Case Studies for Nurses: Evolution in Myeloma Treatment

Slides available for download at:

www.imf-ons.myeloma.org/ONS_2019.pdf

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

Thank you for coming!

1.5 CNE credits are jointly provided by the Annenberg Center for Health Sciences and the International Myeloma Foundation. Educational grants provided by Celgene Corporation, Takeda Oncology, Karyopharm Therapeutics Inc., and Janssen Biotech, Inc., administered by Janssen Scientific Affairs, LLC.

NURSE LEADERSHIP BOARD

INTERNATIONAL MYELOMA FOUNDATION

ONS Disclaimer

Meeting space has been assigned to provide a Symposium supported by International Myeloma Foundation during the Oncology Nursing Society's (ONS) 44th Annual Congress, April 11-14, 2019 in Anaheim, CA. The Oncology Nursing Society's assignment of meeting space does not imply product endorsement.

NURSE LEADERSHIP BOARD

INTERNATIONAL MYELOMA FOUNDATION

Accreditation/Certification

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.

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

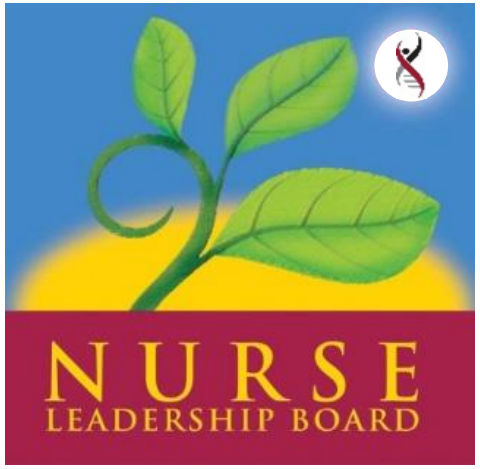
In accordance with accreditation requirements, this program is certified through the joint providership of the Annenberg Center for Health Sciences at Eisenhower and the International Myeloma Foundation (IMF).

NURSE LEADERSHIP BOARD

INTERNATIONAL MYELOMA FOUNDATION

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



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

Off-label use of drugs may be discussed.

Slides available for download at:
www.imf-ons.myeloma.org/ONS_2019.pdf

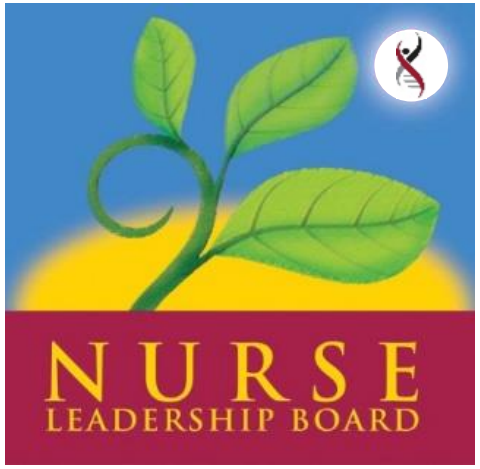
Evaluations with CNE credit are enclosed in the packet, along with the Guidebook.

Presenters' disclosures are in the Guidebook.

NURSE LEADERSHIP BOARD

INTERNATIONAL MYELOMA FOUNDATION

Case Studies for Nurses: Evolution in Myeloma Treatment



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

Kim Noonan, DNP, RN, ANP-BC, AOCN®
Dana-Farber Cancer Institute, Boston, MA

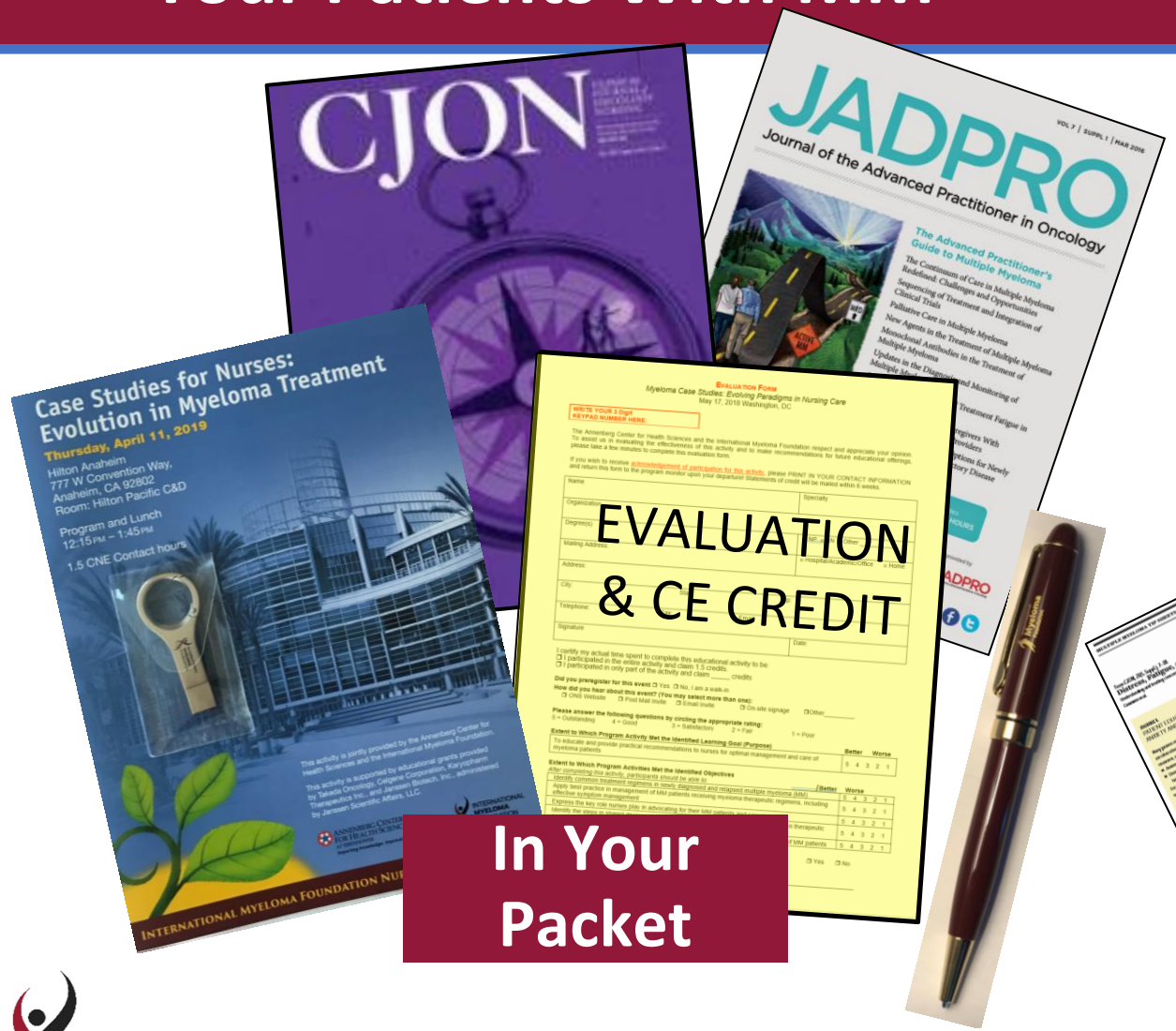
International Myeloma Foundation (IMF)

INTERNATIONAL MYELOMA FOUNDATION

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
- Patient Outreach
  - Support Groups
  - Seminars, Workshops
  - Teleconferences
- Advocacy
- Global Outreach

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



And More

CE = continuing education; MM = multiple myeloma.

Agenda

TIME	TOPIC	FACULTY
12:15 PM – 12:20 PM	Overview	Beth Faiman
12:20 PM – 12:25 PM	Pre-Test	Beth Faiman
12:25 PM – 12:40 PM	Multiple Myeloma Background, Shared Decision-Making, Smoldering Multiple Myeloma Research Update, Finding Clinical Trials	Joseph D. Tariman Beth Faiman
12:40 PM – 1:10 PM	Case Study #1: Newly Diagnosed Multiple Myeloma, Response, Bone Health, Renal Health, Minimal Residual Disease, Survivorship Care	Sandra Rome Beth Faiman
1:10 PM – 1:40 PM	Case Studies #2, #3: Relapsed Myeloma, Treatment for Relapsed Myeloma, Drugs in Development, Knowledge Post-Test	Kimberly Noonan Beth Faiman
1:40 PM – 1:45 PM	Closing Remarks	All

We Hope You Have an Enjoyable and Educational Time: Learning Objectives

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

- Identify common treatment regimens in newly diagnosed and relapsed multiple myeloma
- Discuss nursing management of MM patients receiving myeloma therapeutic regimens, including effective symptom management
- Identify the steps in shared decision-making and strategies to support the patient's input in therapeutic decisions
- Discuss the importance of survivorship care plans and practical tools for long-term management and care of MM patients

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

Multiple Myeloma Background, Shared Decision-Making, SMM Research Update

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

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

NURSE LEADERSHIP BOARD

INTERNATIONAL MYELOMA FOUNDATION

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 MM Patient

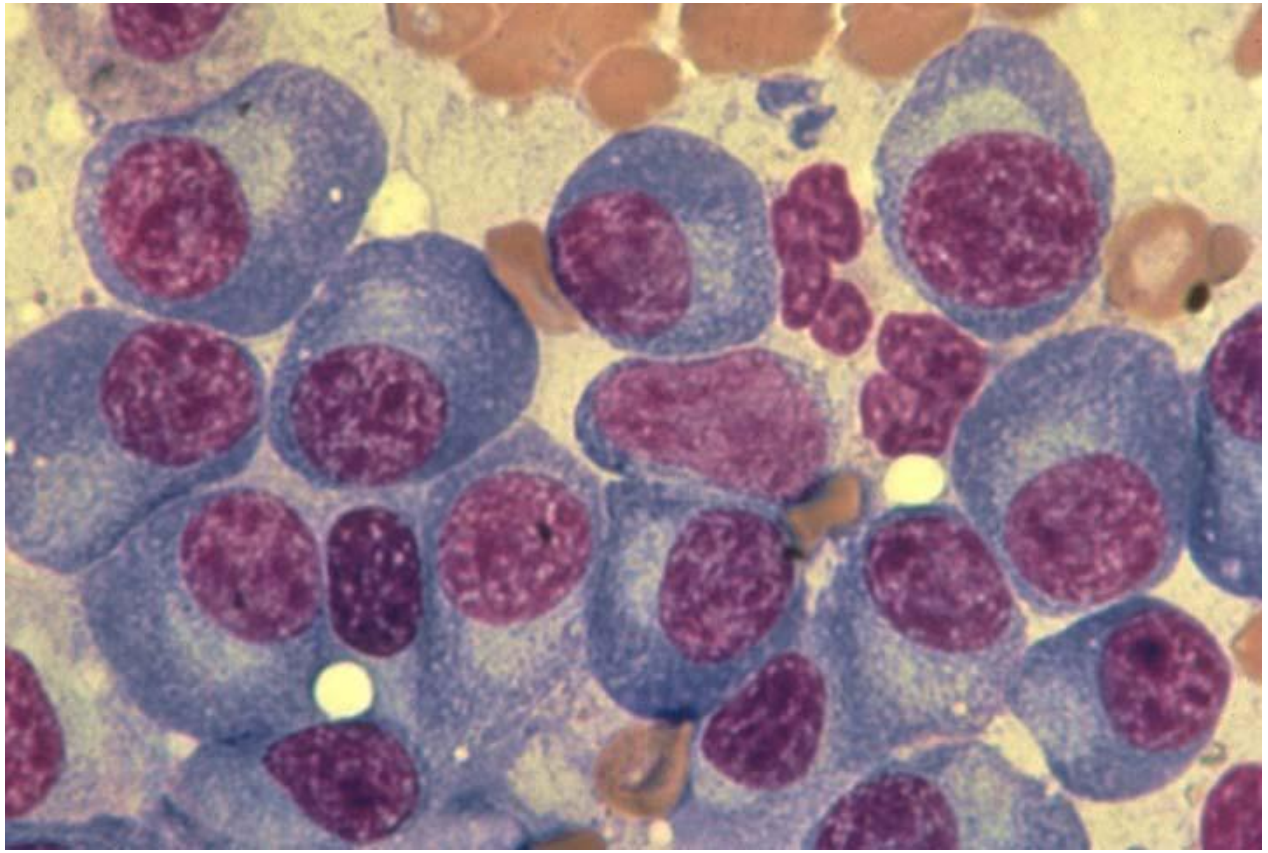
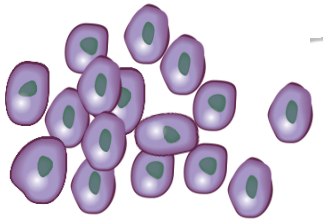


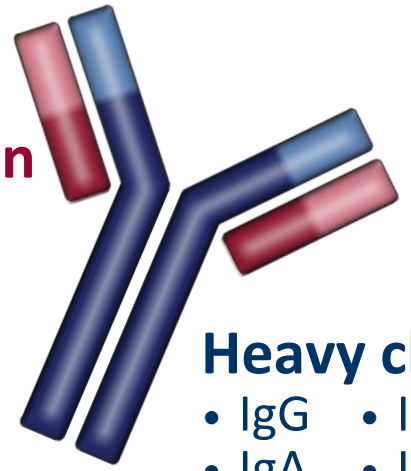
Image: American Society of Hematology

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

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

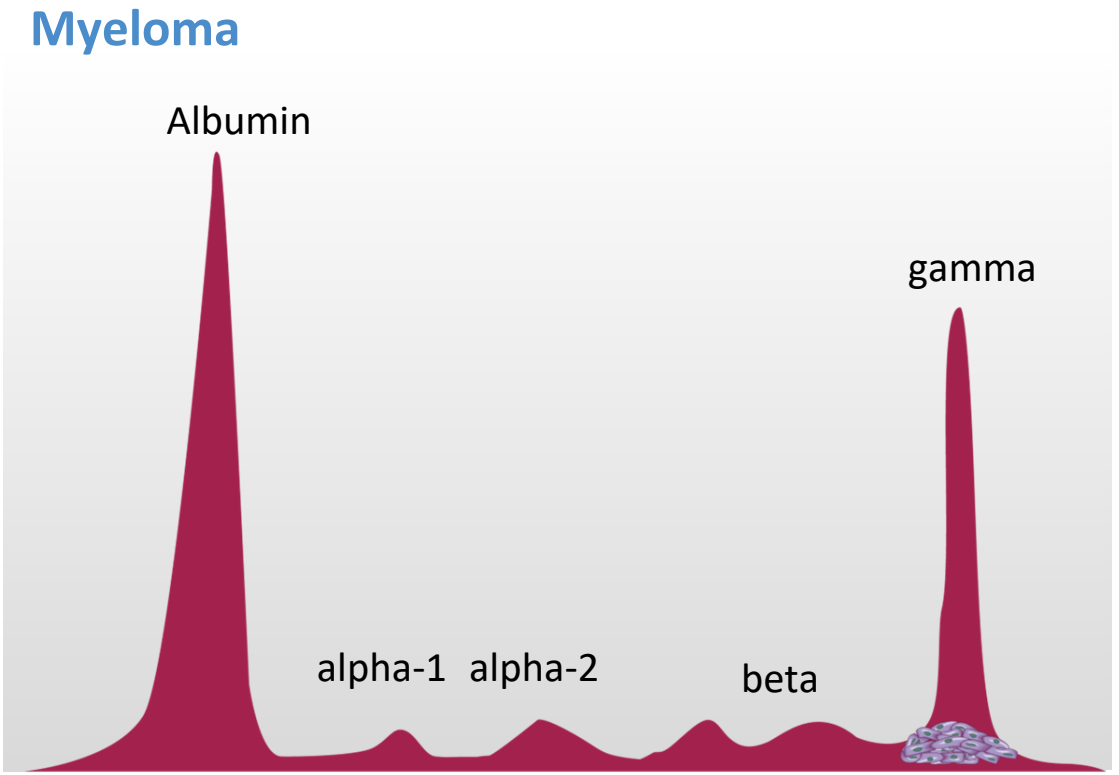


Myeloma cells produce abnormal immunoglobulins continually (nonsecretory disease is rare)



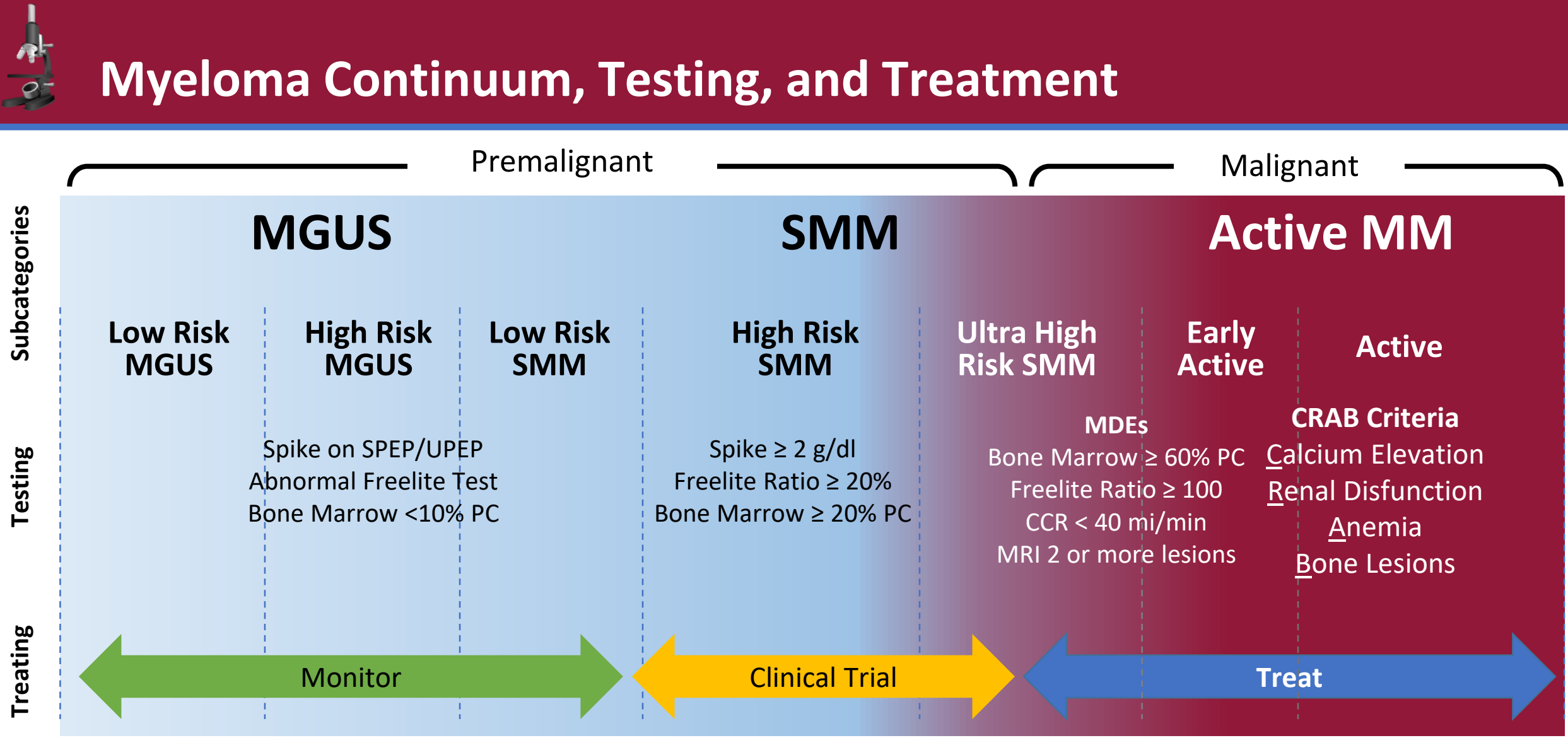
Light chain
- Kappa
- Lambda

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



Understanding Your Test Results, International Myeloma Foundation 2018.

