New Strategies for Multiple Myeloma Care: Case Studies for Nurses
Part 1: Newly Diagnosed Multiple Myeloma


International Myeloma Foundation
800-452-CURE (2873)
http://myeloma.org

Newly Diagnosed Multiple Myeloma

CASE #1: June*

CASE #2: Lisa*

*HIPAA-compliant; not actual patient names

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HIPAA = Health Insurance Portability and Accountability Act.

NURSE LEADERSHIP BOARD

INTERNATIONAL MYELOMA FOUNDATION

Objectives

- Identify common treatment regimens in newly diagnosed multiple myeloma
- Apply recommendations for infection control among an immunocompromised patient population
- Recognize the importance of survivorship care plans and apply practical tools for long-term management and care of patients with multiple myeloma

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Myeloma Is a Cancer of Plasma Cells

- Cancer of plasma cells
- Healthy plasma cells produce immunoglobulins: G, A, M, D, and E
- Myeloma cells produce abnormal immunoglobulin (paraprotein) continually

BONE MARROW OF PATIENT WITH MM

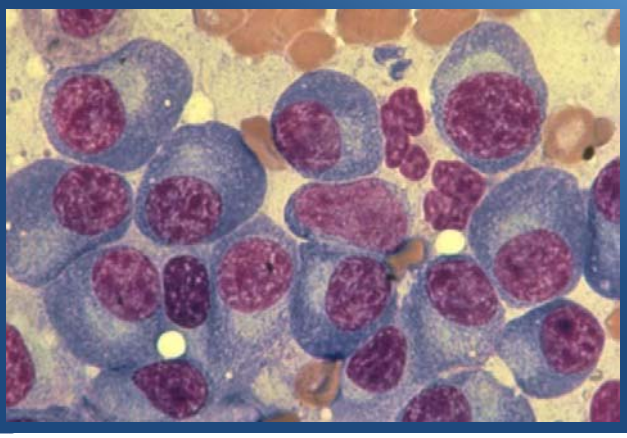
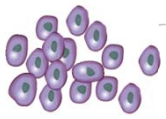


Image: American Society of Hematology

MM = multiple myeloma.
Kyle RA, et al. *Mayo Clin Proc.* 2003;78:21-33.

3

Myeloma Cells Produce Myeloma Protein Continually: Detectable in Plasma and Urine

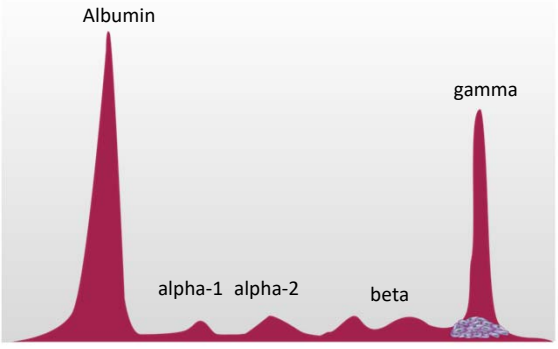


Myeloma cells produce abnormal immunoglobulins continually (nonsecretory disease is rare)

Light chain
- Kappa
- Lambda

Heavy chain
- IgG
- IgA
- IgM
- IgD
- IgE

Myeloma



Ig = immunoglobulin.
Understanding Your Test Results, International Myeloma Foundation 2018.

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CASE #1:

June*

- 76-year-old woman
- Anemia and elevated serum creatinine (1.2gm/dL) on routine annual exam
- Nephrology workup: monoclonal proteinuria, M spike (M-protein) detected
- Referred to heme/onc

*HIPAA-compliant, stock photo (not actual patient).

heme/onc = hematologist/oncologist; HIPAA = Health Insurance Portability and Accountability Act; M-protein = monoclonal protein; M spike = monoclonal spike.

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How Myeloma Patients Commonly Present

Routine Physical ← June

- Patient with few/no symptoms
- Abnormal blood work

Visit for Specific Complaint

- Persistent symptom or injury
- Abnormal test result (eg, x-ray)

Non-emergency; More time for shared decision-making

Emergency Room

- Severe pain—often spinal fractures
- Renal failure

Medical emergencies need immediate treatment!

Brigle K, et al. *Clin J Oncol Nurs*. 2017;21(5 suppl):60-76. Faiman B, et al. *J Adv Pract Oncol*. 2016;2016:7(suppl 1):17-29. Kurtin S, et al. *J Adv Pract Oncol*. 2016;7(suppl 1):59-70.

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CASE #1:

June*

DIFFERENTIAL DIAGNOSIS

- ✓ Multiple myeloma
- ✓ Smoldering multiple myeloma
- ✓ Monoclonal gammopathies of undetermined significance (MGUS)
- ✓ Plasmacytoma
- ✓ Waldenström macroglobulinemia
- ✓ AL amyloidosis
- ✓ Plasma cell leukemia
- ✓ Malignant bone disease
- ✓ POEMS

*HIPAA-compliant, stock photo (not actual patient).

AL = amyloid light chain; HIPAA = Health Insurance Portability and Accountability Act; POEMS = polyneuropathy, organomegaly, endocrinopathy/edema, monoclonal protein, skin changes.

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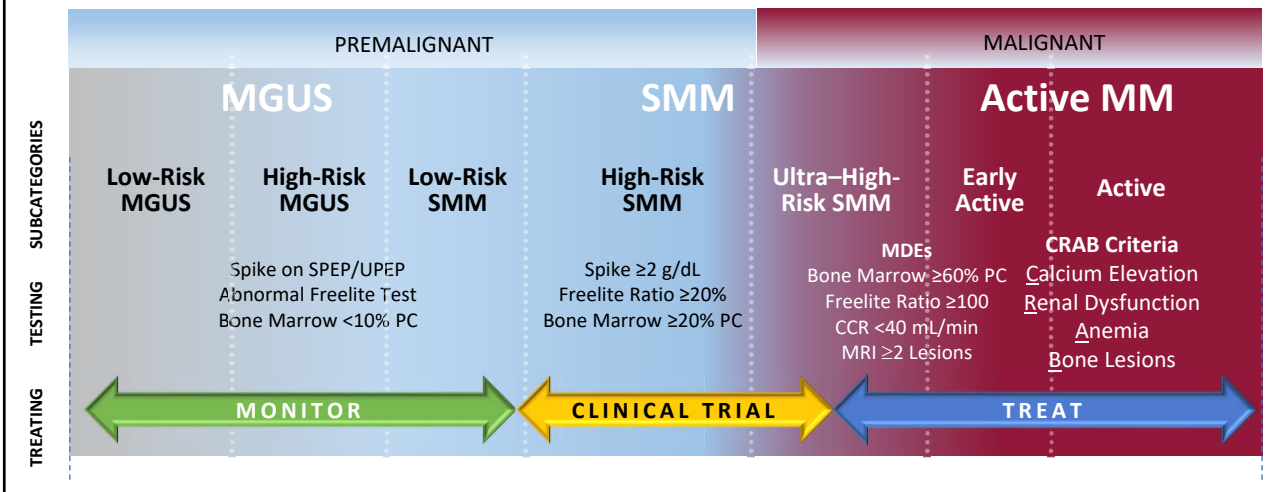
Myeloma Continuum, Testing, and Treatment



