know the treatment options available to you based on your myeloma subtype at each stage of your disease
- Be aware of the pros and cons of each option
- Clearly communicate your treatment goals and concerns to the care team
- Find clinical trials that are right for you

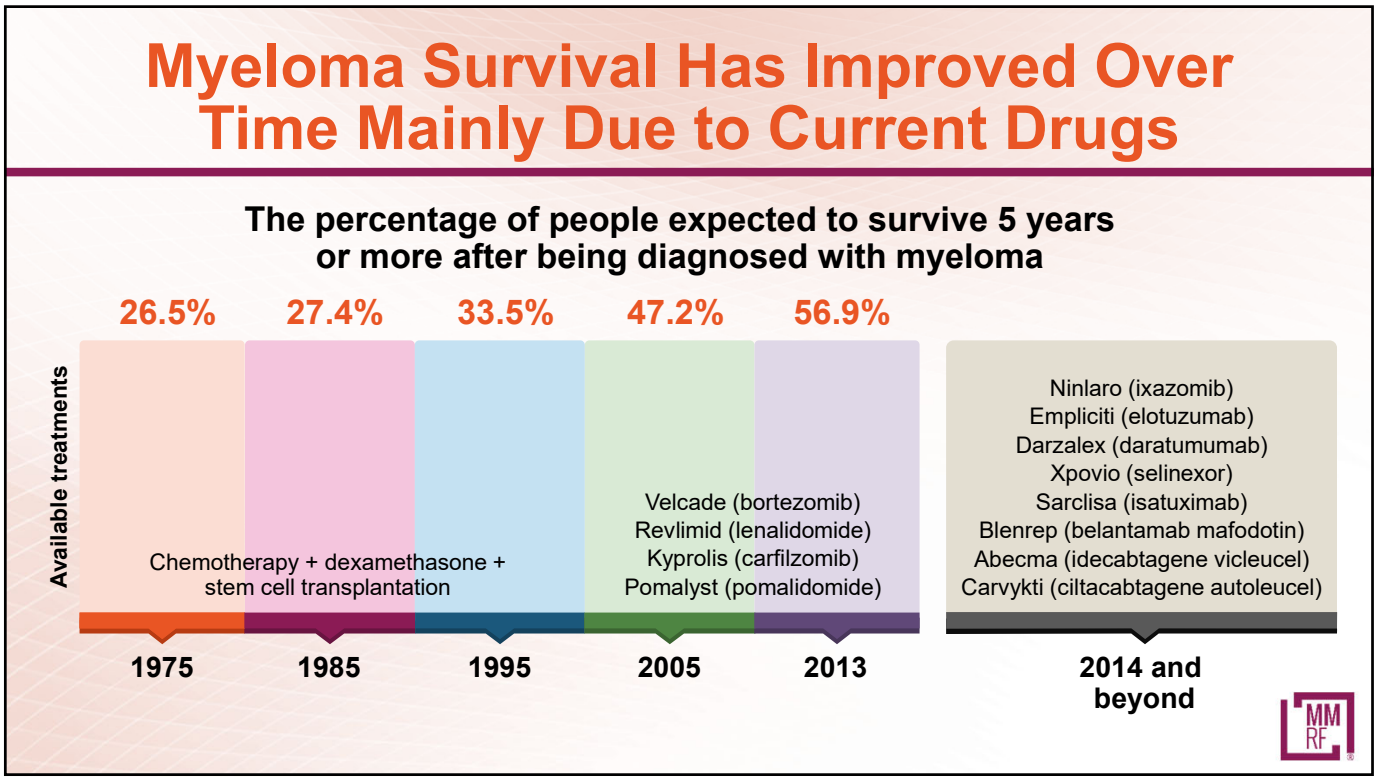
27

Therapeutic Options in Myeloma: The Current Landscape

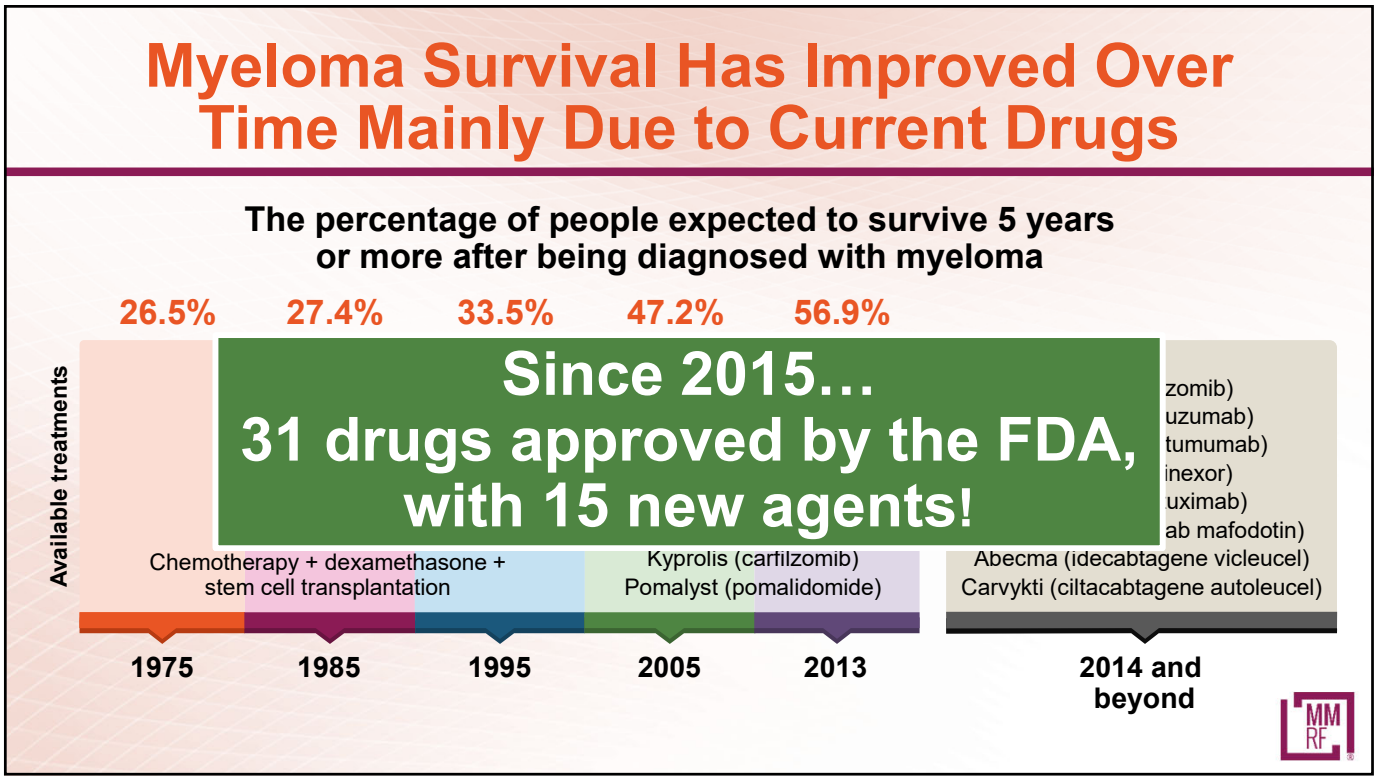
IMiDs	Proteasome inhibitors	Chemotherapy anthracyclines	Chemotherapy alkylators	Steroids	Novel mechanisms of action	mAbs	Cellular therapy
Thalomid (thalidomide)	Velcade (bortezomib)	Adriamycin	Cytoxan (cyclophosphamide)	Dexamethasone	Farydak (panobinostat)	Empliciti (elotuzumab)	Abecma (idecabtagene vicleucel)
Revlimid (lenalidomide)	Kyprolis (carfilzomib)	Doxil (liposomal doxorubicin)	Bendamustine	Prednisone	XPOVIO (selinexor)	Darzalex (daratumumab)	Carvykti (ciltacabtagene autoleucel)
Pomalyst (pomalidomide)	Ninlaro (ixazomib)		Melphalan		Venclexta (venetoclax)*	Sarclisa (isatuximab)	
						Blenrep† (belantamab mafodotin)	

*Not yet FDA-approved for patients with multiple myeloma
†Antibody-drug conjugate

28


Myeloma Survival Has Improved Over Time Mainly Due to Current Drugs
The percentage of people expected to survive 5 years or more after being diagnosed with myeloma
26.5%
27.4%
33.5%
47.2%
56.9%
Available treatments
Chemotherapy + dexamethasone + stem cell transplantation
Velcade (bortezomib)
Revlimid (lenalidomide)
Kyprolis (carfilzomib)
Pomalyst (pomalidomide)
Ninlaro (ixazomib)
Empliciti (elotuzumab)
Darzalex (daratumumab)
Xpovio (selinexor)
Sarclisa (isatuximab)
Blenrep (belantamab mafodotin)
Abecma (idecabtagene vicleucel)
Carvykti (ciltacabtagene autoleucel)
1975
1985
1995
2005
2013
2014 and beyond