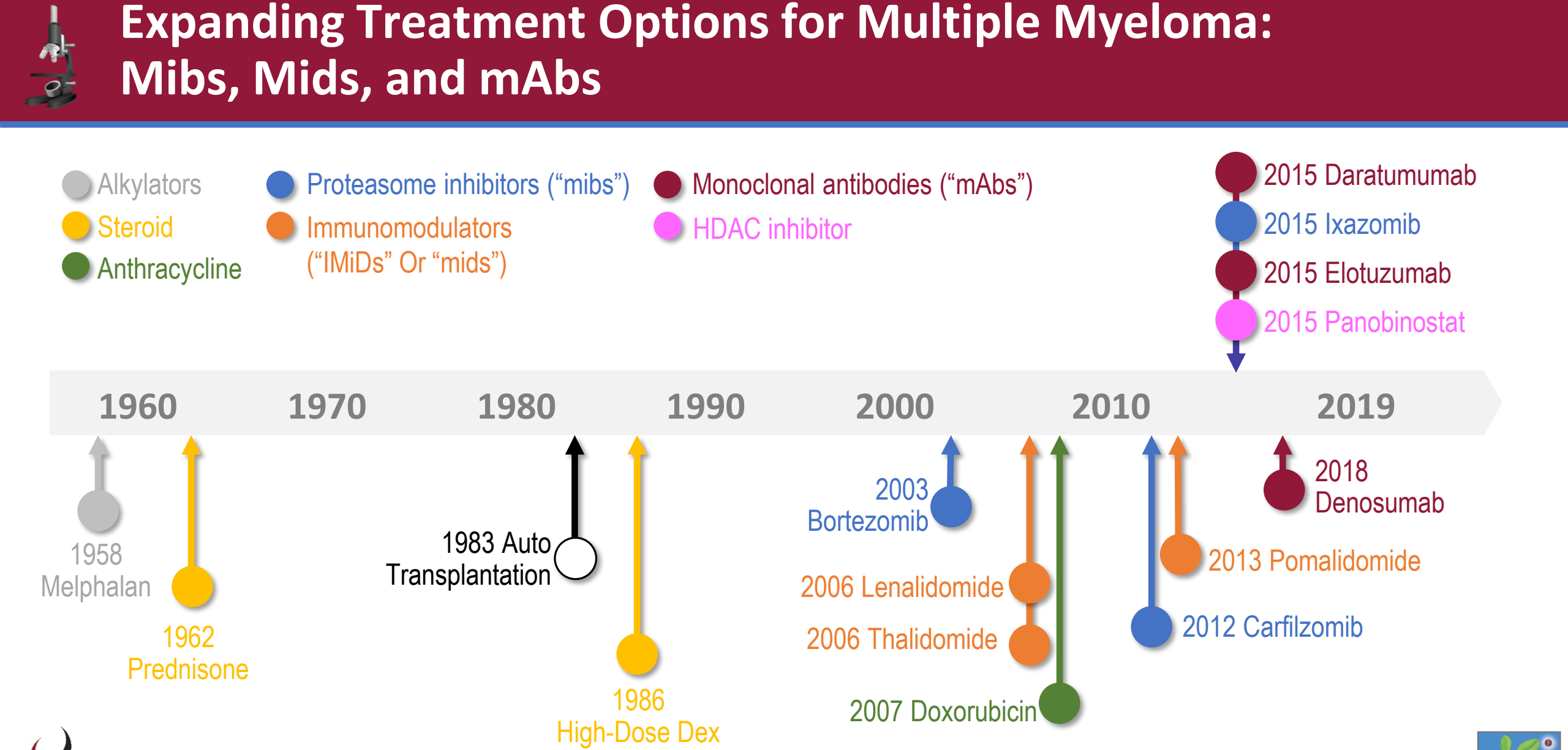
Myeloma Continuum, Testing, and Treatment



CCR = creatinine clearance rate; MDE = myeloma defining event; MGUS = monoclonal gammopathy of undetermined significance; MRI = magnetic resonance imaging; PC = plasma clones; SMM = smoldering multiple myeloma.

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.

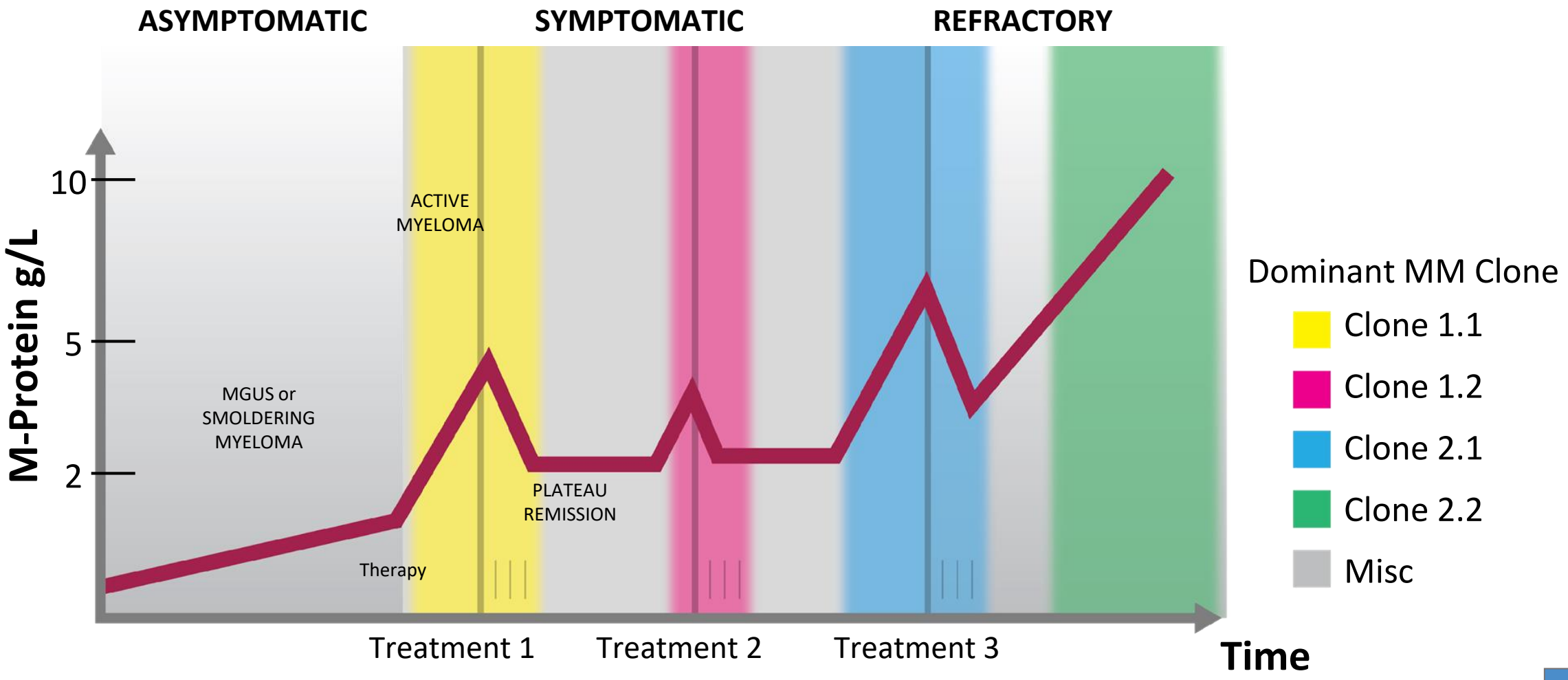
Expanding Treatment Options for Multiple Myeloma: Mibs, Mids, and mAbs



Auto = autologous; Dex= dexamethasone.

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

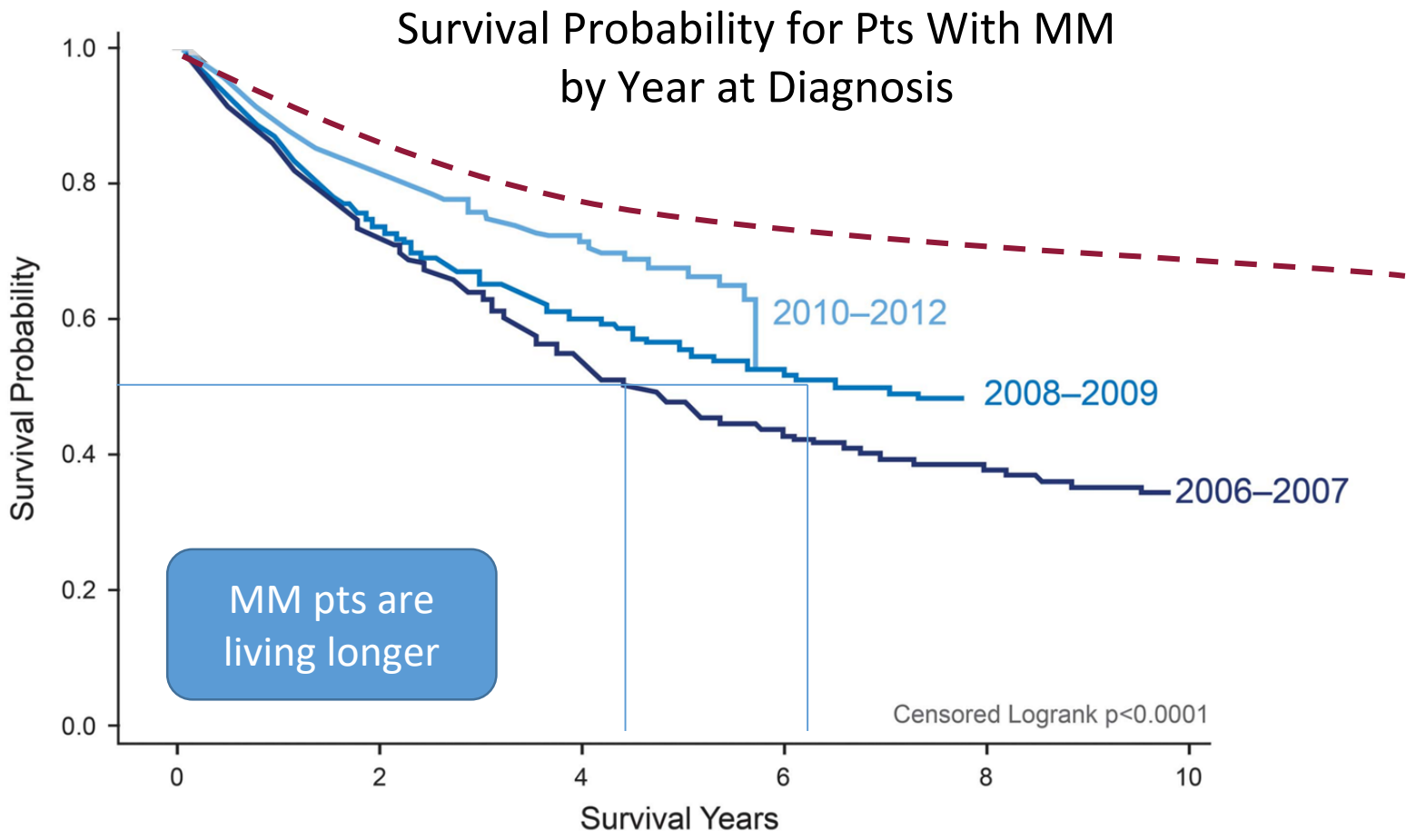
Relapsing Nature of Multiple Myeloma: Clones Change Over Time



MGUS = monoclonal gammopathy of undetermined significance; MM = multiple myeloma.

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

Good News: Myeloma Patients Are Living Longer



How long is a pt diagnosed with MM today likely to live? We don't know. Myeloma is becoming a chronic condition!

dx = diagnosis; MM = multiple myeloma.

Fonseca R, et al. *Leukemia*. 2017;31:1915-1921. Costa LJ, et al. *Blood Advances*. 2017;1(4):282-287.

Patient-Centered Care and Shared Decision-Making

- Plethora of excellent choices for MM treatment!
- Shared decision-making: Including patient preferences in health and treatment decisions
- Aligns with Institute of Medicine Initiatives
- Affordable Care Act emphasizes patient-centered care

Institute of Medicine Publications

MM = multiple myeloma.

Fonseca R, et al. *Leukemia*. 2017;31:1915-1921. Costa LJ, et al. *Blood Advances*. 2017;1(4):282-287.

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: HCP (MD/APP/RN) and patient/caregiver
2. Both parties share information
3. Both parties take steps to build consensus about preferred treatment
4. Mutual agreement is reached between patient and health care team on treatment approach

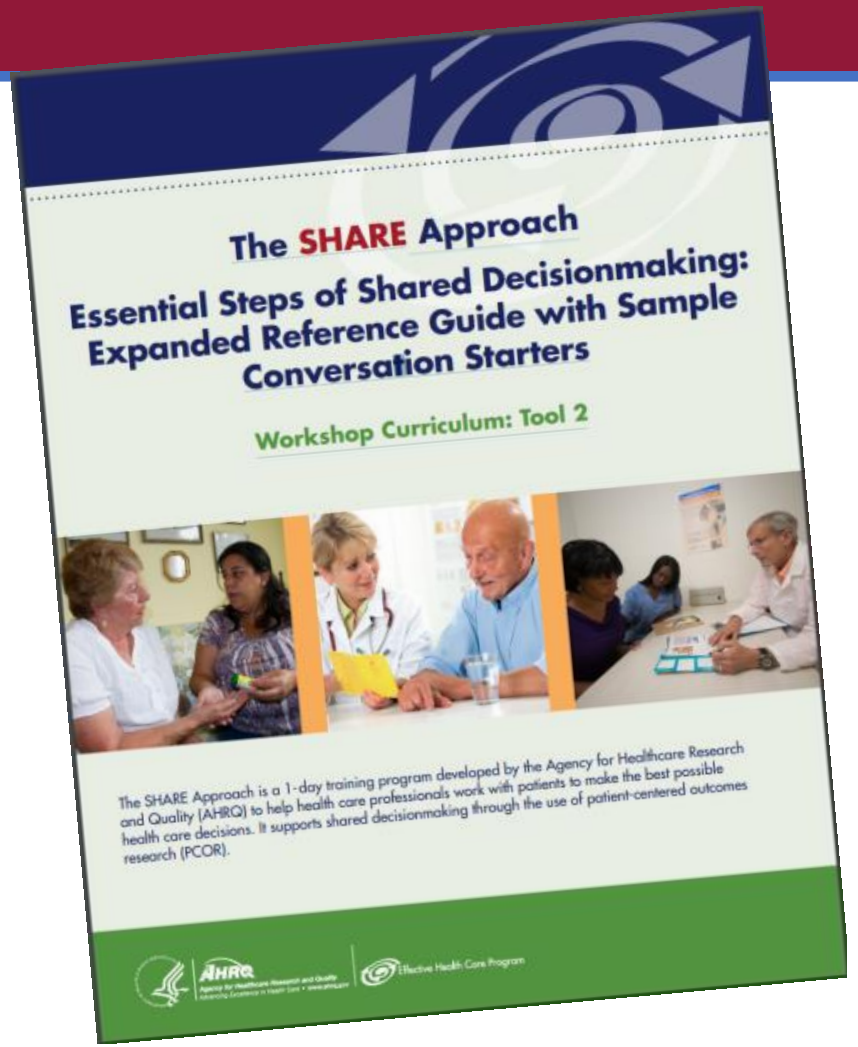
HCP = health care provider.

Adapted from Tariman J, et al. *Clin J Oncol Nurs.* 2015;19:548-556. Tariman J, et al. *Ca Treat Comm.* 2014;*2:*34-37. http://www.ahrq.gov.

Agency for Health Care Research and Quality (AHRQ): SHARE Approach

The 5 steps to SHARE:

1. **S**eek your patient's participation
2. **H**elp your patient explore and compare treatment options
3. **A**ssess your patient's values and preferences
4. **R**each a decision with your patient
5. **E**valuate your patient's decision



The SHARE Approach Essential Steps of Shared Decisionmaking: Expanded Reference Guide with Sample Conversation Starters Workshop Curriculum: Tool 2. Available at https://www.ahrq.gov/sites/default/files/wysiwyg/professionals/education/curriculum-tools/shareddecisionmaking/tools/tool-2/share-tool2.pdf.

Examples of What Shared Decision-Making Sounds Like

"There are two treatment options for your condition. One is…(X), the other is…(Y). Let me first explain to you what the pros and cons of treatment X are."

"Hearing what I just told you, are there any thoughts, concerns, or worries that immediately come to mind?"

"We can make a decision together now, but you might also prefer to have some time to think about things or talk to others, and make it on your own or with your family. Or you can come back to discuss it in another consultation. What would you think is the best for you?"

Stiggelbout AM, et al. *Patient Education and Counseling.* 2015;98:1172–1179.

Nurses Can Reinforce Shared Decision-Making

Empower Patients

"There are many different ways to treat multiple myeloma. The doctor will be in shortly to discuss these. Since they each have their pros and cons, it is important to discuss what is important to you so that the best treatment for you can be decided on together."

Inform Patients

"Did you have questions about the possible treatments that doctor discussed with you that I may be able to answer for you like common side effects or how the treatment is given?"

"Please ask us questions. Our whole office is here for you. A lot of our patients find it helpful to write down their questions and bring them to office visits so they don't forget."

Advocate for Patients

"Mrs. Z said she'd like some time to consider her options. Can I give her a myeloma booklet and schedule a return visit in a few days after she talks with her family?"