CCR = creatinine clearance rate; MDE = myeloma-defining event; MGUS = monoclonal gammopathy of undetermined significance; MM = multiple myeloma; MRI = magnetic resonance imaging; PC = plasma clone; SMM = smoldering multiple myeloma; SPEP = serum protein electrophoresis; UPEP = urine protein electrophoresis.

Adapted from Lakshman A, et al. *Blood Cancer J.* 2018;8(6):59. Rajkumar SV, et al. *Lancet Oncol.* 2014;15:e538-e548. Kyle RA, et al. *Leukemia.* 2010; 24(6):1121-1127. Dr Brian Durie.

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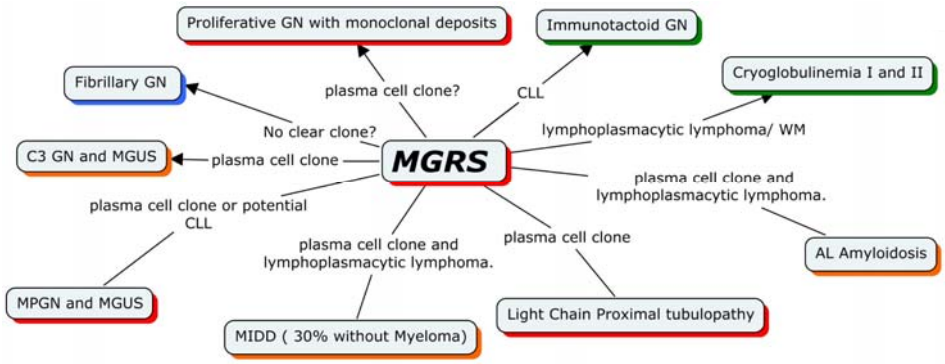
Newly Recognized Phenomenon: MGRS (Monoclonal Gammopathy of Renal Significance)

- Do NOT meet criteria for myeloma
- Have a clone only detected in the kidney; treated much like myeloma
- Kidney biopsy (target organ bx) is gold standard for diagnosis



AL = amyloid light chain; bx = biopsy; CLL = chronic lymphocytic leukemia; GN = glomerulonephritis; MGRS = monoclonal gammopathy of renal significance; MGUS = monoclonal gammopathy of undetermined significance; MIDD = monoclonal immunoglobulin deposition disease; MPGN = membranoproliferative glomerulonephritis; WM, Waldenström macroglobulinemia.

Bridoux F, et al. *Kidney Int.* 2015;87(4):698-711.

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Diagnostic Workup for Multiple Myeloma

LAB TESTS

- Serum protein electrophoresis (SPEP)
- Urine protein electrophoresis (UPEP)
- CBC + differential + chemistry including albumin and β2 microglobulin and LDH
- FLC ratio of free kappa/lambda light chains (plasma)
- Monoclonal protein analysis (MPA)

BONE MARROW BIOPSY

- FISH
- Cytogenetics
- Clonal plasma cell percentage

IMAGING (SEE NEXT SLIDE)

FISH detects abnormalities in multiple myeloma cells by using fluorescent probes

CBC = complete blood count; FISH = fluorescence in situ hybridization; FLC = free light chain; LDH = lactate dehydrogenase.

Ghobrial IM, et al. *Blood*. 2014;124:3380-3388. Rajkumar SV, et al. *Lancet Oncol*. 2014;15:e538-3548. Faiman B. *Clin Lymphoma Myeloma Leuk*. 2014;14:436-440.

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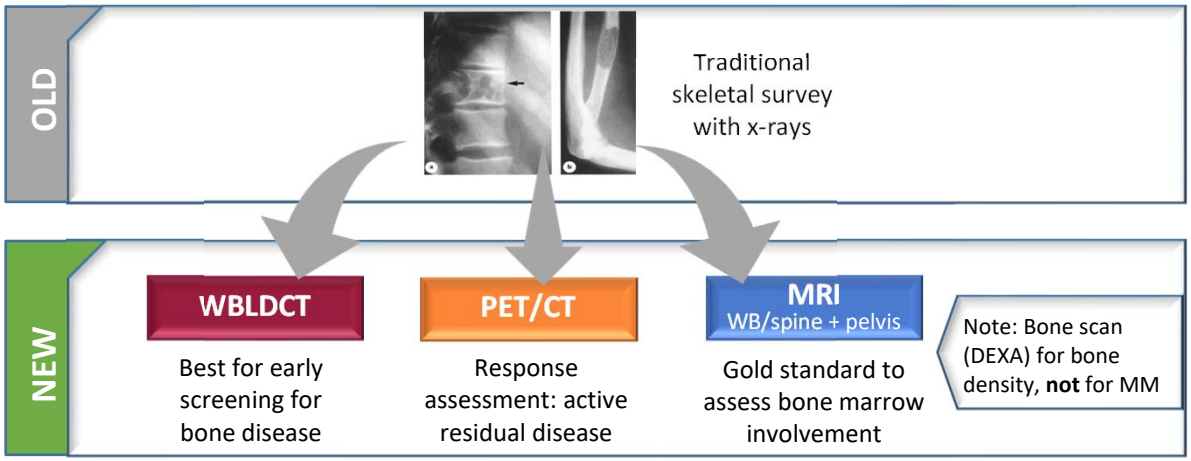
Recommended Imaging for Multiple Myeloma



CT = computed tomography; DEXA = dual-energy x-ray absorptiometry; MM = multiple myeloma; MRI = magnetic resonance imaging; PET = positron emission tomography; WB = whole body; WBLDCT = whole-body low-dose computed tomography.