29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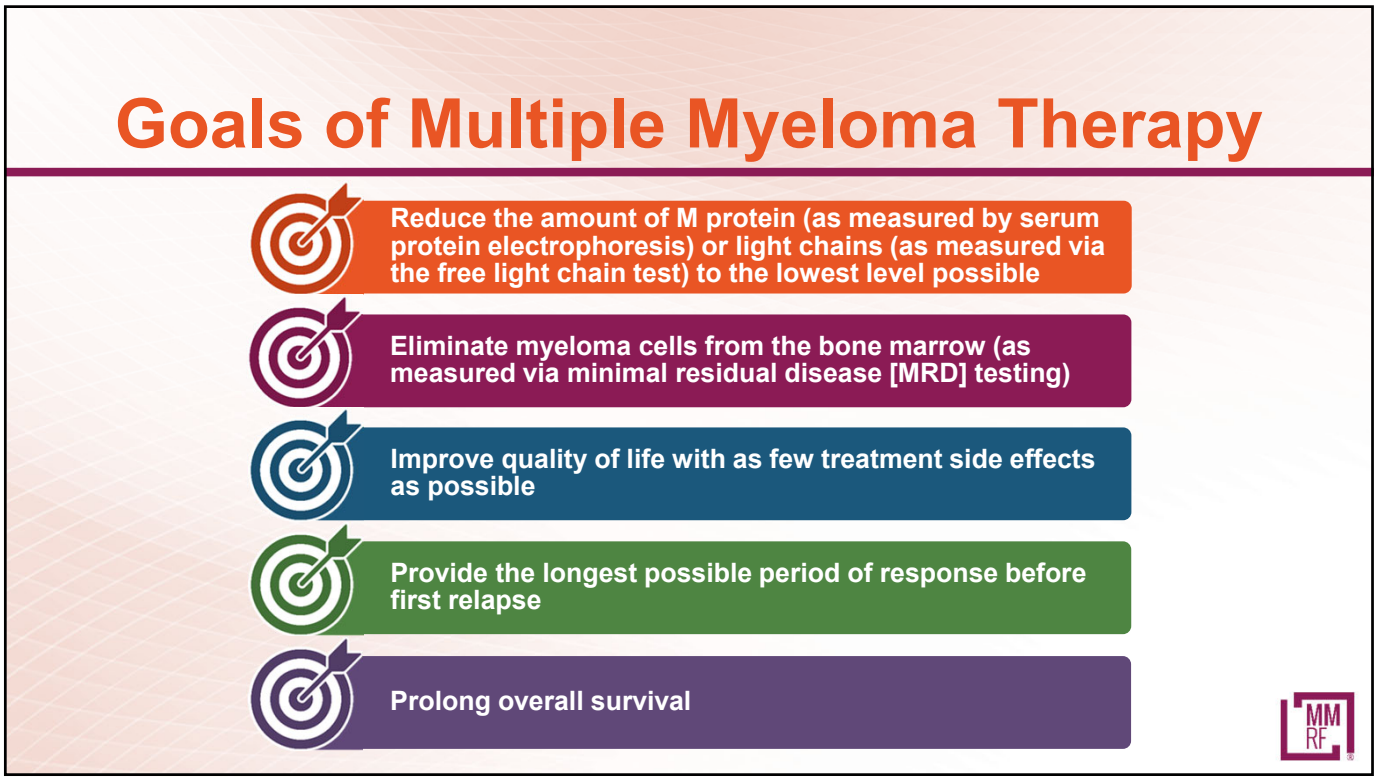
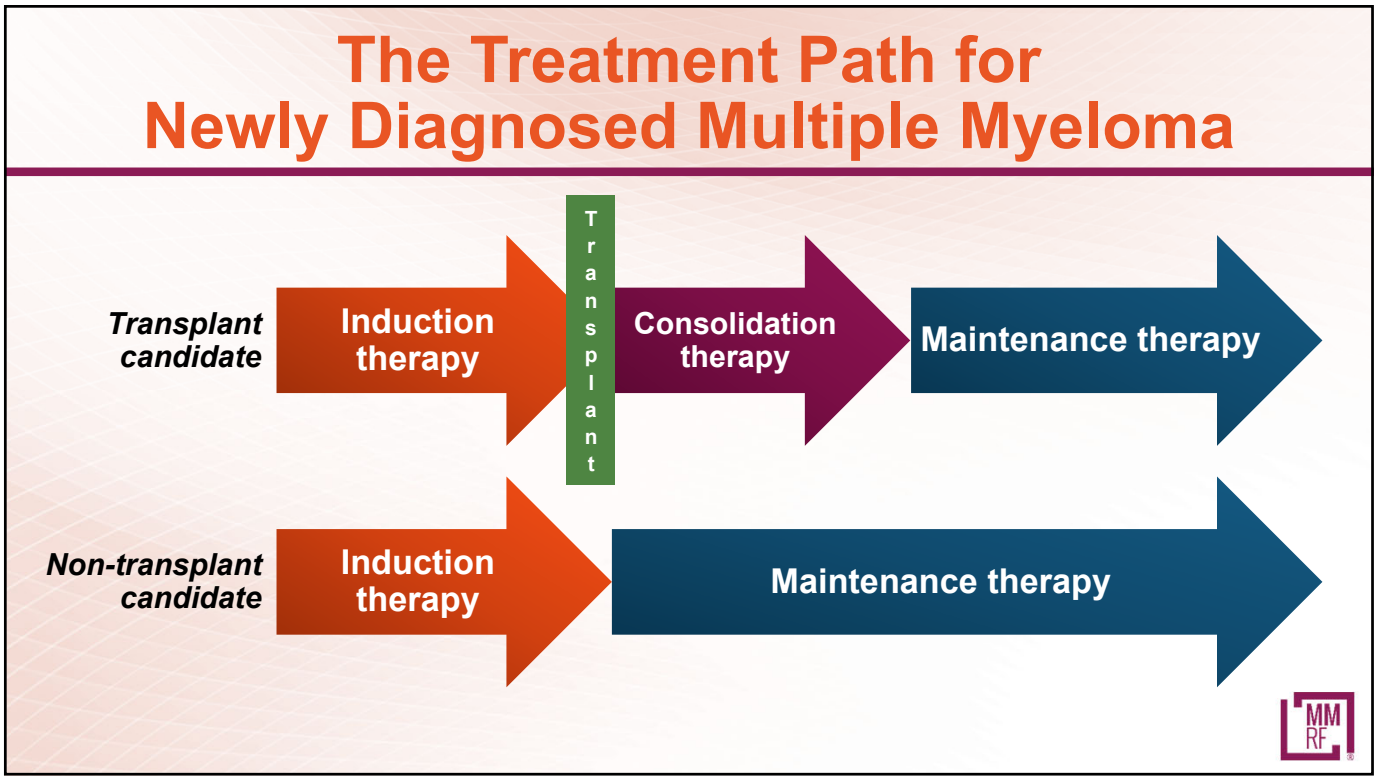
27.4%
33.5%
47.2%
56.9%
Available treatments
Since 2015…
31 drugs approved by the FDA, with 15 new agents!
Chemotherapy + dexamethasone + stem cell transplantation
Kyprolis (carfilzomib)
Pomalyst (pomalidomide)
zomib)
uzumab)
tumumab)
inexor)
uximab)
ab mafodotin)
Abecma (idecabtagene vicleucel)
Carvykti (ciltacabtagene autoleucel)
