Case Studies in Multiple Myeloma:
Best Practices in Patient Care and Symptom Management

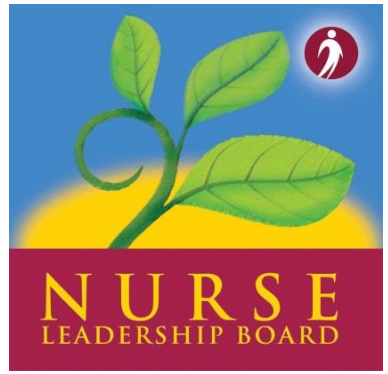
Slides available for download at:

www.imf-ons.myeloma.org/ONS_2017.pdf

Please help us have an on-time start.
Please do not save seats. Please silence cell phones.

Thank you for coming!

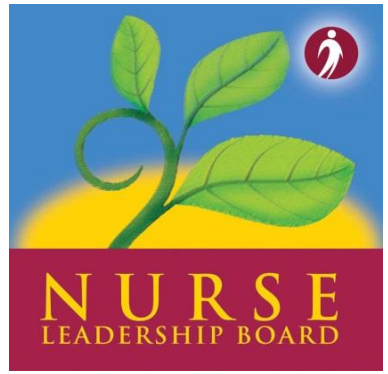
1.5 credits CNE jointly provided by the Annenberg Center for Health Sciences and the International Myeloma Foundation, with the support of educational grants from Takeda Oncology, Janssen Pharmaceuticals, Celgene Corporation, and Bristol-Myers Squibb.



Accreditation/Certification

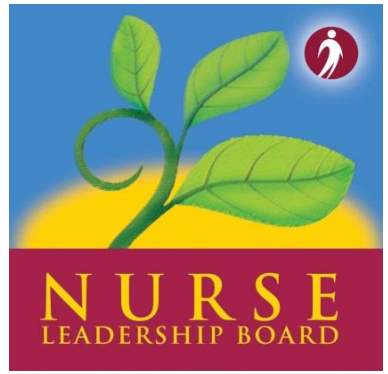
A maximum of 1.5 contact hours may be earned for successful completion of this activity.

In accordance with ACCME requirements, this program will be certified through the joint providership of the Annenberg Center and the International Myeloma Foundation (IMF) for ANCC contact hours. The Annenberg Center for Health Sciences at Eisenhower is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.



Disclosure of Conflicts of Interest

It is the policy of the Annenberg Center for Health Sciences at Eisenhower to ensure balance, independence, objectivity, and scientific rigor in all of its educational activities. In accordance with this policy, the Annenberg Center identifies conflicts of interest with its instructors, content managers, and other individuals who are in a position to control the content of an activity. Conflicts are resolved by the Annenberg Center to ensure that all scientific research referred to, reported, or used in a continuing education activity conforms to the generally accepted standards of experimental design, data collection, and analysis



ONS Disclaimer

Meeting space has been assigned to provide the Symposia, supported by the International Myeloma Foundation (IMF) via an educational grant, during the Oncology Nursing Society's (ONS) 42nd Annual Congress, May 4-May 7, 2017 in Denver, Colorado. The Oncology Nursing Society's assignment of meeting space does not imply product endorsement.

Patient names, demographics and identifying characteristics have been masked to be HIPPA compliant.

Off label use of drugs may be discussed.

Slides available for download at:
www.imf-ons.myeloma.org/ONS_2017.pdf

Evaluations with CNE-credit are enclosed in the packet, along with the Guidebook.

Presenters disclosures are in the Guidebook.

NURSE
LEADERSHIP BOARD

Faculty Introductions

Co-Chairs

Beth Faiman, PhD, RN, MSN, APRN-BC, AOCN®
Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH

Joseph D. Tariman, PhD, RN, ANP-BC, FAAN
DePaul University, Chicago, IL

Faculty

Sandra Rome, RN, MN, AOCN®, CNS
Cedars-Sinai Medical Center, Los Angeles, CA

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Winship Cancer Institute of Emory University, Atlanta, GA

International Myeloma Foundation (IMF)

Dedicated to improving the quality of life of myeloma patients while working toward prevention and a cure

- **Nurse Leadership Board**
- International Myeloma Working Group
- Black Swan Research Projects
- Publications: Brochures, etc.
- IMF Infoline / GLOBAL
- Patient Outreach
  - Support Groups
  - Seminars, Workshops
  - Teleconferences
- Advocacy
- International Outreach

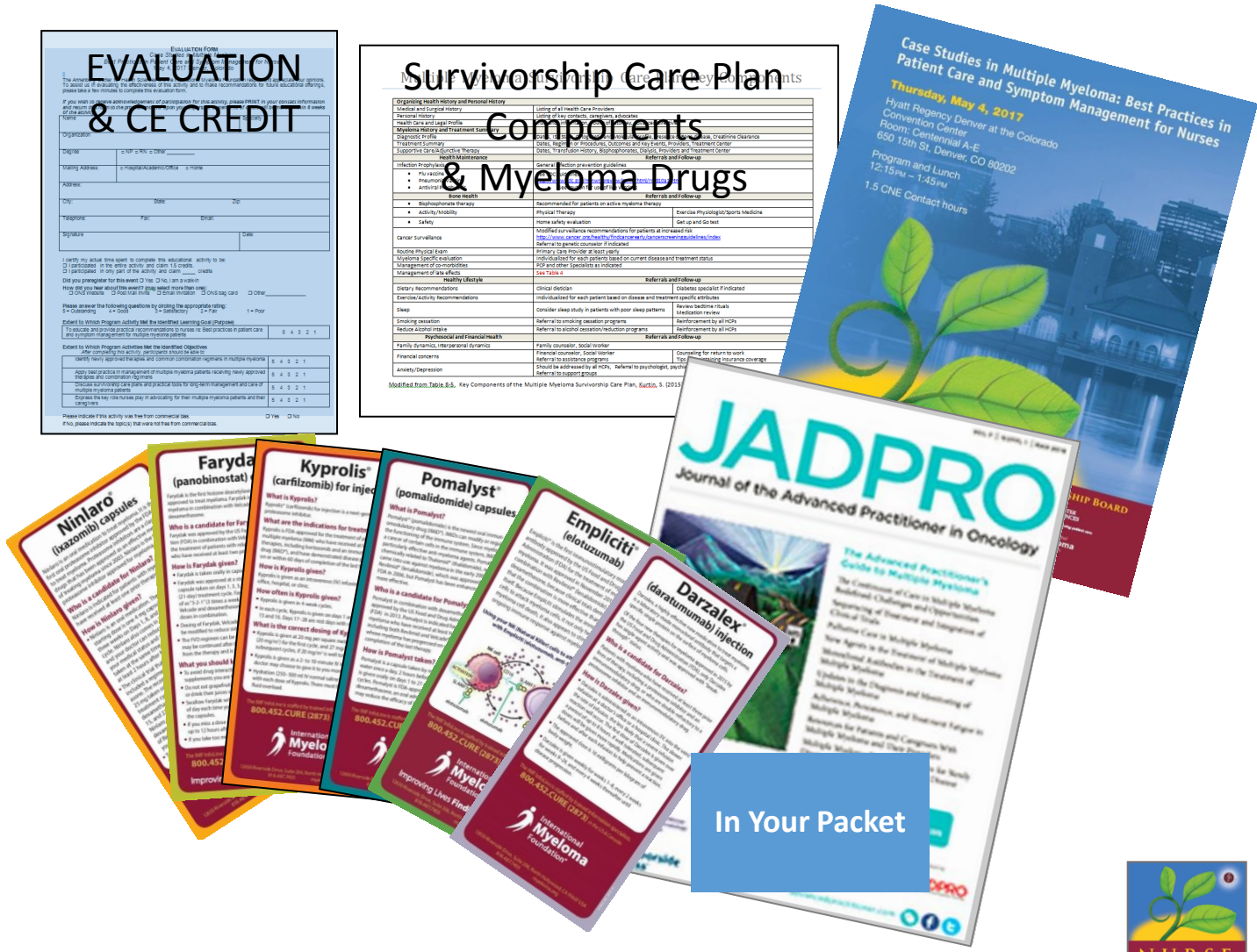
In Your Packet: Resources to Enhance Your Ability to Care for Your MM Patients

Publications from Nurse Leadership Board, International Myeloma Working Group

On USB drive
In small envelope

EVALUATION & CE CREDIT

Survivorship Care Plan Components & Myeloma Drugs



In Your Packet

Agenda

TIME	TOPIC	FACULTY
12:10 PM - 12:15 PM	Welcome, Disclosures & Introductions	Joseph D. Tariman
12:15 PM – 12:40 PM	Multiple Myeloma Background Case Study #1: Diagnostic Criteria, Shared Decision-Making, Clonal Evolution, Clinical Trials	Joseph D. Tariman Beth Faiman
12:40 PM - 1:10 PM	Case Study #2: Newly Diagnosed Multiple Myeloma, Response, Bone Health, Renal Health, Minimal Residual Disease, Adherence, Survivorship Care Case Study #3: Relapsed Myeloma, Multiple Therapeutic Options, Immunotherapy considerations	Sandra Rome Beth Faiman
1:10 PM – 1:40 PM	Case Study #4, #5, #6 #7: Relapsed Myeloma, Treatment for Relapsed Myeloma, Frailty Myeloma, Drugs in Development	Charise Gleason Beth Faiman
1:40 PM - 1:45 PM	Closing Remarks and Q & A	All

Learning Objectives

As a result of this program, you will be able to:

- Identify newly approved therapies and common combination regimens in multiple myeloma
- Apply best practice in management of multiple myeloma patients receiving newly approved therapies and combination regimens
- Discuss survivorship care plans and practical tools for long-term management and care of multiple myeloma patients
- Express the key role nurses play in advocating for their multiple myeloma patients and their caregivers

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

Multiple Myeloma Background

CASE #1: Dolores*

Joseph D. Tariman, PhD, RN, ANP-BC, FAAN

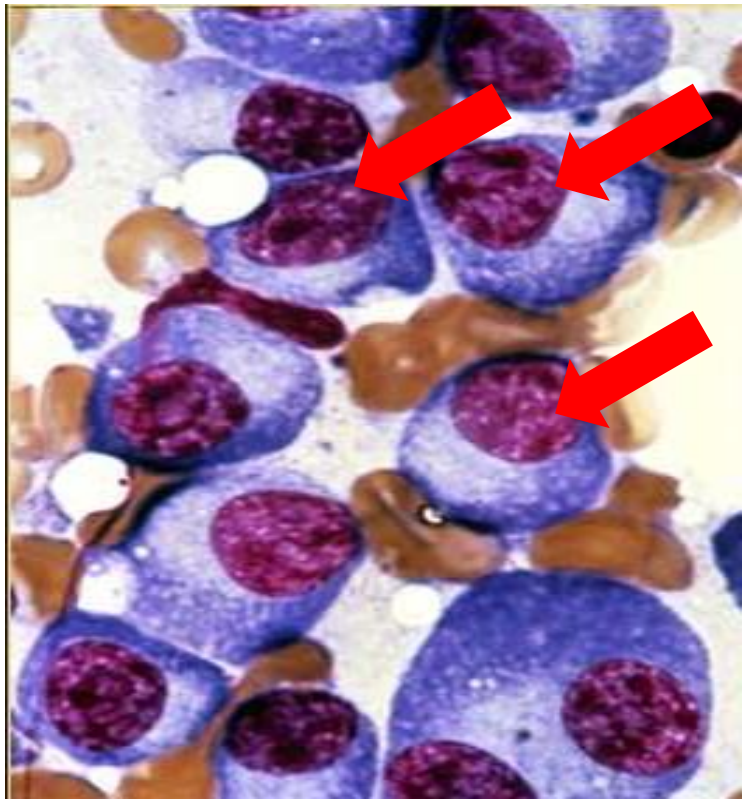
Beth Faiman, PhD, RN, MSN, APRN-BC, AOCN®

*HIPPA-compliant; not actual patient name

Myeloma Is a Cancer of Plasma Cells

- Preceded by nonmalignant state(s): MGUS or SMM
- Cancer of plasma cells
- Healthy plasma cells produce immunoglobulins: G, A, M, D & E
- Myeloma cells produce abnormal immunoglobulin continually
  - 65% IgG
  - 20% IgA
  - 5% to 10% light chains (monoclonal kappa, lambda light chains, Bence-Jones proteins)
  - Rare: IgD, IgE, IgM, or nonsecretory disease

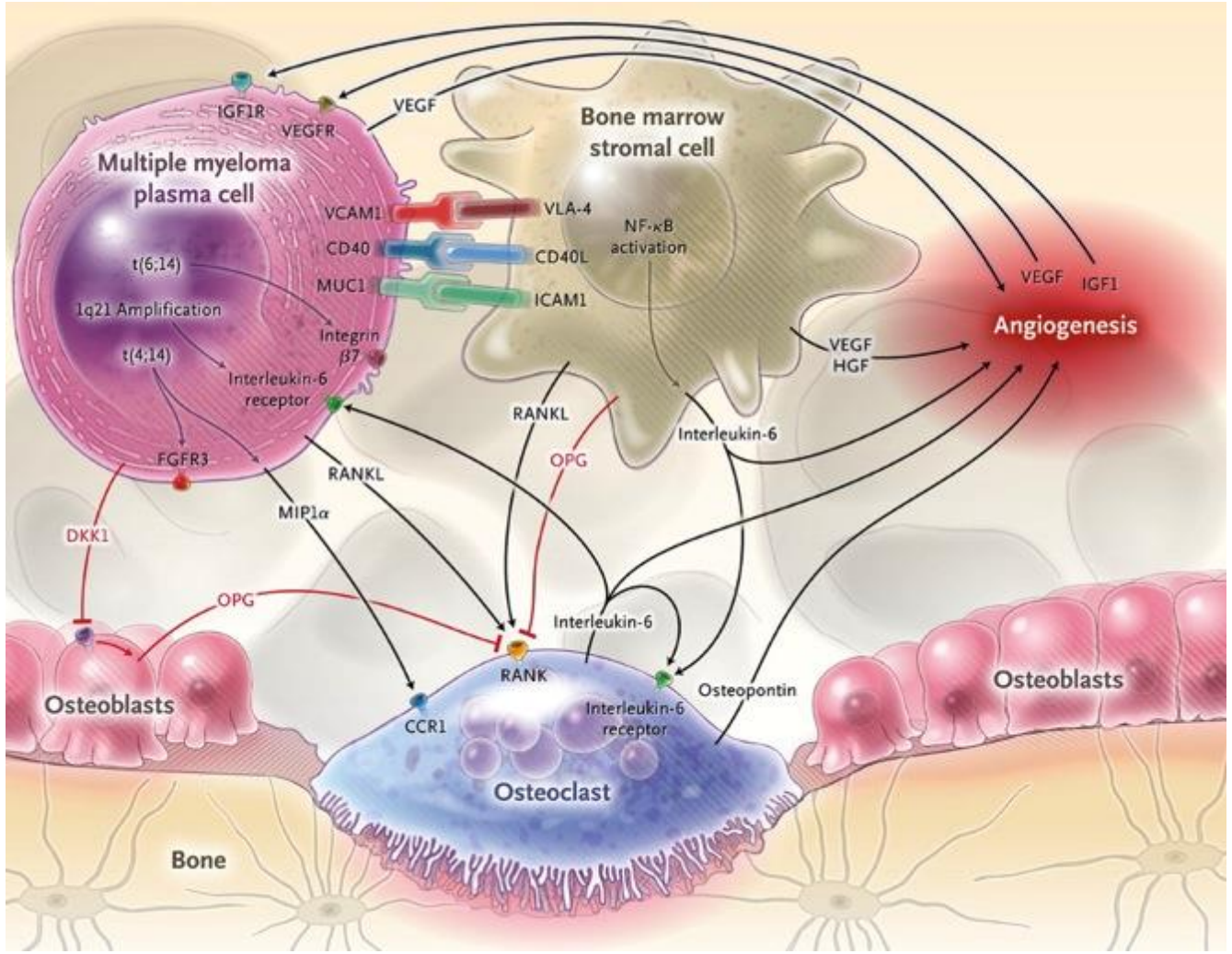
Bone Marrow of MM Patient



Myeloma cells often have large eccentric nuclei

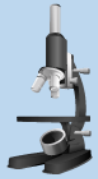
Kyle RA, et al. *Mayo Clin Proc.* 2003;78:21-33.

Immune Basis for Multiple Myeloma



- Complex disease involving:
- Cancerous plasma cell clone(s)
- Genetic changes
- Premalignant conditions: MGUS, SMM at early stages
- Complex interactions of adhesion and cytokines
- Imbalance between osteoclasts (too many) and osteoblasts (too few), resulting in bone damage

Palumbo A, Anderson KC. *N Engl J Med.* 2011;364(11):1046-1060.

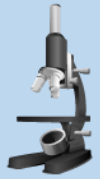


Multiple Myeloma Typically Preceded by Premalignant Conditions

	Premalignant		Malignant
Condition	**MGUS[1-4] (Monoclonal Gammopathy of Undetermined Significance)**	**SMM[1-5,8] (Smoldering Multiple Myeloma)**	**Active Multiple Myeloma[6-8]**
Clonal plasma cells in bone marrow	<10%	10%-60%	≥10%
Presence of Myeloma Defining Events	None	None	Yes
Likelihood of progression	~1% per year	~10% per year	Not Applicable
Treatment	No; observation	Yes for high risk*; No for others	Yes

* In clinical trial (preferred) or offer treatment for those likely to progress within 2 years

1. Kyle RA, et al. *N Engl J Med.* 2007;356:2582-90.
2. International Myeloma Working Group. *Br J Haematol.* 2003;121:749-57.
3. Jagannath S, et al. *Clin Lymphoma Myeloma Leuk*. 2010;10(1):28-43.
4. Kyle RA, et al. *Curr Hematol Malig Rep*. 2010;5(2):62-69.
5. Mateos M-V, et al. *Blood.* 2009;114:Abstract 614.
6. Durie BG, Salmon SE. *Cancer*. 1975;36:842-854.
7. Durie BG, et al. *Leukemia*. 2006;20(9):1467-1473.
8. Rajkumar SV, et al. Lancet *Oncology* 2014; 15:e538-e548.



2014 IMWG Active Myeloma Criteria: Myeloma Defining Events

Clonal bone marrow ≥ 10% or bony/extramedullary plasmacytoma

AND any one or more **M**yeloma **D**efining **E**vents (MDE)

- **C** alcium elevation
- **R** enal complications
- **A** nemia
- **B** one disease

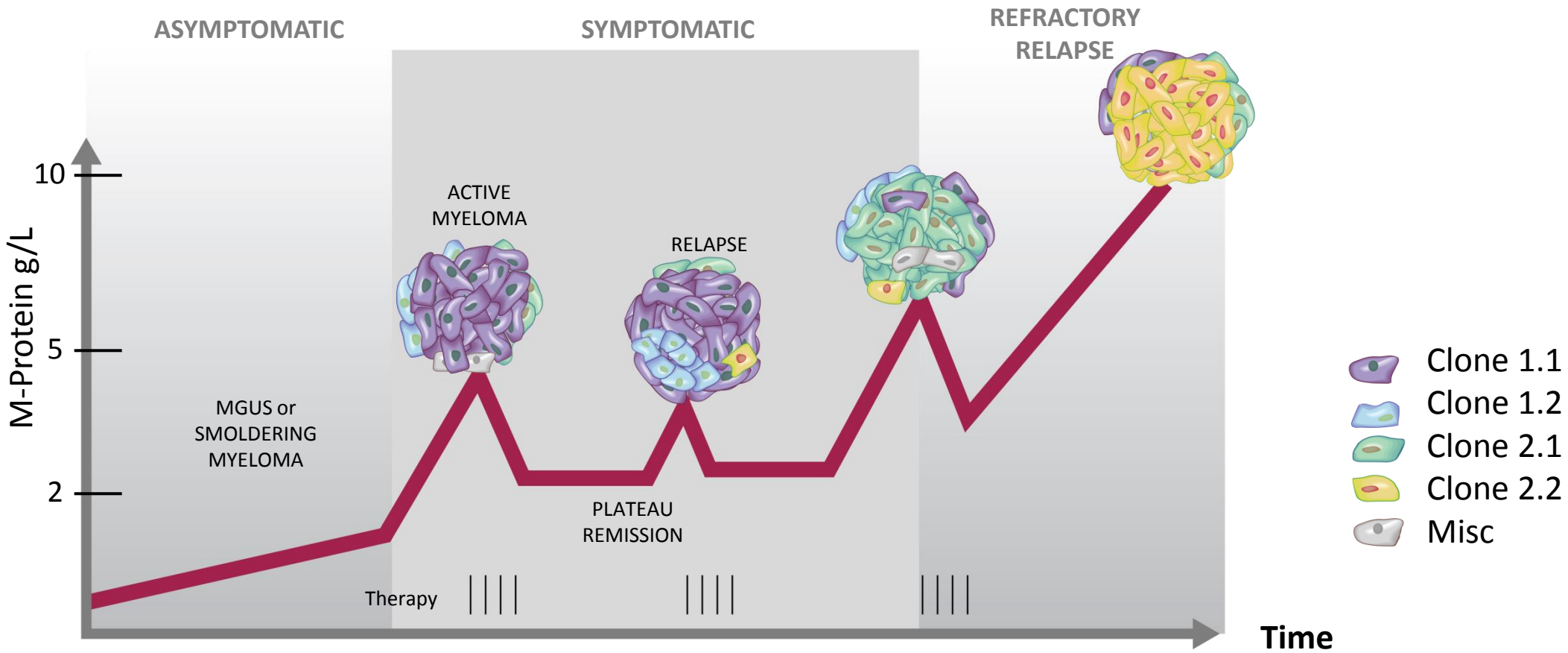
- **BM** Clonal bone marrow ≥ 60%
- **FLC** sFLC ratio >100
- **MRI** >1 focal lesion by MRI

Added in 2014

BM = bone marrow; FLC = free light chain; MDE = myeloma defining event; MRI = magnetic resonance imaging; sFLC = serum free light chain

Rajkumar SV, et al. *Lancet Oncology.* 2014; 15:e538-e548. Kyle RA, et al. *Leukemia.* 2010; 24(6):1121–1127.

Relapsing Nature of Multiple Myeloma

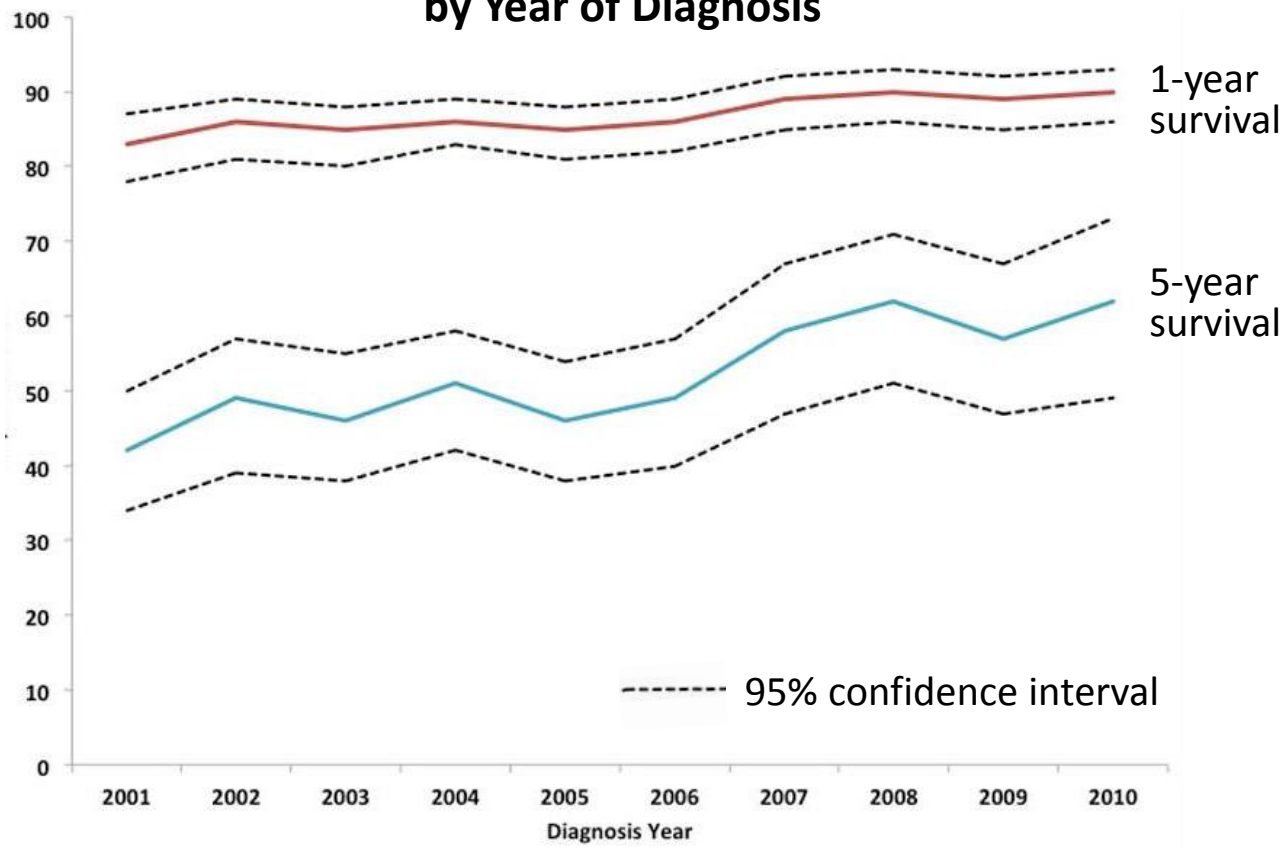


MGUS = monoclonal gammopathy of undetermined significance

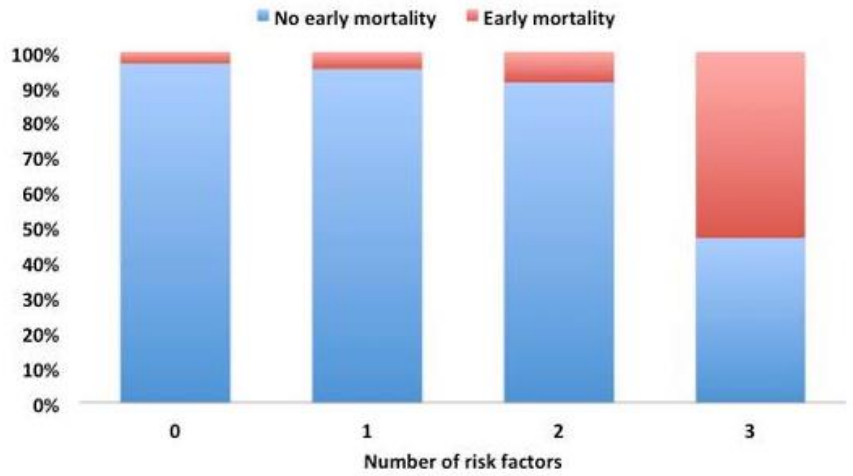
Adapted from Dr. Brian Durie and Keats JJ, et al. *Blood*. 2012;120:1067-1076.