Hillengass J, et al. *Lancet Oncol*. 2019;20(6):e302-e312. Rome SI, et al. *Clin J Oncol Nurs*. 2017;21(5 suppl):47-59. Faiman B. *Clin Lymphoma Myeloma Leuk*. 2014;14:436-440. Dimopoulous M, et al. *Leukemia*. 2009;23(9):1545-1556.

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Revised-ISS (R-ISS) Staging System for MM

Stage	R-ISS	5-Year OS	5-Year PFS
I	• ISS stage I (serum β_2 microglobulin level <3.5 and serum albumin ≥3.5 g/dL) • No high-risk CA [del(17p) and/or t(4;14) and/or t(14;16)] • Serum LDH < ULN (varied by institution)	82%	55%
II	• Not R-ISS stage I or III	62%	36%
III	• ISS stage III (serum β_2 microglobulin level >5.5 mg/L) • High-risk CA [del(17p) and/or t(14;4) and/or t(14;16)] or high serum LDH	40%	24%

BETTER
SURVIVAL
WORSE

CA = chromosomal abnormality; ISS = International Staging System; LDH = lactate dehydrogenase; OS = overall survival; PFS = progression-free survival; ULN = upper limit of normal.

Palumbo A, et al. *J Clin Oncol*. 2015;33:2863-2869.

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CASE #1:

June*

MYELOMA WORKUP

- Peripheral blood:
  - Calcium: 10.2 mg/dL (ULN: 10.6 mg/dL)
  - Albumin: 3.3 mMol/L (LLN: 3.5 mMol/L)
  - B2M: 5.3 mg/dL (ULN: 2.64 mg/dL)
  - LDH: 150 U/mL (ULN: 250 U/mL)
  - Creatinine: 1.2 mg/dL (ULN: 1.3 mg/dL)
    - GFR (calculated): 24 mL/min/1.73 m^2
  - Hgb: 10.8 g/dL
  - κFs: 1832.0 g/dL (normal range: 3.3-19.4 g/dL)
  - κ/λ-light-chain ratio: 122 (ULN: 1.65)
  - Urine M spike: 2.72 g/24 h

*HIPAA-compliant, stock photo (not actual patient).

WHOLE-BODY LOW-DOSE CT: Lytic lesions; arms, ribs, skull, femur

B2M = beta-2 microglobulin; CT = computed tomography; GFR = glomerular filtration rate; Hgb = hemoglobin; HIPAA = Health Insurance Portability and Accountability Act; κ/λ = kappa to lambda; κFs = kappa free serum; LDH = lactate dehydrogenase; LLN = lower limit of normal; M spike = monoclonal spike; ULN = upper limit of normal.

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Nurse's Role Is Crucial to Myeloma Patients

INFORM PATIENTS	• Educate patients and caregivers • Disease, what to watch for, protecting health
EMPOWER PATIENTS	• Encourage questions from patients and caregivers • Encourage communication with medical team • Coach patient how to participate in decision-making
ADVOCATE FOR PATIENTS	• Identify services (eg, financial counseling, financial programs, support groups) • Speak up on behalf of the patient • Ensure medical team is aware of patient concerns/priorities

Gerber L. *Nursing*. 2018;48(4):55-58.

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Steep Learning Curve for Patients Newly Diagnosed With MM

- Patient education is crucial but can be overwhelming
- Shock of diagnosis makes understanding and retaining information difficult
  - Tell patients information, but also give written information they can read later
  - Refer patients to reliable sources of information

https://www.cancer.gov

https://www.cancer.org

IMF Website http://myeloma.org

Free download or order from myeloma.org

IMF TV Teleconferences

Multiple languages

Leukemia & Lymphoma Society
https://www.lls.org

IMF = International Myeloma Foundation; MM = multiple myeloma.

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Relevant Education for Patients With Multiple Myeloma: COVID-19—Advise Precautions

High risk for severe illness from COVID-19:
- Aged ≥65 years
- Living in a nursing home

Underlying medical conditions can increase COVID-19 risk:
- Immunocompromised
- Chronic lung disease
- Severe obesity (BMI ≥40)
- Diabetes
- Chronic kidney disease undergoing dialysis
- Liver disease

Reduce risk of COVID-19 Infection
- Stay home when possible
- Wash hands often
- Maintain 6-foot social distance
- Avoid close contact with others, particularly those who are sick; telemedicine option
- Wear a cloth face cover when around others
- Clean and disinfect frequently touched surfaces
- Avoid travel (cruises, airplanes)
- Get flu and pneumococcal vaccination

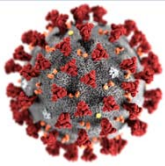

Image: CDC

Have 2+ week supply of medications

Discuss any concerns with your HCP

Call 911 for emergency help

BMI = body mass index; CDC = Centers for Disease Control; COVID-19 = coronavirus 2019; HCP = health care provider.
CDC. Coronavirus disease 2019. URL. Accessed May 1, 2020.

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Additional, Important Education for Newly Diagnosed Patients

INFECTION PREVENTION

- Consider levofloxacin 500 mg once daily for 12 weeks
- Growth factor (eg, filgrastim)
- IVIG for hypogammaglobulinemia
- Immunizations (NO live vaccines)
  - Pneumococcal vaccination (13 and 23)
  - Seasonal inactivated influenza vaccine ×2
  - Shingles vaccine: zoster vaccine recombinant, adjuvanted

RENAL HEALTH

Risks:

- Active MM (M-protein, casts)
- High calcium

Prevention:

- Avoid certain medications (contrast dyes, NSAIDS)
- Hydration

Treatment:

- Address underlying myeloma causing renal disfunction
- Dose adjustments for renal

BONE HEALTH

- Hypercalcemia from bone destruction can affect kidneys
- ≈85% of patients with multiple myeloma develop bone disease

Monitor:

- New or worsening bone pain, serum calcium levels (especially denosumab)

Imaging:

- Depends on type of pain

Bone-modifying agents

- Pamidronate, zoledronic acid
- Denosumab

IVIG = intravenous immunoglobulin; M-protein = monoclonal protein; MM = multiple myeloma; NSAID = nonsteroidal anti-inflammatory drug.