"Mrs. Z expressed concern about…. Is there something that we could do?"

Adapted from Stiggelbout AM, et al. *Patient Education and Counseling.* 2015;98:1172–1179.

Patients AND Oncology Clinicians Need Education and Training on SDM Implementation

- Combined **pt and provider approach** in SDM could **improve mental health-related quality of life** more than professional only or patient only approach for improving SDM outcomes[1]
- Both pt and HCP need to understand the components of SDM as part of cancer care[2,3]
- A new competency scale on SDM for oncology nurses has been developed, validated, and published[4]
  - The new SDM-Nurses instrument has a clinical utility in the assessment of SDM competency (knowledge, attitudes, communication, and adaptability skills) among oncology nurses and other clinicians and for the evaluation of the effectiveness of an educational intervention on SDM among oncology care providers

HCP = health care provider; SDM = shared decision-making.

1. Legare F, et al. *Cochrane Database Syst Rev.* 2018. 2. Stiggelbout AM, et al. *Patient Educ Couns.* 2015;98(10):1172-1179. 3. Kane HL, et al. *CA Cancer J Clin.* 2014;64(6):377-388. 4. Tariman JD, et al. *SAGE Open Med.* 2018;6:2050312118807614.

Smoldering Multiple Myeloma (SMM)

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%

High-Risk SMM

- High likelihood of progression to active myeloma in next 1-2 years
- Treatment recommended in clinical trial
- Criteria vary for defining high risk

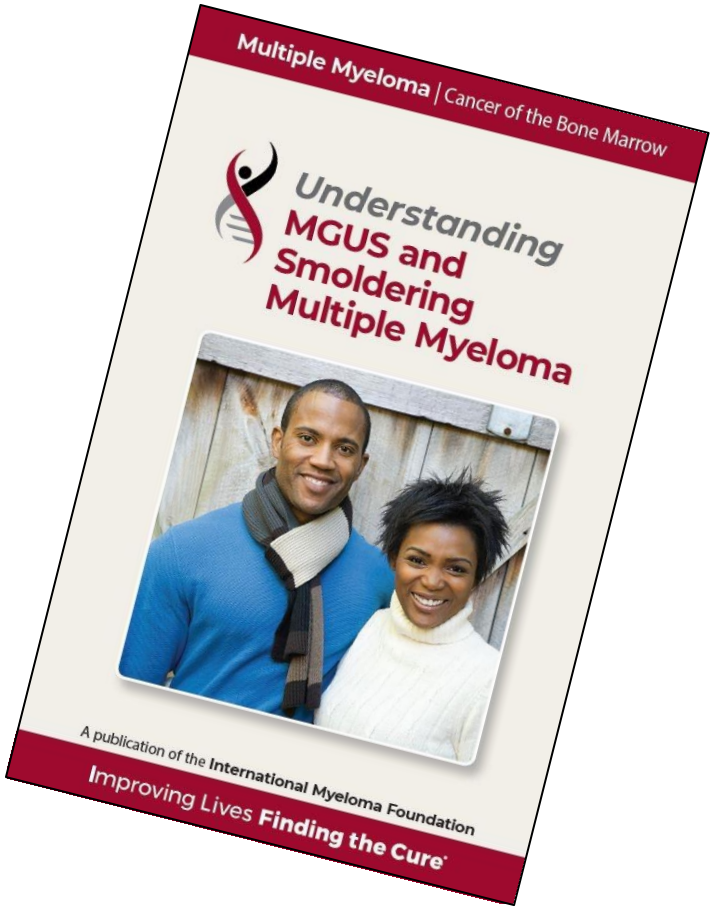
Hr = hour; Ig = immunoglobulin; IMWG = International Myeloma Working Group; MM = multiple myeloma; SMM = smoldering multiple myeloma.

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

SDM for High-Risk SMM

- Options for high-risk SMM
  - Clinical trial
  - Watchful waiting
  - PET-CT or MRI (sensitive test may find evidence of active disease)

- Patient preference important in deciding if/how to address



CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography; SMM = smoldering multiple myeloma.

Phase II Clinical Trials Results for Treating High-Risk SMM

IRd

- 9 cycles of IRd followed by IR maintenance for 15 cycles
- 26 pts (of 56 planned) with high-risk SMM
- Results
  - ORR 89% in pts with 3+ cycles
  - Well tolerated, convenient oral regimen
- **Further studies, longer follow-up needed**

Bustoros M, et al. ASH 2018, #804.

ERd

- ERd for 8 cycles or best response then ER maintenance
- 50 pts with high-risk SMM
- Results
  - ORR 84%
  - Well tolerated
- **Longer follow up and genetic analysis planned**

Liu C, et al. ASH 2018, #154.

KRd + ASCT

- KRd followed by ASCT, consolidation with KRd, maintenance Rd
- 90 pts with high-risk SMM
- Results
  - ORR 98% after 6 cycles KRd
  - Well tolerated
- **Longer follow-up needed**

Mateos MV, et al. ASH 2017, #402.

DARA

- DARA monotherapy (3 regimens: Long, intermediate, short)
- 123 pts with intermediate- or high-risk SMM
- Encouraging results
  - Well tolerated
- **Phase III clinical trial planned**

Hofmeister CC, et al. ASH 2017, #510.

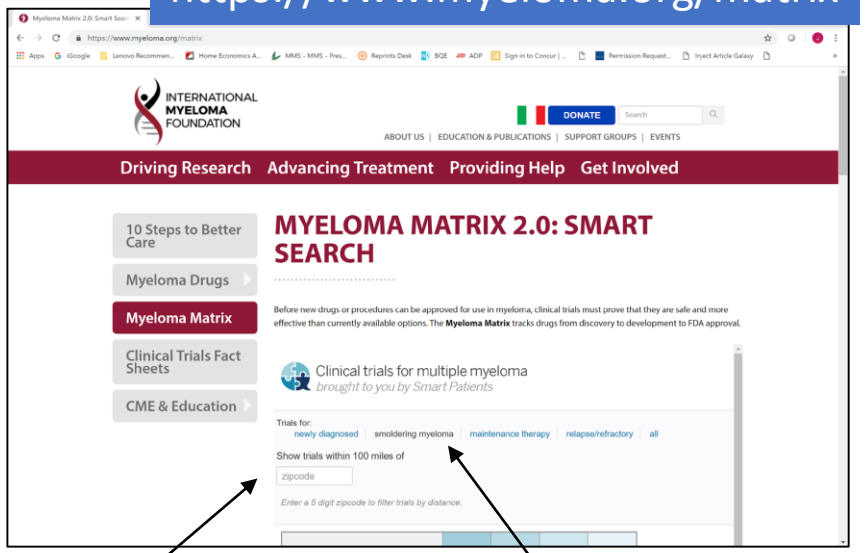
Watch for **Updates as SMM treatment paradigms are evolving**

ASCT = autologous stem cell transplant; DARA = daratumumab; ER = elotuzumab-lenalidomide; ERd = elotuzumab-lenalidomide-dexamethasone; IRd = ixazomib-lenalidomide; IRd = ixazomib-lenalidomide-dexamethasone; KRd = carfilzomib-lenalidomide-dexamethasone; Rd = lenalidomide-dexamethasone; SMM = smoldering multiple myeloma.

Finding Clinical Trials

IMF Infoline
US & Canada 800-452 CURE (2873)
Worldwide: 1-818-487-7455

https://www.myeloma.org/matrix



Search within 100 miles of zip code

Filter trials:

- Newly diagnosis
- Smoldering myeloma
- Maintenance therapy
- Relapse/refractory
- All

multiple myeloma treatments	1 phase 1	6 phase 2	0 phase 3	2 other*
targeted therapy				
carfilzomib (Kyprolis) *proteasome*	0	2	0	0
DKK1 *DKK1*	0	0	0	1
ibrutinib *BTK*	0	1	0	0
ixazomib (Ninlaro) *proteasome*	0	1	0	0
chemotherapy				
cisplatin (Platinol)	0	1	0	0
cyclophosphamide (Cytoxan, Endoxan)	0	1	0	0
doxorubicin (Doxil, Adriamycin)	0	1	0	0
etoposide (Lastet, Vepesid)	0	1	0	0
melphalan flufenamide (Melflufen)	0	1	0	0
thalidomide (Synovir, Thalomid)	0	1	0	0
immunotherapy				
daratumumab (Darzalex) *CD38*	0	2	0	0
durvalumab (MEDI4736) *PD-1*	1	0	0	0
poly iclc (Hiltonol)	1	0	0	0
isatuximab (SAR650984) *CD38*	0	1	0	0
PVX-410 *CS1*	1	0	0	0
lenalidomide (Revlimid)	1	3	0	0
vaccine therapy	0	0	0	1
transplant				
stem cell transplant	0	1	0	0

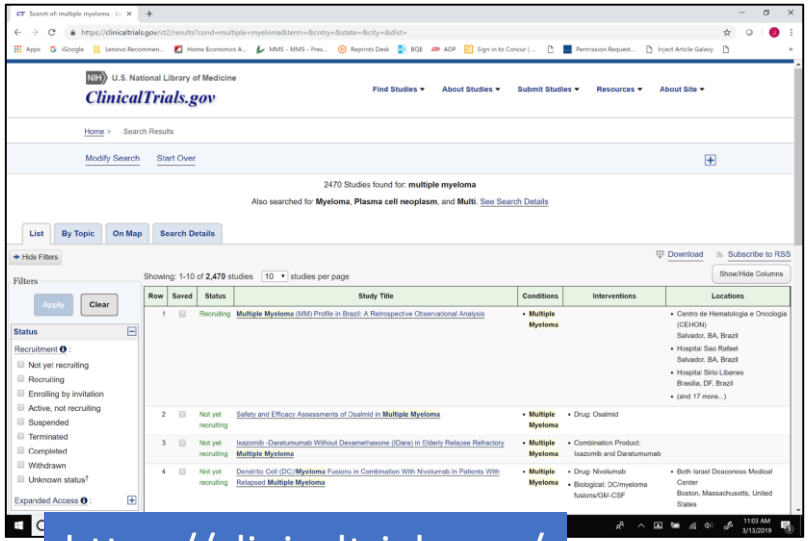
** Phase 4, completed, or compassionate care study*

The table shows only open trials (recruiting, not yet recruiting, or expanded access) in United States. For more options, use the search box below.

Click to expand

NCT02128230
UARK 2012-02 Trial For High-Risk Myeloma Evaluating Accelerating and Sustaining Complete Remission

NCT03289299
Aggressive Smoldering Curative Approach Evaluating Novel Therapies and Transplant



https://clinicaltrials.gov/

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

CASE #1: Mary*

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

*HIPAA-compliant; not actual patient name.

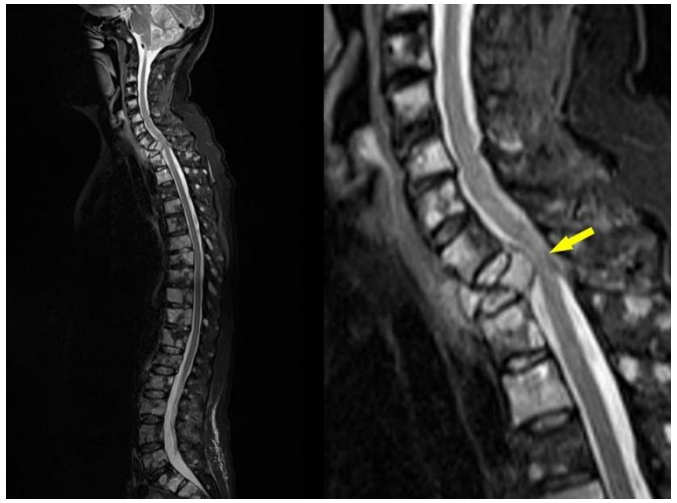
NURSE LEADERSHIP BOARD

INTERNATIONAL MYELOMA FOUNDATION

CASE #1:

Mary*

- 66-year-old retired librarian
  - Married
  - Active and generally good health
    - November 2018 severe back pain
    - Went to ER; T1 fracture spinal compression
    - Lytic lesions
    - Creatinine elevated



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

MRI = magnetic resonance imaging; NSAID = non-steroidal anti-inflammatory drug; PCP = primary care physician.

How Myeloma Patients Commonly Present

Emergency Room

Mary

- Severe pain—often spinal fractures
- Renal failure

Medical emergencies need immediate treatment!

Visit for Specific Complaint

- Persistent symptom or injury
- Abnormal test result

Routine Physical

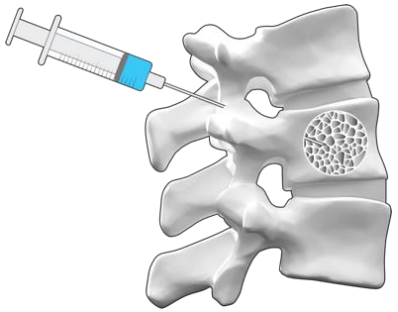
- Patient with few/no symptoms
- Abnormal blood work or x-rays

Non-emergency
More time for shared decision-making

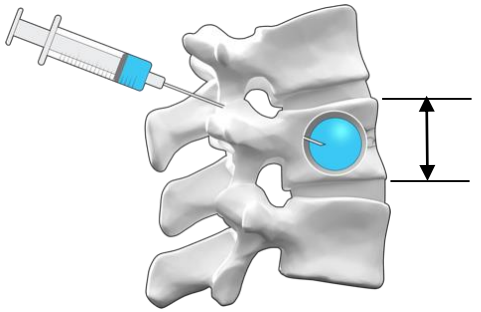
Brigle K, et al. *Clin J Oncol Nursing*. 2017 Oct 1;21(5 Suppl):60-76. Faiman B, et al. *J Adv Pract Oncol.* 2016;2016:7(suppl 1):17-29. Kurtin S, et al. *J Adv Pract Oncol.* 2016;7(suppl 1):59-70.

Procedures to Address Painful Bone Lesions

- **Local radiation:** Radiation to only the bone lesion, delivered by radiation oncologist. Can kill myeloma cells at lesion site



- **Vertebroplasty:** Bone cement injected to stabilize spine
- **Kyphoplasty**: Uses special balloons to create spaces within the vertebra that are then filled with bone cement. Can correct spinal deformity and restore lost height

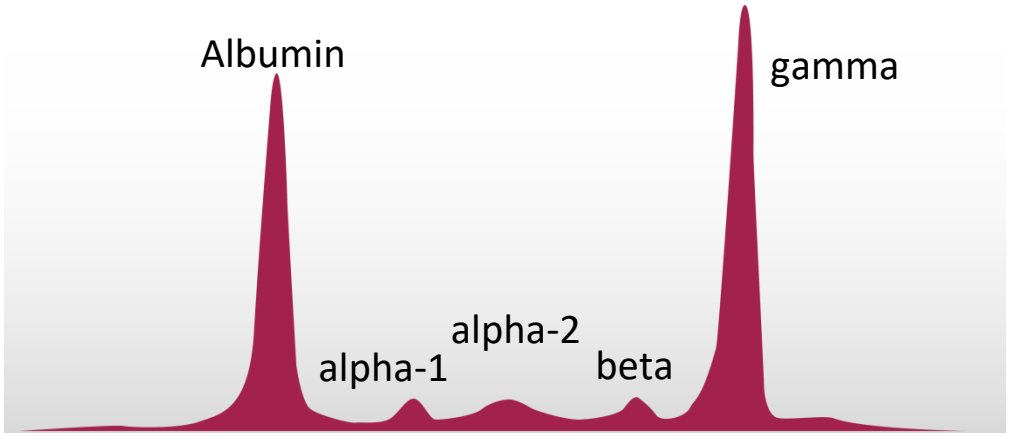


- **Orthopedic surgery**: Pinning or stabilizing procedures done in the operating room

Rome SI, et al. *Clin J Oncol Nursing*. 2017;21(5 Suppl):47-59. Miceli TS, et al. *Clin J Oncol Nursing*. 2011;15(4)suppl:9-23.

Diagnostic Workup for Multiple Myeloma

- Lab tests
  - Serum protein electrophoresis (SPEP)
  - Urine protein electrophoresis (UPEP)
  - CBC + differential + chemistry including albumin and β_2 microglobulin and LDH
  - FLC ratio of free kappa/lambda light chains (plasma)
  - Monoclonal protein analysis (MPA)
- Bone marrow biopsy
  - FISH
  - Cytogenetics
  - Gene expression profiling (GEP)
  - PCLI
- Imaging

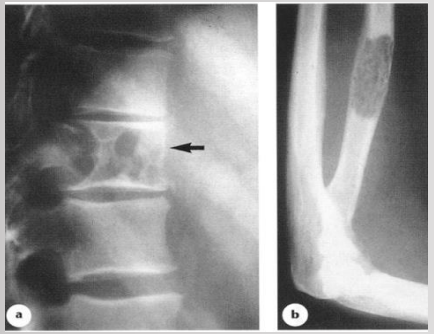


CBC = complete blood count. FISH = fluorescent in situ hybridization; FLC = free light chain; LDH = lactate dehydrogenase; PCLI = plasma cell labeling index.

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.

Recommended Imaging for Multiple Myeloma

OLD



Traditional skeletal survey with x-rays

NEW

WBLDCT

Best for early screening for bone disease

PET/CT

Response assessment: active residual disease

MRI
WB/spine + pelvis

Gold standard to assess bone marrow involvement

Note: Bone scan (DEXA) for bone density, not MM

CT = computed tomography; MM = multiple myeloma MRI = magnetic resonance imaging; PET = positron emission tomography; WBLDCT = whole body low dose computed tomography.

Rome SI, et al. *Clin J Oncol Nursing*. 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.

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(14;4) 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%

CA = chromosomal abnormalities; 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.