1975
1985
1995
2005
2013
2014 and beyond

30

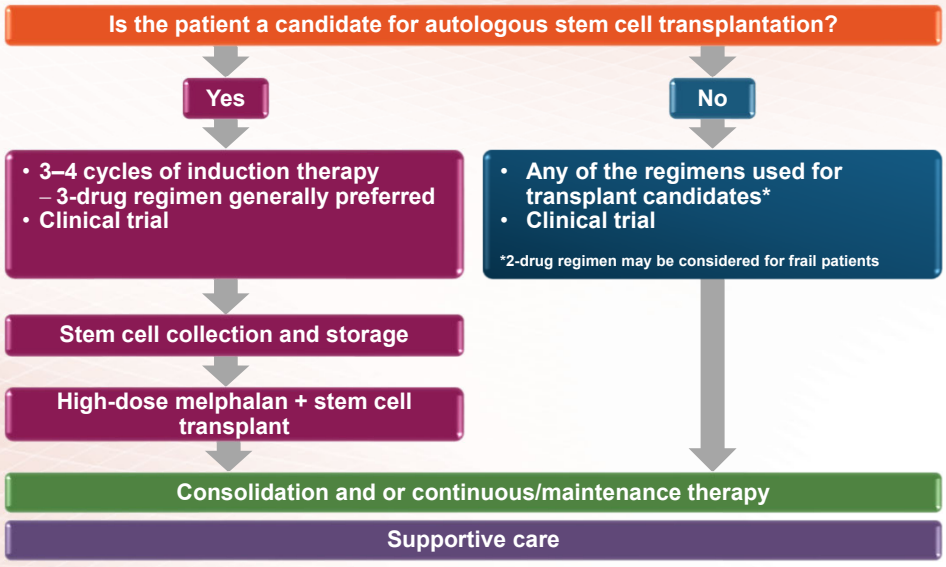

Goals of Multiple Myeloma Therapy
Reduce the amount of M protein (as measured by serum protein electrophoresis) or light chains (as measured via the free light chain test) to the lowest level possible
Eliminate myeloma cells from the bone marrow (as measured via minimal residual disease [MRD] testing)
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
MM RF