Hillengass J, et al. *Lancet Oncol.* 2019;20(6):e302-e312. Faiman B, et al. *Clin J Oncol Nurs.* 2017;21(5 suppl):19-36. Faiman B, et al. *Clin J Oncol Nurs.* 2011;15(suppl):66-76. Miceli TS, et al. *Clin J Oncol Nurs.* 2011;15(4):9-23. Rome SJ, et al. *Clin J Oncol Nurs.* 2017;21(5 suppl):47-59. Miceli TS, et al. *Clin J Oncol Nurs.* 2011;15(4)suppl:9-23. Dimopoulous M, et al. *Leukemia.* 2009;23(9):1545-1556. Brigle K, et al. *Clin J Oncol Nurs.* 2017;21(5)suppl:60-76. Faiman B, et al; IMF Nurse Leadership Board. *Clin J Oncol Nurs.* 2011;15(suppl):66-76. Miceli TS, et al. *Clin J Oncol Nurs.* 2011;15(4):9-23.

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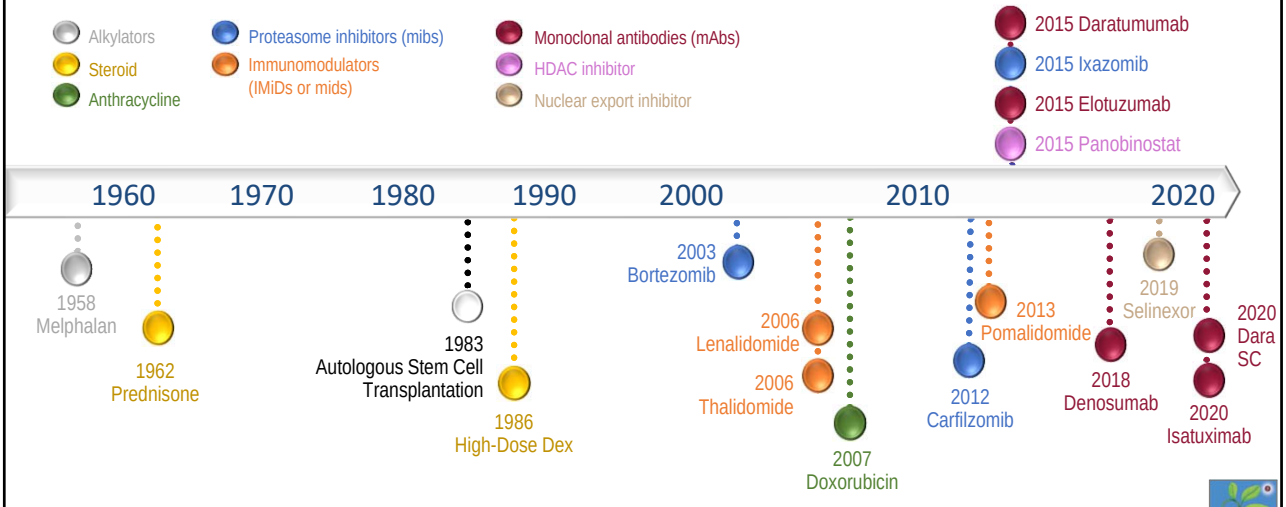
Expanding Treatment Options for Multiple Myeloma



Auto = autologous; Dara = daratumumab; Dex = dexamethasone; HDAC = histone deacetylase; SC = subcutaneous.

Tariman J. *Nurs Clin North Am.* 2017;52(1):65-81. DRUGS@FDA.gov.

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Myeloma Common Frontline Regimens

NEWLY DIAGNOSED MM

PRIMARY TREATMENT†

Common Regimens for Transplant Candidate

- VRd*: bortezomib lenalidomide dex
- VCd: bortezomib cyclophosphamide dex
- KRd: carfilzomib lenalidomide dex
- IRd: ixazomib lenalidomide dex
- Dara-Rd: daratumumab lenalidomide dex
- Dara-Td: daratumumab thalidomide dex
- Dara-VRd: daratumumab bortezomib lenalidomide dex

Common Regimens for Non-Transplant Candidate

- VRd*: bortezomib lenalidomide dex
- Dara-Rd*: daratumumab lenalidomide dex
- Rd*: lenalidomide low-dose dex
- VCd: bortezomib cyclophosphamide dex
- KRd: carfilzomib lenalidomide dex
- Id: ixazomib dex
- Dara-VMP: daratumumab melphalan prednisone

MAINTENANCE†

- Lenalidomide*
- Ixazomib*
- Lenalidomide + proteasome inhibitors (for high risk)

- Lenalidomide*
- Ixazomib
- Lenalidomide + proteasome inhibitors (for high risk)

dex = dexamethasone; MM = multiple myeloma; NCCN = National Comprehensive Cancer Network.
*NCCN Category 1. †Clinical trial participation is recommended.

Faiman B, et al. *J Adv Pract Oncol.* 2016:7(suppl 1):17-29. Mikhael J. https://www.medscape.com/viewarticle/882042. Accessed May1, 2020. Rajkumar SV. How I treat. 2020. https://twitter.com/vincentrk/status/1203058085776035840. Accessed May 1, 2020. NCCN Guidelines. Multiple Myeloma. V3.2020. Accessed May 1, 2020.

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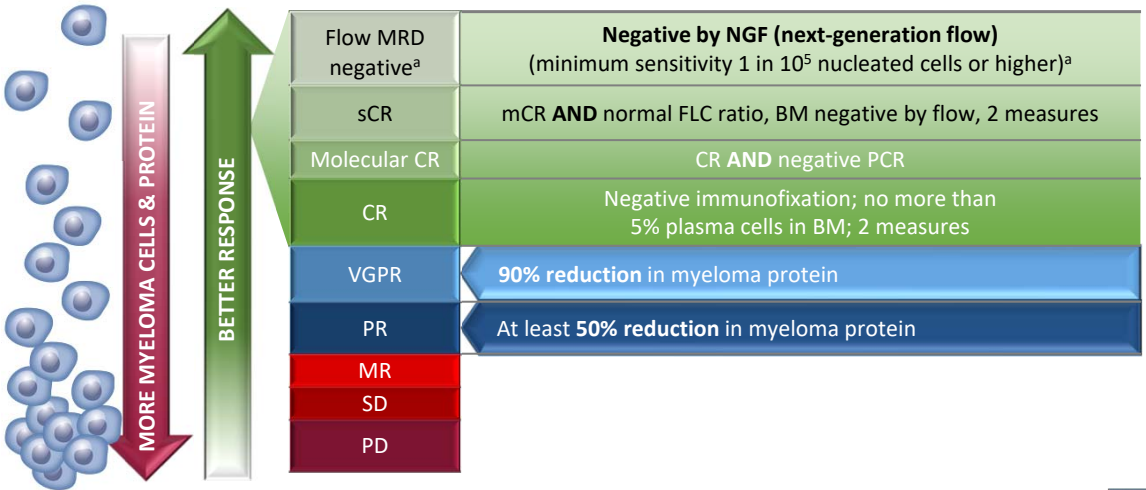
Patients Want to Know Whether Treatment Is Working: IMWG Myeloma Response Criteria



BM = bone marrow; CR = complete response; FLC = free light chain; IMWG = International Myeloma Working Group; mCR = molecular CR; MR = minimal response (only in relapsed); MRD = minimal residual disease; NGS = next-generation sequencing; PD = progressive disease; PR = partial response; sCR= stringent complete response; SD = stable disease; VGPR = very good partial response.
[a]IMWG minimal residual disease consensus criteria published August 2016.