CASE #1:

Mary*

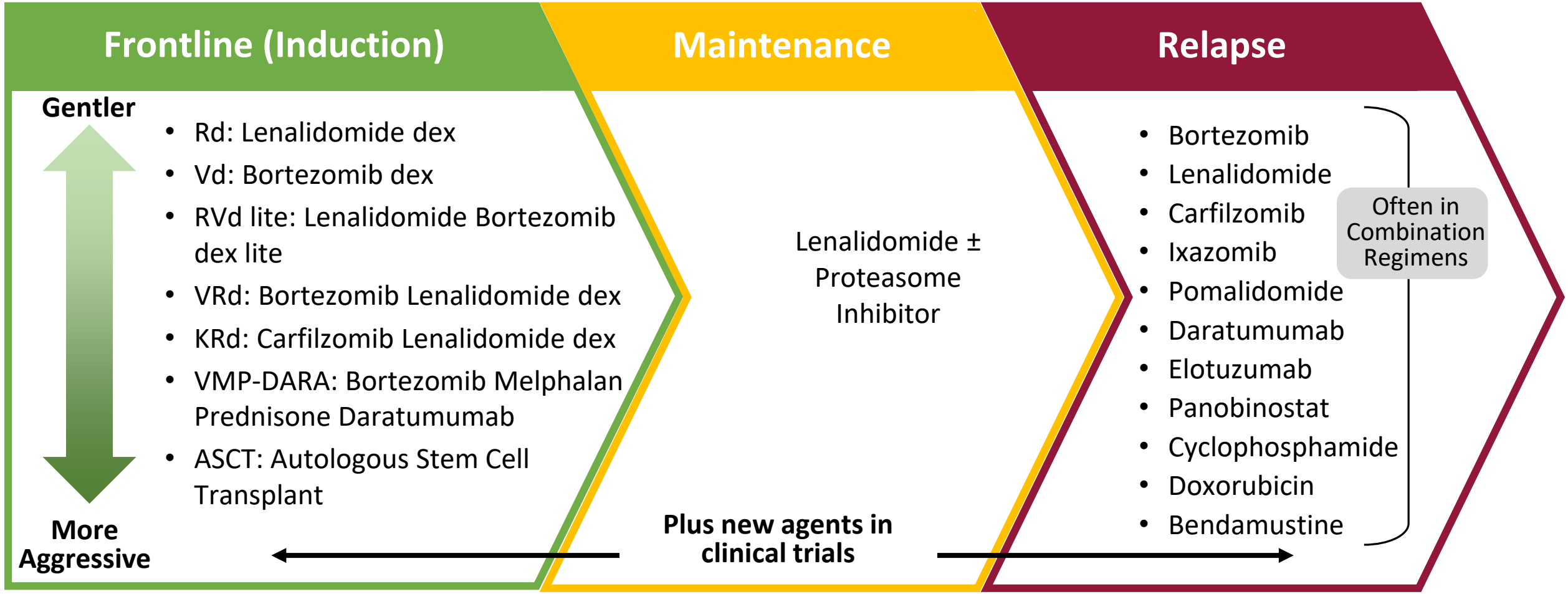
- Myeloma Workup
  - Peripheral blood:
    - Calcium: 10.2 mg/dL (ULN 10.6 mg/dL)
    - Albumin: 3.3 mMol/L (LLN 3.5 mMol/L)
    - B_2M: 5.3 mg/dL (ULN 2.64 mg/dL)
    - LDH: 150 U/mL (ULN 250 U/mL)
    - **Creatinine: 2.1 mg/dL (ULN 1.3 mg/dL)**
      - GFR (calculated): 24 mL/min/1.73 m^2
    - Hgb: 10.8 g/dL
    - **κ: 1832.0 g/dL (normal range 3.3-19.4 g/dL)**
    - **κ/λ-light-chain ratio: 122 (ULN: 1.65)**
  - Bone marrow biopsy:
    - 60% +kappa PC
    - Cytogenetics: 46xx; FISH: normal
  - Whole body low dose CT:
    - Lytic lesions: arms, ribs, skull, femur
- Diagnosis: Active myeloma R-ISS Stage II

translocations t(4;14), t(14;16), t(14;20), and del(17/17p) and any nonhyperdiploid karyotype are high risk
Sonneveld P, et al. *Blood.* 2016;127:2955-2962.

*HIPAA-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.

Common Treatments for Multiple Myeloma



Faiman B, et al. *J Adv Pract Oncol.* 2016:7(suppl 1):17-29. Joseph Mikhael, MD, Med https://www.medscape.com/viewarticle/882042. NCCN Guidelines. Multiple Myeloma. V2.2019.

Autologous Stem Cell Transplant (ASCT) Remains Standard of Care for Eligible Patients; Timing Is Optional

- Role of ASCT in MM is evolving
- Eligibility for ASCT depends on age, comorbidities, and performance status
  - Pts up to age 75 considered for ASCT in the US
  - Ineligible if poor performance status (ECOG 3 or 4), poor heart health (New Haven III or IV), or poor organ function
- Newer drugs are highly effective so decision when (upfront or at relapse) is debated

"Therefore, although ASCT is considered a part of initial therapy, delaying [ASCT] until relapse remains an acceptable approach."

Nursing Implications for ASCT

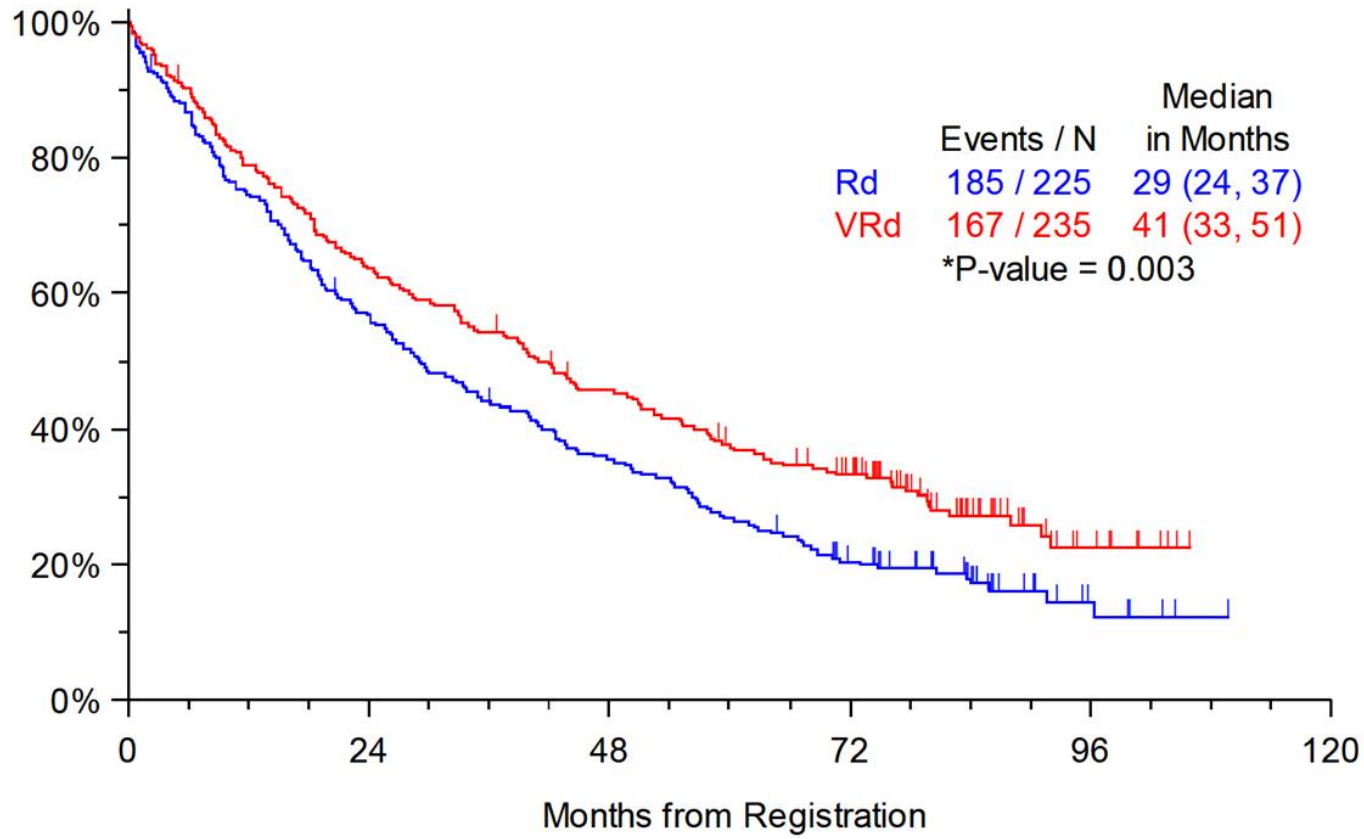
- Ensure pts referred for ASCT consult as soon as possible
- Stem cell harvest is typically after 4-6 cycles of treatment

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

Mahajan S, et al. *Ther Adv Hematol.* 2018;9(5):123-133.

3-Drug Combination Better Than 2 in Newly Diagnosed Multiple Myeloma With Delayed ASCT SWOG 0777 UPDATE

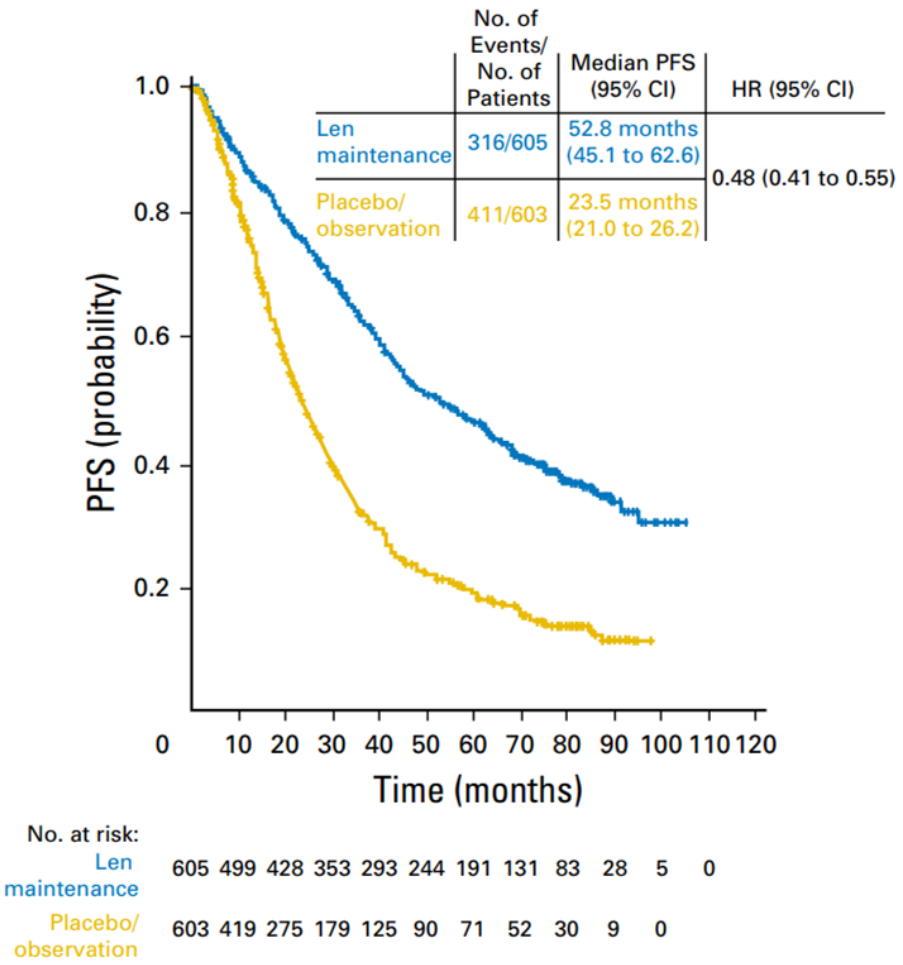
PFS



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 2018. Abstract 1992.

Meta-Analysis: Lenalidomide Maintenance After ASCT Demonstrates Improved PFS and OS vs Placebo/Observation



PFS and OS benefit observed across subgroups:

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

Multiple clinical studies have confirmed the benefits of lenalidomide maintenance in MM pts after ASCT

ASCT = autologous stem cell transplant; CI = confidence interval; HR = hazard ratio; ISS = International Staging System; NDMM = newly diagnosed multiple myeloma; OS = overall survival; PFS = progression-free survival.

McCarthy PL, et al. *J Clin Oncol.* 2017;35(29):3279-3289.

Lenalidomide Maintenance Improves PFS for All Patient Subgroups Including Non-Transplant

- Phase III NCRI Myeloma XI study: 1970 newly diagnosed MM patients **(both transplant eligible and ineligible)** randomized to receive R maintenance OR observation

- Conclusions: Consistent PFS benefit for lenalidomide maintenance across ALL patients
  - Transplant
  - **Non-transplant**
  - All risk groups (standard, high risk, ultra-high risk)
  - All ISS stages
  - Patents with t(4;14) or del17(p)

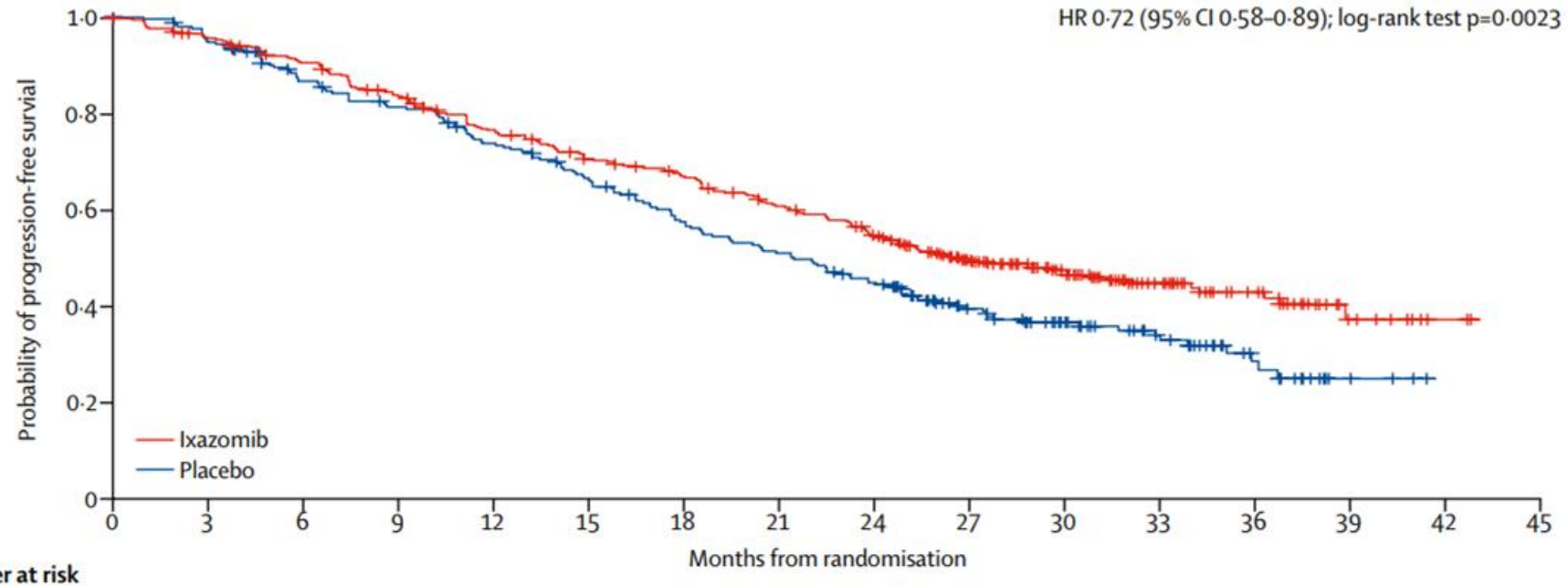
"All risk groups and stages benefitted from maintenance therapy"

ISS = International Staging System; NCRI = National Cancer Research Institute; PFS = progression-free survival; R = lenalidomide.

Jackson G, et al. ASCO 2017. Abstract 436.

Tourmaline-3 Ixazomib Maintenance After Transplant Data

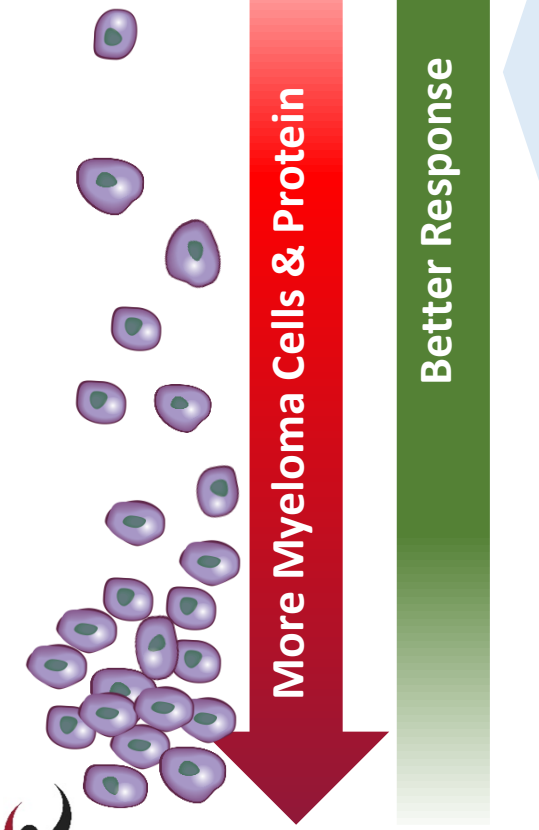
PFS



Number at risk (number censored)																
Ixazomib	395	363	340	311	279	255	238	213	187	135	93	56	35	9	3	0
	(0)	(15)	(19)	(22)	(26)	(30)	(33)	(37)	(41)	(76)	(112)	(146)	(165)	(188)	(194)	(197)
Placebo	261	238	210	195	174	153	130	117	100	69	46	32	15	3	0	0
	(0)	(10)	(18)	(20)	(22)	(25)	(27)	(27)	(29)	(50)	(68)	(78)	(91)	(102)	(105)	(105)

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

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



Flow MRD negative*	**Negative by NGF (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
CR	Negative immunofixation; no more than 5% plasma cells in BM; 2 measures
VGPR	90% reduction in myeloma protein
PR	At least 50% reduction in myeloma protein
MR	
SD	
PD	

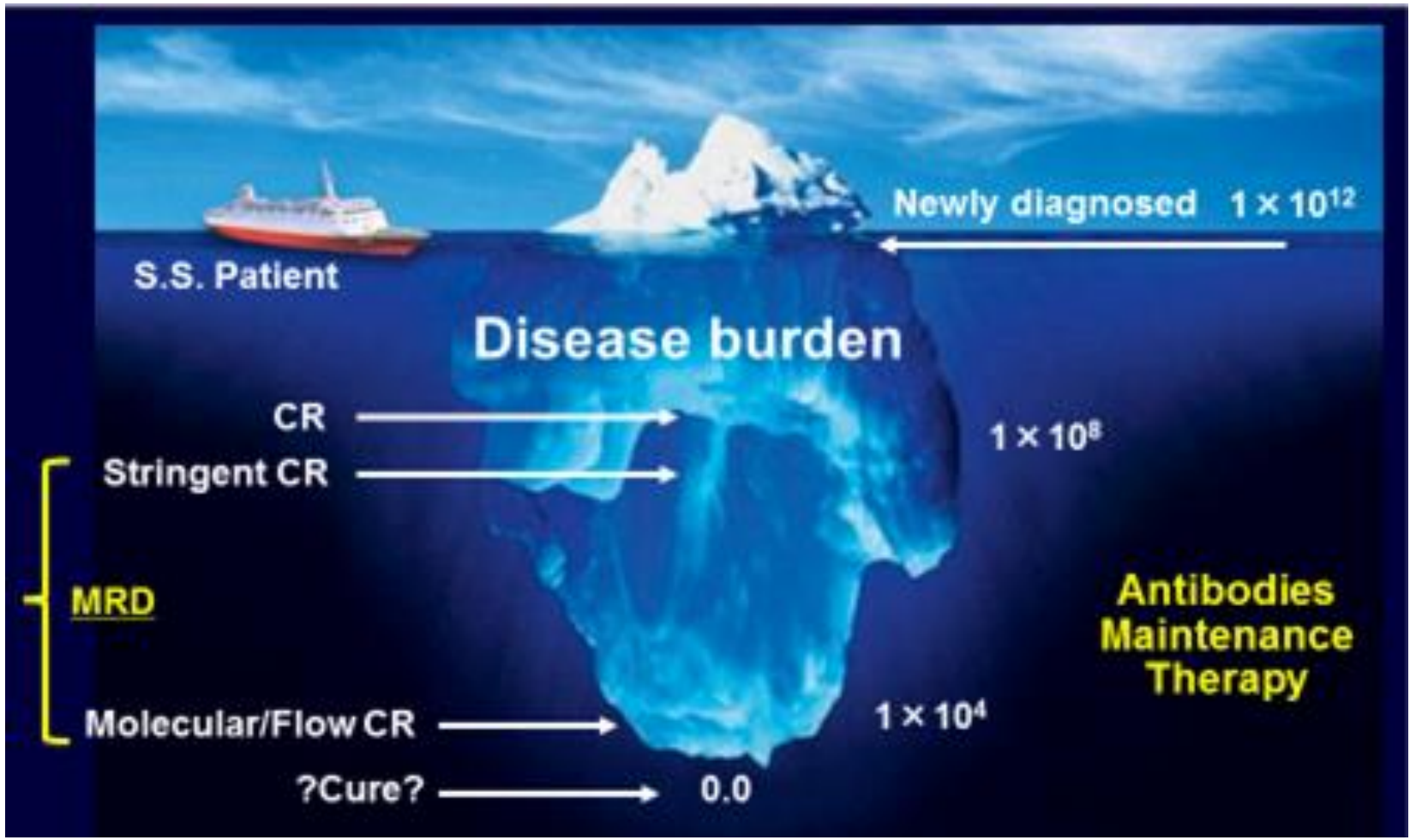
BM = bone marrow; CR = complete response; FLC = free light chain; mCR = molecular CR; MR = minimal response (only in relapsed); NGS = next-generation sequencing; PD = progressive disease; PR = partial response; sCR= stringent complete response; SD = stable disease; VGPR = very good partial response.