31


The Treatment Path for Newly Diagnosed Multiple Myeloma
Transplant candidate
Induction therapy
Transplant
Consolidation therapy
Maintenance therapy
Non-transplant candidate
Induction therapy
Maintenance therapy
MM RF

32

Overview of Treatment Approach for Active Multiple Myeloma



33

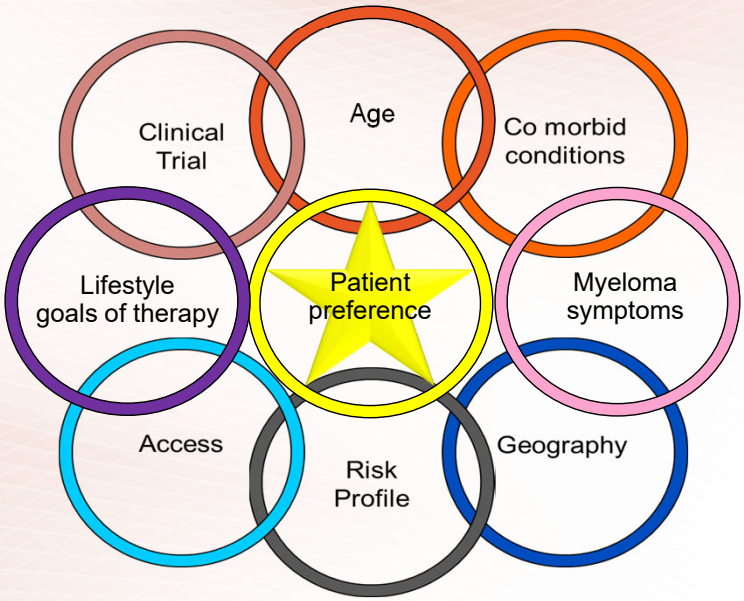
Induction Therapy Regimens

	Preferred	Recommended	Certain circumstances
Transplant eligible	• **Revlimid-Velcade-dex (RVd)***	• Kyprolis-Revlimid-dex (KRd) • Ninlaro-Revlimid-dex (IRd) • Darzalex-Revlimid-Velcade-dex (D-RVd)	• Velcade-Cytoxan-dex (VCd) • Kyprolis-Cytoxan-dex (KCd) • Ninlaro-Cytoxan-dex (ICd) • Revlimid-Cytoxan-dex (RCd) • Velcade-Thalomid-dex (VTd)* • Velcade-Doxil-dex (VDd) • Darzalex-Velcade-Revlimid-dex (D-VRd) • Darzalex-Kyprolis-Revlimid-dex (D-KRd) • Darzalex-Cytoxan-Velcade-dex (D-VCd) • Darzalex-Velcade-Thalomid-dex (D-VTd) • VTD-PACE
Transplant ineligible	• **Revlimid-Velcade-dex (RVd)*** • Darzalex-Revlimid-dex (DRd)*	• Kyprolis-Revlimid-dex (KRd) • Ninlaro-Revlimid-dex (IRd) • Darzalex-Velcade-melphalan-prednisone (D-VMP)* • Darzalex-Cytoxan-Velcade-dex (D-VCd)	• 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 upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
National Comprehensive Cancer Network Guidelines Version 1.2022. Multiple Myeloma.

34

Which is the right therapy for YOU?



35

Main Body Systems Affected by Myeloma Treatment

Blood

- Myeloma patients are at increased risk of developing blood clots
- Several myeloma drugs are associated with an increased risk of deep vein thrombosis (DVT)

CNS

- Peripheral neuropathy is a condition that affects the nerves, resulting in pain, tingling, burning sensations, and numbness in the hands and feet
- Peripheral neuropathy may be caused by multiple myeloma or its treatments

Cardio-vascular

- Cardiovascular side effects (including high blood pressure or congestive heart failure) can occur with some multiple myeloma drugs

Gastro-intestinal

- Commonly used multiple myeloma drugs may cause a variety of gastrointestinal problems, such as constipation, diarrhea, and nausea/vomiting

36

Side Effects of Steroids (dexamethasone)

Insomnia

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

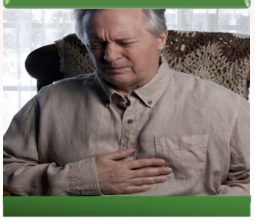
Fluid retention

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

Mood changes

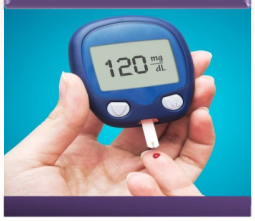
- Irritable, anxiety, difficulty concentrating
- Severe cases → depression, euphoria