Myeloma Patients Are Living Longer

Survival of Newly Diagnosed Myeloma Patients by Year of Diagnosis



Risk of Early Mortality (Death 1 Year After Diagnosis) by Number of Risk Factors

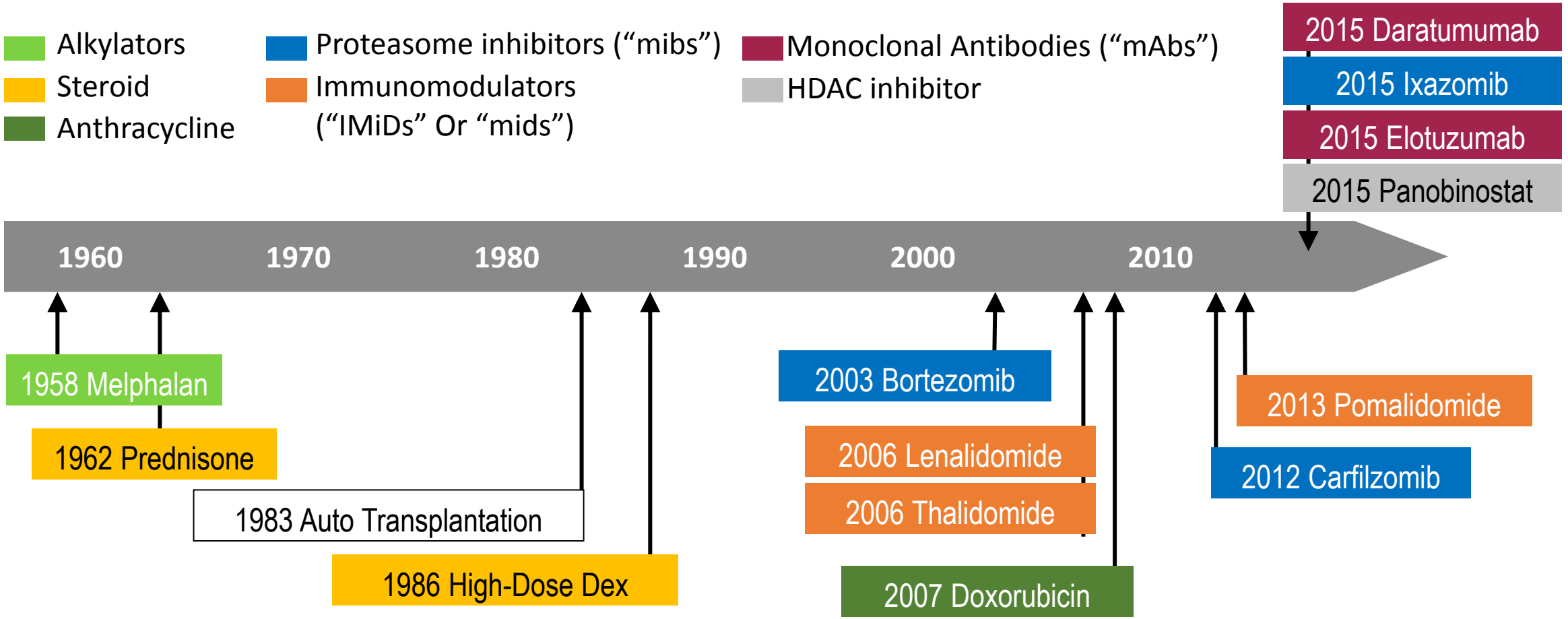


Early Mortality Risk Factors:

- >70 years old
- Serum albumin <3.5 g/dL
- Serum beta-2 microglobulin >6.5 mg/dL

Kumar SK et al. *Leukemia*. 2014;28(5):1122-1128.

Expanding Treatment Options for Multiple Myeloma: Mibs, Mids, and Mabs



DRUGS@FDA.gov Auto = Autologous; Dex= Dexamethasone

Tariman, J.D. (2017). Changes in cancer treatment: Mabs, Mibs, Mids, Nabs, and Nibs. *Nurs Clin North Am,* 52(1):65-81. doi: 10.1016/j.cnur.2016.10.004.

CASE #1:

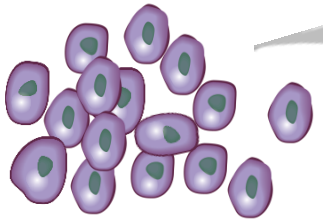
Dolores*

- 61 year old retired teacher
  - Active & generally good health
  - Family history of heart disease
  - Routine physical
  - Elevated total protein in bloodwork
    - Total serum proteins: 10.2 g/dL (ULN 8.5)
    - Calcium: 8.5mg/dL (ULN 10.6mg/dL)
    - Albumin: 3.5 mMol/L (LLN 3.5 mMol/L)
    - B_2M: 2.44 mg/dL (ULN 2.64mg/dL)
    - Creatinine: 1.1 mg/dL (ULN 1.3mg/dL)
    - Hgb: 11.9g/dL
  - Further testing

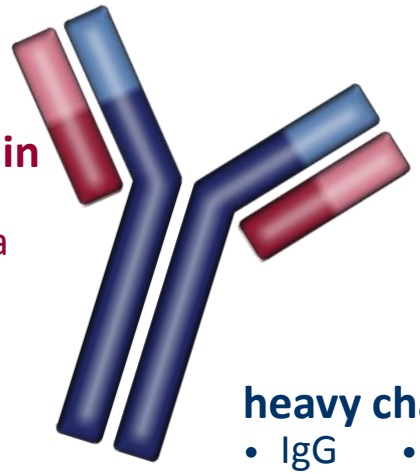
*HIPPA-compliant stock photo (not actual patient)

B_2M = beta-2 microglobulin; FISH = fluorescent in situ hybridization; Hgb = hemoglobin; LLN = lower limit of normal; PC = plasma cells; ULN = upper limit of normal

SPEP / UPEP



Myeloma cells produce abnormal immunoglobulins continually

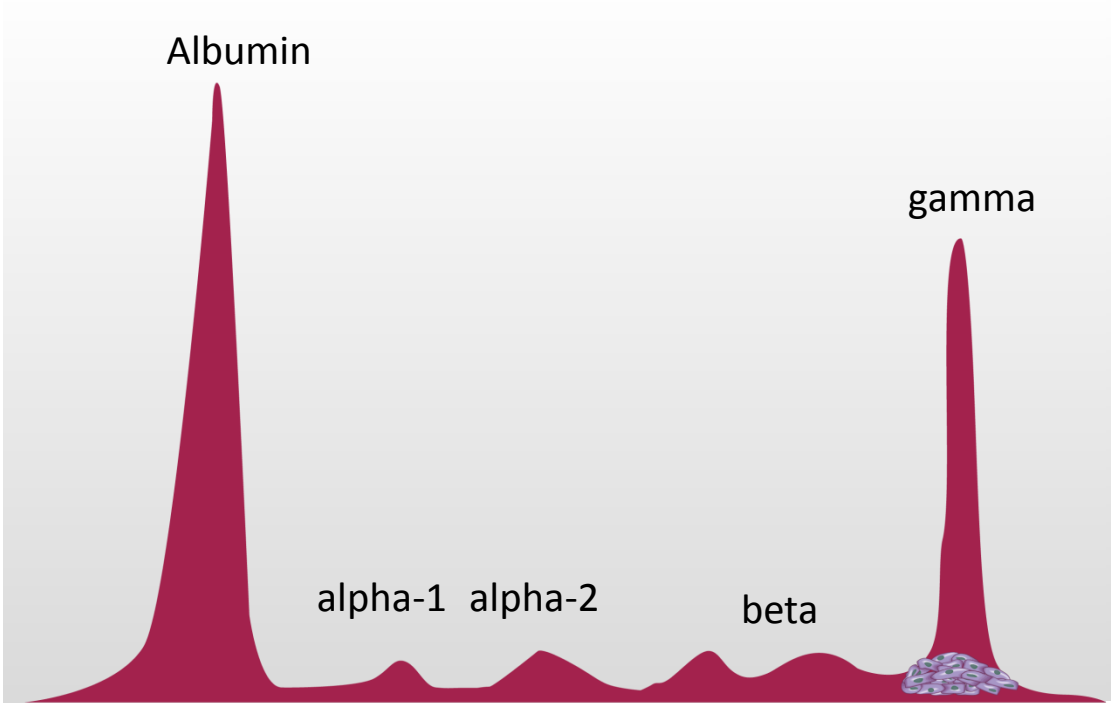


light chain
- Kappa
- Lambda

heavy chain
- IgG
- IgA
- IgM
- IgD
- IgE

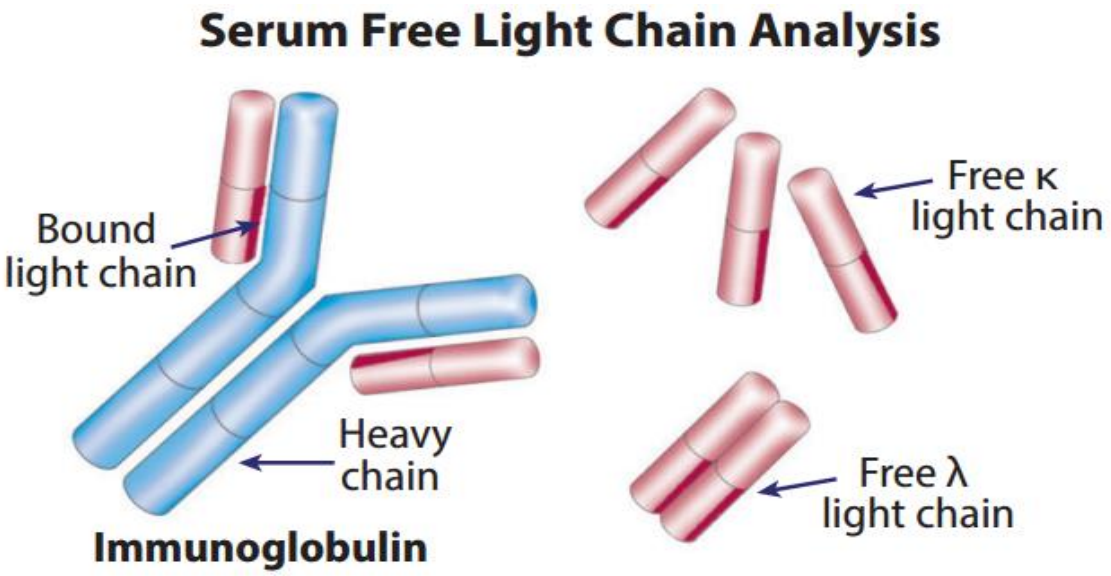
SPEP = serum protein electrophoresis
UPEP = urine protein electrophoresis

Myeloma



Understanding Your Test Results, International Myeloma Foundation 2016.

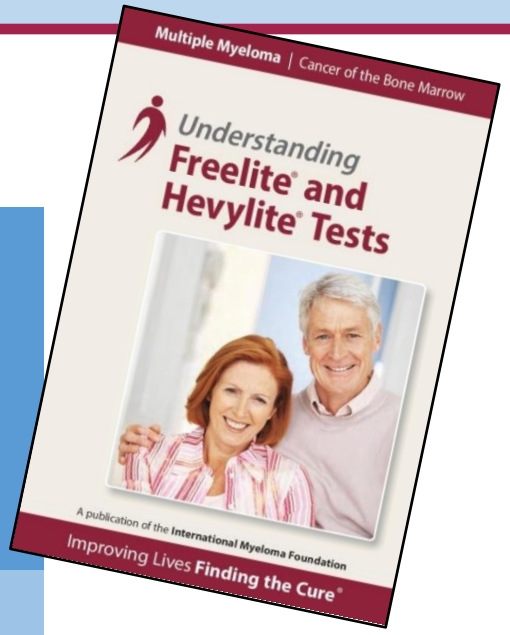
Serum Free Light Chain Assay



Normal Ranges:

- Free kappa: 3.3-19.4 mg/L
- Free lambda: 5.71-26.3 mg/L
- Kappa/lambda ratio: 0.26 – 1.65

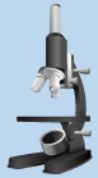
2014 MM criteria:
Free Light Chain ratio >100 is an MDE



Free light chain assay recommended by IMWG and NCCN guidelines

IMWG = International Myeloma Working Group; NCCN = National Comprehensive Cancer Network; MDE = Myeloma Defining Event

Rajkumar SV, et al. *Lancet Oncology.* 2014; 15:e538-e548; NCCN Guidelines for Multiple Myeloma Version 3.2017; International Myeloma Foundation Freelite® tip card; The Binding Site Group Ltd http://www.thebindingsite.com/

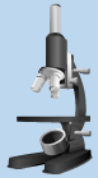


Myeloma Bone Imaging Methods

- Historical Gold Standard
  - Skeletal survey
- Other Testing
  - MRI
  - CT
  - PET Scan (± MRI or CT)
  - Whole body low-dose CT (WBLDCT)
- Not Appropriate for evaluation of lytic lesions – look for osteoporosis, rapid BMD decline
  - DXA (DEXA)

DXA = Dual-energy X-ray absorptiometry (previously DEXA);
CT = computed tomography;
MRI = magnetic resonance imaging;
PET = positron emission tomography;
WBLDCT = whole body low-dose CT

Miceli TS, et al. *Clin J Oncol Nurs.* 2011; 15(4):9-23; Roodman GD, et al. *Hematology AM Soc Hematol Educ Program.* 2008:313-319; Walker R, et al. *Oncol.* 2007:25(9):1121-1128; Durie BG, et al. *Leukemia*. 2006;20(9):1467-1473; Tariman JD. *Clin J Oncol Nurs.* 2004:8(3):317-320; Guise TA et al. *Endocr Rev.* 1998:19(1):18-54; Gralow JR, et al. *J Natl Compr Canc Netw.* 2009:7 Suppl 3:S1-32; Dimopoulous M, et al. *Leukemia.* 2009; 23(9):1545-56.



2014 Updated IMWG Smoldering MM Criteria

2014 IMWG Criteria for SMM, BOTH criteria must be met:

1. Absence of myeloma defining events or amyloidosis
2. Serum monoclonal IgG or IgA ≥30 g/L
   or urinary monoclonal protein ≥500 mg/24 hr
   and/or clonal bone marrow plasma cells 10 to 60%

IMWG = International Myeloma Working Group; MM = multiple myeloma;
SMM = Smoldering multiple myeloma

Rajkumar SV, et al. *Lancet Oncology.* 2014; 15:e538-e548; Clinicaltrials.gov accessed 3/11/2015.

CASE #1:

Dolores*

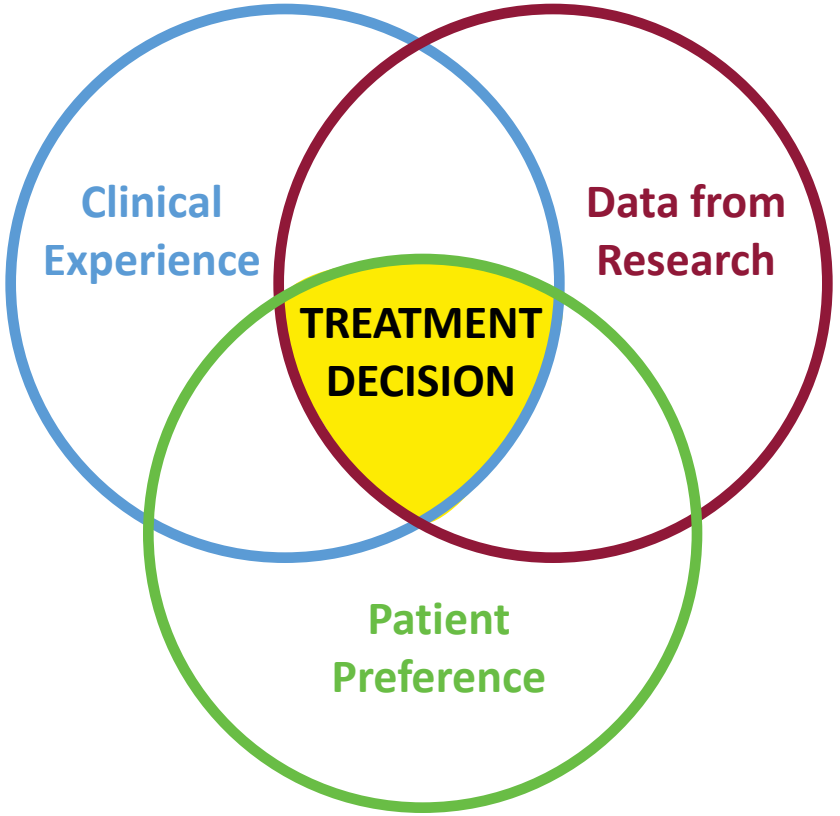
- SPEP: 3.2 g/dL IgG Lambda
- 24-hr UPEP: 520 mg lambda monoclonal protein
- Serum Free Light Chain Assay (FLC ratio)
  - Lambda FLC: 72.0
- Bone Marrow Biopsy:
  - 30% +lambda PC
  - Cytogenetics: 46xx; FISH: normal
- MRI & Skeletal survey: negative
- Diagnosis: High-Risk Smoldering MM

*HIPPA-compliant stock photo (not actual patient)

FISH = fluorescent in situ hybridization; FLC = free light chain; MM = multiple myeloma

Deciding on Treatment

- Considerations
- Options for high-risk SMM
  - Watchful waiting
  - Clinical trial
- Lifestyle and Quality of Life (IV/oral)
- Second opinion or consultation with a myeloma specialist



Philippe Moreau, ASH 2015

Clinical Trials: Access to New Agents and Regimens

- Phase 1 or 2
- Smaller trial, fewer centers
- Often no randomization
  - Single arm: all same regimen
  - Multi arm: multiple dose levels of active drug
- Phase 3
- Larger trial, more centers
- Randomization is often involved
  - Standard of care regimen vs. experimental regimen
  - Regimen ± experimental drug

IMF Myeloma Matrix 2.0: Clinical Trials for MM by Disease Stage, Phase, Location

multiple myeloma treatments	3 phase 1	5 phase 2	1 phase 3	1 other*
targeted therapy				
carfilzomib (Kyprolis) *proteasome*	0	1	0	0
ibrutinib *BTK*	0	1	0	0
ixazomib (Ninlaro) *proteasome*	1	1	0	0
immunotherapy				
anakinra (Kineret) *IL-1*	1	1	0	0
durvalumab (MEDI4736) *PD-1*	1	0	0	0
poly iclc (Hiltonol)	1	0	0	0
pembrolizumab (Keytruda) *PD-1*	0	0	0	1
nivolumab (Opdivo) *PD-1*	0	1	0	0
lenalidomide (Revlimid)	2	4	1	0
chemotherapy				
cisplatin (Platinol)	0	1	0	0
cyclophosphamide (Cytoxan, Endoxan)	0	1	0	0

myeloma.org/matrix

IMF Info Line
1-800-452-CURE
9am to 4pm PST

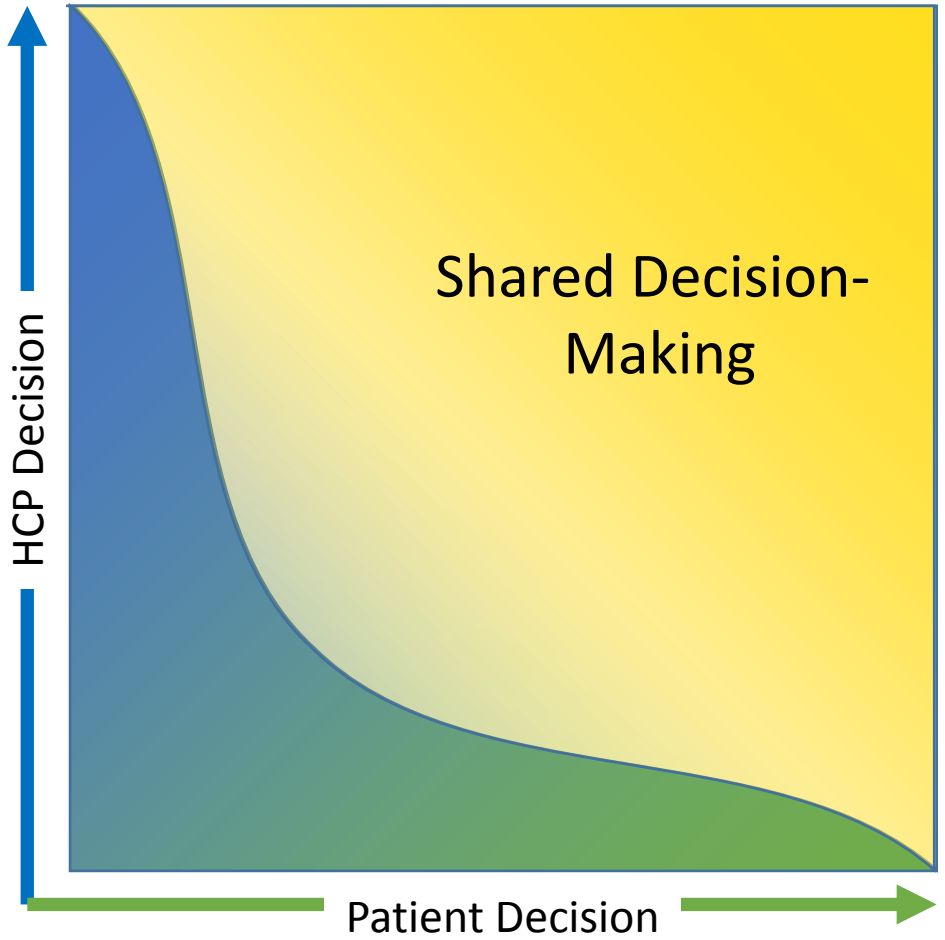
International Myeloma Foundation Understanding Clinical Trials 2016. myeloma.org/matris accessed 4.16/2017.

What Is Shared Decision-Making?

Shared decision-making is a model of treatment decision-making in the patient encounter

4 essential elements:

1. 2 participants: healthcare providers (MD/APP/RNs) and patient
2. Both parties share information
3. Both parties take steps to build consensus about preferred treatment
4. Mutual agreement is reached between patient and healthcare member on treatment approach



The New Era of Shared Decision-Making Benefits Both Patients and Health Care Providers

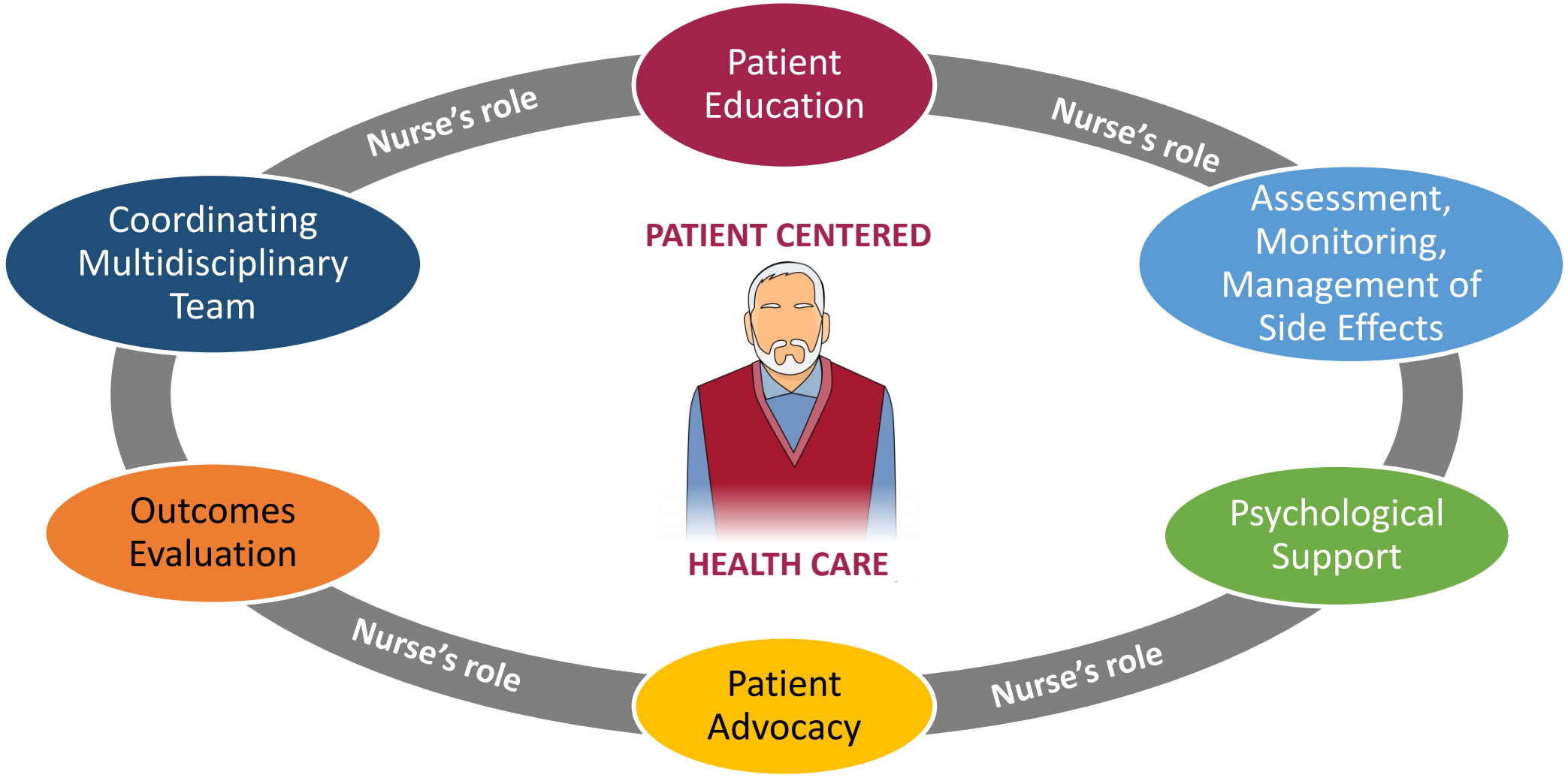
- In the past, paternalistic or provider-driven decision-making model was dominant
- Increased patient burden on cost and healthcare consumerism in US and elsewhere shifted the model from provider-driven to patient-centered care
- Oncology nurses are involved in shared decision-making[1]; nurses are a trusted source of patient information[2]
- Increased emphasis on patient-centered care[3-6]

Shared Decision-Making Benefits & Outcomes[7]

Short-Term Benefits
• Increased confidence with treatment decisions • Higher satisfaction with treatment decisions • Enhanced trust in healthcare team • Improved self-efficacy • Avoidance of decisional regrets • Decreased patient/caregiver stress and anxiety related to cancer treatment decisions
Long-Term Outcomes
• Treatment adherence • Better quality of life • Improved treatment outcomes: disease remission

1. Tariman J, et al. *Clin J Oncol Nurs.* 2015;19:548-556. 2. Tariman J, et al. *Ca Treat Comm.* 2014;*2:*34-37. 3. http://www.ahrq.gov. 4. Institute of Medicine Committee on Quality of Health Care in America. 5. Patient Protection and Affordable Care Act. 6. AACN Competencies for Baccalaureate and Graduate Nurses. 7. Kane HL, et al. *CA Cancer J Clin*. 2014;64:377-388.