Palumbo A, et al; International Myeloma Working Group. *J Clin Oncol.* 2014;32:587-600. Durie BM, et al; International Myeloma Working Group. *Leukemia.* 2006;20(9):14671473. Kumar S, et al. *Lancet Oncol.* 2016;17(8):e328-e346.

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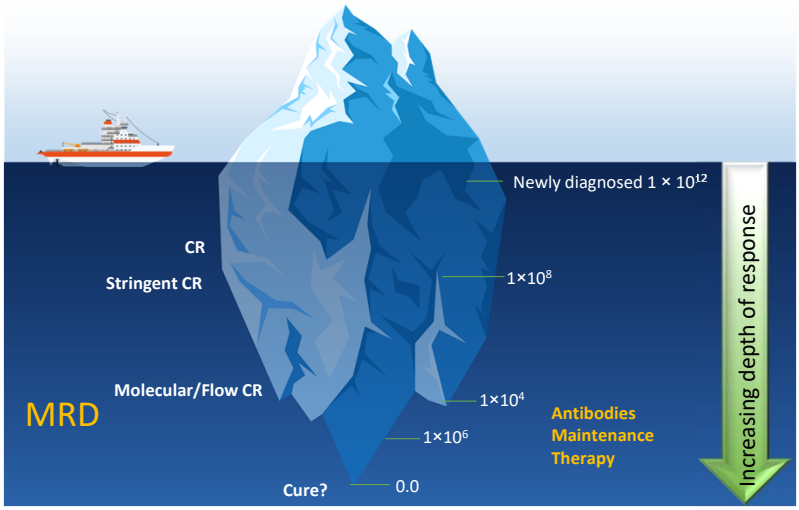
Getting to Minimal Residual Disease (MRD): New Definitions Deeper Than CR



Key concept:
Deeper responses
(less residual disease)
generally means better patient outcomes

MANY ways to get to deeper responses:

- Multi-drug regimens
- ASCT
- Longer therapy duration (eg, continuous regimens or maintenance)

ASCT = autologous stem cell transplant; CR = complete response.
Kumar S, et al. *Lancet Oncol.* 2016;17(8):e328-e346.

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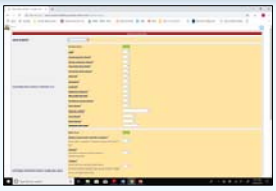
Frailty Score Can Predict Survival and Rate of Treatment Discontinuation



Online myeloma frailty score calculator at **http:/www.myelomafrailtyscorecalculator.net/**

Fit = 0, intermediate = 1, frail = 3

Calculator takes into account age, comorbidity, and ability to manage daily activity

Score	Percentage	3-Year Survival (%)	Treatment Discontinuation (%)
0	39	84	17
1	31	76	22
≥2	31	57	25

Palumbo A, et al. *Blood.* 2015;125(13):2068-2074. International Myeloma Working Group. Myeloma Frailty Score Calculator. http:/www.myelomafrailtyscorecalculator.net/. Accessed June 30, 2020.

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RVd Lite Regimen: Reduced Intensity Regimen for Transplant-Ineligible Patients

RVd Lite Phase 2 Study

- Transplant ineligible: N=53
- Median age: 72 years (range, 65-91)
- Grade 3 toxicities:
  - 34% Hypophosphatemia
  - 24% Neutropenia
  - 10% Rash
- ORR: 86%
- PFS: 41.9
- 5-year OS: 61.3

Conclusions: well-tolerated and highly effective regimen for transplant-ineligible population

Induction (cycles 1-9)
Repeat q35 days ×9 cycles

Lenalidomide 15 mg PO days 1-21

Bortezomib 1.3 mg/m^2 SC days 1, 8, 15, 22

Dexamethasone 20 mg PO days 1, 2, 7, 8, 15, 16, 22, 23 (patients aged ≤75 years)

Consolidation (cycles 10-15)
Repeat q35 days ×9 cycles

Lenalidomide 15 mg PO days 1-21 (or last tolerated dose as of cycle 9)

Bortezomib 1.3 mg/m^2 SC days 1, 15, 22 (or last tolerated dose as of cycle 9)

ORR = overall response rate; OS = overall survival; PFS = progression-free survival; PO = by mouth; q = every; RVd = lenalidomide bortezomib dexamethasone; SC = subcutaneous.

O'Donnell EK, et al. *Blood.* 2019;134(suppl 1):3178. O'Donnell EK, et al. *Br J Haematol.* 2018;182(2):222-230.

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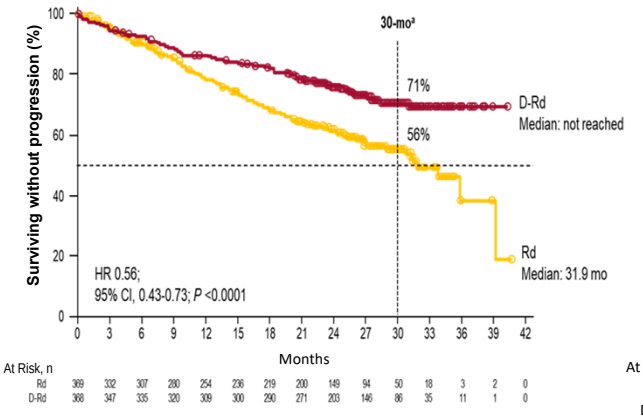
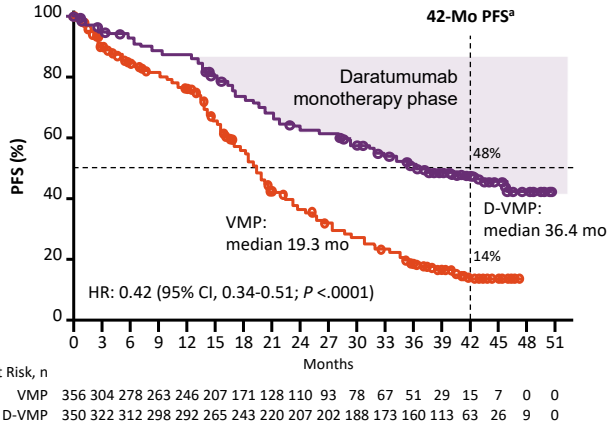
Daratumumab-Based Regimens for Patients With MM Who Are Transplant Ineligible