Dyspepsia–heartburn



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

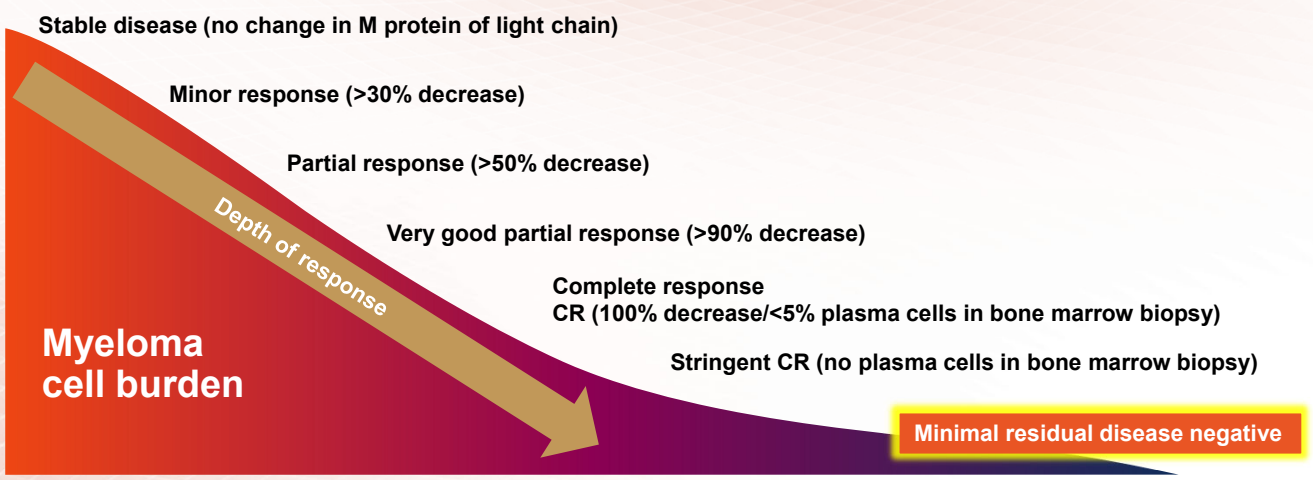
Elevation in glucose



- Monitor glucose and refer/treat as needed

37

Measuring Response to Therapy

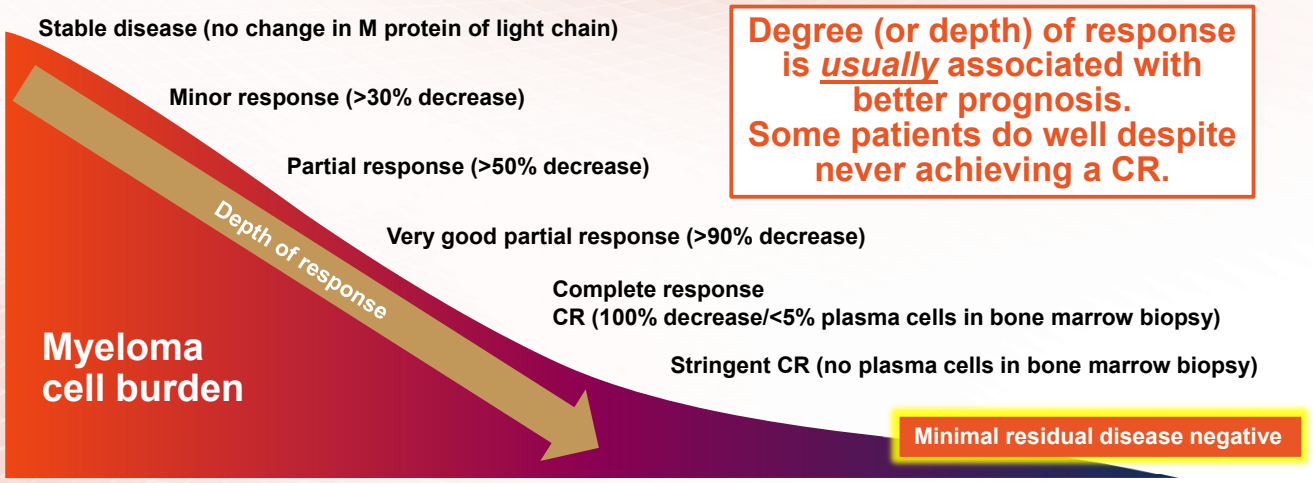


ClonoSEQ is an FDA-approved next-generation sequencing (NGS) test to measure MRD in MM patients

Palumbo A et al. *J Clin Oncol.* 2014;32:587.
Kumar S et al. *Lancet Oncol.* 2016;17:e328.

38

Measuring Response to Therapy



Degree (or depth) of response is *usually* associated with better prognosis. Some patients do well despite never achieving a CR.

ClonoSEQ is an FDA-approved next-generation sequencing (NGS) test to measure MRD in MM patients

Palumbo A et al. *J Clin Oncol*. 2014;32:587.
Kumar S et al. *Lancet Oncol*. 2016;17:e328.

39

What is minimal residual disease (MRD)?

The presence of small amounts of myeloma cells left in the bone marrow following the achievement of a CR after treatment

MRD tests can detect at least 1 cell in 100,000 or better.
Ideally, we want to use more sensitive assays that can find 1 cell in a million.

40

Key Terms for MRD

MRD positive or MRD positivity (MRD+)

- Myeloma cells are still detectable*

MRD negative or MRD negativity (MRD-)

- Myeloma cells are not detected*

*Level of sensitivity can be different depending on methodology used: next-generation sequencing (NGS) or next-generation flow cytometry (NGF).

Patients who achieve MRD negativity following treatment live longer than those who are MRD positive.

41

Multiple Myeloma Care Among Black Patients

Time to therapy initiation

- Median time to first-line therapy initiation significantly longer in Black patients[1]
- Black patients less likely to initiate first-line therapy for multiple myeloma[1]

Utilization of stem cell transplant

- Significantly lower stem cell transplant utilization in Black patients[1-5]

Treatment outcomes

- Outcomes of Black patients same as White patients in cooperative-group clinical trials[6]
- Response rates and survival of Black and White patients after transplant similar in equal-access system[7]

1. Ailawadhi S et al. *Cancer*. 2018;124:1710; **2.** Ailawadhi S et al. *Cancer Med*. 2017;6:2876; **3.** Fiala M et al. *Cancer*. 2017;123:1590;
4. Ailawadhi S et al. *Cancer*. 2018;124:1710; **5.** Costa LJ et al. *Biol Blood Marrow Transplant*. 2015;21:701; **6.** Ailawadhi S et al. *Blood Cancer J*. 2018;8:67.
7. Verma PS et al. *Am J Hematol*. 2008;83:355.