Nurse's Role in Shared Decision-Making

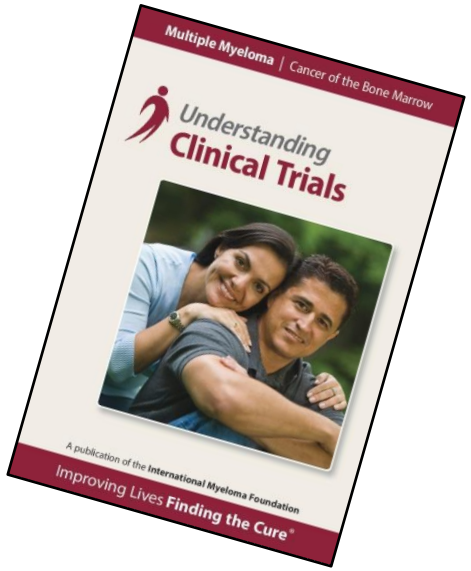


Adapted from Tariman JD, et al. *Clin J Oncol Nurs*. 2015;19:548-556.

CASE #1:

Dolores*

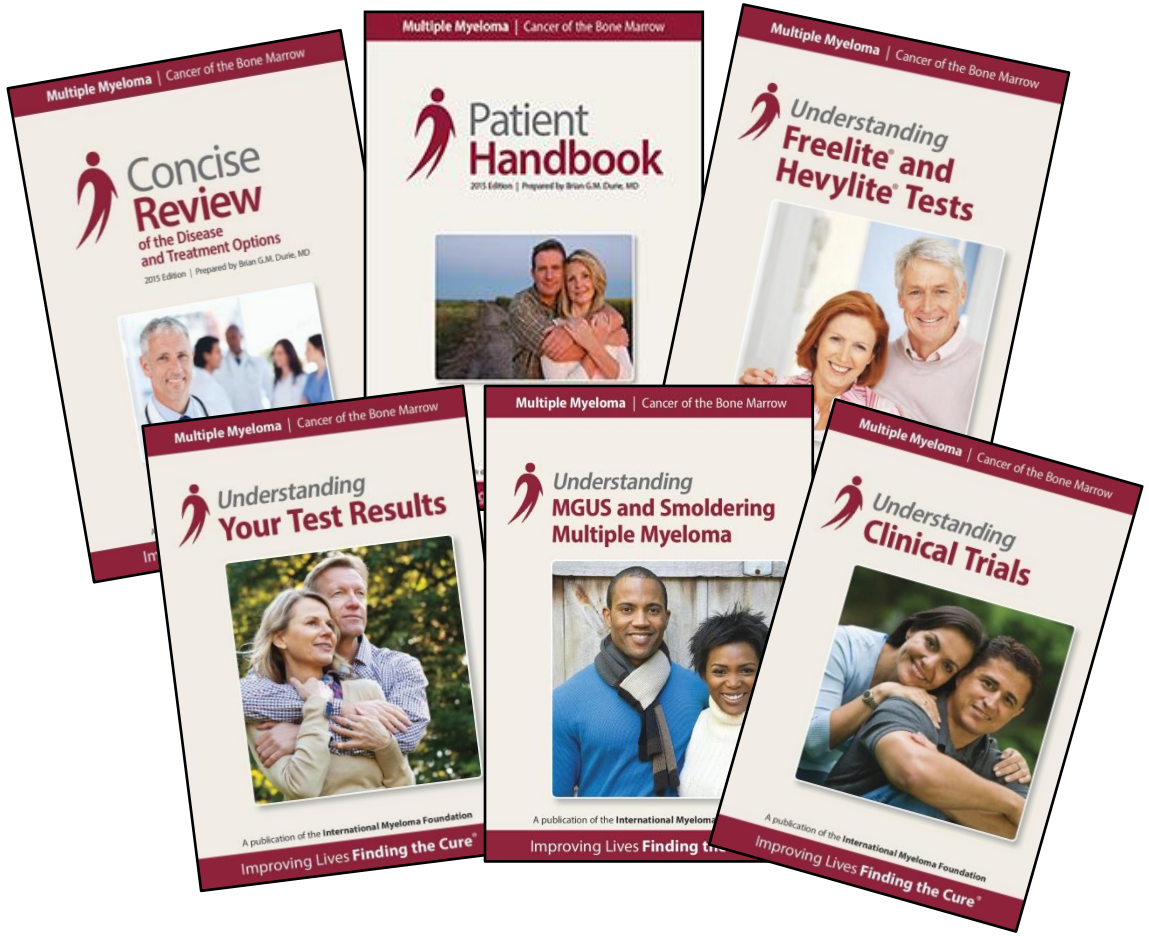
- Decided to enter clinical trial
- **NCT01169337** Lenalidomide or Observation in Treating Patients With Asymptomatic High-Risk Smoldering Multiple Myeloma
  - National Cancer Institute
  - Phase III
  - Lenalidomide vs. observation
  - Qualifies as she has no CRAB criteria (end organ damage)



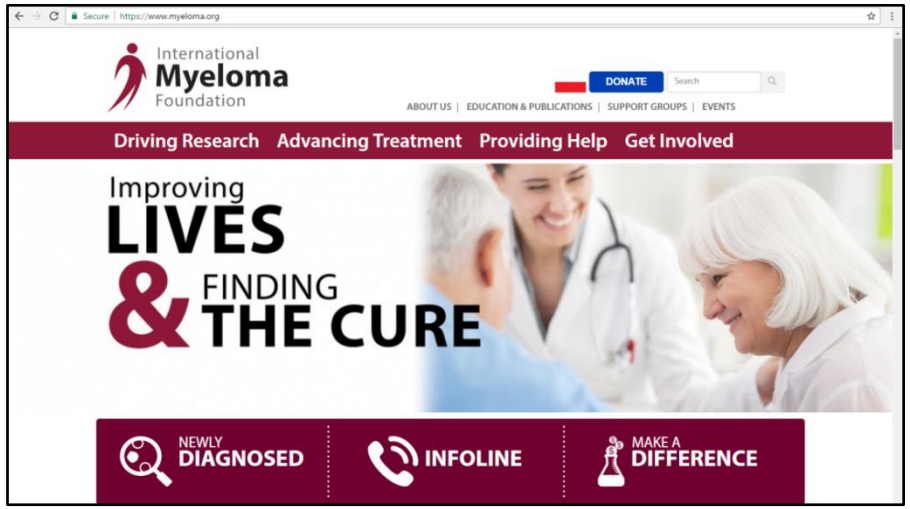
*HIPPA-compliant stock photo (not actual patient)

B_2M = beta-2 microglobulin; FISH = fluorescent in situ hybridization; Hgb = hemoglobin; PC = plasma cells; PCLI = plasma cell labeling index; ULN = upper limit of normal

Patient Education Tools for MGUS and SMM From IMF



Free download or order hard copy at myeloma.org



IMF website with many resources including for those newly diagnosed at myeloma.org

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

CASE #2: Mark*
CASE #3: Julia*

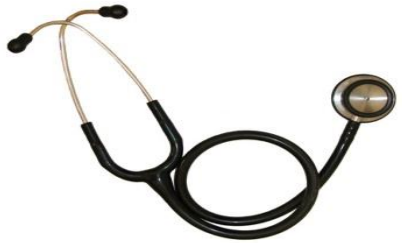
Sandra Rome, RN, MN, AOCN®, CNS
Beth Faiman, PhD, RN, MSN, APRN-BC, AOCN®

*HIPPA-compliant; not actual patient names

How Myeloma Patients Commonly Present?

In ER

- Severe pain – often spinal fractures
- Renal failure
- Medical emergencies need immediate treatment



During Routine Physical

- Patient with few/no symptoms
- Abnormal blood work
- Patient and caregivers can discuss options with health care team

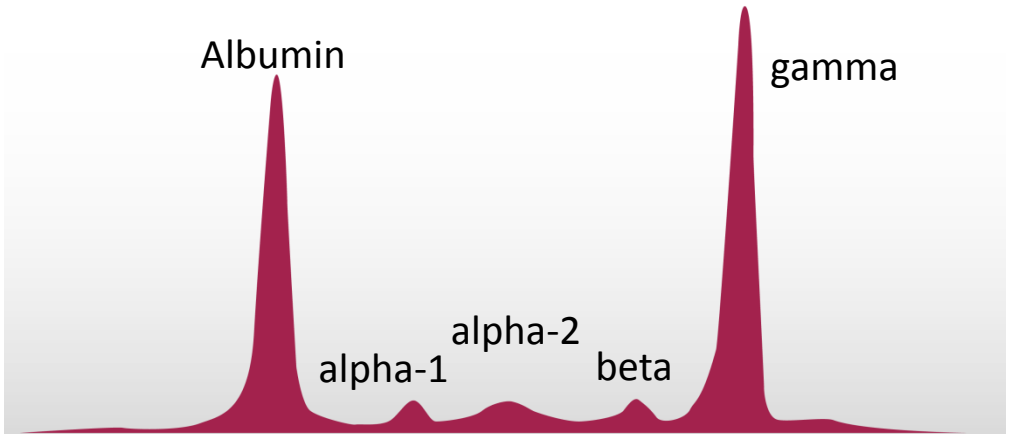
Top Choices for Newly Diagnosed MM

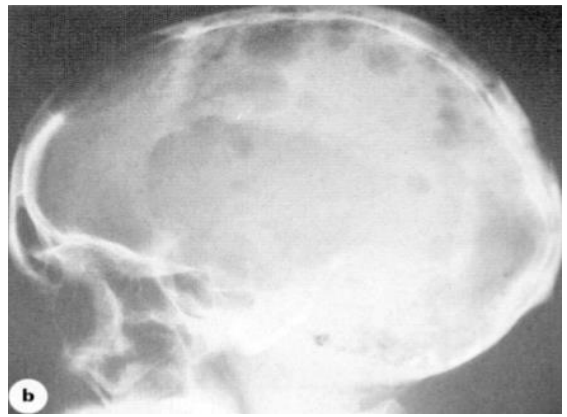
- IMiD and Mibs-based (eg, 3 drug regimen VRd)
- IMiD-based (eg, Rd) or Mibs-based (eg, Vd) (for frail/elderly)
- mAbs-based (in clinical trial) (eg, DRd)

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.

Diagnostic Workup for Multiple Myeloma

- Lab tests
  - Serum protein electrophoresis (SPEP)
  - Urine protein electrophoresis (UPEP)
  - CBC + differential + Chemistry including Albumen and B2microglobin and LDH
  - FLC ratio of free kappa/lambda light chains (plasma)
  - Monoclonal protein analysis (MPA)
- Bone marrow biopsy
  - FISH, cytogenetics, and gene expression profiling (GEP)
- Imaging:
  - Skeletal survey
  - MRI, CT
  - PET scan ± MRI, CT





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.

Updated MM Staging: Revised-ISS considers FISH and High LDH

BETTER SURVIVAL

WORSE SURVIVAL

Stage	ISS	Revised-ISS (R-ISS)
I	Serum beta-2 microglobulin < 3.5 mg/dL Serum albumin ≥ 3.5 g/dL	ISS stage I and standard risk chromosomal abnormalities by iFISH AND Serum LDH < ULN (varied by institution)
II	Not ISS stage I or II	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** **OR** **Serum LDH > ULN (varied by institution)**

iFISH = interphase FISH; ISS = International Staging System; PFS = progression-free survival.

Greipp PR, et al. *J Clin Oncol* 2005;23:3412-20; Palumbo A, et al. *J Clin Oncol* 2015;33:2863-9.

CASE #2:

Mark*

- 63-year-old engineer
  - Active & generally good health
    - Statin for high cholesterol
    - Beta-blocker for high blood pressure
  - Sharp back pain July 2016
  - Went to ER – Lumbar spine x-ray, then MRI
    - Spinal fracture and lytic lesions
  - Treated for spinal fracture
    - Kyphoplasty
  - Heme-onc consulted

*HIPPA-compliant stock photo (not actual patient)

CASE #2:

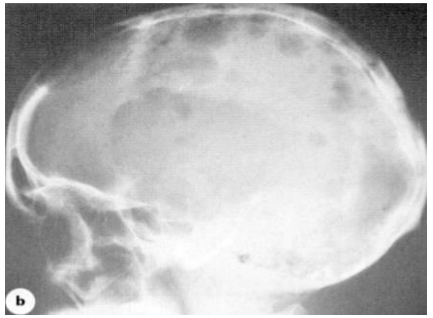
Mark*

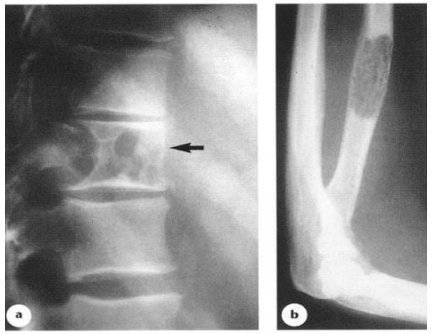
- Myeloma Work Up
  - Peripheral blood:
    - Calcium: 9.5mg/dL (ULN 10.6mg/dL)
    - Albumin: 3.3mMol/L (LLN 3.5 mMol/L)
    - B_2M: 2.58 mg/dL (ULN 2.64mg/dL)
    - Creatinine: 2.1 mg/dL (ULN 1.3mg/dL)
    - Hgb: 10.9g/dL
    - κ/λ-light-chain ratio: 185 (ULN: 1.65)
  - Bone Marrow Biopsy:
    - 70% +kappa PC
    - Cytogenetics: 46xy; FISH: normal
  - Skeletal survey & spine MRI:
    - Lytic lesions on ribs, skull, femur
- Diagnosis: Active Myeloma ISS Stage 2

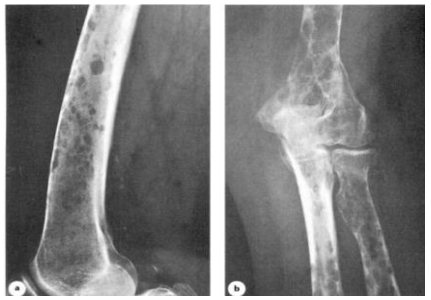
*HIPPA-compliant stock photo (not actual patient)

B_2M = beta-2 microglobulin; FISH = fluorescent in situ hybridization; Hgb = hemoglobin; PC = plasma cells; PCLI = plasma cell labeling index; ULN = upper limit of normal

Multiple Myeloma and Bone Lesions







At relapse

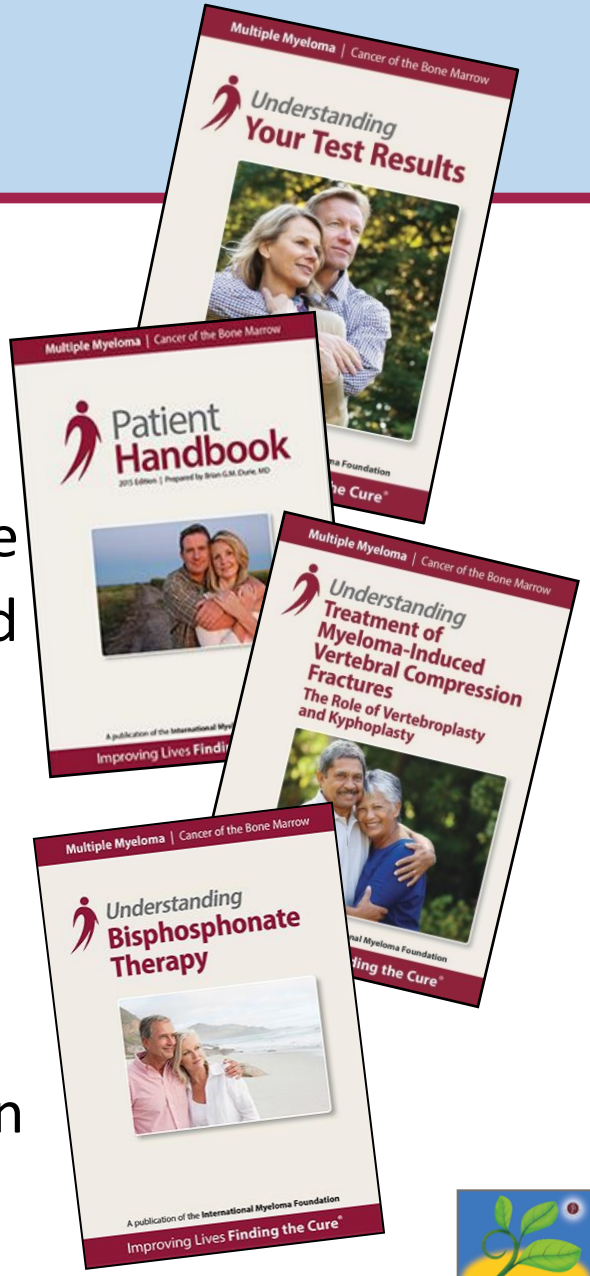
Bone imaging – type depends on symptoms

Bone Disease in Myeloma

- ~85% of myeloma patients develop bone disease
- Bone destruction may lead to hypercalcemia and contribute to renal impairment

Nursing Implications

- Coordinate among treatment team if needed
- Educate patients on protecting bone health
- Educate patients on symptoms of bone disease
- Are fracture precautions necessary—ask clinician



Miceli TS, et al. *Clin J Oncol Nursing.* 2011;15(4)suppl:9-23; Dimopoulous M, et al. *Leukemia.* 2009; 23(9):1545-56.

Bone Health Supportive Care

Kyphoplasty or vertebroplasty for vertebral compression:

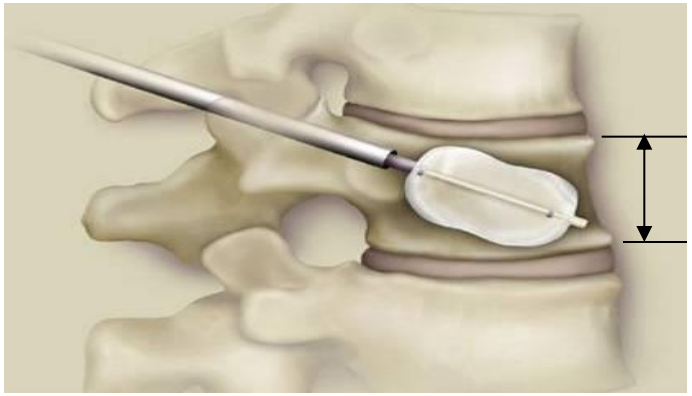
- Other bone interventions include surgery or radiation (used less often)

Bisphosphonates to improve bone health recommended for all patients receiving anti-myeloma therapy

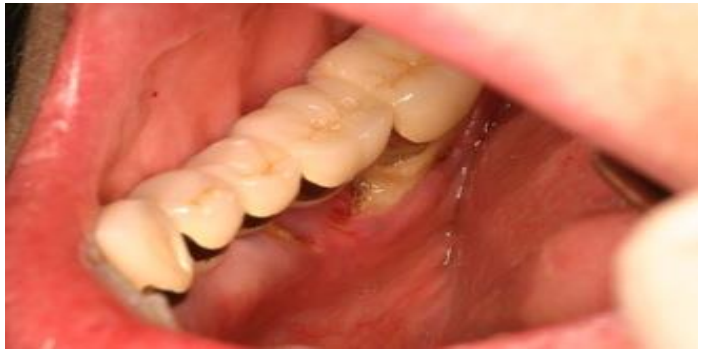
- Pamidronate
- Zoledronic acid (zol)

} bisphosphonates

- Denosumab monoclonal antibody non-inferior to zoledronic acid*



Kyphoplasty for Vertebral Compression



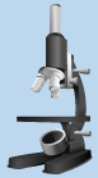
Osteonecrosis of the jaw

Nursing implications for bisphosphonates:

- Acute phase reaction: 11% fever, chills
- Dental health (dental exams every 6 months)
- Renal (24-hr urine)

* Recent research results; currently not FDA-approved (Amgen press release October 20, 2016).

Terpos E, et al. *J Clin Oncol.* 2013;31:2347-2357; NCCN Multiple Myeloma Guidelines v3.2015; Miceli TS, et al. *Clin J Oncol Nursing*. 2011;15(4)suppl:9-23; Coleman RE. *Br J Cancer.* 2008;98(11):1736-1740; Morgan GJ, et al. ASH 2010 #311; Witzig T, et al. ASH 2010 #3053; Berenson J, et al. *Lancet Oncol.* 2011;12:225-235; Medtronic, Kyphon Products Division; Amgen press release October 20, 2016.



Induction Regimens for Newly Diagnosed MM Patients

Common Induction Regimens

- **Transplant eligible:** three drug induction regimen: VRd (also written RVd)

- **Transplant ineligible:**
  - Three drug induction VRd for fit patients
  - Two drug regimens (eg, Rd or Vd) in frail or elderly patients
  - Continuous Rd therapy was superior to shorter duration Rd or MPT (FIRST trial)

Clinical Trials

- Experimental front line regimens in phase III
  - KRd vs VRd (NCT01863550)
  - Daratumumab (monoclonal antibody) Rd vs Rd (NCT02252172)
  - Pembrolizumab (immuno-oncology agent) Rd vs Rd (NCT02579863)
  - DVMP vs VMP (NCT02195479)
- Many, many phase I and II trials

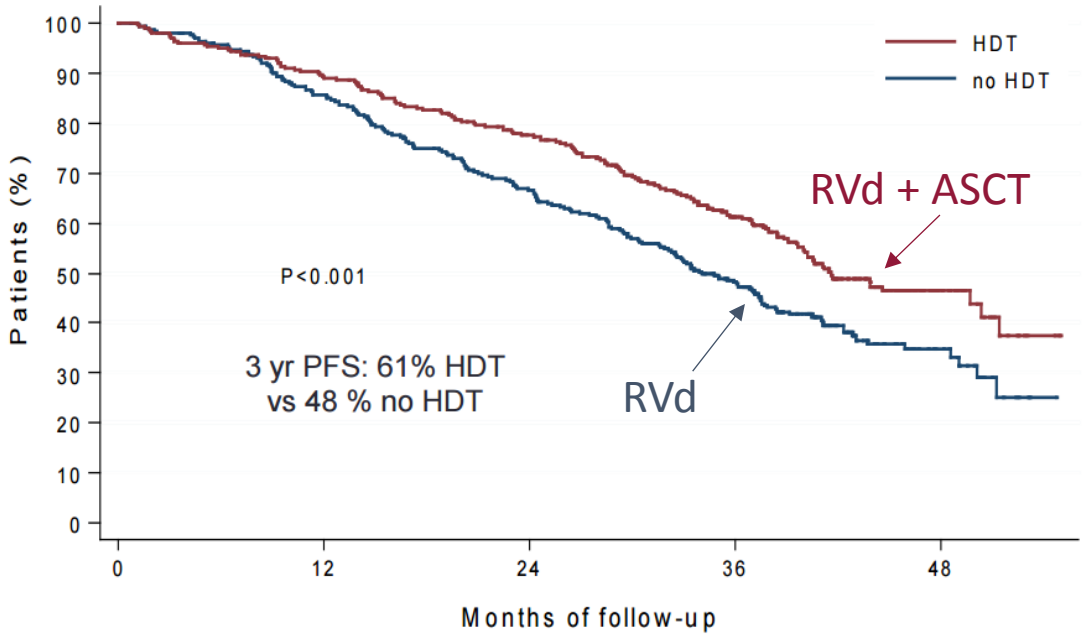
KRd = carfilzomib- lenalidomide-dexamethasone; MPT = melphalan-prednisone-thalidomide; Rd = lenalidomide-dexamethasone; Vd = bortezomib-dexamethasone; VRd = bortezomib-lenalidomide-dexamethasone.

Faiman B, et al. *J Adv Pract Oncol* 2016; 2016: 7(suppl 1):17-29; Palumbo A, et al. *NEJM.* 2014; 371(10):895-905; Attal et al. ASH 2015 #319; Lentzsch S, et al. ASH 2015 #1975; Attal M, et al. ASCO 2016 #8001; Hulin C, et al. *J Clin Oncol*. 2016;34:3609-3617; Clinicaltrials.gov accessed April 11, 2017.