MAIA Phase 3



ALCYONE Phase 3



D = daratumumab; HR = hazard ratio; MM = multiple myeloma; PFS = progression-free survival; Rd = lenalidomide dexamethasone; VMP = bortezomib melphalan dexamethasone.

[a]Kaplan-Meier estimate.

Facon T, et al. ASH 2018. Abstr #LBA-2. Mateos MV, et al. ASH 2019. Abstr #859.

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CASE #1:

June*

TREATMENT DECISION

- Continuous therapy: RVd lite

SURVIVORSHIP CARE PLAN

- Diagnosis and test results
- Treatment received
- Follow-up plan
- Coordination with PCP
- Long-term health maintenance

*HIPAA-compliant, stock photo (not actual patient).

Remember:
- Shingles prevention
- DVT prophylaxis
- Monitor sugars

DVT = deep vein thrombosis; HIPAA = Health Insurance Portability and Accountability Act; MRI = magnetic resonance imaging; NSAID = nonsteroidal anti-inflammatory drug; PCP = primary care provider; RVd = lenalidomide bortezomib dexamethasone.

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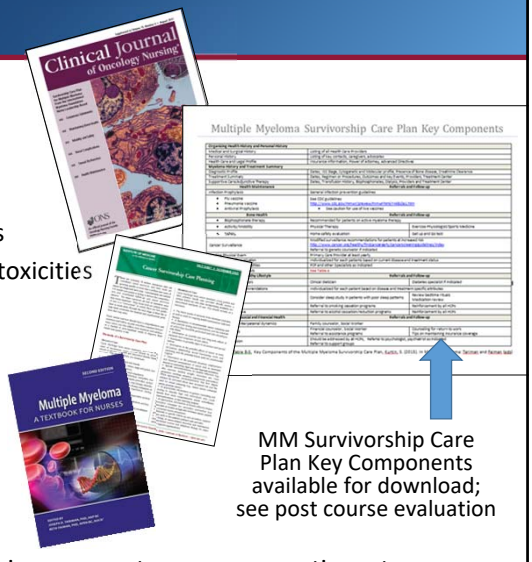
Survivorship Care Plan: Recommended for Each Survivor and His/Her PCP

- Institute of Medicine Recommendation:
  A Survivorship Care Plan for Each Survivor
  - **Record of care**
    - Diagnosis, including diagnostic tests and results
    - Treatments received, total dosage, responses, toxicities
    - Other supportive services (psychosocial, etc)
    - Contact information for key providers
    - Point of contact for continuing care
  - **Follow-up plan**
    - Ongoing health maintenance therapy/testing
    - Recommended screenings
    - Late/long-term effects of treatments
    - Recommendations/resources for healthy behaviors, support, cancer prevention, etc



MM Survivorship Care Plan Key Components available for download; see post course evaluation

MM = multiple myeloma; PCP = primary care provider.

Institute of Medicine. Cancer Survivorship Care Planning. Fact Sheet Nov 2005. https://apos-society.org/wp-content/uploads/2016/06/factsheetcareplanning.pdf. Accessed May 1, 2020. Salz T, et al. *Cancer.* 2014;120(5):722-730. Bilotti E, et al. *Clin J Oncol Nurs.* 2011;15(4)suppl. Kurtin S. In: Tariman JD, et al, eds. *Multiple Myeloma: A Textbook for Nurses.* 2nd ed. 2015.

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CASE #2

Lisa*

- Lisa is a 56-year-old woman with no significant comorbidities
  - FISH: del(17p)
  - Transplant eligible

*HIPAA-compliant, stock photo (not actual patient).

FISH = fluorescence in situ hybridization; HIPAA = Health Insurance Portability and Accountability Act.

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Risk With Multiple Myeloma

STANDARD RISK

No abnormalities detected

OR

Abnormalities that are not defined as high risk

HIGH RISK

Identified by FISH

- t(4;14)[a]
- t(14;16)
- t(14;20)
- del(17/17p)
- gain(1q)[a]

Identified by karyotyping

- nonhyperdiploid karyotype
- del(13)

Genetic analysis

- Double hit (biallelic *TP53* inactivation or amplification of *CKS1B* [1q21])

Other disease characteristics

- Extramedullary disease
- Plasma cell leukemia

CKS1B = Cyclin-dependent kinases regulatory subunit 1; FISH = fluorescence in situ hybridization; *TP53* = tumor protein 53.
[a]Intemediate risk according to Rajkumar SV, high risk according to Sonneveld P, et al.
Sonneveld P, et al. *Blood*. 2016;127:2955-2962. Rajkumar SV. *Am J Hematol*. 2018;93:1091-1110. Walker BA, et al. *Leukemia*. 2019;33(1):159-170.

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Myeloma Common Frontline Regimens

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- IRd: ixazomib lenalidomide dex
- Dara-Rd: daratumumab lenalidomide dex
- Dara-Td: daratumumab thalidomide dex
- Dara-VRd: daratumumab bortezomib lenalidomide dex

Common Regimens for Non-Transplant Candidate

- VRd*: bortezomib lenalidomide dex
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- VCd: bortezomib cyclophosphamide dex
- KRd: carfilzomib lenalidomide dex
- Id: ixazomib dex
- Dara-VMP: daratumumab melphalan prednisone

MAINTENANCE†

- Lenalidomide*
- Ixazomib*
- Lenalidomide + proteasome inhibitors (for high risk)

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- Ixazomib
- Lenalidomide + proteasome inhibitors (for high risk)

dex = dexamethasone; MM = multiple myeloma; NCCN = National Comprehensive Cancer Network.
*NCCN Category 1. †Clinical trial participation is recommended.