42

Summary

- Multiple myeloma is a rare blood cancer that can negatively affect the bones, kidneys, and the bone marrow, leading to lowered blood counts.
- Multiple myeloma compromises the immune system; therefore, infection prevention is key.
- Bone marrow biopsies give us key insights into the biology of your myeloma, and the genetic information we obtain from the biopsy can provide prognostic information and help guide the optimal drug choice.
- Survival rates are improving because of new drugs and new combinations of drugs.
- Treatment paradigm will continue to change with the approval of additional novel agents.

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

43

Recent Updates

44

What has changed recently?

- Tecvayli approval granted (October 2022)
- Blenrep approval withdrawn (November 2022)

45

Blenrep Withdrawn From US Market
What happened?

Blenrep was granted accelerated approval in 2020 by the FDA, which required further clinical studies to verify a drug's clinical benefit.

Results from the confirmatory phase 3 DREAMM-3 study comparing Blenrep with Pomalyst-dex in patients with RRMM after at least two prior lines of therapy showed that progression-free survival with Blenrep was not improved versus Pomalyst-dex → withdrawn November 2022*

Patients already enrolled in the Blenrep Risk Evaluation and Mitigation Strategy program have the option to enroll in a compassionate use program to continue to access treatment. Patients currently being treated with Blenrep should consult their health care provider

The DREAMM clinical study program is continuing as a path forward for approval with two ongoing phase 3 studies (DREAMM-7, DREAMM-8) testing Blenrep in combinations in an earlier treatment setting for patients who have tried at least one prior line of therapy. Results are anticipated in the first half of 2023.

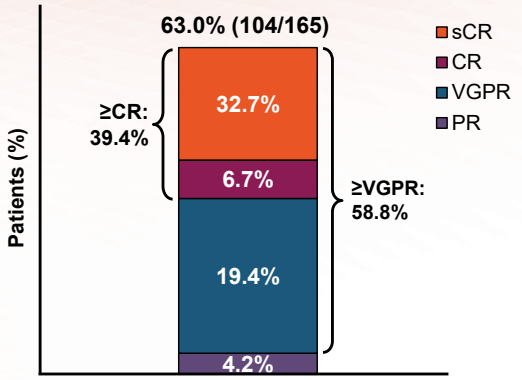
*Marketing of Blenrep continues in other countries where it has been approved.

46

FDA Has Approved the First Bispecific Antibody in Myeloma: Tecvayli!

Drug	Formulation	Approval
Tecvayli (teclistamab)*	Step-up dosing† the first week then once weekly thereafter by subcutaneous injection	For **relapsed/refractory** myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb)

IMiD, immunomodulatory agent; PI, proteasome inhibitor; mAb, monoclonal antibody
*Black box warning: cytokine release syndrome; neurologic toxicities
†Patients are hospitalized for 48 hours after administration of all step-up doses.
Tecvayli is available only through a restricted distribution program.



Median duration of response 18.4 months

Moreau P et al. *N Engl J Med*. 2022;387:495.

47

Tecvayli Side Effects

Side Effects

- Cytokine release syndrome
- Injection-related reactions
- Injection-site reaction
- Infections
- Neutropenia
- Anemia
- Thrombocytopenia
- Neurotoxicity

Side Effect Management

- Available only through a Risk Evaluation and Mitigation Strategies (REMS) due to the risk of cytokine release syndrome
- Patients will receive step-up dosing and will be monitored in an inpatient setting
- Cytokine release syndrome is managed in the same fashion as it is with CAR T therapy
- Injection reactions are managed with oral antihistamines and topical steroids
- Infection prevention!
- COVID precautions

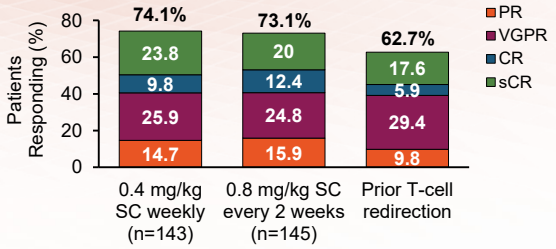
48

Another Bispecific Antibody on the Horizon: Talquetamab

Phase 1/2 study (MonumenTAL-1) in RRMM

288 patients—with no prior T-cell redirecting therapies—received treatment with talquetamab at 2 different doses (0.4 mg/kg every week and 0.8 mg/kg every other week) subcutaneously

Data from this trial was recently used to submit a Biologics License Application to the US Food and Drug Administration for the treatment of patients with relapsed or refractory multiple myeloma.