ASCT Remains Standard of Care for Eligible Patients

IFM 2009 Clinical Trial

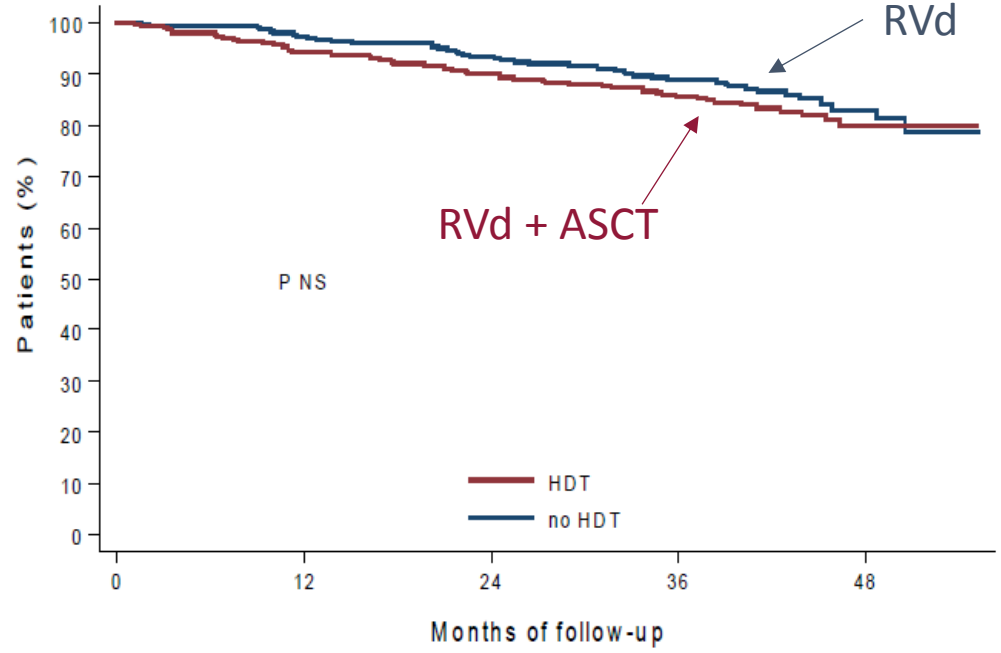
PFS



N at risk					
ASCT	350	309	261	153	27
No ASCT	350	296	228	128	24

IFM 2009 Clinical Trial

OS



N at risk					
ASCT	350	328	309	226	55
No ASCT	350	338	320	244	56

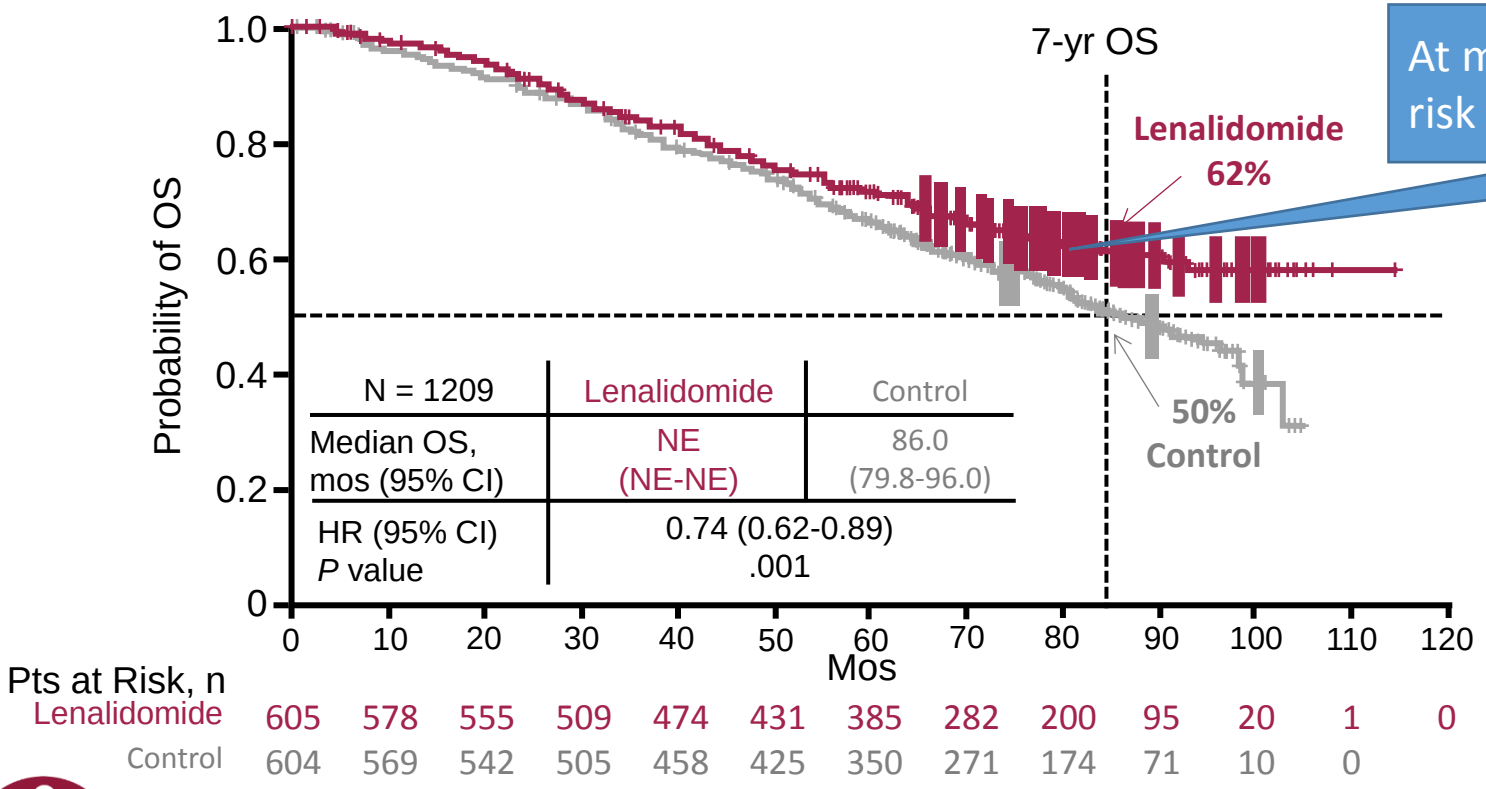
ASCT = autologous stem cell transplant; NS = not significant; OS = overall survival; PFS = progression-free survival; RVd = bortezomib-lenalidomide-dexamethasone.

Attal M, et al. ASH 2015. Abstract 391.

Lenalidomide Maintenance After ASCT Improves OS (Meta-analysis)

Trials: IFM 2005-02, CALGB 100104, GIMEMA RV-209 (N = 1209)

Treatment: lenalidomide maintenance (n = 605) vs placebo or no maintenance (n = 604)

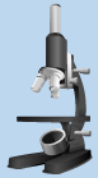


At median follow-up of 80 mos, 26% decrease in risk of death and 2.5-yr increase in median OS

OS, %	Lenalidomide	Control	P Value
OS at 5 yrs	71	66	.001
OS at 6 yrs	65	58	.001
OS at 7 yrs	62	50	.001

Risk of secondary primary malignancy post-ASCT higher in lenalidomide group (HR: 2.03; 95% CI: 1.14-3.61)

Attal M, et al. ASCO 2016. Abstract 8001.



Lenalidomide Maintenance After ASCT Is FDA-Approved

- After ASCT, lenalidomide maintenance increased PFS
  - GALGB 100104 PFS 5.7 years with maintenance vs. 1.9 years without
  - IFM 2005-02 PFS 3.9 years with maintenance vs. 2 years without
- After ASCT, lenalidomide maintenance increased OS

Lenalidomide maintenance after ASCT
10 mg Day 1-28 of 28 day cycle
FDA approved February 2017

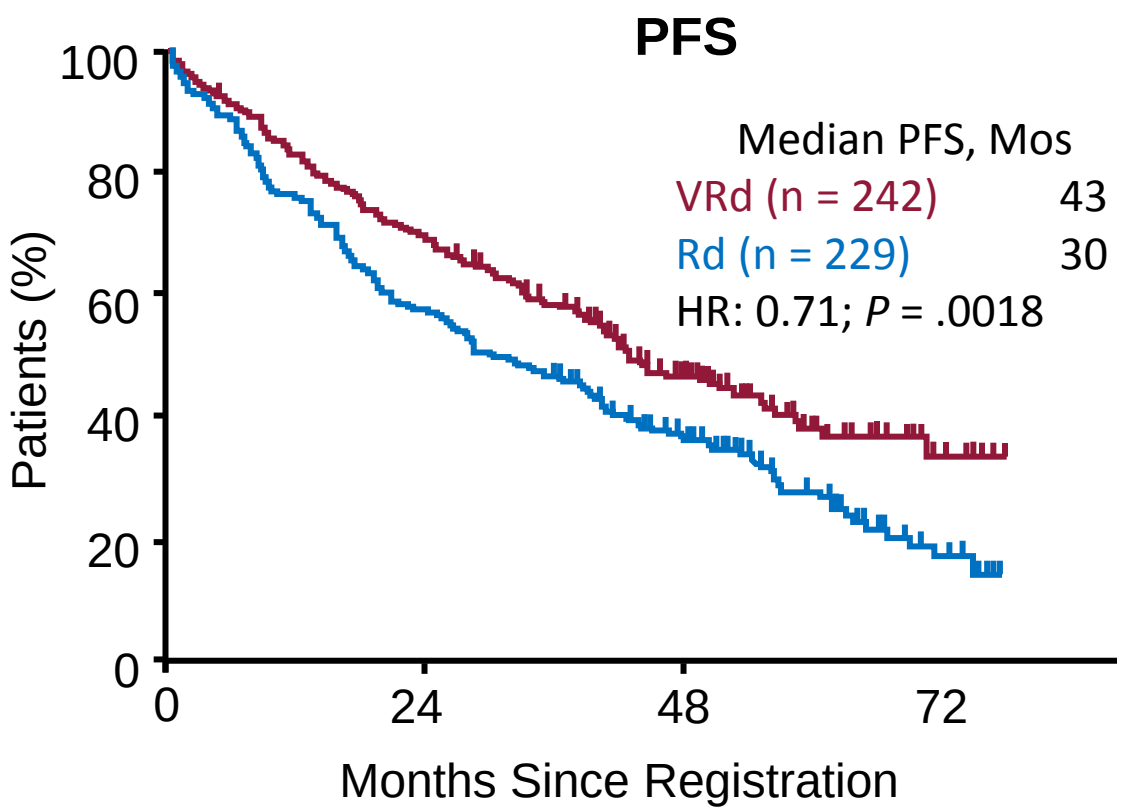
Nursing Implications

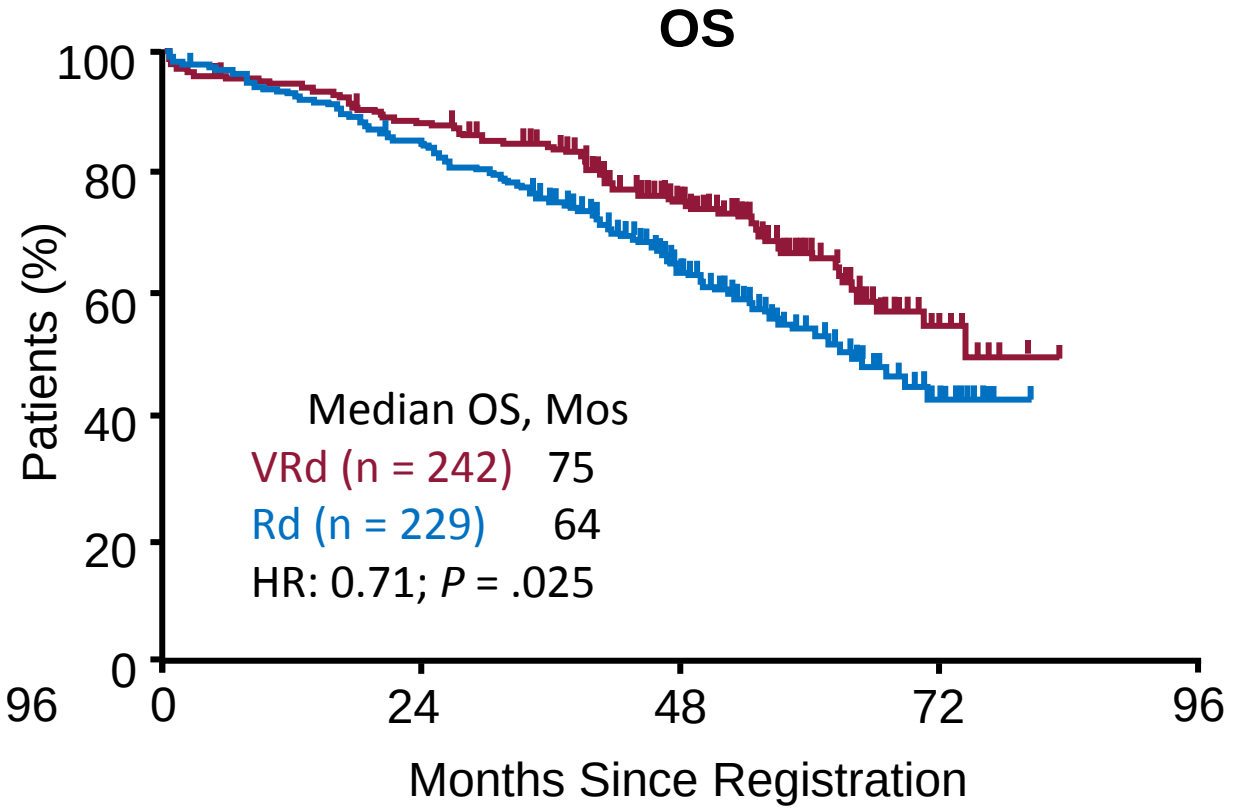
- Patients on therapy for long time: AE management, adherence, treatment fatigue, no pregnancy
  - Short term (many AEs subside after first few months) vs. long term effects (health screening)
- Patients living longer: survivorship care, coordination with PCP, emphasis on healthy behaviors
- Patient advocacy: understanding patient's changing needs/desires; advocating with extended health care team

AE = adverse event; ASCT = autologous stem cell transplant; len = lenalidomide; OS = overall survival; PCP = primary care physician; PFS = progression free survival.

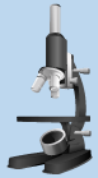
Hulin C, et al. ASH 2014 #81; Facon T, et al. ASH 2013 #2; Palumbo A, et al. *NEJM.* 2014; 371(10):895-905; Attal et al. ASH 2015 #319; Lentzsch S, et al. ASH 2015 #1975; Attal M, et al. ASCO 2016 #8001; Celgene press release February 22,2017.

3 Drug Combination Better Than 2 in Newly Diagnosed Multiple Myeloma With Delayed ASCT





ASCT = autologous stem cell transplant; HR = hazard ratio; OS = overall survival; PFS = progression-free survival; Rd = lenalidomide-dexamethasone; VRd = bortezomib-lenalidomide-dexamethasone;
Durie B, et al. ASH 2015. Abstract 25.



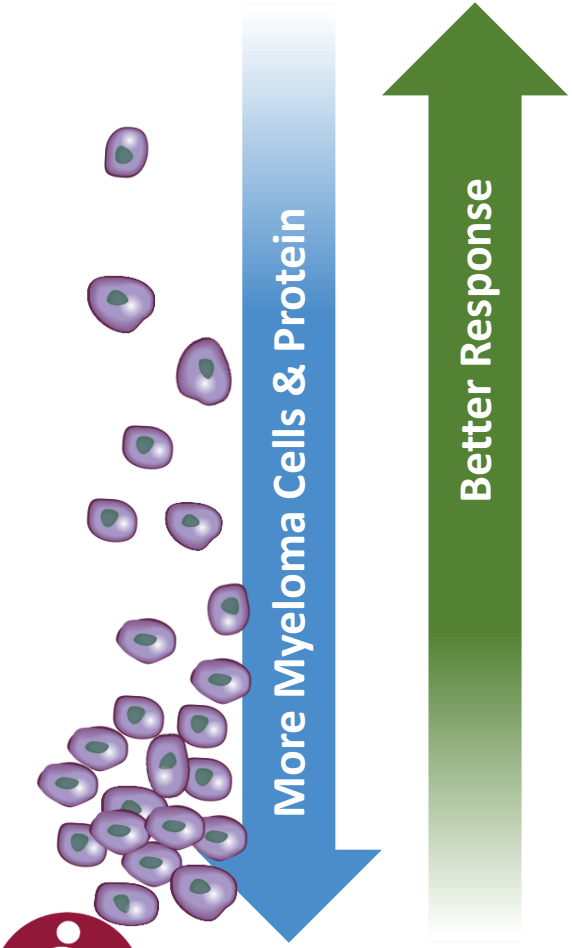
Experiment Regimen: KRd in Newly Diagnosed MM

- 8 cycles of induction and consolidation with KRd in pts with newly diagnosed MM was highly effective
  - 61% CR/sCR at end of consolidation (primary endpoint)
  - 70% of pts with negative MRD at end of consolidation
- Time to response quicker than standard intensive VRd
  - At time of transplant, 78% achieved ≥ VGPR with KRd vs ~ 50% in historical VRD studies
- No peripheral neuropathy observed with KRd but cardiovascular toxicity a concern
  - Mechanism of cardiovascular events needs further investigation

CR = complete response; KRd = carfilzomib-lenalidomide-dexamethasone; MM = multiple myeloma; MRD = minimal residual disease; sCR = stringent complete response; VGPR = very good partial response

Roussel M, et al. ASH 2016. Abstract 1142

IMWG Myeloma Response Criteria



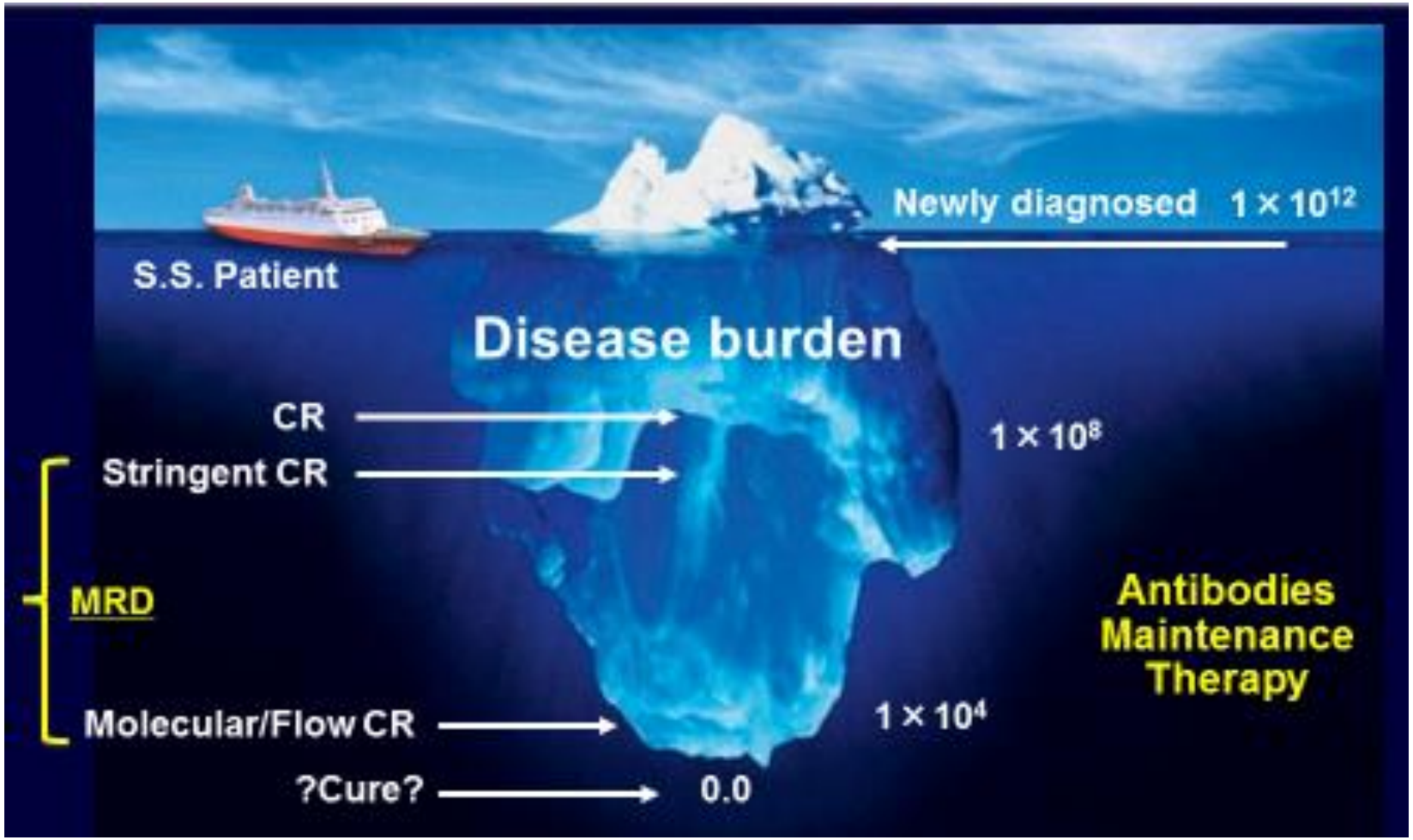
Flow MRD negative*	negative by next generation flow (minimum sensitivity 1 in 10^5 nucleated cells or higher)*
sCR	mCR AND normal FLC ratio, BM negative by flow, 2 measures
Molecular CR	CR AND negative PCR
Complete Response (CR)	Negative immunofixation; no more than 5% plasma cells in BM; 2 measures
VGPR	VGPR: 90% reduction in myeloma protein
PR	PR: at least 50% reduction in myeloma protein
MR	
SD	
PD	

sCR= Stringent Complete Response; CR = Complete Response; VGPR = Very Good Partial Response; PR = Partial Response; SD = Stable Disease; MR = Minimal Response (only in relapsed); PD = Progressive Disease

*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. *The Lancet Oncology.* 2016; 17(8):e328–e346.

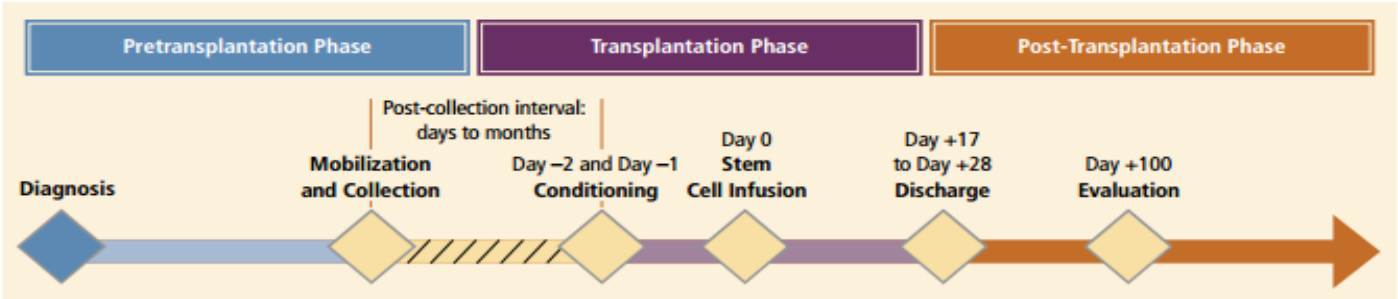
Getting to Minimal Residual Disease (MRD): New Definitions for CR



from S. Lonial; Kumar S, et al. *The Lancet Oncology.* 2016; 17(8):e328–e346.

NLB: CJON Supplement on Transplantation in MM

Clinical Pearls for Transplant Patients



- **Arrange consult early for transplant**
  - Stem cells typically collected from newly diagnosed after 3-4 cycles
- **Avoid alkylating agents and high cycles before stem cell collection**
- **Plan for receiving patients back from transplant center**
  - Maintenance therapy after transplant improves outcomes
  - Adherence to consolidation/maintenance
  - Monitoring blood counts; council patient on avoiding infection
  - Screen for depression; refer if needed
  - Recommended revaccinations
  - Survivorship care plan

Resources for Nurses:

- Clinical update
- Transplant process
- Caregiver information
- FAQ

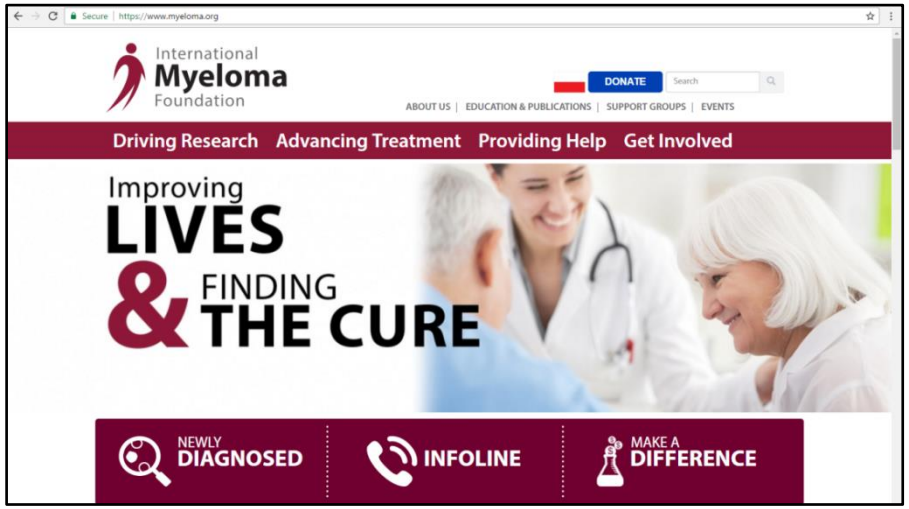
In your packet on USB drive and free on myeloma.org

CJON = Clinical Journal of Oncology Nursing; MM = multiple myeloma; NLB = Nurse Leadership Board

NLB Transplantation supplement. *Clin J Oncol Nurs*. 2013;17(6) suppl; NLB survivorship care plan supplement. *Clin J Oncol Nursing.* 2011;15(4)suppl; NLB consensus guidelines supplement. *Clin J Oncol Nursing.* 2008;12(3)suppl. Tariman JD et al. *J Adv Pract Oncol.* 2014;5:115–122. Palumbo A, et al. *NEJM.* 2014; 371(10):895-905.