Faiman B, et al. *J Adv Pract Oncol.* 2016:7(suppl 1):17-29. Mikhael J. https://www.medscape.com/viewarticle/882042. Accessed May1, 2020. Rajkumar SV. How I treat. 2020. https://twitter.com/vincentrk/status/1203058085776035840. Accessed May 1, 2020. NCCN Guidelines. Multiple Myeloma. V3.2020. Accessed May 1, 2020.

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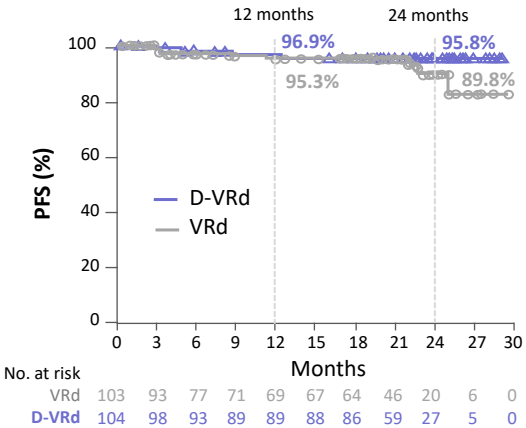
GRIFFIN Phase 2 Clinical Trial: Dara-RVd Regimen in Transplant-Eligible Patients

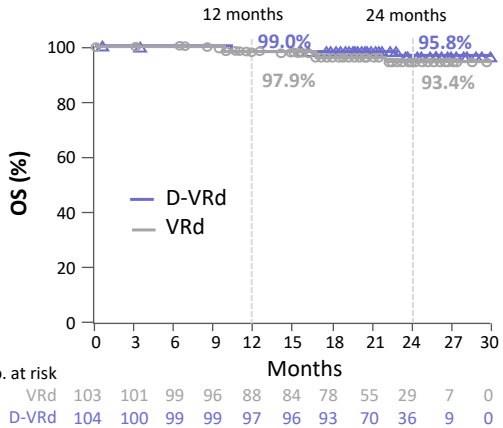
Progression-Free Survival



No. at risk

VRd	103	93	77	71	69	67	64	46	20	6	0
D-VRd	104	98	93	89	89	88	86	59	27	5	0

Overall Survival



No. at risk

VRd	103	101	99	96	88	84	78	55	29	7	0
D-VRd	104	100	99	99	97	96	93	70	36	9	0

Dara = daratumumab; D-VRd = daratumumab bortezomib lenalidomide dexamethasone; OS = overall survival; PFS = progression-free survival; VRd = bortezomib lenalidomide dexamethasone.

Voorhees PM, et al. ASH 2019. Abstr #691.

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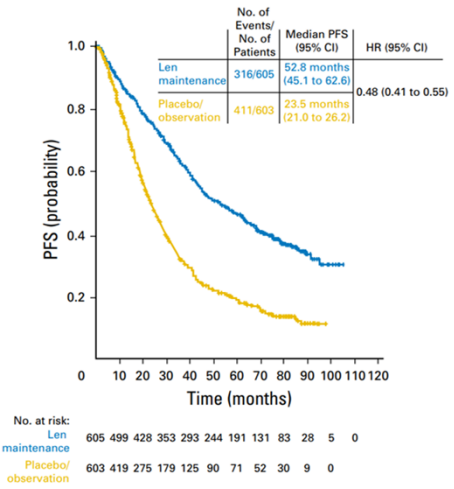
Meta-Analysis: Lenalidomide Maintenance After ASCT Demonstrates Improved PFS and OS



PFS and OS benefit observed across subgroups:

- Older or younger than 60 years
- Male or female
- ISS stage I/II or III
- Response after ASCT (prior to maintenance)
- Different induction regimens

NEW DATA at ASCO 2020

STaMINA clinical trial

- Benefit of len maintenance until progression post ASCT
- Double ASCT has benefit for patients with high-risk MM

SWOG1212 clinical trial

- Benefit to IMiD + PI maintenance for high-risk MM

ASCT = autologous stem cell transplant; ASCO = American Society of Clinical Oncology; HR = hazard ratio; IMiD = immunomodulatory drug; ISS = International Staging System; len = lenalidomide; NDMM = newly diagnosed multiple myeloma; OS = overall survival; PI = proteasome inhibitor; PFS = progression-free survival; SWOG = Southwest Oncology Group.

McCarthy PL, et al. *J Clin Oncol.* 2017;35(29):3279-3289. Hari P, et al. ASCO 2020. Abstr #8506. Usmani SZ, et al. ASCO 2020. Abstr #8507.

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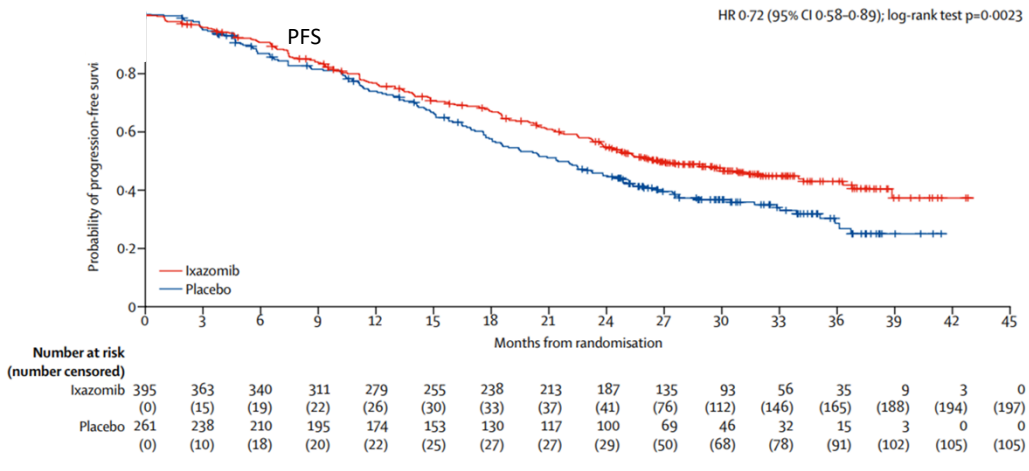
TOURMALINE-MM3 Phase 3 Clinical Trial: Ixazomib Maintenance After Transplant



R = hazard ratio; PFS = progression-free survival.