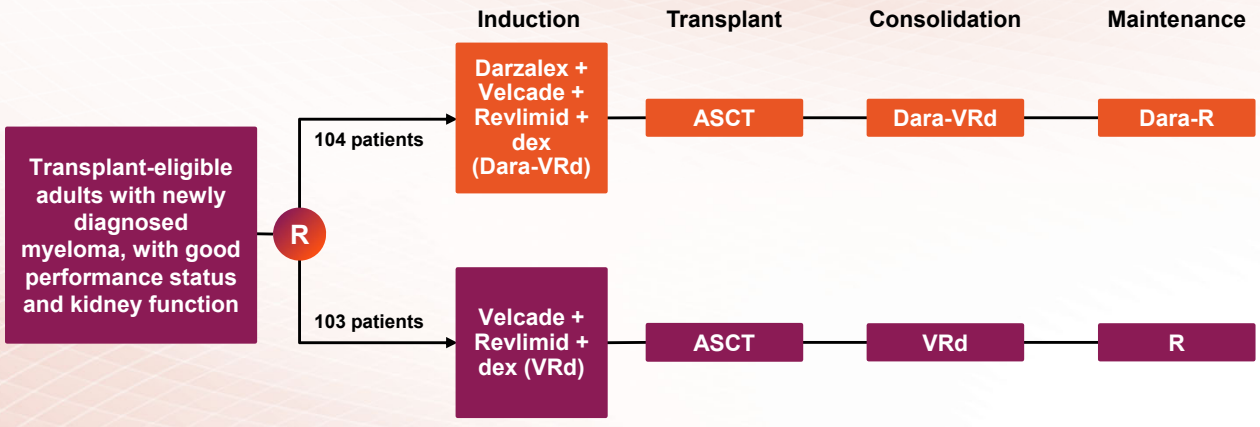


	0.4 mg/kg		0.8 mg/kg	
Most frequent adverse events, %	Any grade	Grade 3/4	Any grade	Grade 3/4
Hematologic				
Anemia	44.8	31.5	39.3	24.8
Neutropenia	34.3	30.8	28.3	22.1
Lymphopenia	28	25.9	26.2	25.5
Thrombocytopenia	27.3	20.3	26.9	16.6
Infections	57.3	16.8	50.3	11.7

IMiD, immunomodulatory drug; PI, proteasome inhibitor
Chari A et al. *Blood*. 2022;140. Abstract 157.

49

GRIFFIN Study: Phase 2 Study of Dara-VRd vs VRd in Transplant-Eligible Newly Diagnosed Multiple Myeloma

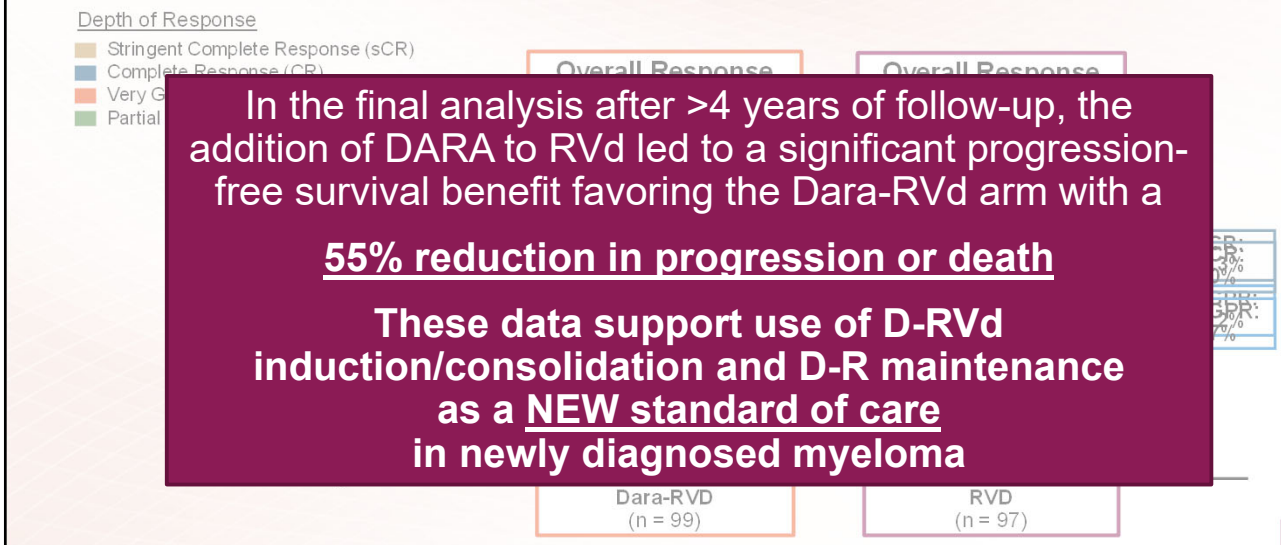


Primary end point: CR by end of consolidation

Dara, daratumumab (Darzalex); ASCT, autologous stem cell transplant
Voorhees PM et al. *Blood*. 2020;136:936.

50

GRIFFIN Randomized Phase II: Dara-RVD vs. RVD in Newly Diagnosed Multiple Myeloma



In the final analysis after >4 years of follow-up, the addition of DARA to RVd led to a significant progression-free survival benefit favoring the Dara-RVd arm with a

55% reduction in progression or death

These data support use of D-RVd induction/consolidation and D-R maintenance as a NEW standard of care in newly diagnosed myeloma

Voorhees PM et al. *Blood*. 2020 Aug 20;136(8):936-945. Sborov et al. IMS Annual Meeting. 2022 Aug 26; Abst# OAB-057

51

Health-Related Quality of Life for Patients With Newly Diagnosed Multiple Myeloma

Transplant-eligible patients[1]

Phase 2 GRIFFIN trial comparing daratumumab, lenalidomide, bortezomib, and dexamethasone (Dara-RVd) with RVd

- Both groups of patients had meaningful reduction in pain symptoms
- Large reductions in pain symptoms favored Dara-RVd (post-consolidation and throughout maintenance)
- Greater reduction in fatigue symptoms at maintenance for patients treated with Dara-RVd than RVd

Frail, transplant-ineligible patients[2]

Phase 3 MAIA trial comparing daratumumab, lenalidomide, and dexamethasone (Dara-Rd) with Rd

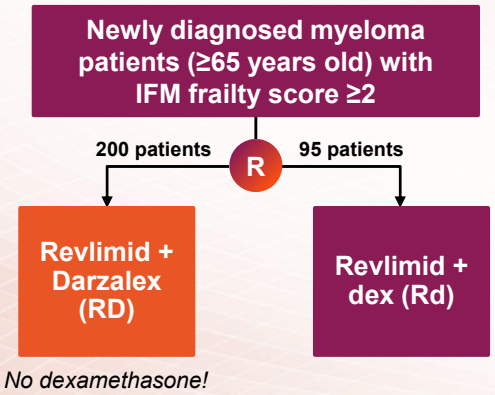
- Patients treated with Dara-Rd showed large reductions in pain from baseline, and pain symptoms improved compared with Rd
- Fatigue moderately improved in both treatment groups, but Dara-Rd did not increase fatigue
- Global health status improvements were consistent over time for patients in both treatment groups
- Emotional and social functioning improvements observed in both groups
- Physical functioning improved from baseline in patients treated with Dara-Rd
- No meaningful changes observed for nausea and vomiting in either group

1. Silbermann R et al. *Blood*. 2022;140. Abstract 473.
2. Perrot A et al. *Blood*. 2022;140. Abstract 472.

52

Dexamethasone-Sparing Regimen for Frail Patients

IFM2017-03 Trial



No dexamethasone!