Many Resources From IMF for Newly Diagnosed Patients

Multiple languages available
Free download or order hard copies at myeloma.org



IMF website with many resources including newly diagnosed at myeloma.org

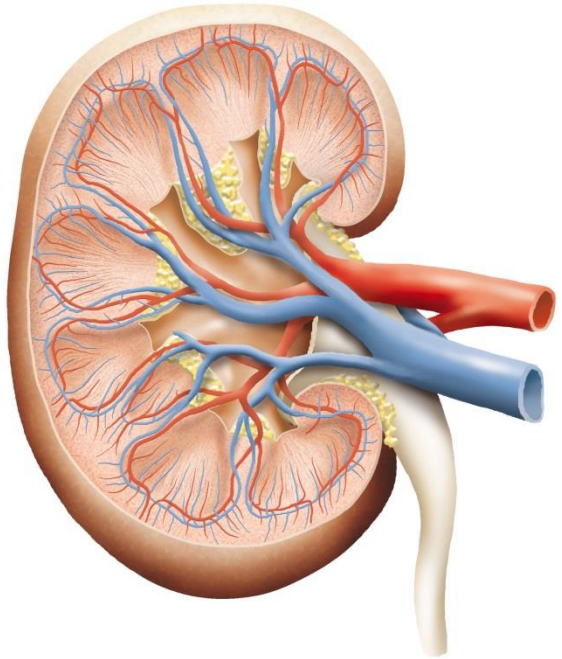
Infection Prevention: Crucial in Myeloma Patients

- Compromised immunity from MM disease & treatment
  - Good personal hygiene (skin, oral)
  - Environmental control (wash hands, avoid crowds and sick people, etc)
  - Prompt medical attention at signs of infection(e.g., fever, chills)
  - Medications (antibacterial, antiviral)
  - Growth factor (e.g., filgrastim)
  - Intravenous immunoglobulin for hypogammaglobulinemia
  - Immunizations (NO live vaccines)
    - Pneumococcal vaccination (13 and 23)
    - Seasonal inactivated influenza

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

Renal Health

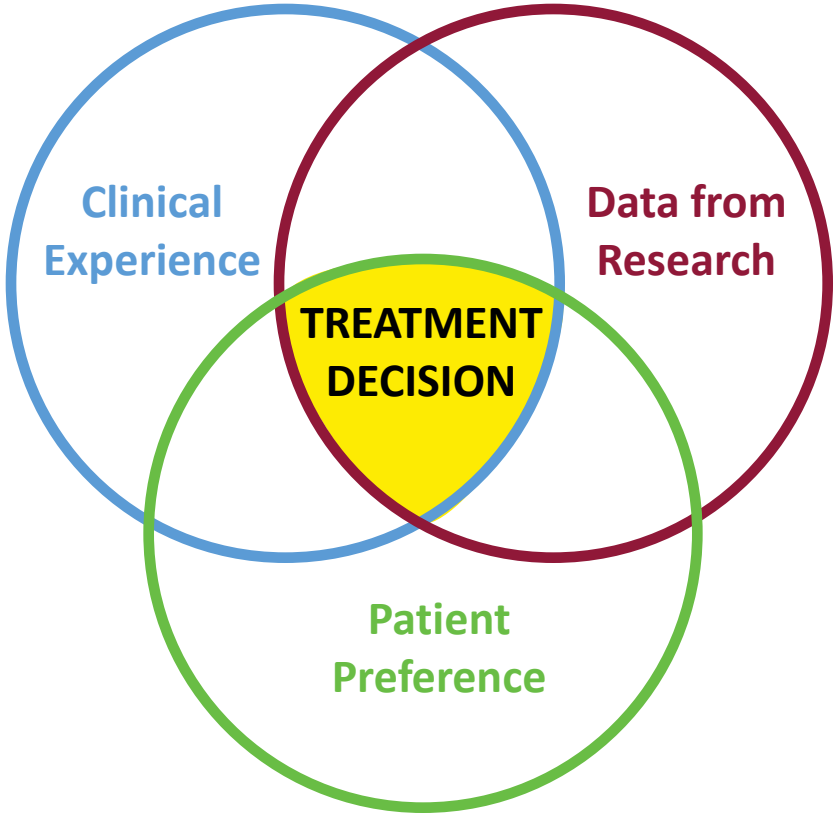
- Risk Factors
  - Active multiple myeloma (protein, casts)
  - High calcium
  - Other medical issues
- Symptoms
- Prevention
  - Avoid certain medications (IV contrast, NSAIDs)
  - Hydration (DRINK WATER)
- Treatment
  - Correct underlying cause e.g., treat myeloma causing renal dysfunction
  - Use myeloma treatments that have quick response and minimal kidney excretion



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

Case #2: Mark*

- Treatment Decision
  - Considered available trials
    - Concerns about office visits with working
  - Decided on three drug induction regimen:
    - VRd bortezomib/lenalidomide/dex
  - Supportive agents:
    - Zoledronic acid
  - Nursing key points
    - Kidney function and bone health
    - Subcutaneous bortezomib (reduced PN)
    - Dex same time each day
    - Aspirin, acyclovir prophylaxis



Philippe Moreau, ASH 2015

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

- Institute of Medicine Recommendation:
  A Survivorship Care Plan for Each Survivor
  - Record of Care
    - Diagnosis including diagnostic tests & 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 & who provides them
    - Late/long-term effects of treatments
    - Recommendations/resources for healthy behaviors, support, cancer prevention, etc.

Institute of Medicine. Cancer Survivorship Care Planning. Fact Sheet Nov 2005. www.iom.edu. Salz T, et al. *Cancer*. 2013 Dec 10. doi: 10.1002/cncr.28472; *Clin J Oncol Nursing.* 2011;15 (4)suppl. Kurtin, S. (2015). Multiple Myeloma (second edition): Tariman and Faiman (eds).

CASE #2:

Mark*

- Achieved a CR after 4 cycles
  - Stem cell collection
  - Autologous stem cell transplant
  - Len maintenance therapy
- MRD testing planned for 1 year
- Survivorship care plan
  - Diagnosis and test results
  - Treatment received
  - Follow up plan
  - Coordination with PCP
  - Long-term risks

*HIPPA-compliant stock photo (not actual patient)

CASE #3:

Julia*

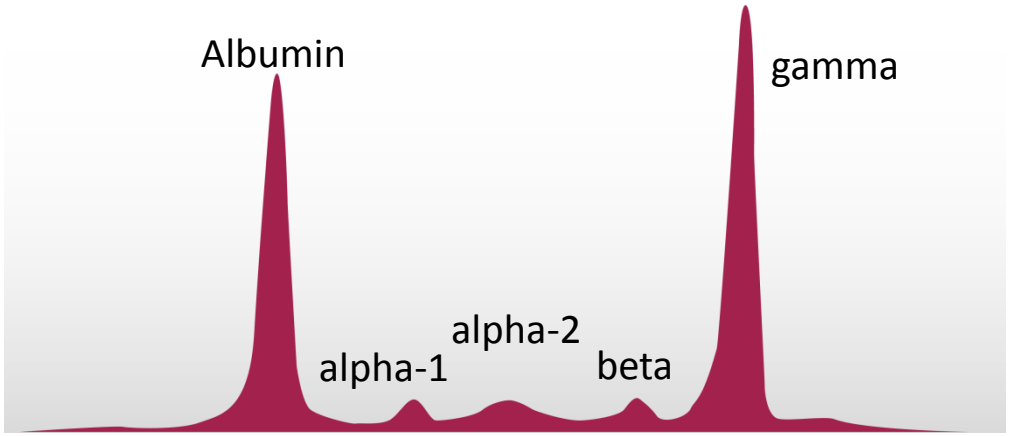
- Widowed, retired teacher 62 years old
- September 2014
  - Suspicious blood work at check up
  - Multiple myeloma diagnosed
  - VRd 8 cycles induction + lenalidomide maintenance
  - Declined ASCT
  - Normal cytogenetics
- January 2017: biochemical relapse
  - Asymptomatic rising sFLC and M spike over 9 mos
  - Protein of 1.4 g/dL
  - Mild anemia
  - Skeletal survey: suspected new lesions
  - No neuropathy

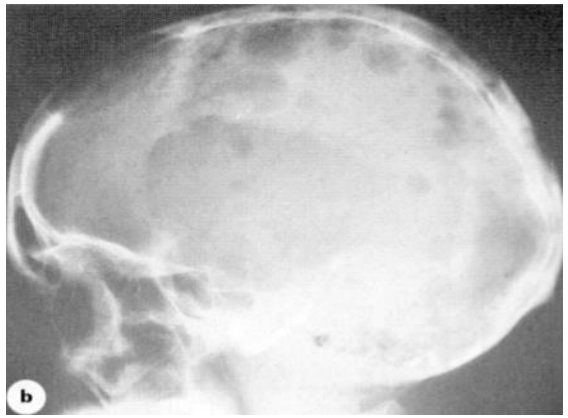
*HIPPA-compliant stock photo (not actual patient)

ASCT = autologous stem cell transplantation; sFLC = serum free light chain; VRd = bortezomib-lenalidomide-dexamethasone.

Relapse Workup

- **Lab tests**
  - Serum protein electrophoresis (SPEP)
  - Urine protein electrophoresis (UPEP)
  - CBC + differential + Chemistry (metabolic panel)
  - FLC ratio of free kappa/lambda light chains (plasma)
  - Monoclonal protein analysis (MPA)
- **Cytogenetics & FISH**
- **Imaging:**
  - Skeletal survey
  - MRI, CT, PET scan ± MRI depending on situation



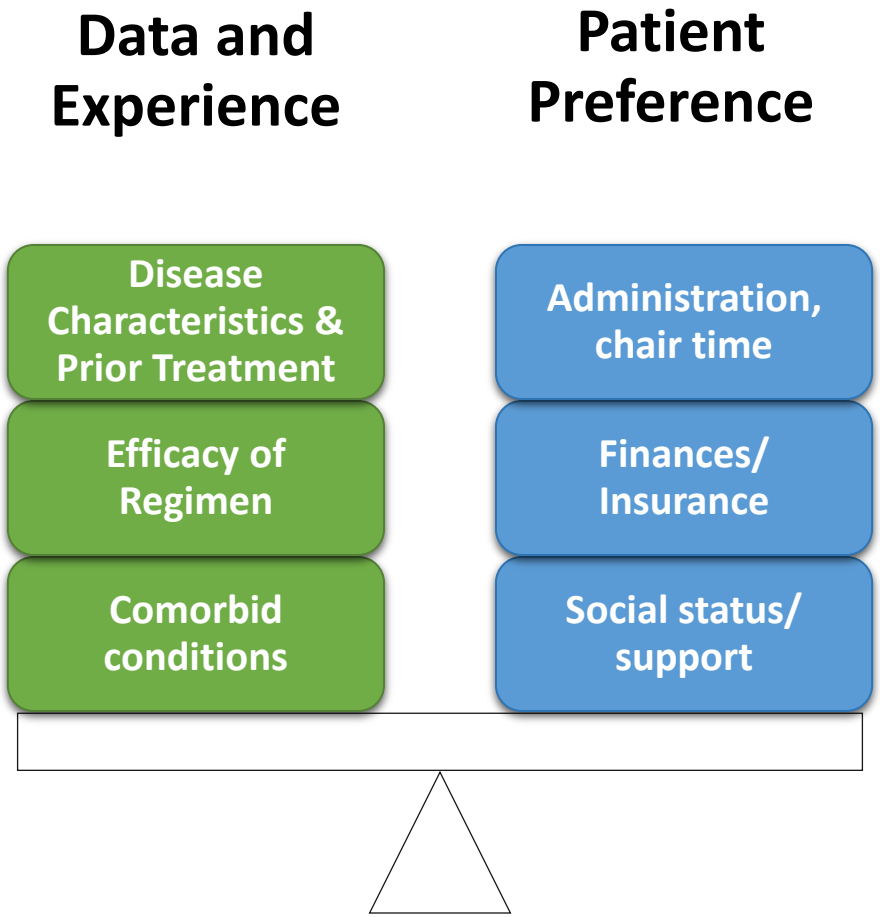


Ghobrial IM, et al. *Blood*. 2014;124:3380-3388. Rajkumar SV, et al. *Lancet Oncol.* 2014;15:e538-3548.
Faiman B. *Clin Lymphoma Myeloma Leuk*. 2014;14:436-440.

Many, Many Choices at Relapse/After 1+ Prior Myeloma Therapies

Newer FDA-approved after 1+ myeloma therapies*	Comments	Combinations*
Carfilzomib	IV	KRd, Kd
Pomalidomide	oral	Pd
Elotuzumab	IV	ERd
Daratumumab	IV/oral	DRd, DVd
Ixazomib	oral	IRd
Panobinostat	oral/IV	Pano-Vd

*Lenalidomide (R) and/or Bortezomib (V) are used in second-line combinations

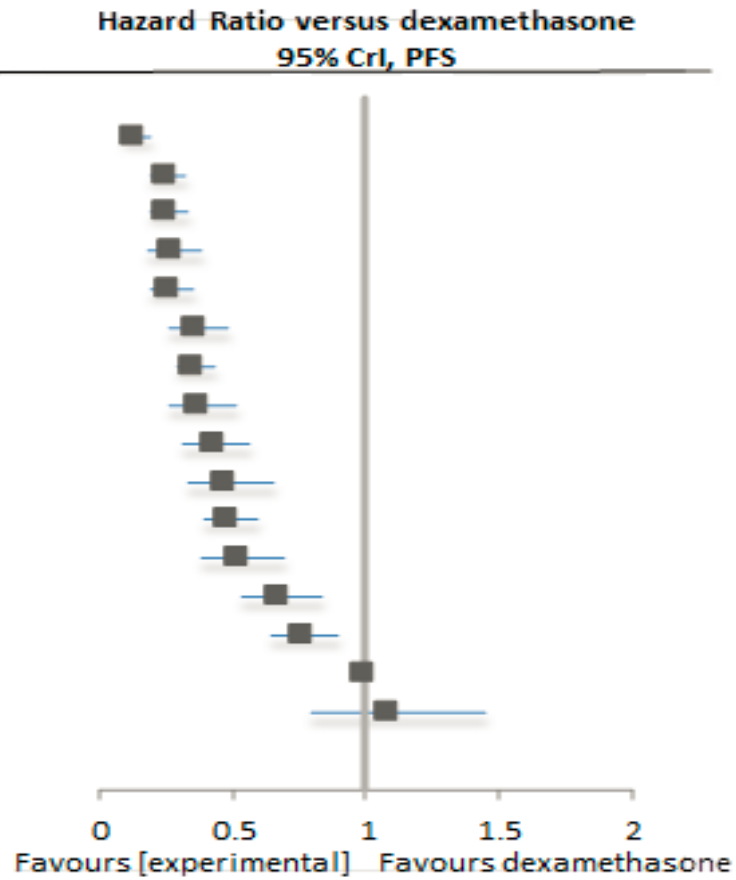


Faiman B, et al. *J Adv Pract Oncol* 2016; 2016: 7(suppl 1):17-29; Philippe Moreau, ASH 2015.

Meta-Analysis of Treatments for RRMM

- Since 2000, 15 new treatments were approved for relapsed/refractory MM
- Systematic literature review of all available phase 3 randomized controlled trials on PFS

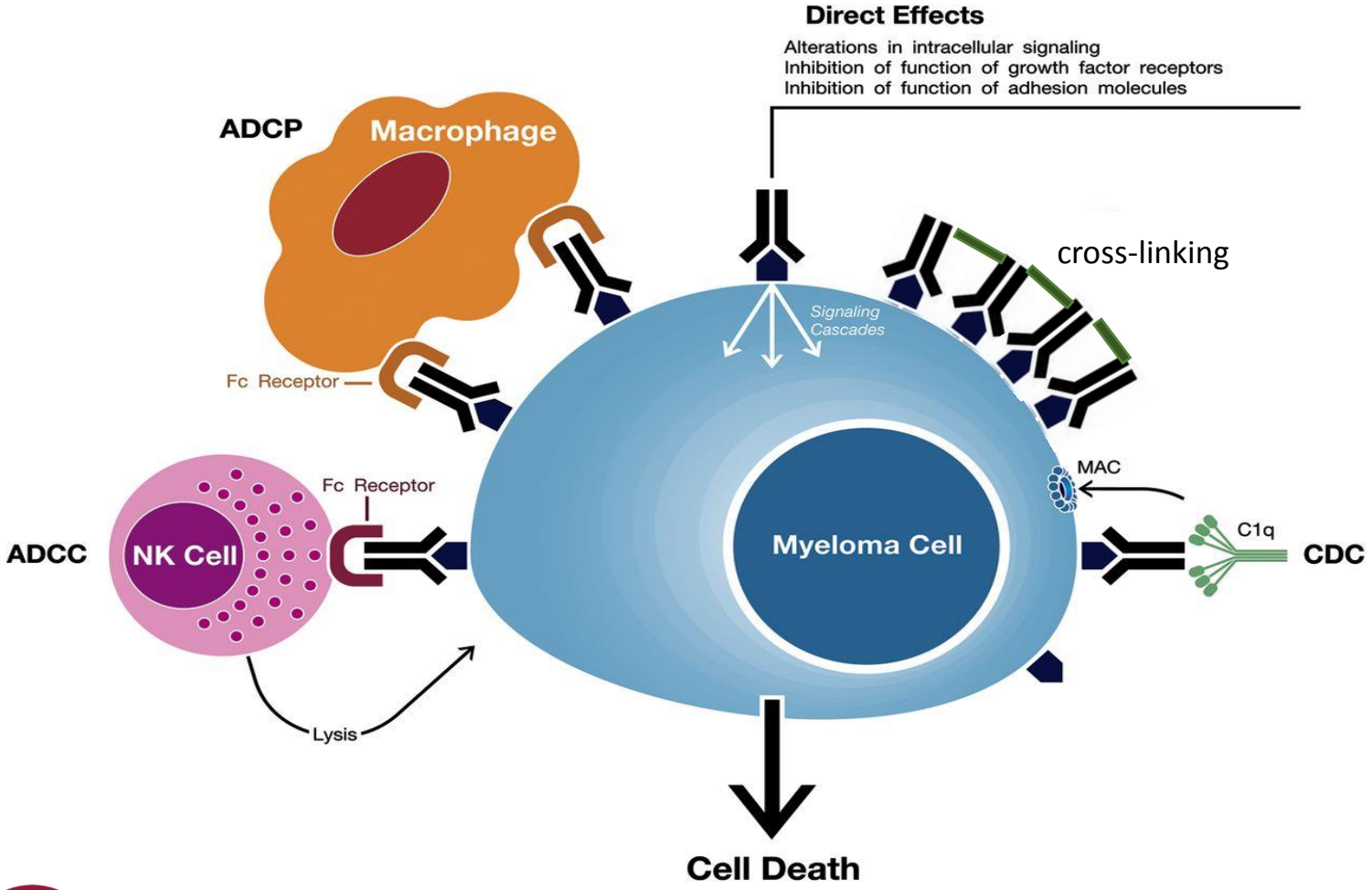
Treatment	% being best treatment	Hazard Ratio vs dexamethasone 95% CrI, PFS
DaraLenDex	99%	0.13 [0.09,0.19]
CarLenDex	0%	0.24 [0.18,0.32]
EloLenDex	0%	0.25 [0.19,0.33]
DaraBorDex	1%	0.27 [0.18,0.38]
IxaLenDex	0%	0.26 [0.19,0.35]
CarDex	0%	0.36 [0.26,0.48]
LenDex	0%	0.35 [0.29,0.43]
PegIDoxBor	0%	0.37 [0.26,0.52]
PanoBorDex	0%	0.43 [0.31,0.56]
BorThalDex	0%	0.47 [0.33,0.65]
PomDex	0%	0.48 [0.39,0.6]
VorinoBor	0%	0.52 [0.38,0.69]
Bor/BorDex	0%	0.67 [0.53,0.84]
Thal/ThalDex	0%	0.76 [0.64,0.9]
Dex	0%	1
ObIDex	0%	1.08 [0.79,1.45]



RRMM = relapsed/refractory multiple myeloma; PFS = progression-free survival.

Van Beurden-Tan, C. Systematic Literature Review and Network Meta-Analysis of Treatments for Relapsed/Refractory Multiple Myeloma Patients. ASH 2016.

Daratumumab Mechanism



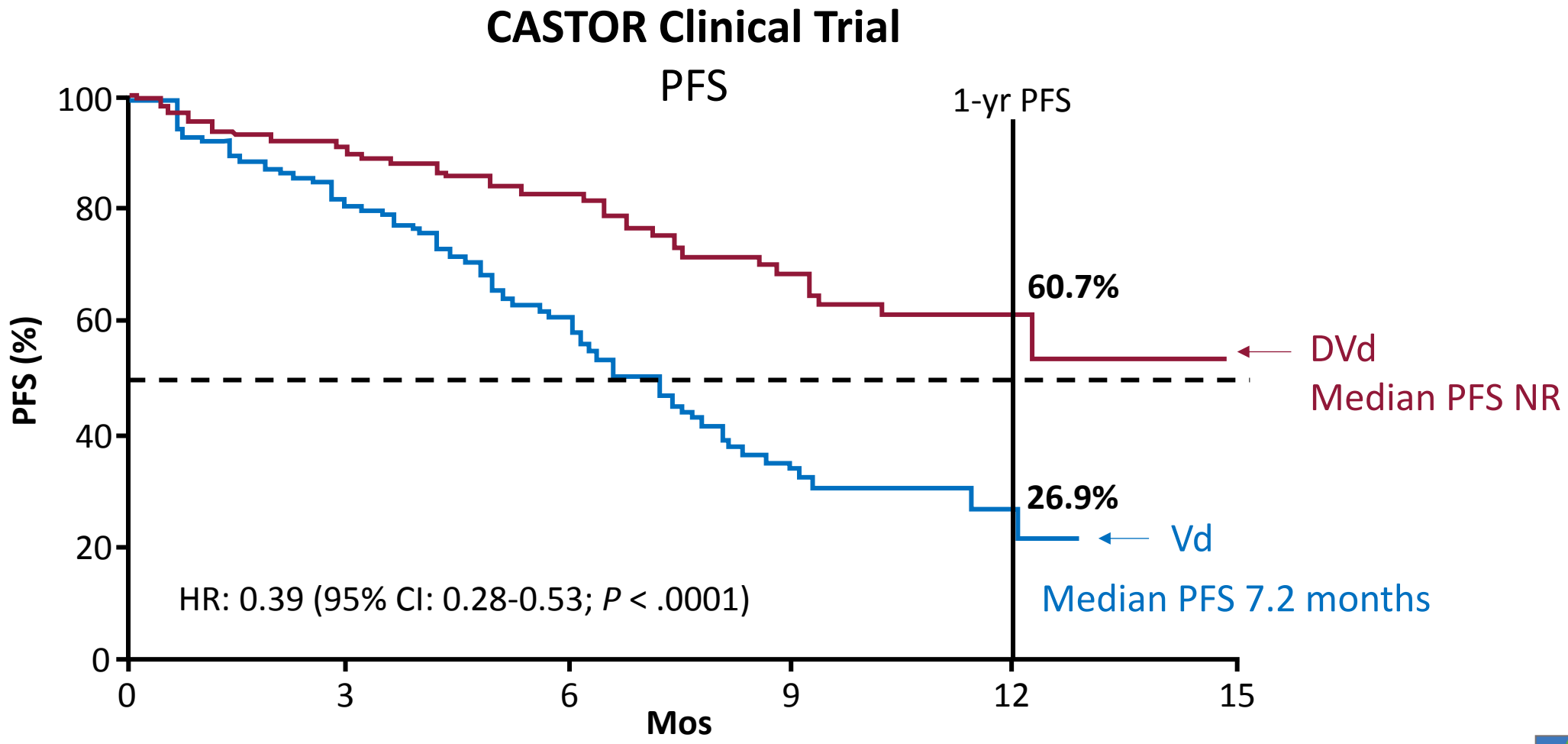
Daratumumab FDA approved November 2015

The mechanism of action of daratumumab includes immunomodulatory effects:

- ADCC = antibody-dependent cell-mediated cytotoxicity
- ADCP = antibody-dependent cellular phagocytosis
- CDC = complement-dependent cytotoxicity
- MAC = membrane attack complex.

Image adapted from Van de Donk N, et al. *Blood 2016*; 127(6):681-695; Gleason C, et al. *J Adv Pract Oncol* 2016; 7 (suppl 1): 53-57.

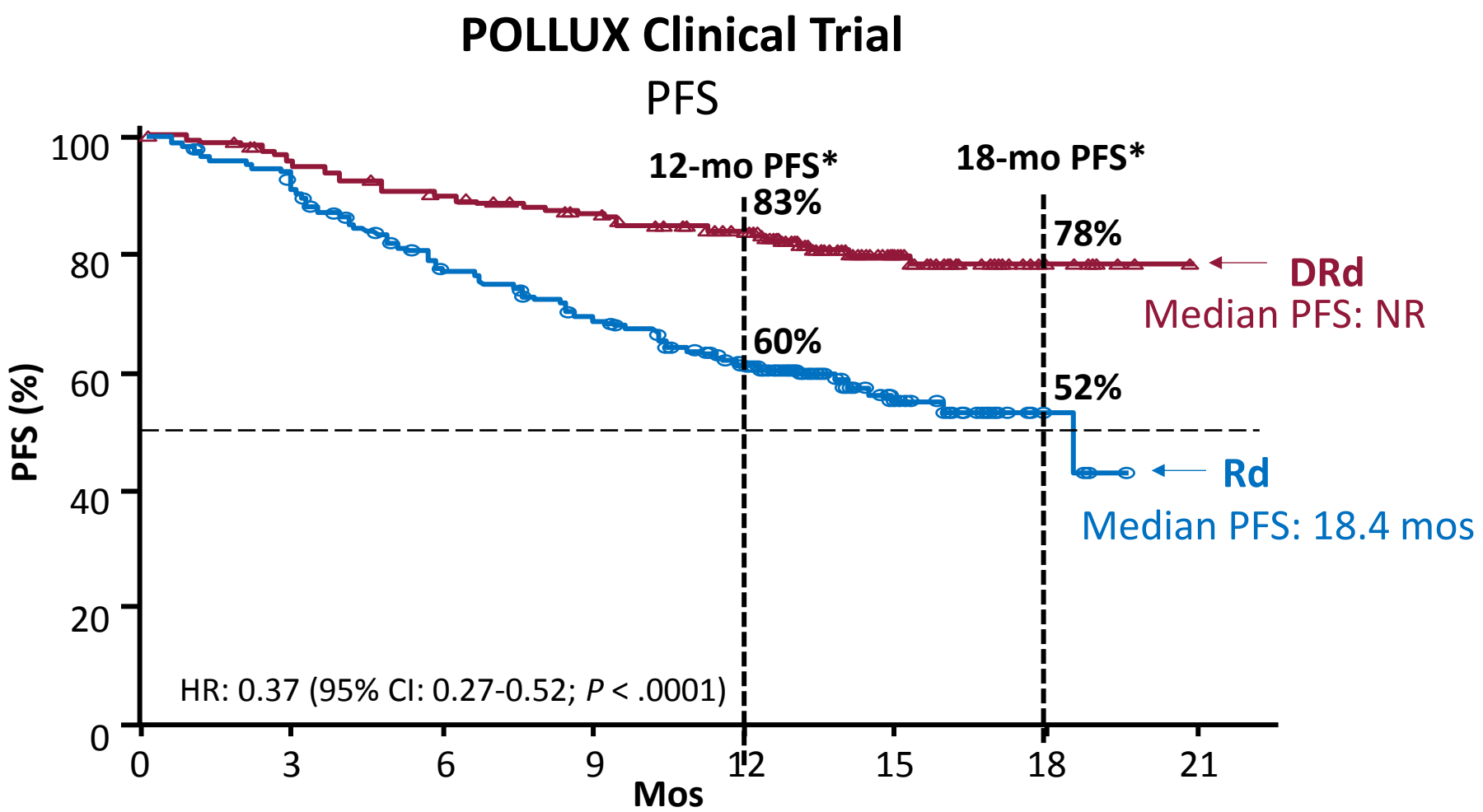
Daratumumab Improved PFS Added to Vd (bortezomib-dex)



CI = confidence interval; dex = dexamethasone; DVd = daratumumab-bortezomib-dexamethasone; HR = hazard ratio; Mos = months; PFS = progression-free survival; Vd = bortezomib-dexamethasone.