Dimopoulos MA, et al. *Lancet.* 2019;393(10168):253-264. Dimopoulos MA, et al. ASH 2018. Abstr #301.

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FORTE: Carfilzomib Regimens in Transplant-Eligible Patients With Newly Diagnosed MM

Design

- 474 patients with newly diagnosed MM
- Randomized to KRd_ASCT_KRd or KRd12 or KCd_ASCT_KCd

Results

- 12 cycles of KRd vs KRd + ASCT: both were equally effective in producing deep responses
  – GOOD FOR HIGH RISK
- In R-ISS stage I disease, impressive MRD-negative rates of 69% and 62%

NEW DATA at ASCO 2020

ENDURANCE phase 3: KRd did not improve PFS over VRd in patients with newly diagnosed MM without high-risk features

	KRd_ASCT_KRd (n=158)	KRd (n=157)	R-ISS I		R-ISS II/III
			KRd_ASCT_KRd (n=48)	KRd_12 (n=39)	KRd_ASCT_KRd (n=92)
sCR	44%	43%	46%	49%	39%
≥CR	60%	61%	66%	64%	56%
≥VGPR	89%	87%	92%	79%	86%
MRD-negative	58%	54%	69%	62%	51%

ASCT = autologous stem cell transplant; ASCO = American Society of Clinical Oncologists; CR = complete response; KCd = carfilzomib cyclophosphamide dexamethasone; KRd = carfilzomib lenalidomide dexamethasone; MM = multiple myeloma; MRD = minimal residual disease; R-ISS = revised International Staging System; sCR = stringent complete response; VGPR = very good partial response; VRd = bortezomib lenalidomide dexamethasone.
Gay F, et al ASCO 2019. Abstr #8002. Kumar S, et al. ASCO 2020. Abstr #LBA3.

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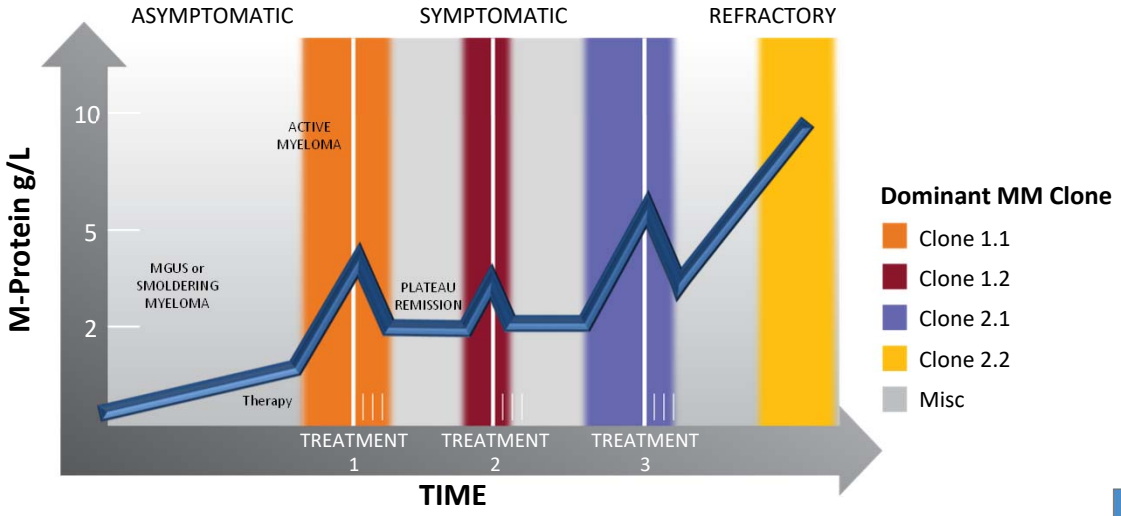
Relapsing Nature of MM With Clonal Evolution: Dominant Clones Change Over Time



M-protein = monoclonal protein; MGUS = monoclonal gammopathy of undetermined significance; MM = multiple myeloma.
Adapted. Durie B. Keats JJ, et al. *Blood*. 2012;120:1067-1076.

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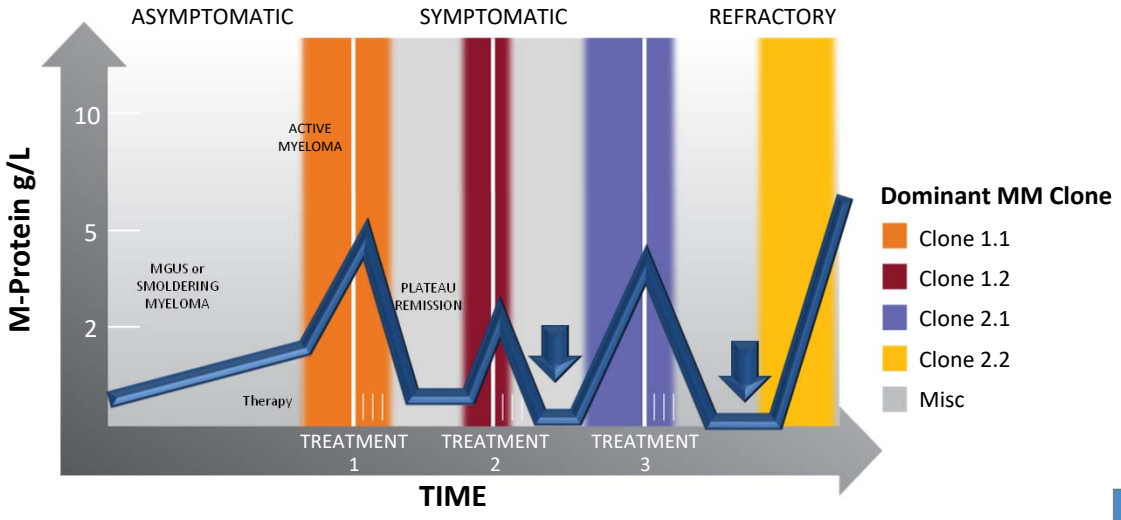
However, With New Agents, Some Patients Achieve Deep Responses Even After Many Treatments



M-protein = monoclonal protein; MGUS = monoclonal gammopathy of undetermined significance; MM = multiple myeloma.
Adapted. Durie B. Keats JJ, et al. *Blood*. 2012;120:1067-1076.

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Resources to Enhance Your Ability to Care for Your Patients With MM: Download or Receive a USB Drive by Mail

…and Much, Much More

Instructions for accessing these resources are provided in the post-course evaluation

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