- Deeper responses observed with RD vs Rd at 4, 8, and 12 months (≥VGPR rates 41% vs 26%; 68% vs 48%; 71% vs 55%, respectively).
- Favorable safety profile without increased infection or pneumonia with RD vs Rd

Encouraging results for a dexamethasone-sparing strategy for frail MM patients.

Manier S et al. *Blood*. 2022;140. Abstract 569.

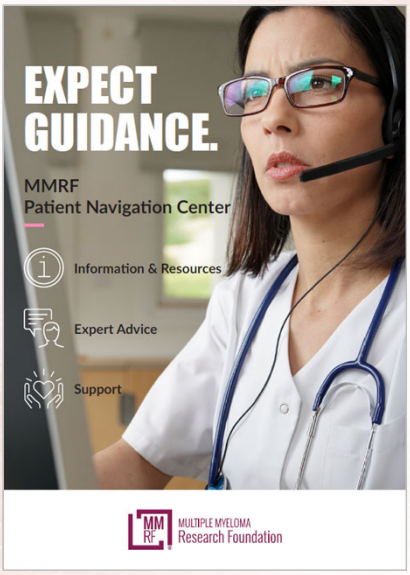
53

Questions & Answers

54

55

MMRF Patient Resources



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 Mensching, 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-MMRF (6673) Online: TheMMRF.org/PatientNavigationCenter
Email: patientnavigator@themmrf.org

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56

Myeloma Mentors®

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.

57

A Cure Is Within Reach

Join the myeloma community from around the world as a member of the MMRF Team for Cures and become an integral part of the team, accelerating a cure for each and every patient! The MMRF is determined to make multiple myeloma curable, and we will stop at nothing to reach that goal.

Find your event today!
theMMRF.org/Events

5K Walk/Run
Taking steps to cure cancer

Join one of 15 MMRF Team for Cures 5K Walk/Runs across the country or from anywhere in the world as a virtual participant! Participation brings the myeloma community together for camaraderie and knowledge sharing in a family-friendly fundraising event.

theMMRF.org/5K

Current Walk/Run Events
South Florida • Scottsdale • San Francisco • Boston • Atlanta Dallas • Southeast Michigan • Connecticut • Charlotte Chicago • Twin Cities • Washington, DC • Philadelphia New York City • Los Angeles

Marathons & Half-Marathons
Crossing a finish line for a cure

Since 2007, over 2,700 athletes have raised more than $13.6 million to accelerate a cure for multiple myeloma. We offer entry to some of the top marathons and half marathons in the world, including five of the six Abbott World Marathon Majors.

theMMRF.org/Marathon

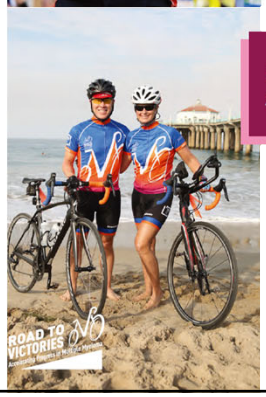
Current Marathons and Half-Marathons
United Airlines NYC Half Marathon • Boston Marathon
BMW Berlin Marathon • Virgin Money London Marathon
Bank of America Chicago Marathon • TCS New York City Marathon

Moving Mountains for Multiple Myeloma
Reach new heights, accelerate cures

Myeloma patients, doctors, nurses, and other caregivers have been taking on epic peaks across the globe for this program since 2016. Each trek emphasizes the collaboration necessary to drive toward cures and the incredible feats that can be accomplished when the myeloma community comes together to raise critical funds.

theMMRF.org/Hike

Current and Past Treks
Mount Kilimanjaro • Grand Canyon • Machu Picchu
Mount Fuji • Everest Base Camp • Mount Washington
Sweden • Colorado • Greenland • Patagonia • Iceland



Road to Victories
Achieving victories over cancer

These inspirational cross-country rides take cyclists on epic journeys on multiple continents, all to raise critical funds to fight myeloma. Patients, caregivers, doctors, and pharma partners have conquered over 3,400 miles and counting for this incredible cycling program.

RoadtoVictories.com

Current and Past Rides
Vermont to Quebec • London to Paris • Glacier National Park
Bryce Canyon and Zion National Park • The Coast of Maine

58

Upcoming Patient Education Events

Save the Date

Topic	Date and Time (ET)	Speakers
Facebook Live	Wednesday, February 15 3:00 to 4:00 PM ET	Benjamin Derman, MD Sarah Major, PA-C, MMS, MPH Julia Grosch
Webinar (rebroadcast): *Focus on Treatments, Monitoring, and Maintenance for Newly Diagnosed Multiple Myeloma Patients*	Friday, February 17 12:00 to 1:00 PM ET	Suzanne Lentzsch, MD, PhD Cesar Rodriguez, MD
Webinar (rebroadcast): *Management of Patients Who Have Relapsed After One to Three Prior Lines of Therapy*	Wednesday, March 8 1:00 to 2:00 PM ET	Larry Anderson, Jr, MD, PhD Faith Davies, MBBCh, MD
Patient Summit Hackensack, NJ	Saturday, March 11 9:00 AM to 2:00 PM ET	David Vesole, MD, PhD

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

59

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REGENERON SCIENCE TO MEDICINE Takeda ONCOLOGY

60

61