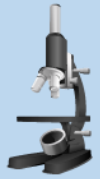
Avet-Loiseau H, et al. ASH 2016. Abstract 246.

Daratumumab Improved PFS Added to Rd (lenalidomide-dex)



CI = confidence interval; dex = dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone; HR = hazard ratio; Mos = months; PFS = progression-free survival; Vd = bortezomib-dexamethasone.

Avet-Loiseau H, et al. ASH 2016. Abstract 246.



Daratumumab

- Human CD38-directed monoclonal antibody
- Indication
  - In combination with Rd or Vd in MM patients with at least one prior therapy
  - As a monotherapy in MM patients who have received at least 3 prior lines of therapy including a PI and an IMiD OR are double-refractory to a PI and an IMiD
- Clinical Pearls:
  - Schedule: Wks 1-8 @ Weekly (1st dose 12 hrs; 3-4 hrs after 1st/2nd dose)
    Wks 9-24 @ every 2 weeks
    Wks 25 on @ every 4 weeks
  - Premeds: corticosteroids, antipyretics, and antihistamine
  - Post med: oral corticosteroid for 2 days after infusion
  - Educate patients about infusion expectations (schedule, reactions, etc)
  - Herpes prophylaxis

Daratumumab combinations
DRd DVd
FDA approved
November 2016

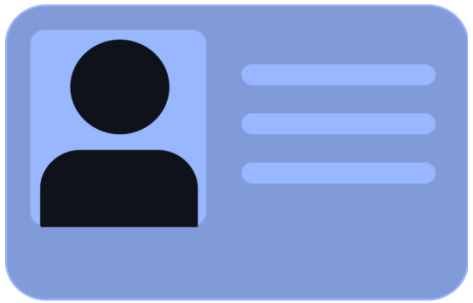
DRd = daratumumab-lenalidomide-dexamethasone; DVd = daratumumab-lenalidomide-dexamethasone; hrs = hours; IMiD = immunomodulatory agent; PI = proteasome inhibitor; Wks = weeks;

Darzalex ™ (daratumumab) Prescribing Information; Gleason C, et al. *J Adv Pract Oncol* 2016; 7 (suppl 1): 53-57.

Type and Cross Match Needs to Be Done Before Daratumumab Because of Antibody Interference With IAD

- RBC- CD38 weakly expressed on erythrocytes
  - Interference by CD38 monoclonal ABs
  - Leads to pan reactivity
  - Interference with indirect antiglobulin tests
  - Detection of irregular antibodies masked for 6 months
  - Leads to difficulty pre-transfusion testing

- Solutions for IAT interference
  - RBC genotyping before C1D1 CD38 monoclonal antibodies
  - In life-threatening situation, 0 RHD-negative blood or KELL negative blood
  - Patients should be provided with a card
  - Close monitoring for reactions with transfusion

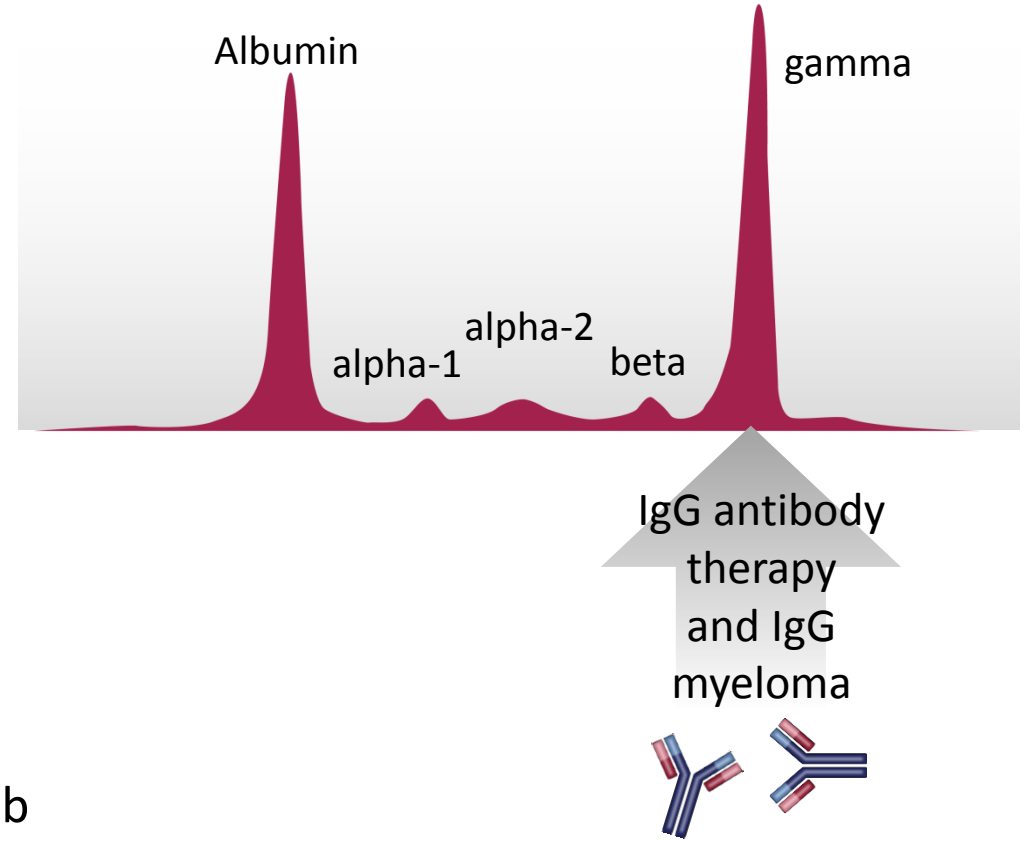


IAT = indirect antiglobulin test

Chari A, et al. ASH 2015 #3571; Van de Donk N, et al. *Blood* 2016; 127(6):681-695; Catamero D and Imran Khan ONS 2016.

Special Considerations With Antibodies (mAbs): Interference With Laboratory Tests

- Potential interference with laboratory tests
  - Antibodies can be detected in the gamma region
  - 50% of IgG Kappa M bands co-migrate with daratumumab and elotuzumab -- overestimation of M protein & reduced CR rates
  - Interference reduces after completion of therapy
- SPEP and Immunofixation Solutions
  - Development of daratumumab interference reflex assay (DIRA assay)
  - Shifts migration of daratumumab
  - Performed in IgG K <2 and deep response achieved
  - New assays in development for elotuzumab, isatuximab



Chari A, et al. ASH 2015 #3571; Van de Donk N, et al. *Blood* 2016; 127(6):681-695; Catamero D and Imran Khan ONS 2016.

CASE #3:

Julia*

- Treatment
  - DVD (daratumumab, bortezomib, dexamethasone)
  - Just finished first 2 months
  - Tolerating therapy well
- Survivorship Care Plan
  - Prior diagnosis & treatments
  - Test results
  - Current treatment plan
  - Coordination with PCP for vaccinations & health screenings
- Health promotion; diet, exercise, lifestyle
- Support group

*HIPPA-compliant stock photo (not actual patient)

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

CASE #4: Susan*

CASE #5: William*

CASE #6: Margaret*

CASE #7: Miguel*

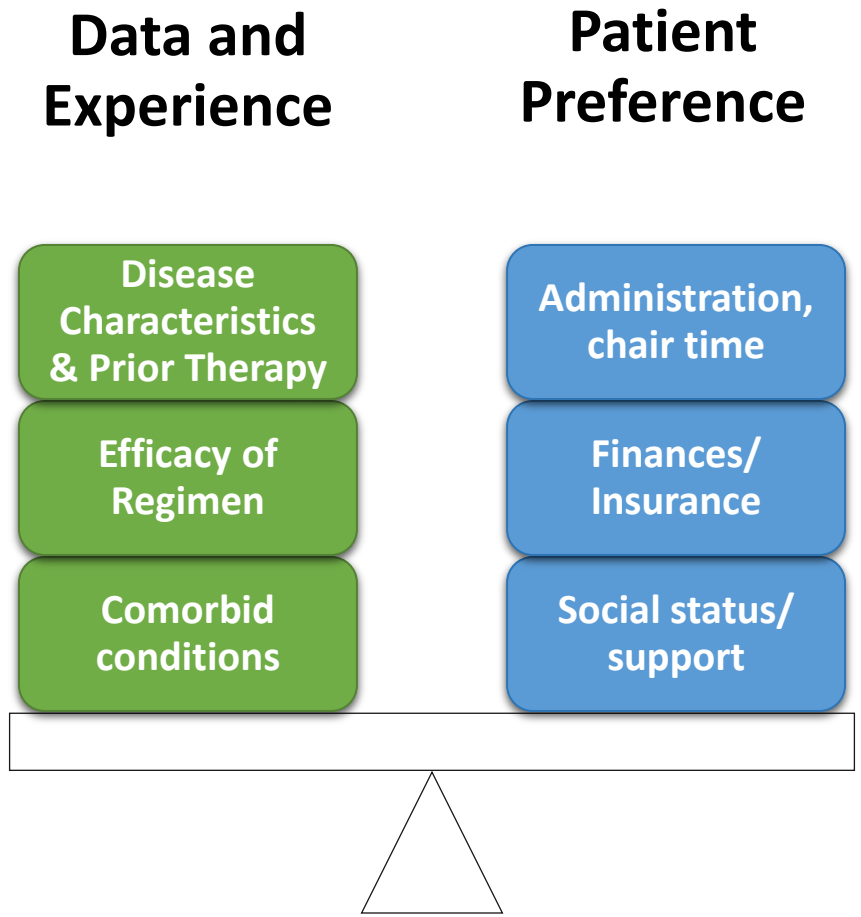
Charise Gleason, MSN, NP-BC, AOCNP

Beth Faiman, PhD, RN, MSN, APRN-BC, AOCN®

*HIPPA-compliant; not actual patient names

Practical Approach to Treatment of Patients With Relapsed Myeloma

- Disease-related factors
  - Duration of response to initial therapy
  - High-risk vs low-risk status
  - Molecular disease progression vs symptomatic progression
  - Other comorbid conditions, patient frailty
- Treatment-related factors
  - Previous therapy exposure (relapsed or refractory)
  - Toxicity/tolerability of previous regimen (combination vs single agent)
  - Mode of administration (i.e., PO or IV)
  - Cost and convenience (out-of-pocket copays for IV vs PO)
  - Patient Preference



Faiman B, et al. *J Adv Pract Oncol* 2016; 2016: 7(suppl 1):17-29; Philippe Moreau, ASH 2015.

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Risk Stratification

Mayo Clinic Risk Stratification for Multiple Myeloma (mSMART)		
Standard Risk	**Intermediate Risk**	**High Risk**
Trisomies t(11;14) t(6;14)	t(4;14) Gain(1q)	t(14:16) t(14;20) del(17p)

Mikhael et al, 2013; Rajkumar, 2016.

Less Intense Therapy Recommended for Frail Individuals; Determining Frailty: Charlson Comorbidity Index

- Predicts 10-year mortality for patients by summing scores associated with comorbid conditions and age scores by assigning points to factors
  - 1 point each: myocardial infarct, congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic lung disease, connective tissue disease, ulcer, chronic liver disease, diabetes
  - 2 points each: hemiplegia, moderate or severe kidney disease, diabetes with end organ damage, tumor, leukemia, lymphoma
  - 3 points each: moderate or severe liver disease
  - 6 points each: malignant tumor, metastasis, AIDS
  - Age scores <50 years: 0 points
    Age 50-59 years: 1 point
    Age 60-69 years: 2 points
    Age 70-70 years: 3 points

- Doublet instead of triplet therapy (e.g., Rd continuous therapy; FIRST trial)
- No ASCT
- Lower starting doses (e.g., Palumbo recommendations)

Charlson M, et al. *J Clin Epidemiol* 1994;47(11):1245-1251. D'Hoore W, et al. *J Clin Epidemiol* 1996:49(12):1429-1433. Palumbo A, et al. *Blood*. 2015;125:2068-2074

Proposed Drug Dosing by Frailty/Risk Score

Agent	Dose Level 0 (No Risk Factors)	Dose Level -1 (≥ 1 Risk Factor)	Dose Level -2 (≥ 1 Risk Factor + Grade 3/4 Nonheme AE)
Thalidomide	100 mg/day	50 mg/day	50 mg QOD
Lenalidomide	25 mg/day Days 1-21/4 wks	15 mg/day on Days 1-21/4 wks	10 mg/day Days 1-21/4 wks
Pomalidomide	4 mg/day Days 1-21/4 wks	Reduce dose to 3 mg/day or further due to hematologic toxicity, reduce dose by 50% with strong CYP1A2 inhibitor	
Bortezomib	1.3 mg/m^2 2x/wk Days 1, 4, 8, 11/3 wks	1.3 mg/m^2 1x/wk Days 1, 8, 15, 22/5 wks	1.0 mg/m^2 1x/wk Days 1, 8, 15, 22/5 wks
Ixazomib	4 mg/day Days 1, 8, 15/4 wks	First reduction: 3 mg Hold Tx if low blood counts or PN (resume at lower dose)	Second reduction: 2.3 mg/day; discontinue if grade 4 PN
Dexamethasone	40 mg/day Days 1,8,15, 22/4 wks	20 mg/day Days 1, 8, 15, 22/4 wks	10 mg/day Days 1, 8, 15, 22/4 wks
Prednisone	60 mg/m^2 Days 1-4 or 50 mg QD	30 mg/m^2 Days 1-4 or 25 mg QD	15 mg/m^2 Days 1-4 or 12.5 mg QD
Cyclophosphamide	100 mg/day Days 1-21/4 wks or 300 mg/m^2/day Days 1, 8, 15/4 wks	50 mg/day Days 1-21/ 4 wks or 150 mg/m^2/day Days 1, 8, 15/4 wks	50 mg/day Days 1-21/4 wks or 75 mg/m^2/day Days 1, 8, 15/4 wks
Melphalan	0.25 mg/kg or 9 mg/m^2 Days 1-4/4-6 wks	0.18 mg/kg or 7.5 mg/m^2 Day 1-4/4-6 wks	0.13 mg/kg or 5 mg/m^2 Day 1-4/4-6 wks

Palumbo A, et al. *Blood*. 2011;118:4519-4529. Palumbo A, et al. *Blood*. 2015;125:2068-2074.
Ixazomib [package insert]. Pomalidomide [package insert].

CASE #4:

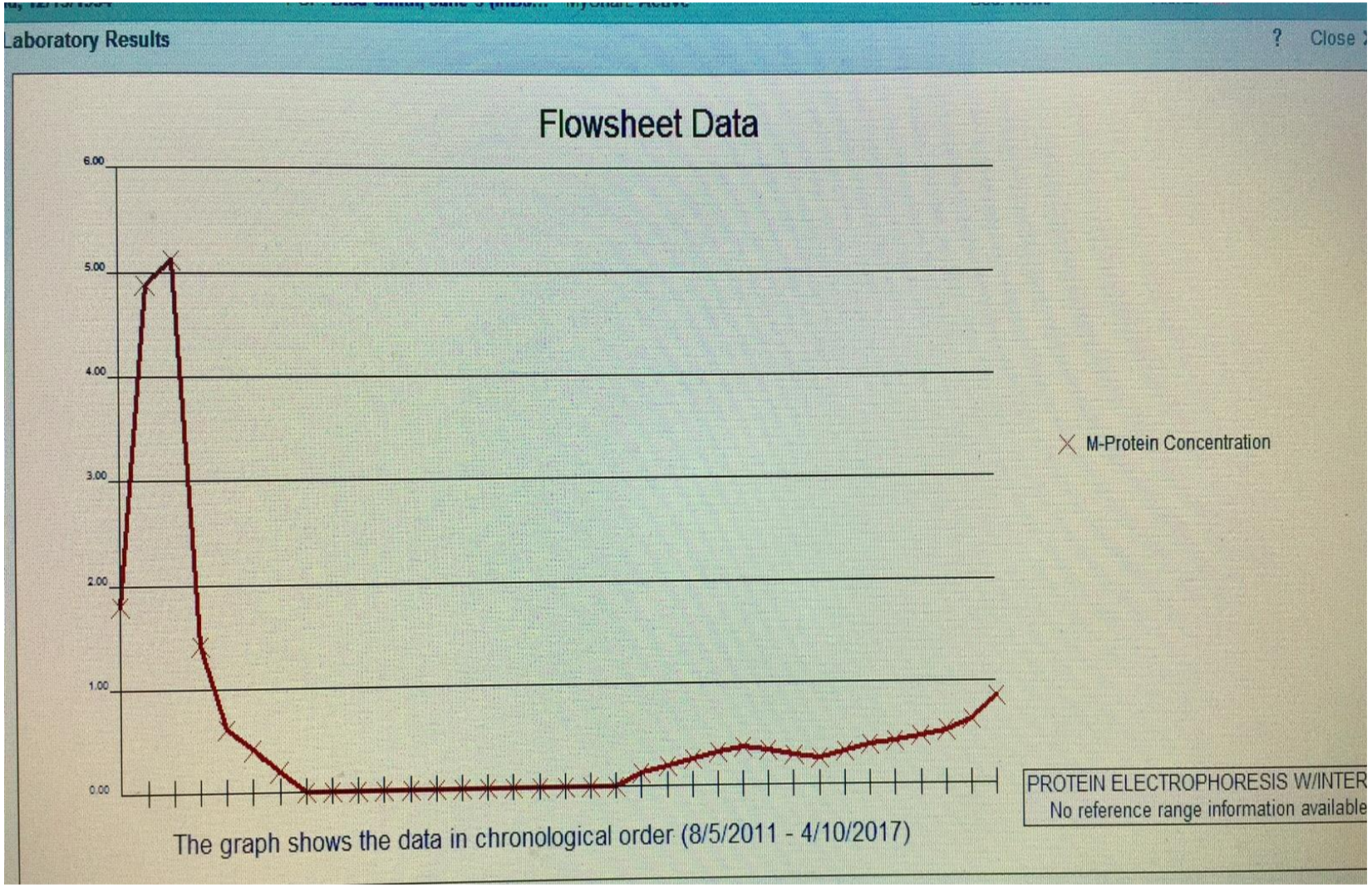
Susan*

- Divorced regional manager, 52 years old
- July 2011
  - Multiple myeloma diagnosed
  - Standard risk
  - Vd induction + ASCT
  - Len maintenance 2 years
- November 2016, now 57 years old
  - Biochemical relapse
    - PET and bone marrow genetics
  - No new genetic abnormalities
  - Unpredictable travel schedule for work
  - College-age children
  - Current smoker
  - Preferred minimal disruption to work schedule (oral regimen)

*HIPPA-compliant stock photo (not actual patient)

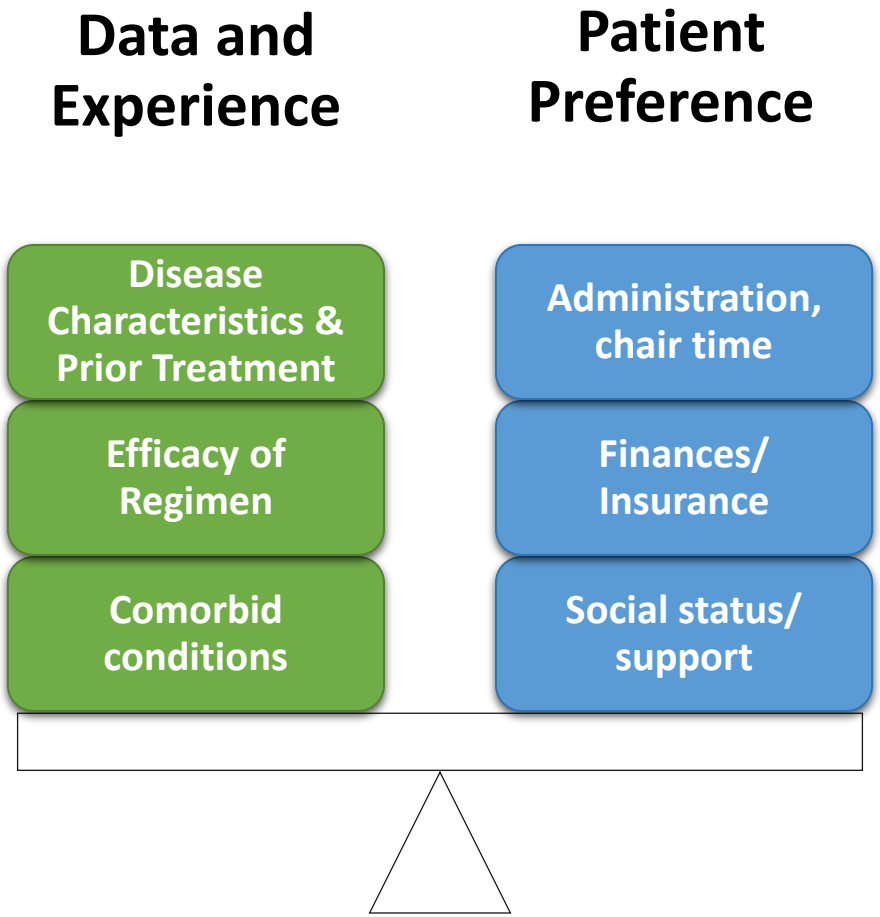
ASCT = autologous stem cell transplantation; Vd = bortezomib-dexamethasone

M spike 2011; Slow Relapse Over the Last Few Years but No Evidence of Recurrent CRAB



Oral Choices at Relapse/After 1+ Prior Myeloma Therapies

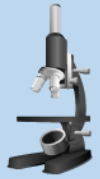
FDA-approved after 1+ myeloma therapies*	Combinations*	Comments
Carfilzomib	KRd, Kd	IV
Pomalidomide	**Pd**	**oral**
Elotuzumab	ERd	IV
Daratumumab	DRd, DVd	IV
Ixazomib	**IRd**	**oral**
Panobinostat	**Pano-Vd**	**oral but V is IV/SQ**



*Lenalidomide (R) or Bortezomib (V) are used in many 2+L combinations

IV = intravenous; SQ = subcutaneous

Faiman B, et al. *J Adv Pract Oncol* 2016; 2016: 7(suppl 1):17-29; Philippe Moreau, ASH 2015.



Ixazomib: Oral Proteasome Inhibitor

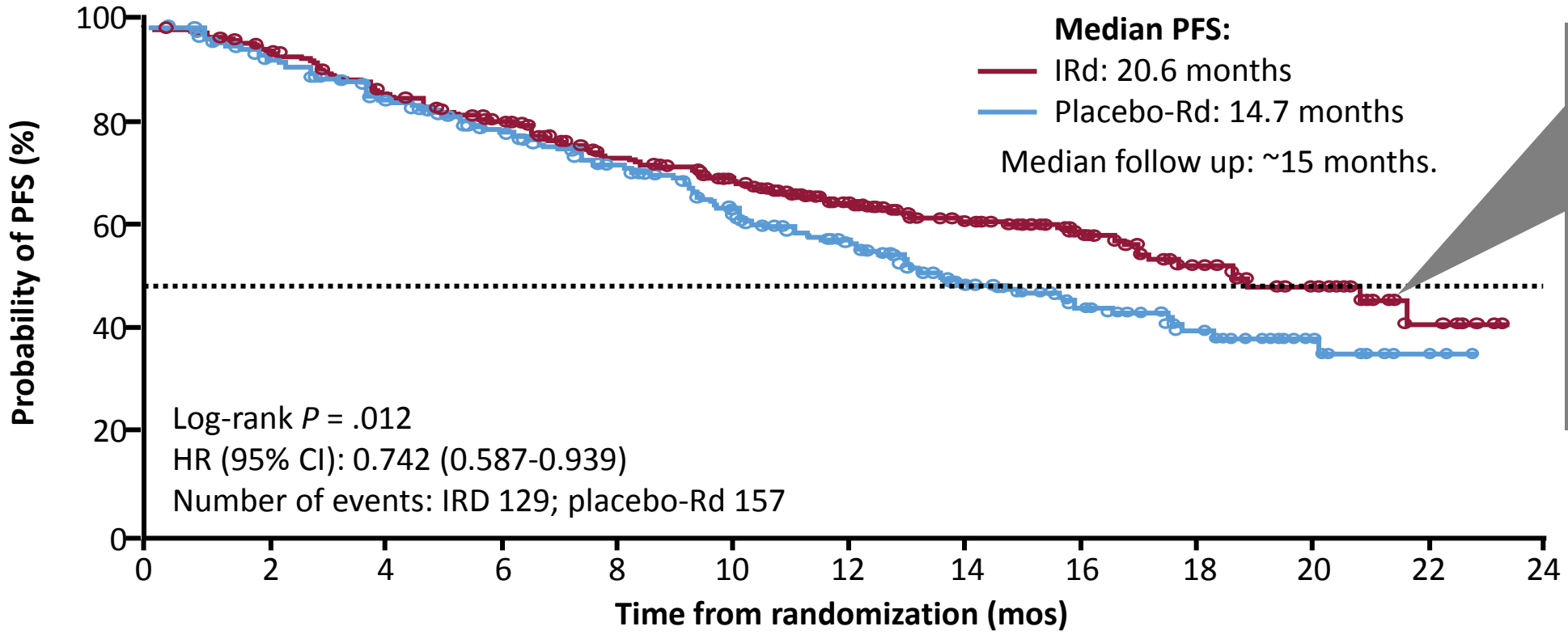
- Oral proteasome inhibitor
  - Indication: Patients with Multiple Myeloma who have received at least one prior therapy
  - In combination with Rd
- Administration
  - Oral capsule 1X per week; do not crush or chew capsules or open capsule
  - Empty stomach: 1 hr before or 2 hrs after food
- Clinical Pearls
  - Adherence, schedule, viral prophylaxis
  - Rapid response (1.1 months); fast absorption (if vomit, do NOT repeat dose)
  - Cyclic thrombocytopenia
  - Peripheral neuropathy, peripheral edema

Ixazomib+Rd
FDA approved
November 2015

Rd = lenalidomide, dexamethasone; hr = hour; hrs = hours

NINLARO® (ixazomib) prescribing information; Faiman B, et al. *J Adv Pract Oncol* 2016;7:45–52.