*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.

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

Increasing depth of response



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

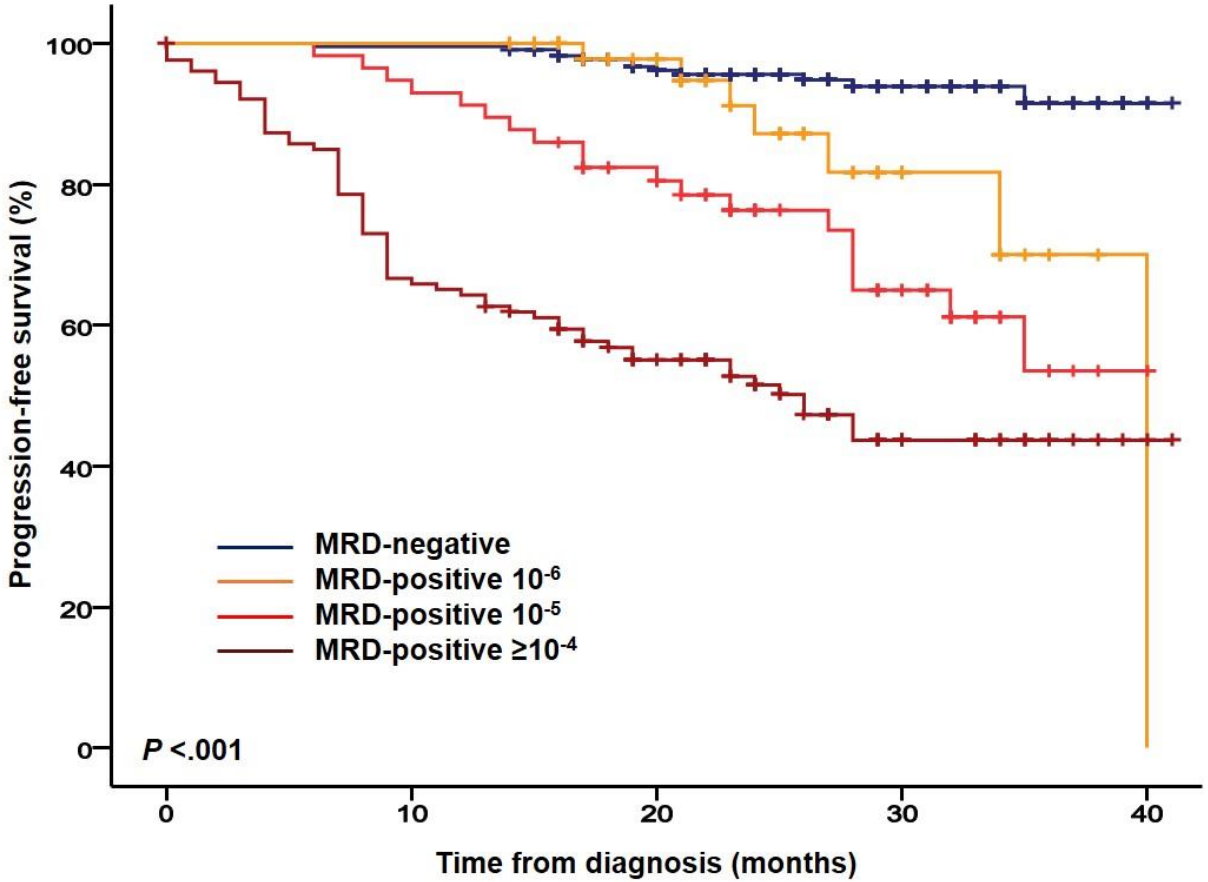
MANY ways to get to deeper responses:

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

ASCT = autologous stem cell transplant; CR = complete response.

From S. Lonial; Kumar S, et al. *Lancet Oncol.* 2016; 17(8):e328-e346.

PETHEMA/GEM2012 Trial: MRD-Negative Patients Had Best PFS



MRD-negative had 3-year PFS = 92%

"Overall, this study defines MRD-negativity as the most relevant clinical endpoint for both standard- and high-risk transplant-eligible MM patients."

MM = multiple myeloma; MRD = minimal residual disease; PFS = progression-free survival.
Pavia B, et al. ASH 2017. Abstract 905.

MRD Testing for MM Now Commercially Available

- **Bone marrow** samples from pts with MM can now be tested for MRD via FDA-cleared assay
- Reimbursed by Medicare

Watch for

Updates to MRD testing. Although commercially available, clinical application (eg, when and how to initiate treatment based on test results) is evolving

ClonoSEQ website. https://www.clonoseq.com/. Accessed March 13, 2019. Adaptive press release January 17, 2019. https://www.adaptivebiotech.com/adaptive-biotechnologies-announces-medicare-coverage-of-the-clonoseq-assay-for-mrd-testing-in-patients-with-multiple-myeloma-and-acute-lymphoblastic-leukemia-at-multiple-timepoints-throughout-treatmen/. Accessed March 13, 2019.

Steep Learning Curve for Pts Newly Diagnosed With MM

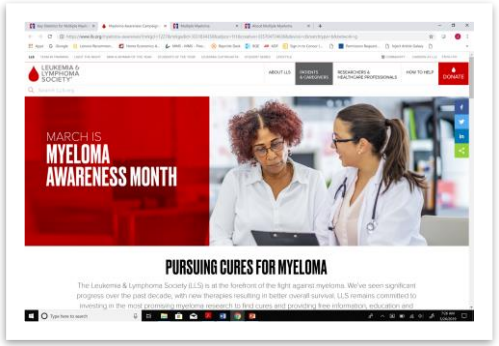
- Patient education is crucial but can be overwhelming
- Shock of diagnosis makes understanding and retaining information difficult
  - Tell patient information but also give written information they can read later
  - Refer patients to reliable sources of information

NIH NATIONAL CANCER INSTITUTE

https://www.cancer.gov

American Cancer Society®

https://www.cancer.org



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

IMF Website http://myeloma.org

IMF TV Teleconferences

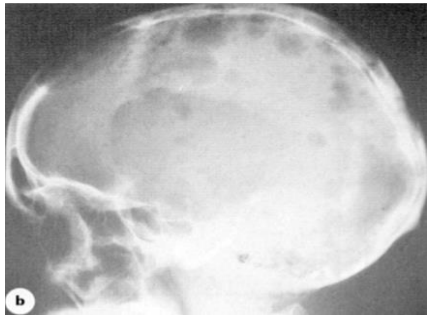
Free download or order from myeloma.org

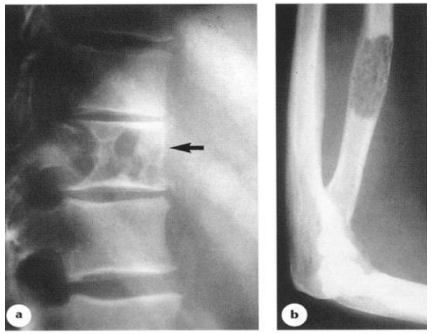
Multiple languages

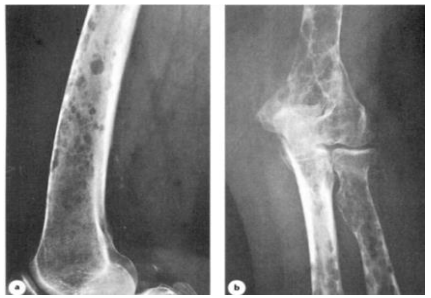
MM = multiple myeloma.

NURSE LEADERSHIP BOARD

Newly Diagnosed MM Patient Education: Bone Health







Bone Disease in Myeloma

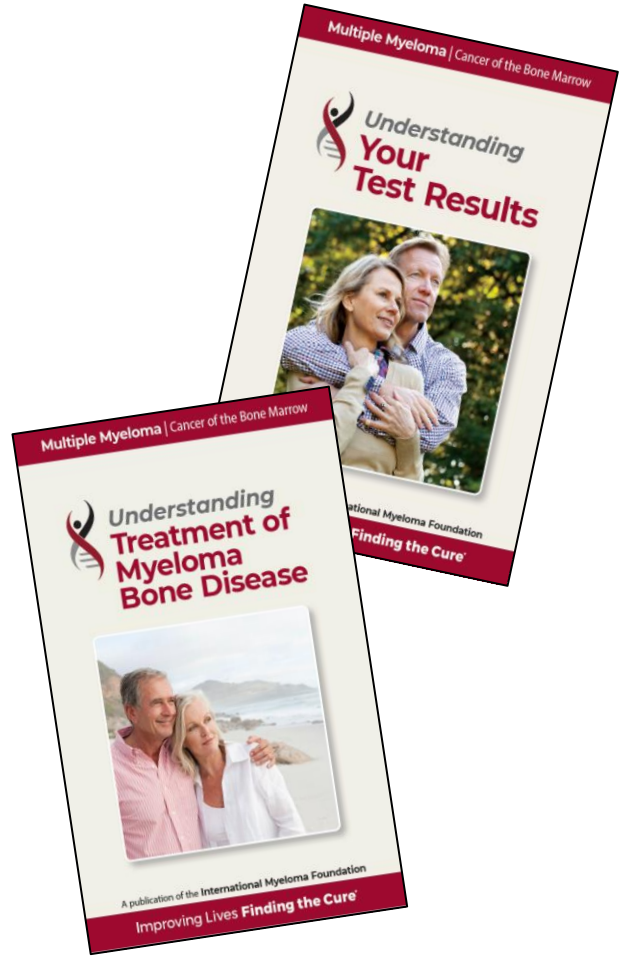
- ≈85% of myeloma patients develop bone disease
- Bone destruction may lead to hypercalcemia and contribute to renal impairment
- Spinal cord compression can be an emergency!

Symptoms

- Pain, fracture—report to Myeloma Team
- Bone imaging—type depends on symptoms

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

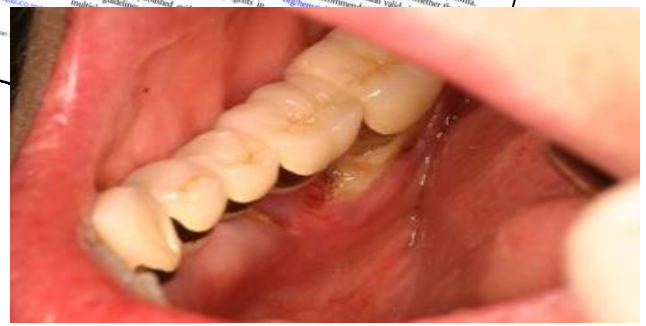


Rome SI, et al. *Clin J Oncol Nursing*. 2017;21(5 Suppl):47-59. Miceli TS, et al. *Clin J Oncol Nursing.* 2011;15(4)suppl:9-23. Dimopoulous M, et al. *Leukemia.* 2009;23(9):1545-56.

ASCO Guideline Update: Bone-Modifying Agents

A **bone-modifying agent** is recommended for ALL pts receiving anti-myeloma therapy regardless of bone disease status for up to 2 years. **Three options:**

- **Pamidronate:** 90 mg over 2+ hrs every 3-4 weeks
  - In pts with severe renal impairment (CrCl <30 mL/min): 90 mg over 4-6 hrs
  - Consider dose adjustment for mild-moderate preexisting renal impairment
- **Zoledronic acid:** 4 mg over 15+ min every 3-4 weeks
  - Dose adjust for mild-moderate renal impairment (CrCl 30 to 60 mL/min) per PI
  - Not recommended (nor studied) in pts with sever renal impairment
- **Denosumab:** Demonstrated non-inferiority to zoledronic acid in SRE
  - Fewer renal AEs; may be preferred in pts with renal comorbidities; hypocalcemia



Osteonecrosis of the Jaw

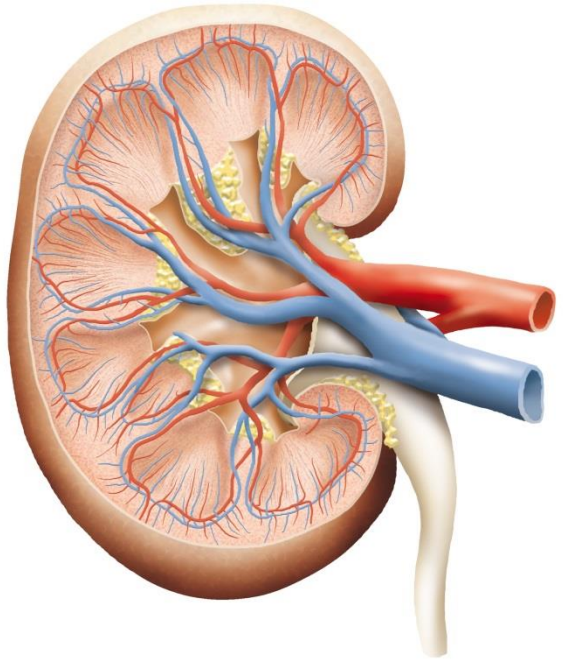
Continuous bone-modifying agent treatment by physician discretion.
Retreatment with bone-modifying agent recommended at relapse.

CrCl = creatinine clearance; PI = prescribing information; SRE = skeletal related events.

Anderson K, et al. *J Clin Oncol.* 2018;36:812-818.

Newly Diagnosed MM Patient Education: Renal Health

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



NSAID = non-steroidal anti-inflammatory drug.

Faiman B, et al. *Clin J Oncol Nurs.* 2017 Oct 1;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 Nursing.* 2011;15(4):9-23.

NDMM Patient Education: Infection Prevention

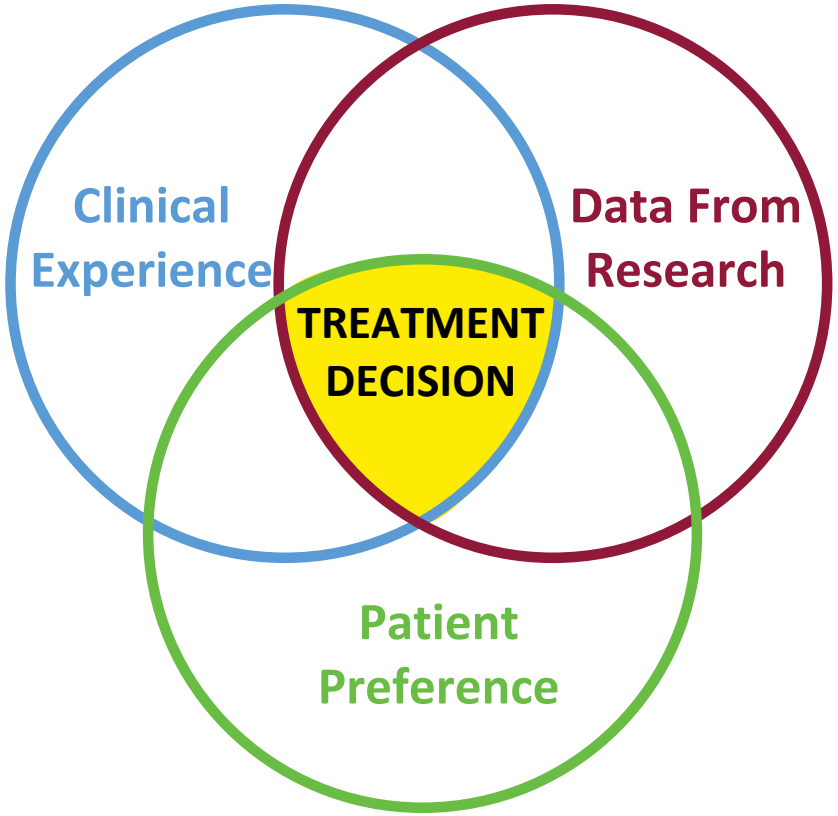
- Compromised immunity from MM disease and treatment
  - Good personal hygiene (skin, oral)
  - Environmental control (wash hands, avoid crowds and sick people, etc)
  - Prompt medical attention at signs of infection (eg, fever, chills)
  - Medications (antibacterial, antiviral)
    - For patients receiving active myeloma therapy, levofloxacin 500 mg once daily for 12 weeks reduced infection (fevers, death) (ASH 2017 #903)
  - Growth factor (eg, filgrastim)
  - Intravenous immunoglobulin for hypogammaglobulinemia
  - Immunizations (NO live vaccines)
    - Pneumococcal vaccination (13 and 23)
    - Seasonal inactivated influenza X 2
    - Shingles vaccine: Zoster vaccine recombinant, adjuvanted

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 Nursing.* 2011;15(4):9-23. CDC https://www.cdc.gov/vaccines/vpd/shingles/public/shingrix/index.html.

CASE #1:

Mary*

- Treatment Decision
  - Considered available trials
  - Decided on three-drug induction regimen:
    - VRd (bortezomib/lenalidomide/dex)
      - 10 mg lenalidomide (renal dose adjustment)
  - Supportive agents options:
    - Denosumab subcutaneous injection + Ca supplement
  - Nursing key points
    - Kidney function and bone health
    - Subcutaneous bortezomib (reduced PN)
    - Dex same time each day
    - Aspirin, acyclovir prophylaxis

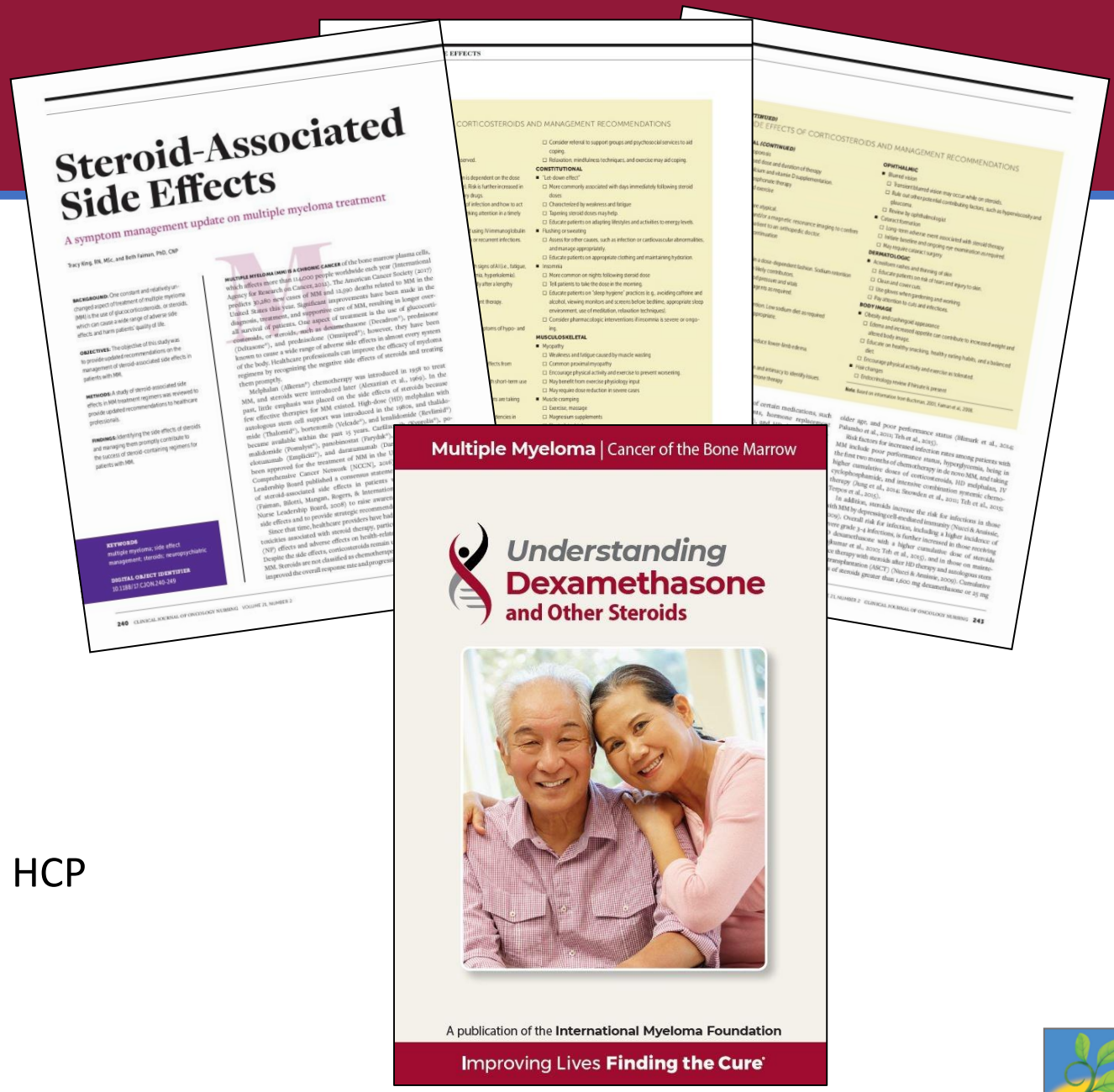


Philippe Moreau. ASH 2015.

Dex = dexamethasone; PN = peripheral neuropathy.
*HIPAA compliant; not actual patient name.

Clinical Pearls for Steroids

- Patient education
  - Steroids kill myeloma cells
  - Don’t stop or change dose without discussing with provider
- Consistent schedule (AM vs PM)
- Take with food
- Proactively manage side effects
  - Glucose
  - Checklists
  - Consider dose/timing adjustments with HCP (if needed)



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

CASE #1:

Mary*

- Achieved a VGPR after 4 cycles
  - Kidney function improved (creatinine 1.2 mg/dL)
  - Stem cell collection
  - Autologous stem cell transplant planned (PFS, OS benefit)
  - Maintenance therapy planned
  - MRD testing planned at 1 year (if molecular CR)
- Survivorship care plan
  - Diagnosis and test results
  - Treatment received
  - Follow-up plan
  - Coordination with PCP
  - Long-term risks

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

CR = complete response; MRD = minimal residual disease; Len = lenalidomide; OS = overall survival; PFS = progression-free survival; PCP = primary care physician.

Maintenance Therapy 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

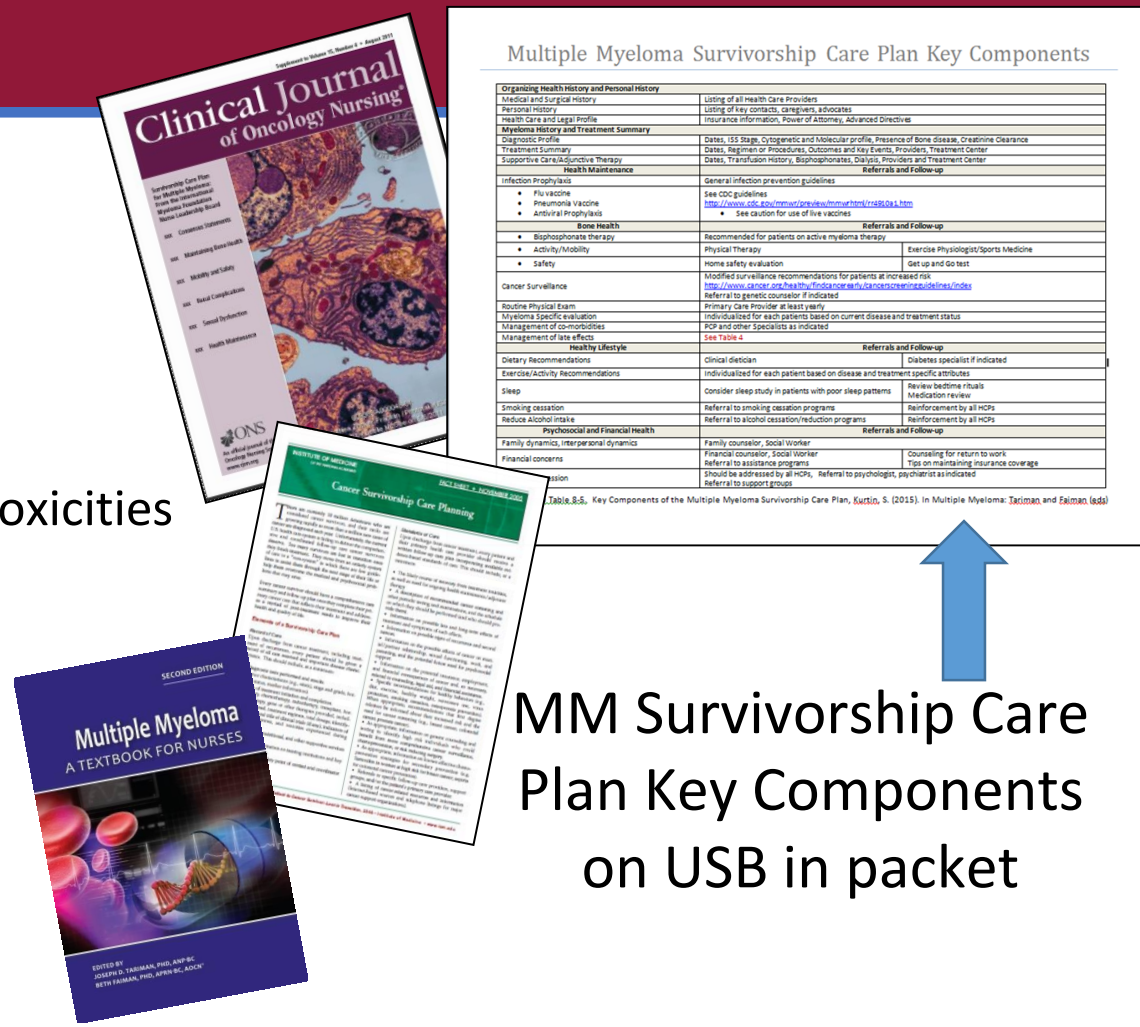
Lenalidomide maintenance after ASCT
10 mg Day 1-28 of 28-day cycle
FDA approved February 2017

AE = adverse event; ASCT = autologous stem cell transplant; PCP = primary care physician.

Hulin C, et al. ASH 2014, #81. Facon T, et al. ASH 2013, #2. Palumbo A, et al. *N Engl J Med.* 2014; 371(10):895-905. Attal M, 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.

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 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

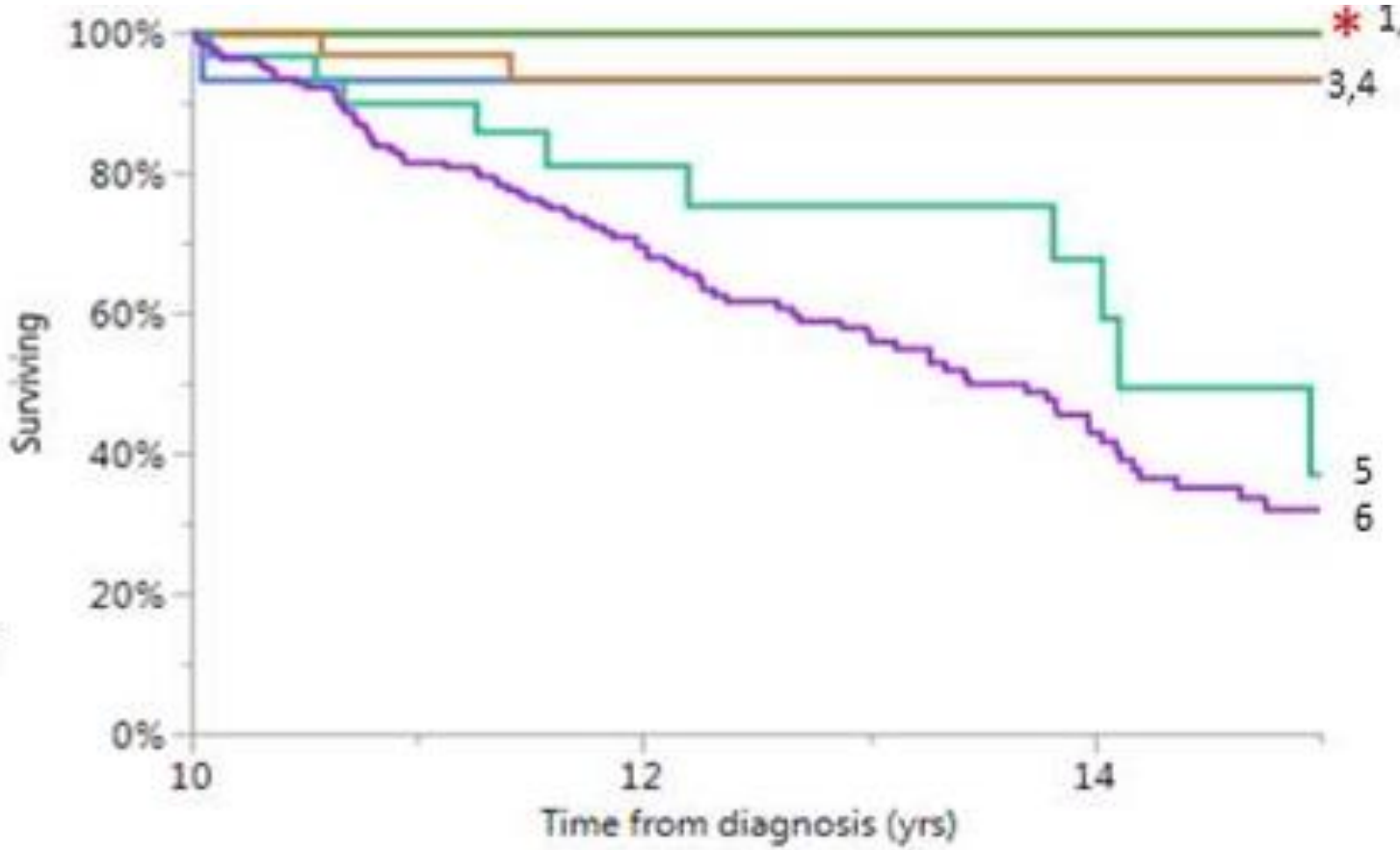


MM Survivorship Care Plan Key Components on USB in packet

Institute of Medicine. Cancer Survivorship Care Planning. Fact Sheet Nov 2005. www.iom.edu. Salz T, et al. *Cancer.* 2014;120(5):722-730. *Clin J Oncol Nursing.* 2011;15(4)suppl. Kurtin, S. *Multiple Myeloma.* 2nd ed. Tariman and Faiman (eds). 2015.

Some MM Pts (~17%) Experience Long-Term Remissions

Mayo Clinic follow-up of 2,125 pts with MM at ≥ 10 years



≥ 5 year remission off Rx

≥ 5 year remission on maintenance

~17% of long-term MM survivors may represent patients "operationally cured"

Watch for

Updates since research is ongoing to characterize which pts achieve long-term remissions

Grieb B, et al. ASH 2018. Abstract #1912.

IMF's Research Initiatives: Black Swan and iStopMM 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

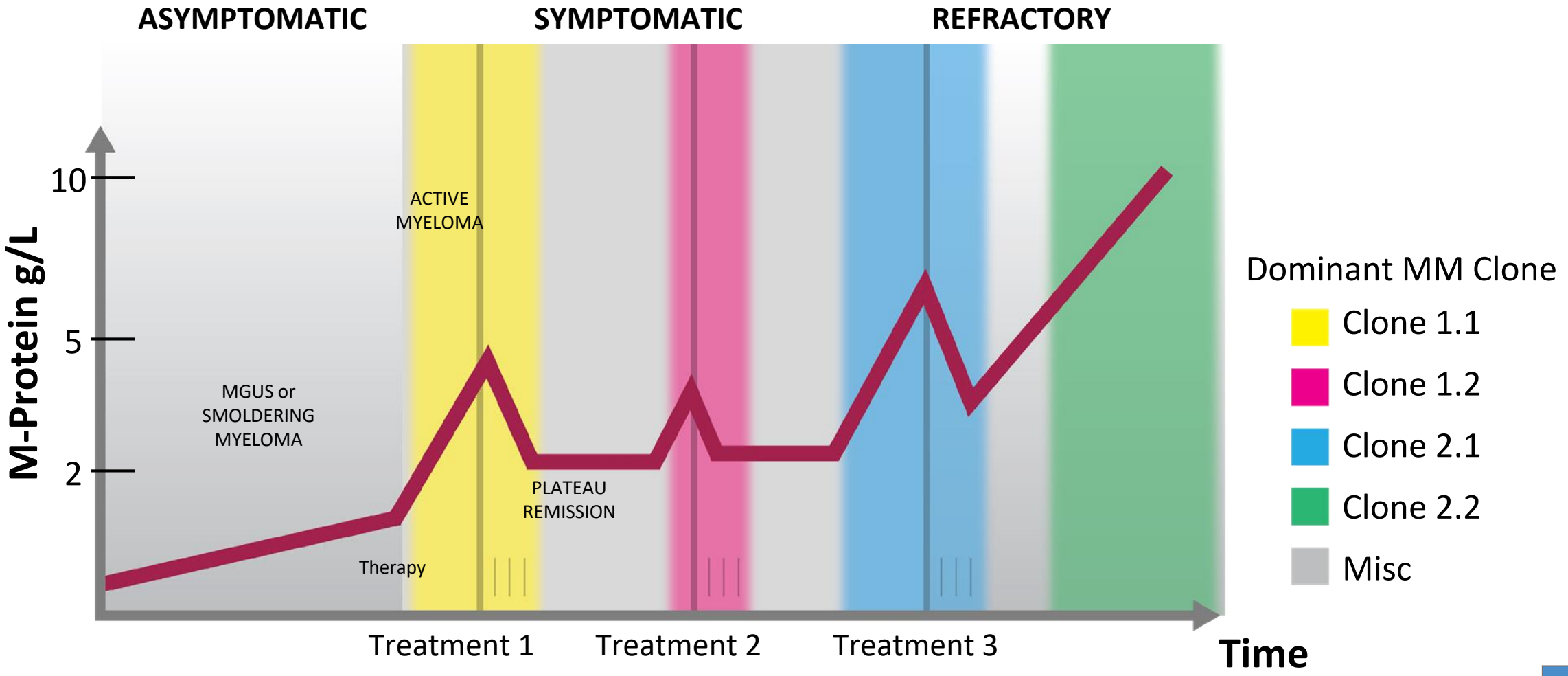
iStopMM (one of the Black Swan Trials)

- 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.

Unfortunately Most Pts With MM Eventually Relapse: Relapsed Disease Is Different—Clonal Evolution



MGUS = monoclonal gammopathy of undetermined significance; MM = multiple myeloma.

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

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

CASE #3: Aaron*
CASE #4: James*

Kimberly Noonan, DNP, RN, ANP-BC, AOCN®
Beth Faiman, PhD, RN, MSN, APRN-BC, AOCN®

*HIPAA-compliant; not actual patient names.