Ixazomib: PFS Improvement Added to Rd



CI = confidence interval; IRd = ixazomib-lenalidomide-dexamethasone; PFS = progression free survival; Rd = lenalidomide-dexamethasone

Moreau P, et al. ASH 2015. Abstract 727.

Ixazomib Dosing Calendar

Ixazomib Dosing
28-day Cycle

Recommended starting doses:

- Ixazomib 4 mg
- Lenalidomide 25 mg
- Dexamethasone 40 mg

1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28

NINLARO® (ixazomib) prescribing information; Faiman B, et al. *J Adv Pract Oncol* 2016;7:45–52.

Nurse's Role in IV and Oral Adherence

- Essential in both IV and oral therapy adherence
- Reinforce the rationale for ongoing treatment plan
  - Myeloma is a chronic condition, ongoing therapy needed
  - Patients who receive therapy live longer
  - Pill in bottle or at pharmacy are not able kill myeloma cells
- Encourage shared decision-making and mutual treatment/quality-of-life goals
- Optimize treatment; prevent and/or reduce the severity of adverse events
- Provide tools, education for AE awareness, and management
- Engage caregivers in the treatment process and education
- Offer advice (consistent time, alarm clocks, pillboxes, smart phone "alerts")
- Engage members of the interdisciplinary team to identify solutions and resources
- Combat treatment fatigue

Faiman BM. *J Adv Pract Oncol.* 2012;2:26-34; Miaskowski C, et al. *Clin J Oncol Nurs.* 2008;12(2):213-221; Gleeson T, et al. *Osteoporos Int.* 2009;20(12):2127-2134; Accordino MK and Hershman DL. *Am Soc Clin Oncol Educ Book.* 2013:271-276. Kurtin S, et al. *J Adv Pract Oncol* 2016; 7(suppl 1):71-77.

CASE #4:

Susan*

- IRd regimen chosen
  - Tolerating regimen well
  - Careful with infection prevention especially when traveling
  - Acyclovir prophylaxis
  - DVT prophylaxis
  - GI
  - Remind schedule for best absorption

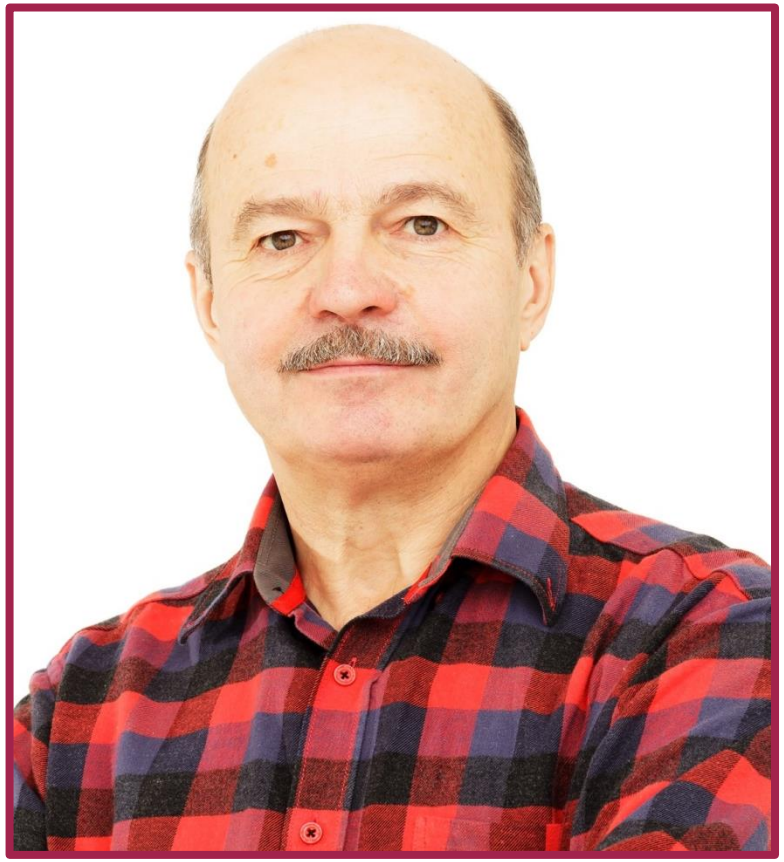
*HIPPA-compliant stock photo (not actual patient)

DVT = deep vein thrombosis; IRd = ixazomib-lenalidomide-dexamethasone

CASE #5:

William*

- Married retired contractor 74 years old
- July 2015 diagnosed with multiple myeloma
  - Standard risk
  - Rd continuous therapy; VGPR best response
- Relapse November 2016
  - Mild anemia
  - Rising paraprotein
- Considerations
  - Diabetes
  - Lives close by center
  - Some peripheral neuropathy
  - Interest in immunotherapy



*HIPPA-compliant stock photo (not actual patient)

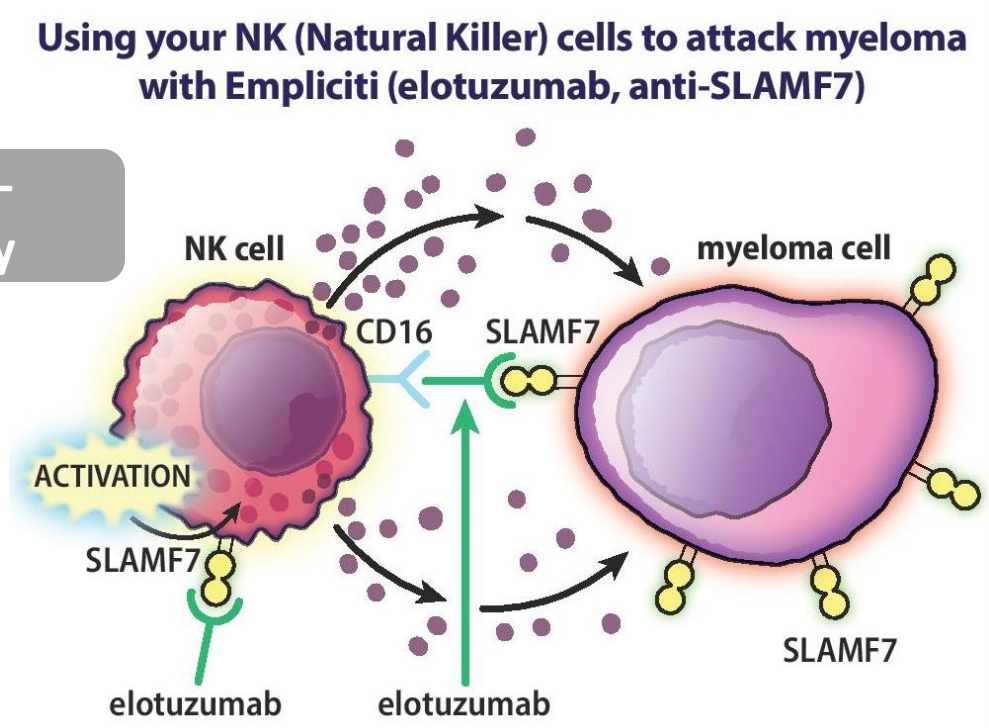
Rd = lenalidomide –dexamethasone.; VGPR = very good partial response.

Immuno-Oncology: Elotuzumab Enhances Natural Killer Cell Activity

- Monoclonal Antibody
  - For multiple myeloma patients with 1-3 prior therapies
  - In combination with len-dex

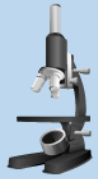
Elotuzumab+Rd
FDA approved
November 2015

Immuno-Oncology



Dex = dexamethasone; Len = lenalidomide; NK = natural killer; Rd = lenalidomide-dexamethasone; SLAMF7 = signaling lymphocytic activation molecule F7

FDA News Release Nov. 30, 2015; Liu Y-C, et al. *Blood Lymphatic Cancer: Targets Therapy*. 2014; 4:15-27; Empliciti™ Tip Card from International Myeloma Foundation.



Clinical Pearls for Elotuzumab

Immuno-Oncology

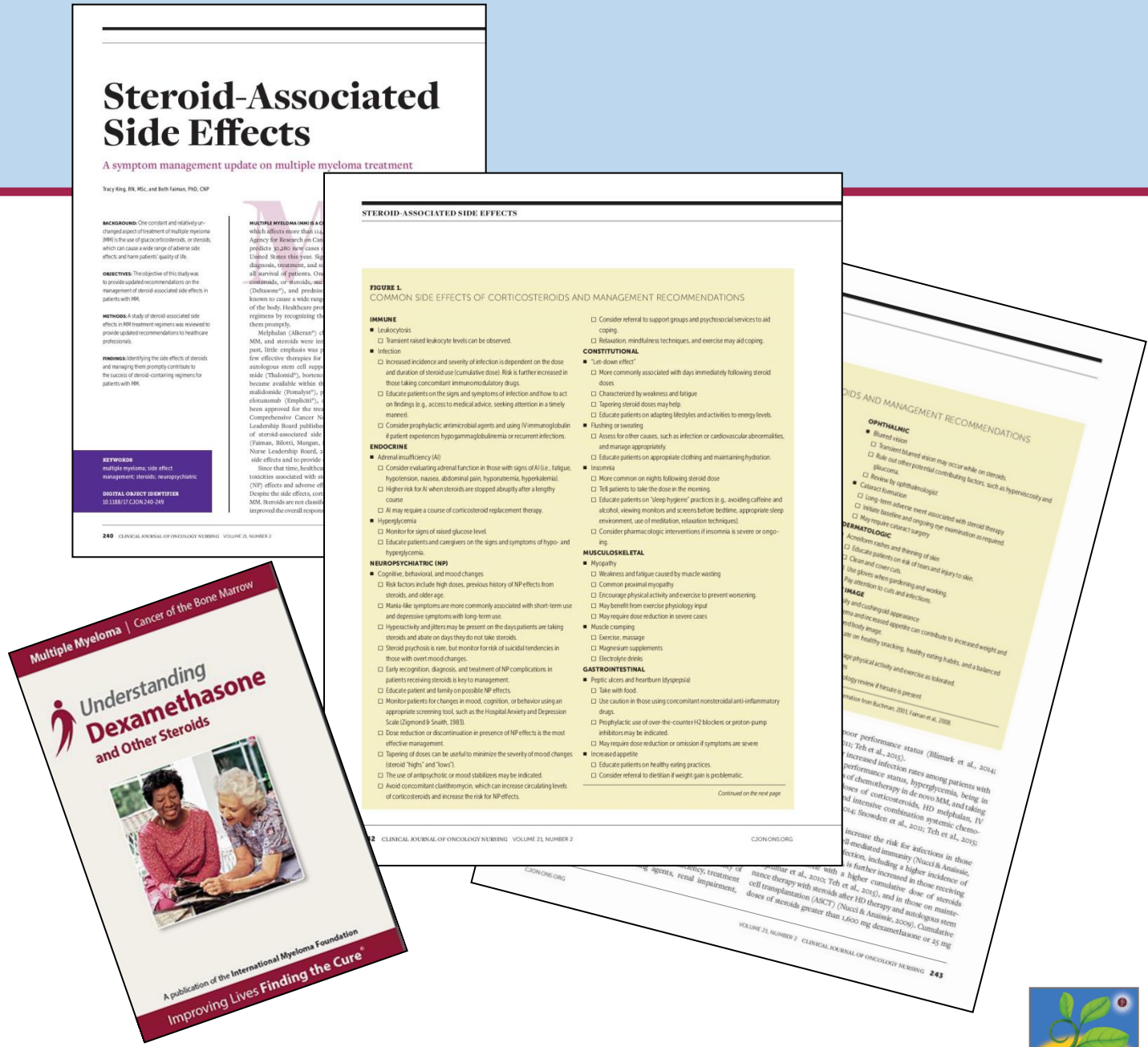
- Antibody administration
  - Risk of infusion reaction: 10%
    - 3-24 hrs before= Dex 28 mg; 45-90 mins before= Dex 8mg IV, H1, H2 and acetaminophen
  - Infuse at rate of 0.5ml/min and escalate to 5ml/min over time
  - Give weekly for 8 weeks then twice monthly until PD
- Prescribed with len-dex
  - DVT prophylaxis (for len)
  - Steroid side effects & schedule (am vs. pm)
- Monitoring
  - Blood counts (hold/adjust dose if needed)
  - Response assessment (monthly)
  - Glucose (dex can affect)
  - Renal, hepatic function

dex = dexamethasone; len = lenalidomide; DVT = deep vein thrombosis; PD = Progressive Disease

Empliciti™ (elotuzumab) Prescribing Information; Gleason C, et al. *J Adv Pract Oncol* 2016; 7 (suppl 1): 53-57.

Clinical Pearls for Steroids

- Patient education
- Consistent schedule (am vs. pm)
- Take with food
- Proactively manage side effects
  - Glucose
  - Checklists
  - Consider dose/timing adjustments (if needed)

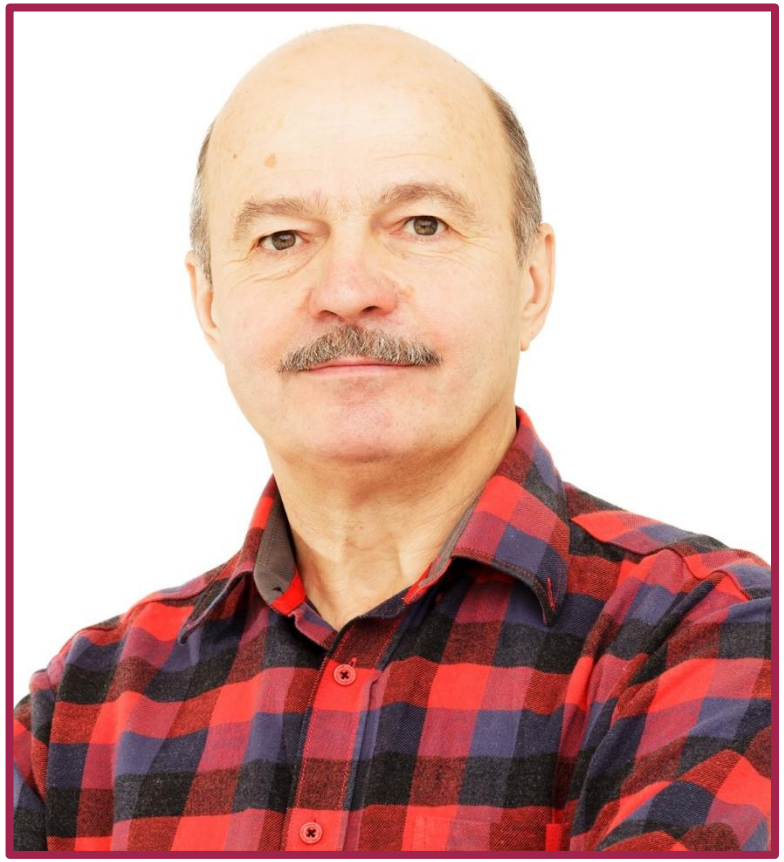


King T, Faiman B. *Clin J Oncol Nurs*. 2107;21(2):240-249.

CASE #5:

William*

- Discussed therapy options
  - Decided to add elotuzumab to Rd
- After 4 cycles:
  - VGPR
  - Tolerating treatment well
  - Adjusted insulin
  - Liver function normal



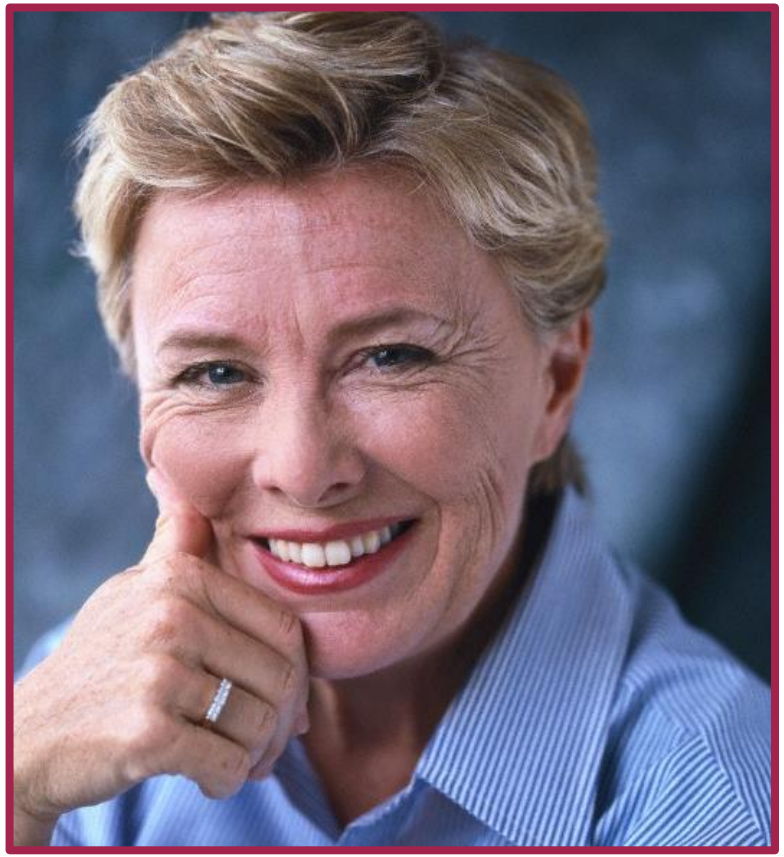
*HIPPA-compliant stock photo (not actual patient)

Rd = lenalidomide-dexamethasone; VGPR = very good partial response.

CASE #6:

Margaret*

- Married office manager 61
- July 2012
  - Multiple myeloma diagnosed
  - RVd induction + ASCT
  - Len maintenance continuous
- January 2017:
  - Biochemical relapse on Len maintenance
  - Skeletal survey: no new lesions
  - New 17p deletion
- Discussed options:
  - DPd in clinical trial



*HIPPA-compliant stock photo (not actual patient)

ASCT = autologous stem cell transplantation; DPd = daratumumab-pomalidomide-dexamethasone; RVd = bortezomib-lenalidomide-dexamethasone.

Pomalidomide

Pomalidomide ± dex
FDA approved
February 2013

- Oral immunomodulatory agent (IMiD)
- Indication: Patients with Multiple Myeloma who have both:
  - Received at least 2 prior therapies including bortezomib and an immunomodulatory agent
  - Demonstrated disease progression on or within 60 days of completion of last therapy

- Administration
  - Oral; Recommended with low-dose dex
  - Take without food (2 hrs before or 2 hrs after a meal)
  - Do not crush, chew or open capsules

dex = dexamethasone; hrs = hours

POMALYST® (pomalidomide) prescribing information

Pomalidomide Clinical Pearls

- Monitor
  - Blood counts – neutropenia most frequent GR 3/4 AE
  - Liver function
  - Response
- Proactive AE management
- Patient education
  - Adherence and REMS
  - Infection prevention
  - Refrain from smoking (reduces pom exposure)
  - Protect renal health (renal excretion of pom)
    - Hydration
    - Avoid NSAIDS, IV contrast, other drugs with renal interactions

AE = adverse event; GR = grade; pom = pomalidomide

POMALYST® (pomalidomide) prescribing information; Faiman B, et al. *J Adv Pract Oncol* 2016;7:45–52.

Pomalidomide Dosing Calendar

Pomalidomide Dosing 28-day Cycle

Recommended starting doses:

Pomalidomide 4 mg
Dexamethasone 40 mg <75 years; 20 mg >75 years

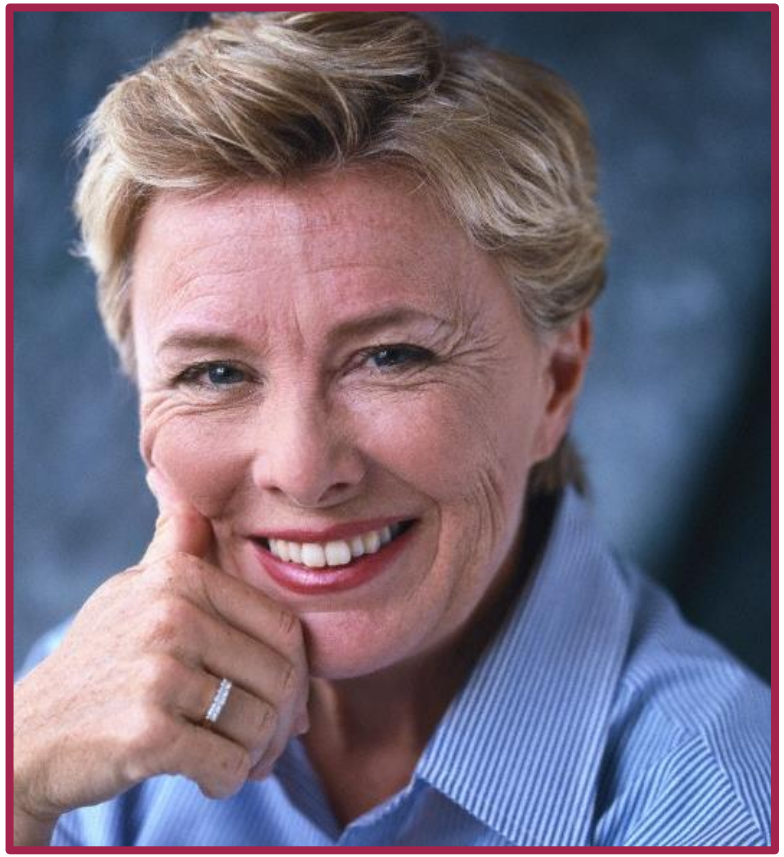
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28

POMALYST® (pomalidomide) prescribing information; Faiman B, et al. *J Adv Pract Oncol* 2016;7:45–52.

CASE #6:

Margaret*

- DPd 4 cycles VGPR
  - Tolerating regimen well
  - Prophylaxis: acyclovir, antithrombotic; PJP



*HIPPA-compliant stock photo (not actual patient)

DPd = daratumumab-pomalidomide-dexamethasone; VGPR, very good partial response.

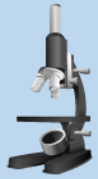
CASE #7:

Miguel*

- Married, retired auto mechanic 66 years old
- November 2013
  - Multiple myeloma diagnosed
  - VRd induction + ASCT + 2 yrs len maintenance
  - No genetic abnormalities
- November 2016:
  - Leg pain
  - Relapse suspected
  - Skeletal survey: new lesions femur, ribs
  - No genetic abnormalities
- Considerations:
  - Side effects
  - Missed doses of len on maintenance
  - Neuropathy
  - No cardiac history
  - Lives near clinic

*HIPPA-compliant stock photo (not actual patient)

ASCT = autologous stem cell transplantation; len = lenalidomide



Carfilzomib: Proteasome Inhibitor

- IV Proteasome Inhibitor, indications:
  - In combination with dex or len-dex in patients with relapsed or refractory MM who have received 1-3 lines of therapy
  - As a single agent in patients with relapsed or refractory multiple myeloma who have received 1 or more lines of therapy

Carfilzomib+Rd
FDA approved
July 2015

- Clinical pearls
  - Avoid starting first cycle at the end of the week – dyspnea
  - Hydration but not over hydration
  - Premedication (dex)
  - Aspirin prophylaxis
  - Monitor blood counts, response
  - Monitor for infection
  - Herpes virus prophylaxis
  - Know cardiac and pulmonary status Cardiac eval/EKG for patients with cardiac history
  - Diuretic (furosemide or torsemide) or inhalers if needed

Carfilzomib+d
56 mg/m^2
FDA approved
January 2016

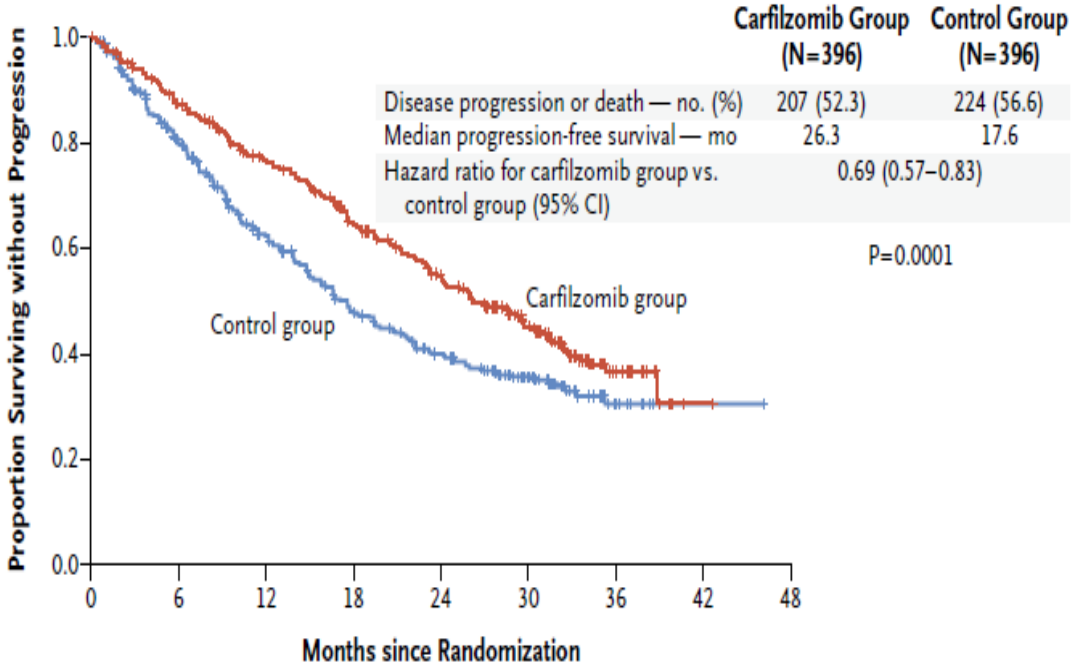
CR = Complete Response; Dex = dexamethasone; KRd = carfilzomib, lenalidomide, dexamethasone; MM = multiple myeloma; OS = Overall Survival; PFS = Progression Free Survival; Rd = lenalidomide, dexamethasone; HRQoL = Health Related Quality of Life

Stewart K, et al. *N Engl J Med.* 2015; 372:142-152.