NURSE LEADERSHIP BOARD

INTERNATIONAL MYELOMA FOUNDATION

CASE #2:

Aaron*

- Married, retired plumber, 68 years old
- May 2014
  - Generalized pain, fatigue
  - X-rays, MRI
  - Multiple myeloma diagnosed
  - Normal cytogenetics
  - Diabetes, pulmonary hypertension (transplant ineligible)
  - Ex-smoker
  - VRd 6 cycles induction; (V was IV and developed PN)
  - Continued R maintenance
  - Zoledronic acid
- CR

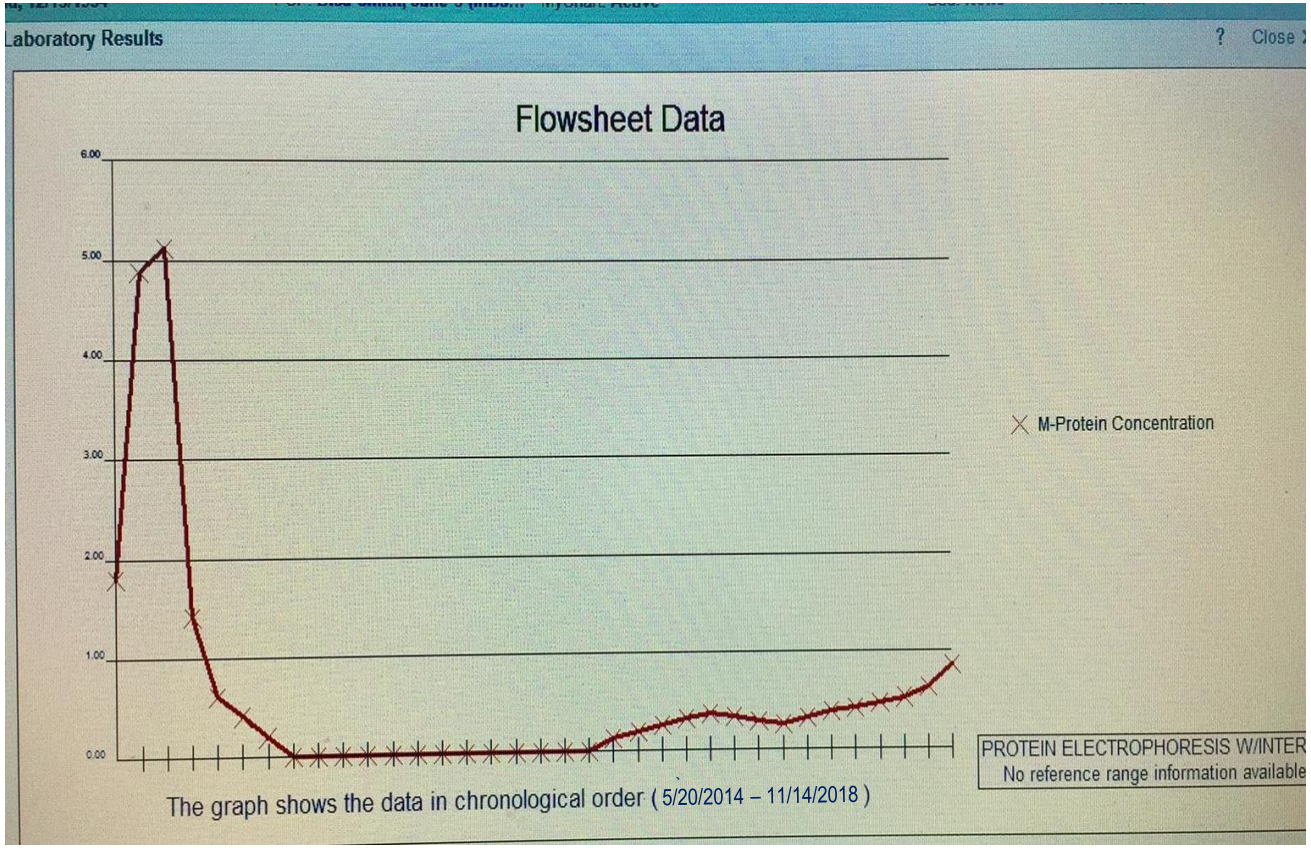
*HIPAA-compliant, stock photo (not actual patient).

ASCT = autologous stem cell transplantation; MRI = magnetic resonance imaging; VGPR = very good partial response; VRd = bortezomib-lenalidomide-dexamethasone.

CASE #2:

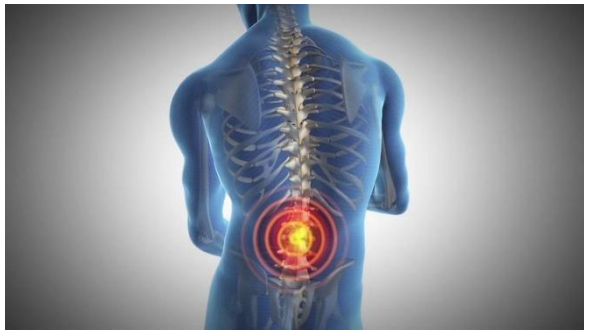
Aaron*

- December 2018: biochemical relapse
  - M-protein from undetectable g/dL to 0.96 g/dL over 2.5 year
  - No other symptoms
  - Lab values normal
  - Low dose whole body CT, no new lesions



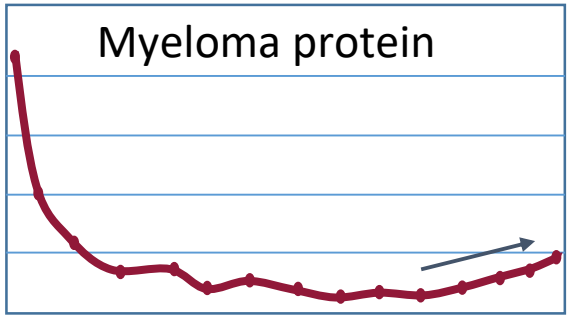
*HIPAA-compliant, identifiers removed.

How Patients with Myeloma Relapse



Symptomatic

- New, worsening bone pain
- Increasing fatigue, anemia
- Next steps: Relapse workup, many therapy choices



Asymptomatic Biochemical Relapse

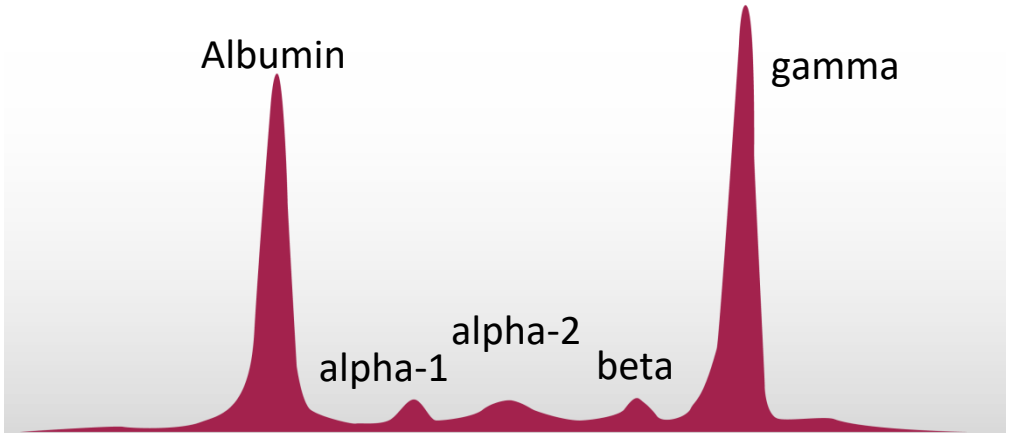
Aaron

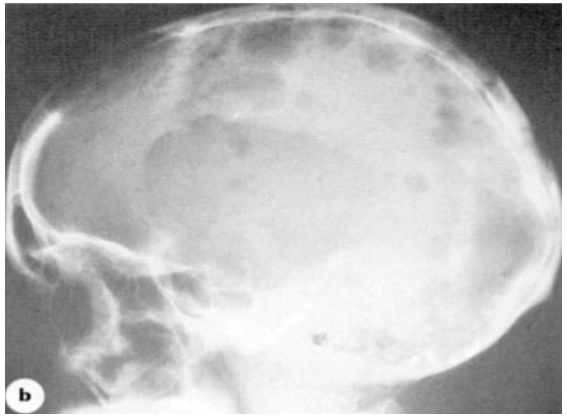
- Sequentially rising myeloma protein, free light chain
- No other symptoms
- Decisions: If, when, how to treat

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.

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)
- **Consider bone marrow biopsy**
  - Cytogenetics and FISH
- **Imaging**
  - Skeletal survey or whole body low dose CT
  - MRI and/or PET/CT for select pts





CT = computed tomography; FISH = fluorescent in situ hybridization; FLC = free light chain; MRI = magnetic resonance imaging; PET = positron emission tomography.

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 Treatment Options at Relapse

Treatment Options

- Bortezomib
- Lenalidomide
- Carfilzomib
- Ixazomib
- Pomalidomide
- Daratumumab
- Elotuzumab
- Panobinostat
- Cyclophosphamide
- Doxorubicin
- Bendamustine

Often in Combination Regimens

New agents in clinical trials

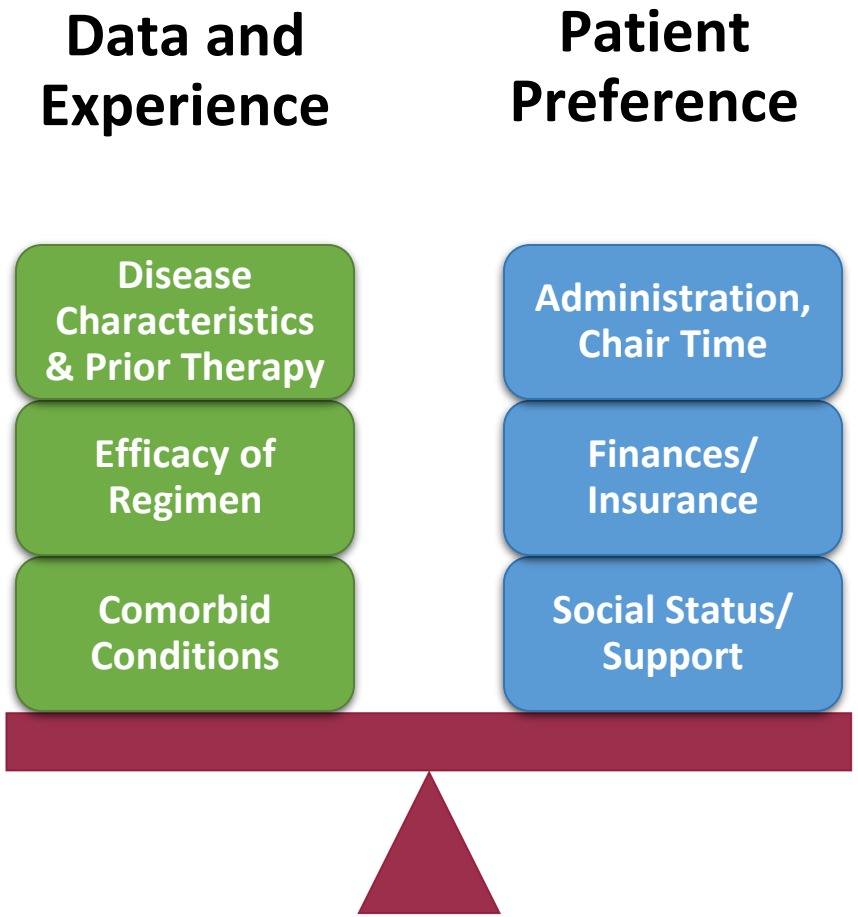
FDA-approved myeloma therapies	Common Combinations
Bortezomib (SQ admin)	VRD, Vd
Lenalidomide	VRD, Rd
Carfilzomib	KRd, Kd
Pomalidomide	Pd, DPd, EPd, PCd
Daratumumab	DRd, DVd, DPd, D-VMP
Elotuzumab	ERd, EPd
Ixazomib	IRd
Panobinostat	Panobinostat + Vd
Doxorubicin	Liposomal doxorubicin + V
Cyclophosphamide	PCd, VTD-PACE

C = cyclophosphamide; D = daratumumab; d = dexamethasone; E = elotuzumab; I = ixazomib; K = carfilzomib; P = pomalidomide; PACE = cisplatin, doxorubicin, cyclophosphamide, etoposide; R = lenalidomide; SQ = subcutaneous; T = thalidomide; V = bortezomib.

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

Practical Approach to Treatment of Patients With Relapsed Myeloma

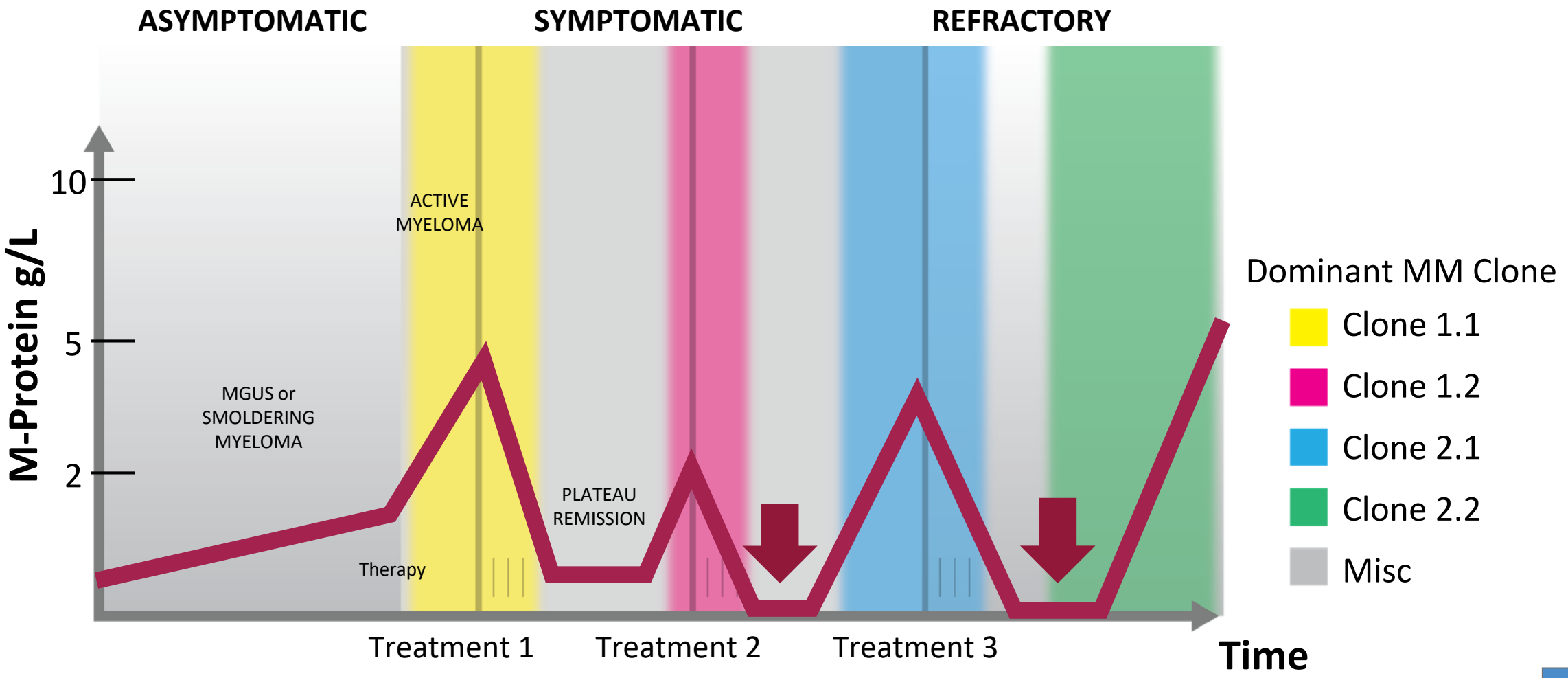
- **Disease-related factors**
  - Duration of response to initial therapy
  - High-risk vs low-risk status
  - Molecular relapse vs symptomatic relapse
  - Other comorbid conditions, patient frailty
- **Treatment-related factors**
  - Previous/current therapy exposure (relapsed or refractory)
  - Toxicity/tolerability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



IV = intravenous; PO = orally.