ASPIRE Trial: PFS & OS

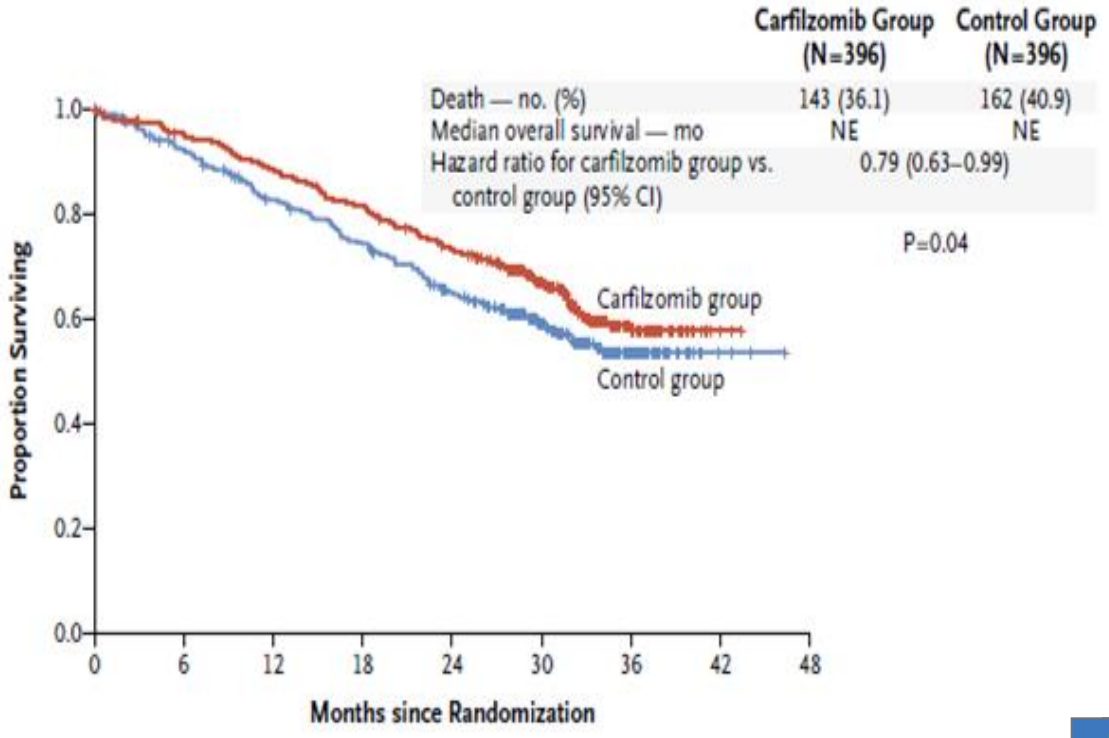
Progression Free Survival (PFS)

PFS significantly improved with KRd
(26.3 months vs. 17.6 months; P=0.0001)



Overall Survival (OS)

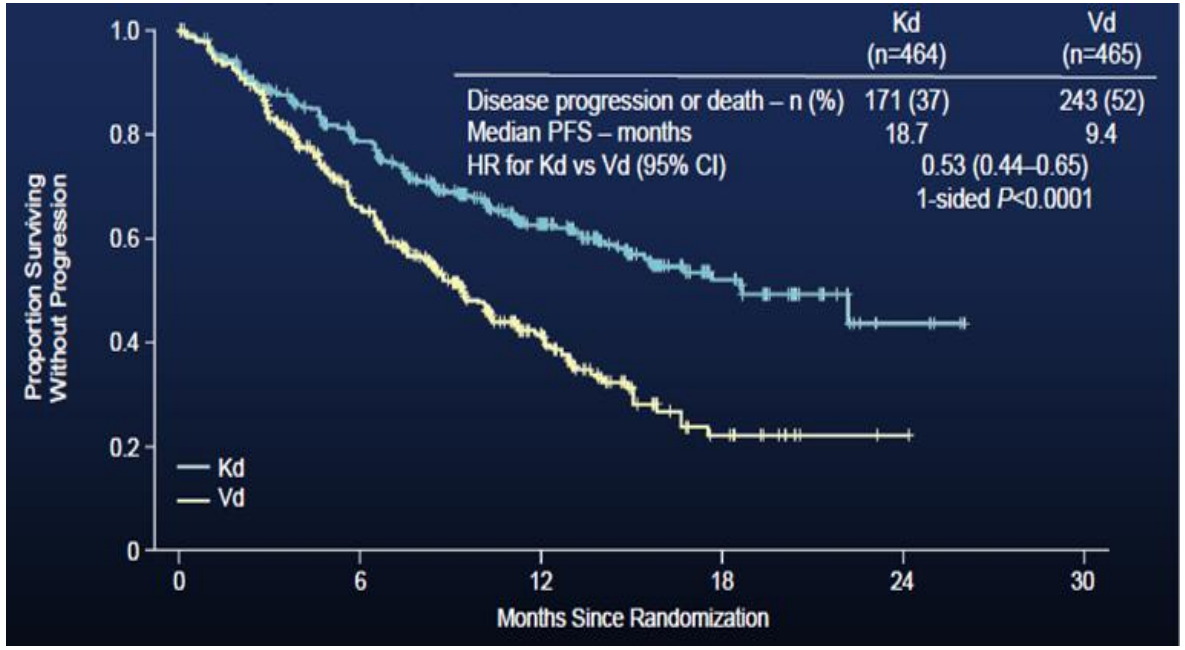
24-month OS favored KRd
(24-mo OS 73.3% KRd vs 65.0% Rd; P=0.04)

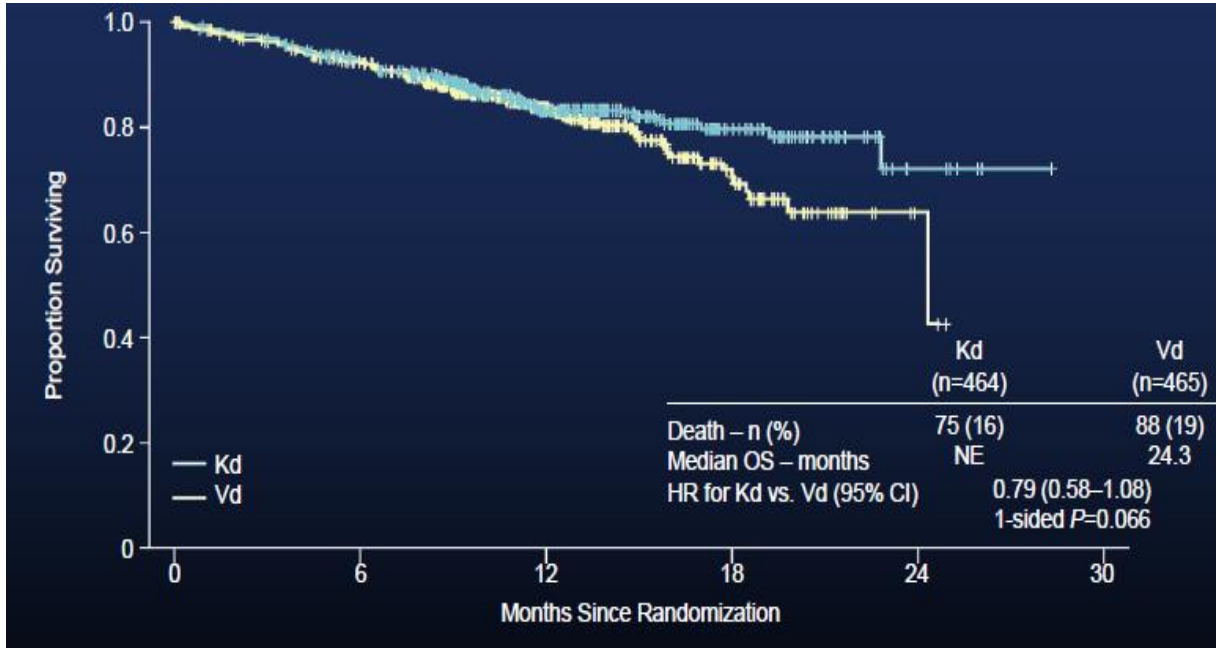


KRd = carfilzomib, lenalidomide, dexamethasone; OS = Overall Survival; PFS = Progression Free Survival

Stewart AK et al. *N Engl J Med.* 2015;372(2):142-52.

ENDEAVOR: PFS & OS





- Double median PFS in Kd arm compared to Vd (18.7 vs 9.4 months)
- PFS subgroup analysis, favor Kd in all subgroups – high ISS, prior bortezomib and IMIDs exposure, high-risk cytogenetics, age ≥75 yo
- Trend for improved OS with Kd (P =0.066)

ISS = International Staging System; IMID = immunomodulatory drug; Kd = carfilzomib-dexamethasone; OS = overall survival; PFS = progression-free survival; Vd = bortezomib-dex

Dimopoulos MA et al. EHA meeting 2015. Abstract LB2071.

Carfilzomib – Lenalidomide - Dexamethasone (KRd) Regimen Dosing Calendar

KRd Dosing 28-day Cycle

Starting dose
20 mg/m^2
day 1&2

Subsequent doses
27 mg/m^2

Cycle 13+:
eliminate day 8 & 9 carfilzomib

Discontinue carfilzomib after cycle 18

Recommended dosing:

- Carfilzomib 10- minute infusion
- Lenalidomide 25 mg
- Dexamethasone 40 mg

1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28

KYPROLIS® (carfilzomib) prescribing information; Faiman B, et al. *J Adv Pract Oncol* 2016;7:45–52.

Carfilzomib – Dexamethasone (Kd) Regimen Dosing Calendar

KD Dosing
28-day Cycle

Recommended dosing:

- Carfilzomib 30- minute infusion
- Dexamethasone 20 mg 30 min to 4 hrs before K

Starting dose
20 mg/m^2
day 1&2

Subsequent doses
56 mg/m^2

1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28

Hrs = hours;
K = carfilzomib;
Kd = carfilzomib - dexamethasone

KYPROLIS® (carfilzomib) prescribing information; Faiman B, et al. *J Adv Pract Oncol* 2016;7:45–52.

CASE #7:

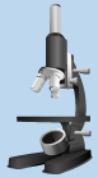
Miguel*

- Discussed options with Miguel, wife and daughter who assist with caregiving
  - Kd selected

- After 3 cycles Kd
  - VGPR
  - Tolerating treatment
  - 2x per week schedule at clinic ensures adherence

*HIPPA-compliant stock photo (not actual patient)

Kd = kyprolis-dexamethasone; VGPR = very good partial response.



Drugs or Regimens in Development

Many myeloma drugs are in development

- Immuno-oncology approaches:
  - Vaccines approaches
  - Pembrolizumab
  - Nivolumab (CheckMate 602 trial)
  - CAR T-Cells
- Approved in other indications
  - Ibrutinib
  - Bevacizumab
  - Venetoclax
  - Ruxolitinib
  - Denosumab
- New myeloma targets / drugs
  - Filanesib / ARRY-520
  - Selinexor
  - Oprozomib

Combinations or sequencing

- First line induction combinations
  - KRd
  - DVd
  - DRd
  - Many in Phase I or II
- Sequencing or timing of therapy
  - Early treatment (SMM)
  - Role of transplantation (early, late)

Watch for new data on myeloma therapies from ASCO June 2-8th

Clinical Trials. gov

IMF's Research Initiatives: Black Swan and ISTOPP Search for Myeloma Cure

Black Swan

- Develop sensitive MRD testing methods
  - Next generation flow: 10-6 level
- Standardize testing across laboratories
- CURE Trials: HR SMM patients treated to achieve MRD negative status
- Studying "resistant" disease in patients not achieving MRD negative status

BLACK SWAN RESEARCH INITIATIVE®
Signature Project of the International Myeloma Foundation

iStopMM (one of Black Swan Trials)

- iStopMM (Iceland Screens Treats or Prevents Multiple Myeloma) clinical study
- Examine blood samples from approximately 140,000 adults over age 40 in Iceland for the earliest signs of myeloma
- Patients with MGUS, SMM and MM will be identified, tested and set up for monitoring or treatment

HR = high risk; MGUS = monoclonal gammopathy of unknown significance; MM = multiple myeloma; MRD = minimal residual disease; SMM = smoldering multiple myeloma

Dr. Brian Durie; International Myeloma Foundation.

Summary

- Myeloma patients are living longer with more therapeutic options
  - Three-drug induction regimens (eg, VRd) are preferred unless frail or elderly
  - Share decision-making by discussing options with patients and taking their priorities into consideration
  - Keep patients on therapy maximizing the full benefit from each drug by sharing decision-making and proactive side effect management
- Many therapeutic options are available for patients after they have received a prior myeloma therapy
  - No one “best” choice; preferred therapy depends on individual patient characteristics and preferences
- Many new potential therapies are on the horizon including some currently approved in other cancers
- Many educational resources are available from the IMF to help patients at all stages of their disease
  - Patients should have a clear understanding of their test results, therapy, and follow up plan (survivorship care plan)

Kumar SK et al. *Leukemia*. 2014;28(5):1122-1128. 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. Tariman J, et al. *Clin J Oncol Nurs.* 2015;19:548-556. Tariman J, et al. *Ca Treat Comm.* 2014;*2:*34-37. Clinicaltrials.gov. Myeloma.org. Kurtin, S. (2015). Multiple Myeloma (second edition): Tariman and Faiman (eds).

Thank You for Sharing in the Stories of Our Patients

We Hope You Had and Enjoyable and Educational Time: Learning Objectives

As a result of this program, you will be able to:

- Identify newly approved therapies and common combination regimens in multiple myeloma
- Apply best practice in management of multiple myeloma patients receiving newly approved therapies and combination regimens
- Discuss survivorship care plans and practical tools for long-term management and care of multiple myeloma patients
- Express the key role nurses play in advocating for their multiple myeloma patients and their caregivers

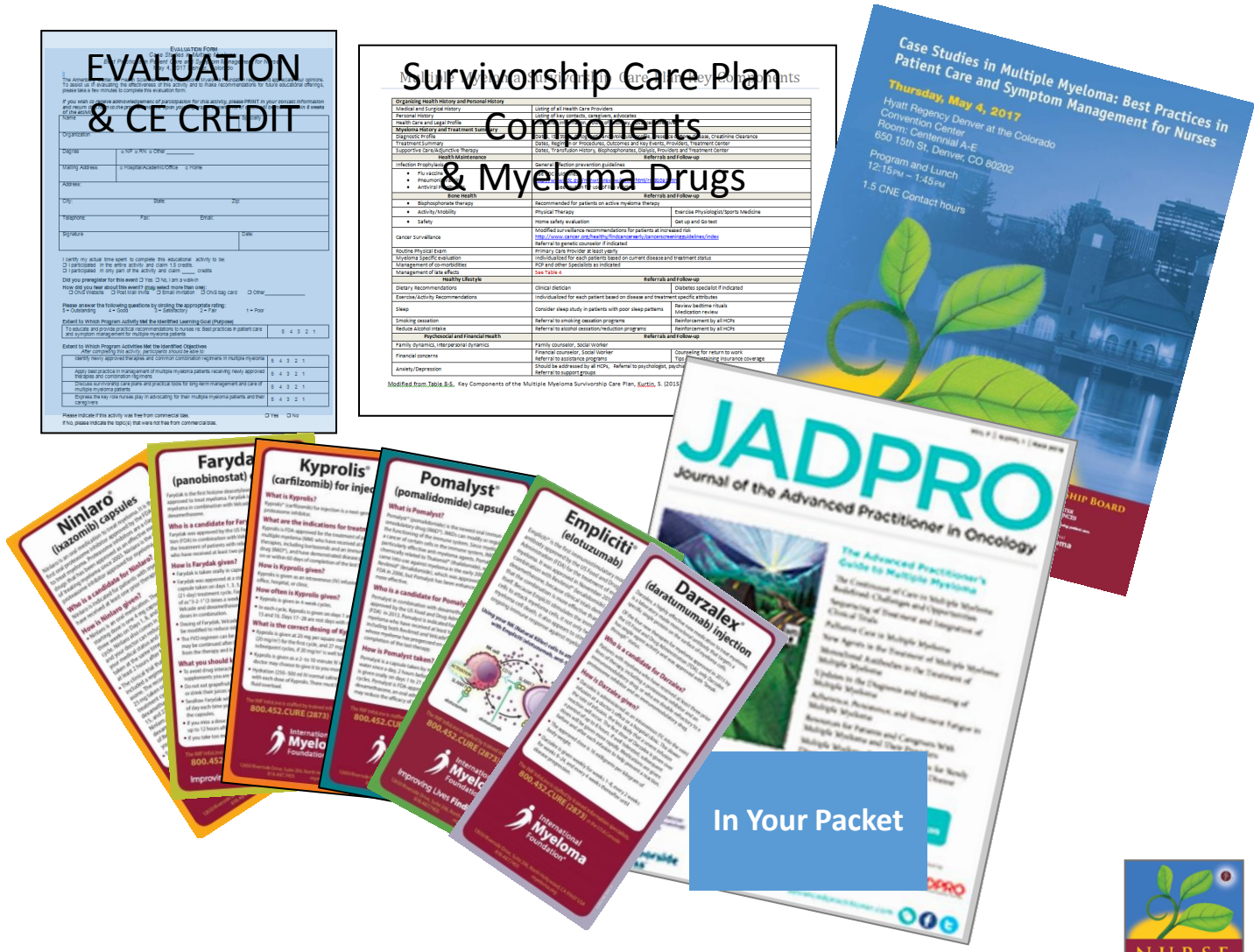
In Your Packet: IMF Nurse Leadership Board Resources to Enhance Your Ability to Care for Your MM Patients

Publications from Nurse Leadership Board, International Myeloma Working Group

On USB drive
In small envelope

EVALUATION & CE CREDIT

Survivorship Care Plan Components & Myeloma Drugs



In Your Packet

Thank You for Your Attendance and Participation

On behalf of the International Myeloma Foundation with the generous support from Takeda Oncology, Janssen Pharmaceuticals, Celgene Corporation, and Bristol-Myers Squibb, ***we thank you****.*

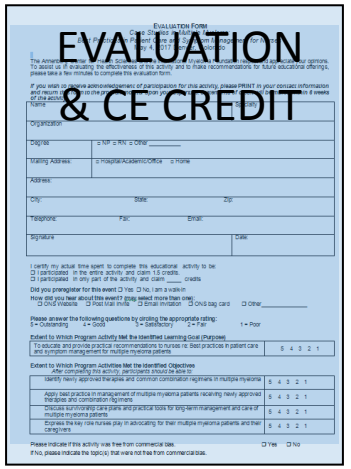
Faculty are available to answer questions.

Please Contact IMF for Further Information and Resources:

1-800-452-CURE
(1-800-452-2873)

TheIMF@myeloma.org

http://myeloma.org



Please leave
CE Credit & Eval Form
at back tables

Slides available for download at
www.imf-ons.myeloma.org/ONS_2017.pdf

Appendix Slides

Drugs and Drug Classes for Treatment of Myeloma

Drug Class	Name	Abbreviations	Brand
Proteasome inhibitor	Bortezomib	btz, bor, V	VELCADE®
	Carfilzomib	cfz, car, K	KYPROLIS®
	Ixazomib	I	NINLARO®
Immunomodulatory agent	Lenalidomide	len, R	REVLIMID®
	Thalidomide	thal, T	THALOMID®
	Pomalidomide	pom, P	POMALYST®
Monoclonal antibodies	Daratumumab	dara, D	DARZALEX™
	Elotuzumab	elo, E	Empliciti™
Alkylating agent	Melphalan	mel, M	ALKERAN®, ALPHALAN®
	Cyclophosphamide	CTX, Cy, C	CYTOXAN®
Corticosteroid	Prednisone	pred, P	DELTASONE®
	Dexamethasone	D, d, dex, DXM	DECADRON®
Histone Deactylase Inhibitor	Panobinostat	pano, F	FARYDAK®
Bisphosphonate	Pamidronate	pmd	AREDIA®
	Zoledronic Acid	zol	ZOMETA®

Classes: Mids, Mibs, MABs and Others

-Mids	-Mibs	-MABs	Others
Immunomodulatory Drugs (IMIDs)	**Proteasome Inhibitors**	**Monoclonal Antibodies**	
Thalidomide (PO)	Bortezomib (IV/SQ)	Daratumumab (IV)	Steroids (IV/PO) • Dexamethasone • Prednisone
Lenalidomide (PO)	Carfilzomib (IV)	Elotuzumab (IV)	Alkylating Agents (IV/PO) • Melphalan • Bendamustine • Cyclophosphamide
Pomalidomide (PO)	Ixazomib (PO)	Denosumab (IV) *	HDAC (PO) • Panobinostat
	Oprozomib (PO) *	SAR650984 (IV) *	Anthracyclines • p-Doxorubicin
		Siltuximab (IV) *	

- In development; not FDA approved for multiple myeloma patients

Prescribing information: thalidomide, lenalidomide, pomalidomide, bortezomib, carfilzomib, ixazomib, daratumumab, elotuzumab, dexamethasone, prednisone, melphalan, bendamustine, cyclophosphamide, panobinostat, p-Doxorubicin; Clinicaltrials.gov.

Side Effects of Common Myeloma Drugs

	thalidomide	lenalidomide	pomalidomide	bortezomib	carfilzomib
Neuropathy (PN)	✓			✓*	
Thrombosis (DVT, PE)	✓more with dex	✓more with dex	✓more with dex		✓
Myelosuppression	✓ neutro	✓anemia, thrombo, neutro	✓ neutro	✓ thrombo	✓ neutro, thrombo
Cardiopulmonary	✓slow heart rate		✓shortness of breath	✓hypotension	✓shortness of breath, other
Fatigue, weakness	✓	✓	✓	✓	✓
Sedation	✓				
Rash	✓	✓	✓		
GI disturbance	✓ constipation	✓ diarrhea, constipation	✓ diarrhea, constipation	✓ nausea, vomiting, diarrhea	✓nausea, vomiting, diarrhea, constipation

* Subcutaneous or weekly administration of bortezomib reduces risk of PN

PN = peripheral neuropathy; DVT = deep vein thrombosis; PE = pulmonary embolism; dex = dexamethasone;
Neutro = Neutropenia (low white blood cell) count; Thrombo = thrombocytopenia (low platelets); GI = gastrointestinal

Prescribing information: thalidomide, lenalidomide, pomalidomide, bortezomib, carfilzomib.

Side Effects of Newly-Approved M Myeloma Drugs

	panobinostat	elotuzumab	daratumumab	ixazomib
Peripheral Neuropathy (PN)				
Infusion reaction		✓	✓	
Myelosuppression	✓ neutro, thrombo		✓neutro, thrombo	✓ thrombo
Cardiopulmonary	✓arrhythmias, ischemia			
Fatigue, weakness	✓	✓	✓	✓
Rash				✓
GI disturbance	✓diarrhea, nausea, vomiting	✓diarrhea, nausea	✓ diarrhea	

Neutro = Neutropenia (low white blood cell) count; PN = peripheral neuropathy; Thrombo = thrombocytopenia (low platelets); GI = gastrointestinal

Prescribing information: panobinostat, elotuzumab, daratumumab, ixazomib.

Common Multiple Myeloma-Related Abbreviations

AE	Adverse Event
Alb	Albumin
AHSCT	Autologous Hematological Stem Cell Transplant
B_2M	Beta-2 Microglobulin
BM	Bone Marrow
BMC	Bone Marrow Concentrate
BMPC	Bone Marrow Plasma Cells
CBC	Complete Blood Count
CLcr	Creatinine Clearance
Cr	Creatinine
CR	Complete Response
CRAB	CRAB Criteria – indicative of active MM
CT	Computed Tomography
Cyto	Cytogenetics
DVT	Deep Venous Thrombosis
FLC	Free Light Chain
FISH	Fluorescent In Situ Hybridization
GFR	Glomerular Filtration Rate
G-CSF	Granulocyte Colony Stimulating Factor
Hgb	Hemoglobin
HLC	Heavy Light Chain Ratio
IFE	Immunofixation Electrophoresis
Ig	Immunoglobulin
IM	Intramuscular
ISS	International Staging System
IMiD	Immunomodulatory Drug
IMWG	International Myeloma Working Group
IV	Intravenous
kFLC	kappa Free Light Chain
MCP	Monoclonal Protein
MDE	Myeloma Defining Event
MDS	Myelodysplastic Syndrome
MGUS	Monoclonal Gammopathy of Undetermined Significance
MP	Melphalan & Prednisone
MRI	Magnetic Resonance Imaging
M-spike	Myeloma Protein Spike
MM	Multiple Myeloma
NCCN	National Comprehensive Cancer Network
nCR	Near Complete Response
NSAID	Non-Steroidal Anti-Inflammatory Drug
PCLI	Plasma Cell Labeling Index
PCP	Primary Care Physician
PD	Progressive Disease
PET	Positron emission tomography
PN	Peripheral Neuropathy
PR	Partial Response
Pts	Patients
QoL	Quality of Life
RR	Relapsed/Refractory
SC	Subcutaneous
sCR	Stringent Complete Response
SFLC	Serum Free Light Chain
SPEP	Serum Protein Electrophoresis
SPM	Secondary Primary Malignancy
SMM	Smoldering Multiple Myeloma
TTP	Time to Progression
UPEP	Urine Protein Electrophoresis
VGPR	Very Good Partial Response
WBC	White Blood Cells