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

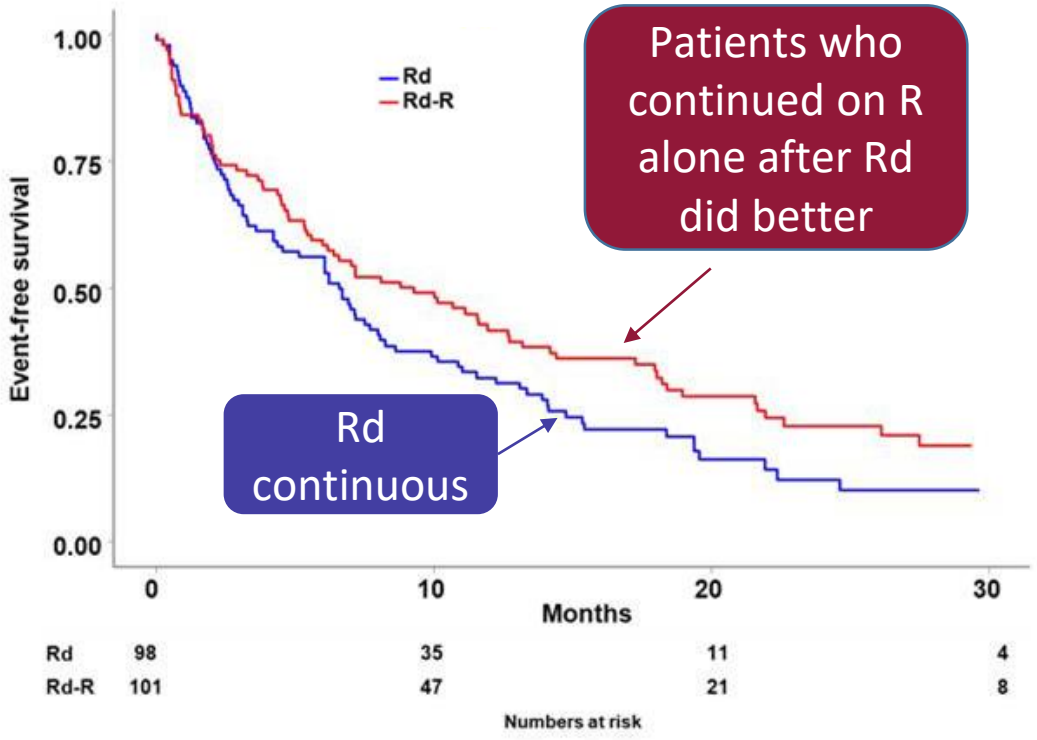
With New Agents, Some Patients Achieve Deep Responses Even After Many Treatments

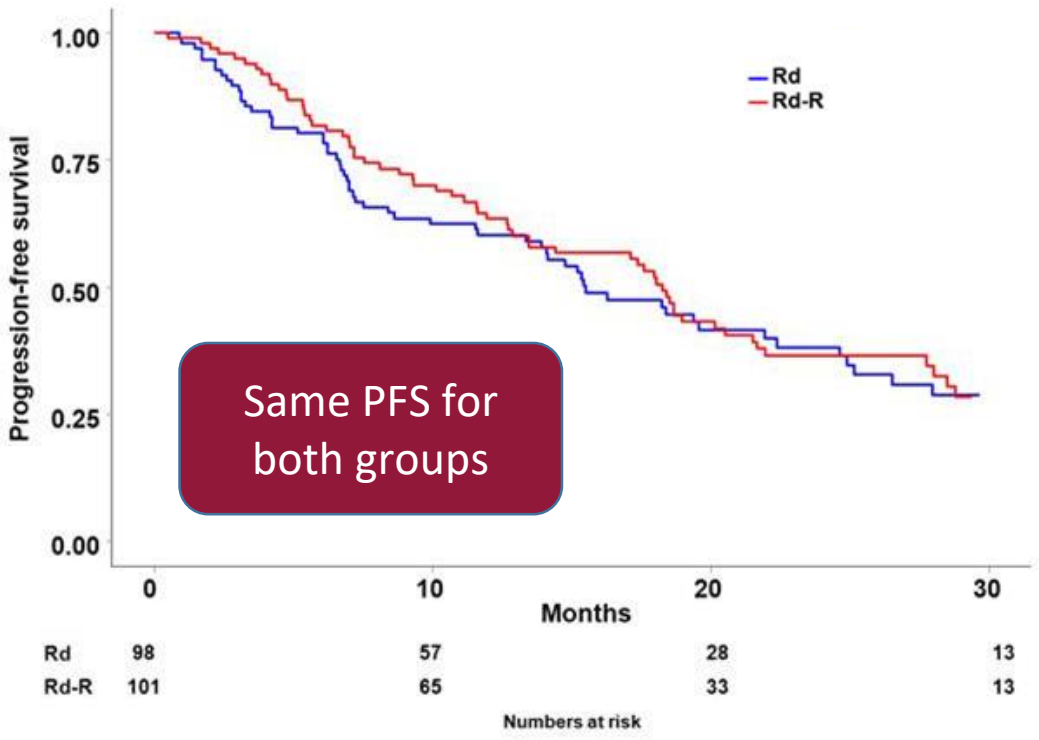


MGUS = monoclonal gammopathy of undetermined significance; MM = multiple myeloma.

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

Less Dexamethasone Improved Event-Free Survival in Elderly/Frail MM Patients



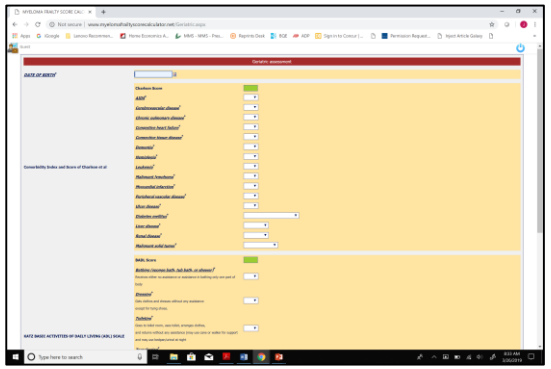


EFS Events: PD or death for any cause or discontinuation of lenalidomide or any hematological grade 4 or non-hematological grade 3-4 AEs, including SPMs

MM = multiple myeloma; PFS = progression-free survival; R = lenalidomide; Rd = lenalidomide dexamethasone; RSPM = second primary malignancy.

Benevolo MG, et al. ASH 2018. Abstract 305.

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

Dose adjustments suggested for myeloma pts based on frailty

See appendix downloaded slides. www.imf-ons.myeloma.org/ONS_2019.pdf

Palumbo A, et al. *Blood.* 2015;125(13):2068-2074. http:/www.myelomafrailtyscorecalculator.net/ accessed March 26,2019.

CASE #2:

Aaron*

- Treatment – Shared decision-making considered options
  - Lives close to clinic
  - Progressing on R maintenance
  - Has peripheral neuropathy
  - Aaron and HCP team prefers combination

FDA-approved myeloma therapies	Common Combinations
Bortezomib (SQ admin)	VRD, Vd
Lenalidomide	VRD, Rd
Carfilzomib	KRd, Kd
Pomalidomide	Pd, DPd, EPd, PCd
Daratumumab	DRd, DVd, DPd, D-VMP
Elotuzumab	ERd, EPd
Ixazomib	IRd
Panobinostat	Panobinostat + Vd
Doxorubicin	Liposomal doxorubicin + V
Cyclophosphamide	PCd, VTD-PACE

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

Pomalidomide Clinical Pearls

- Oral immunomodulatory agent active in R-refractory pts
- Monitor
  - Blood counts—neutropenia most frequent GR 3/4 AE
  - Liver function
  - Response
- Proactive AE management
- Patient education
  - Adherence and REMS
  - DVT prophylaxis
  - AEs: GI, Infection
  - Refrain from smoking (reduces pom exposure)
  - Protect renal health (renal excretion of pom)
    - Hydration
    - Avoid NSAIDS, IV contrast, other drugs with renal interactions

New

EPd
FDA approved
November 2018

Dara-Pd
FDA approved
June 2017

P ± dex
FDA approved
February 2013

AE = adverse event; IV = intravenous; EPd = elotuzumab pomalidomide dexamethasone; GR = grade; NSAID = non-steroidal anti-inflammatory drug; P = pomalidomide; pom = pomalidomide; R = lenalidomide; REMS = Risk Evaluation and Mitigation Strategies.

POMALYST® (pomalidomide) Prescribing Information. Faiman B, et al. *J Adv Pract Oncol.* 2016;7:45-52.

Clinical Pearls for Elotuzumab, Antibody Targeting SLAMF-7

- Antibody administration
  - Risk of infusion reaction: 10%
    - 3-24 hrs before= Dex 28 mg; 45-90 mins before= Dex 8 mg IV, H1, H2, and acetaminophen
  - Infuse at rate of 0. 5ml/min and escalate to 5 ml/min over time
  - Give weekly for 8 weeks then twice monthly until progressive disease
- Prescribed with len-dex or pom-dex
  - DVT prophylaxis (for len or pom)
  - Steroid side effects and schedule (AM vs PM)
- Monitoring
  - Blood counts (hold/adjust dose if needed)
  - Response assessment (monthly); interference
  - Glucose (dex can affect)
  - Renal, hepatic function

New

EPd
FDA approved
November 2018

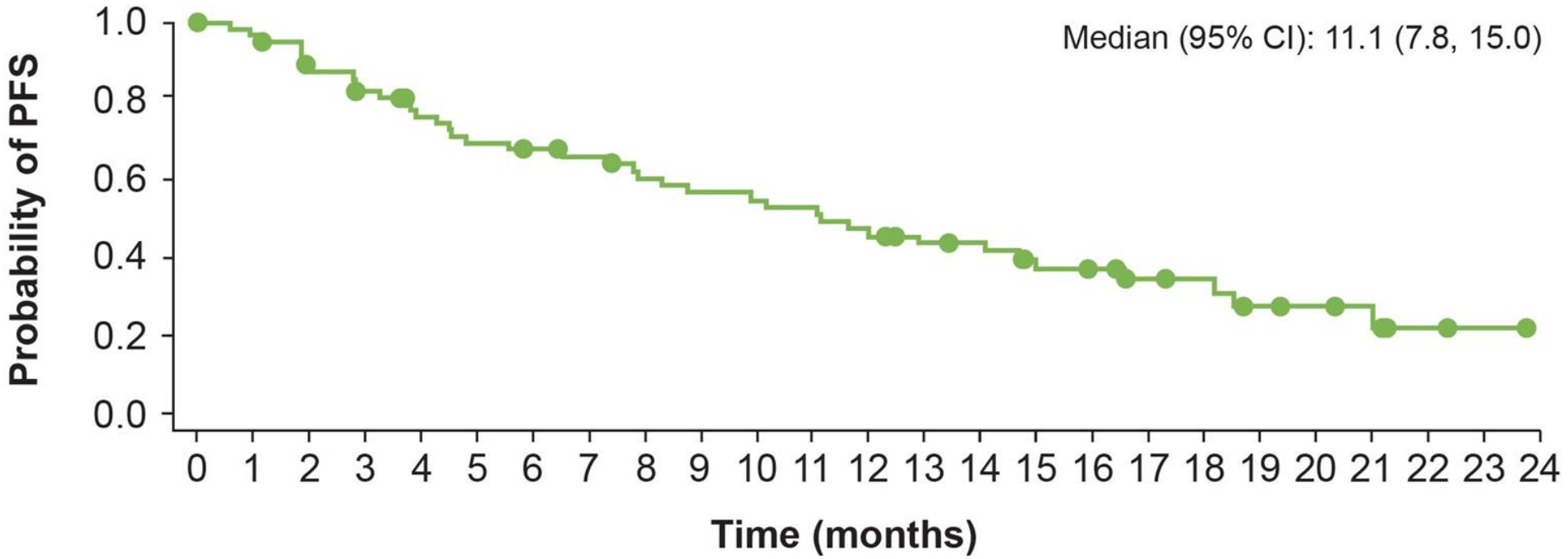
Elotuzumab+Rd
FDA approved
November 2015

dex = dexamethasone; DVT = deep vein thrombosis;
len = lenalidomide; PD = progressive disease; pom = pomalidomide

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

Elotuzumab Pomalidomide Dexamethasone

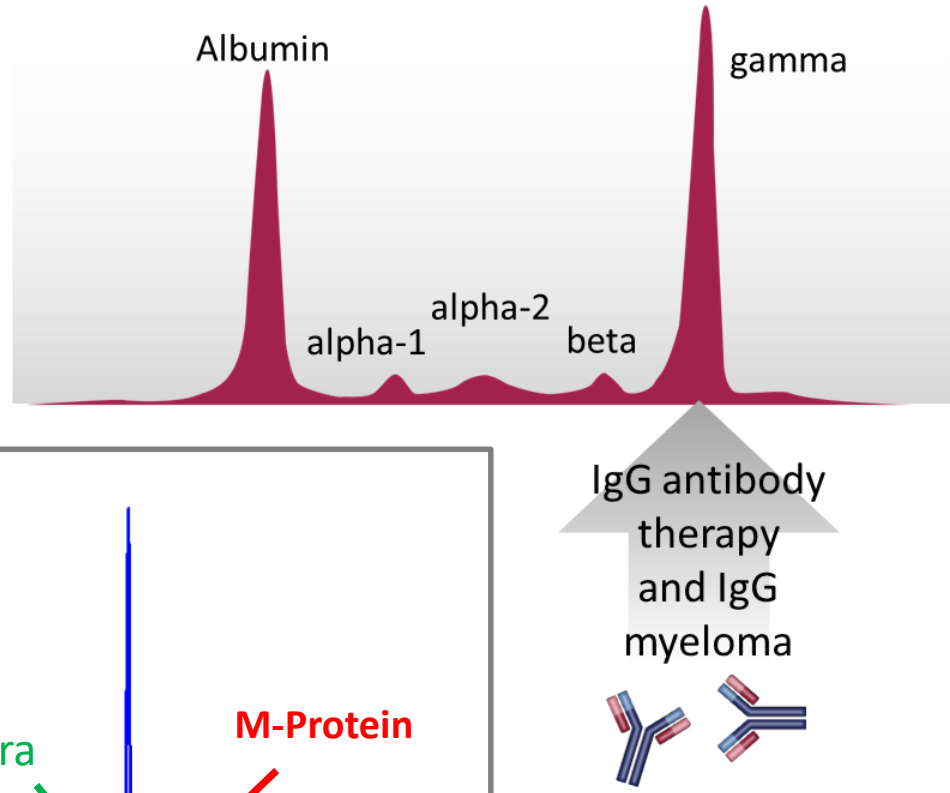
PFS with EPd treatment in Pts with Relapsed/Refractory MM



CI = confidence interval; EPd = elotuzumab pomalidomide dexamethasone; MM = multiple myeloma; PFS = progression-free survival.
Jagannath S, et al. ASH 2018. Abstract 1991.

Special Considerations With Antibody Therapy

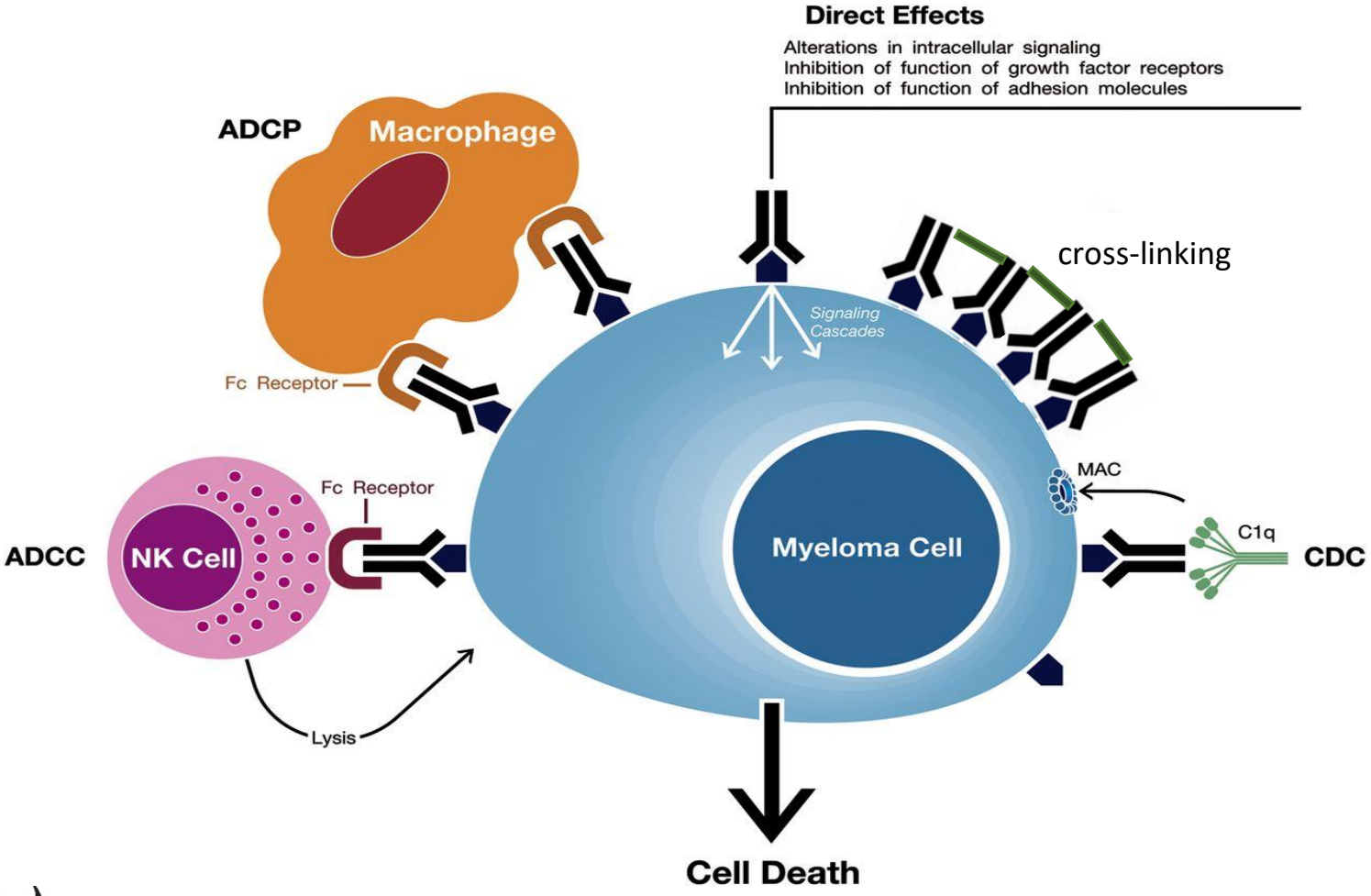
- Potential interference with laboratory tests
  - Co-migration of therapeutic antibody with M protein: Overestimation of M protein and reduced CR rates
- Solutions
  - Laboratory assays to minimize effects (eg, high resolution mass spectrometry)
  - Awareness
- Elotuzumab, daratumumab, isatuximab (in development) are all IgG antibodies



Dara = daratumumab.

Mills JR, Murray DL. *J Appl Lab Med.* 2017;1(4):421-431.

Daratumumab Directed Against CD38 on Myeloma Cells, Multiple Mechanisms of Action



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 (DARA, D)

- Human CD38-directed monoclonal antibody
- Indications
  - In combination with VMP in newly diagnosed MM patients who are not eligible for transplant
  - In combination with Rd or Vd in MM patients with at least 1 prior therapy
  - In combination with pomalidomide and dex in pts with at least 2 prior therapies including lenalidomide and a proteasome inhibitor
  - 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
- Current clinical trials
  - Many underway: watch for new combinations, indications

VMP + DARA
1st line non-transplant
FDA approved May 2018

DRd, DVd
1 prior therapy
FDA approved Nov. 2016

DPd
2 prior therapies
FDA approved June 2017

DARA monotherapy
3 prior therapies
FDA approved Nov. 2015

DRd = daratumumab-lenalidomide-dexamethasone; DVd = daratumumab-lenalidomide-dexamethasone; IMiD = immunomodulatory agent; PI = proteasome inhibitor; Rd = lenalidomide-dexamethasone; Vd = bortezomib-dexamethasone; VMP = bortezomib-melphalan-prednisone.

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

Daratumumab

Clinical Pearls:

- **Slow first infusion** ~7 hrs; then **faster** 3-4 hrs after 1st/2nd dose
- Schedule: Wks 1-8 @ **weekly**
  Wks 9-24 @ every **2 weeks**
  Wks 25 @ every **4 weeks**

Schedule becomes less frequent

IRR most common in first infusion; uncommon thereafter

Watch for early signs of IRR:
- Stuffy nose
- Asking for tissue
- Flushed face

- Premeds: Corticosteroids, antipyretics, and antihistamine
- Post-med: Oral corticosteroid for 2 days after infusion
- Educate patients/caregivers about infusion expectations
  (eg, after first decrease in chair time; injection reactions only first infusion usually)
- Herpes prophylaxis
- Antibody interference—obtain patient blood type BEFORE starting daratumumab

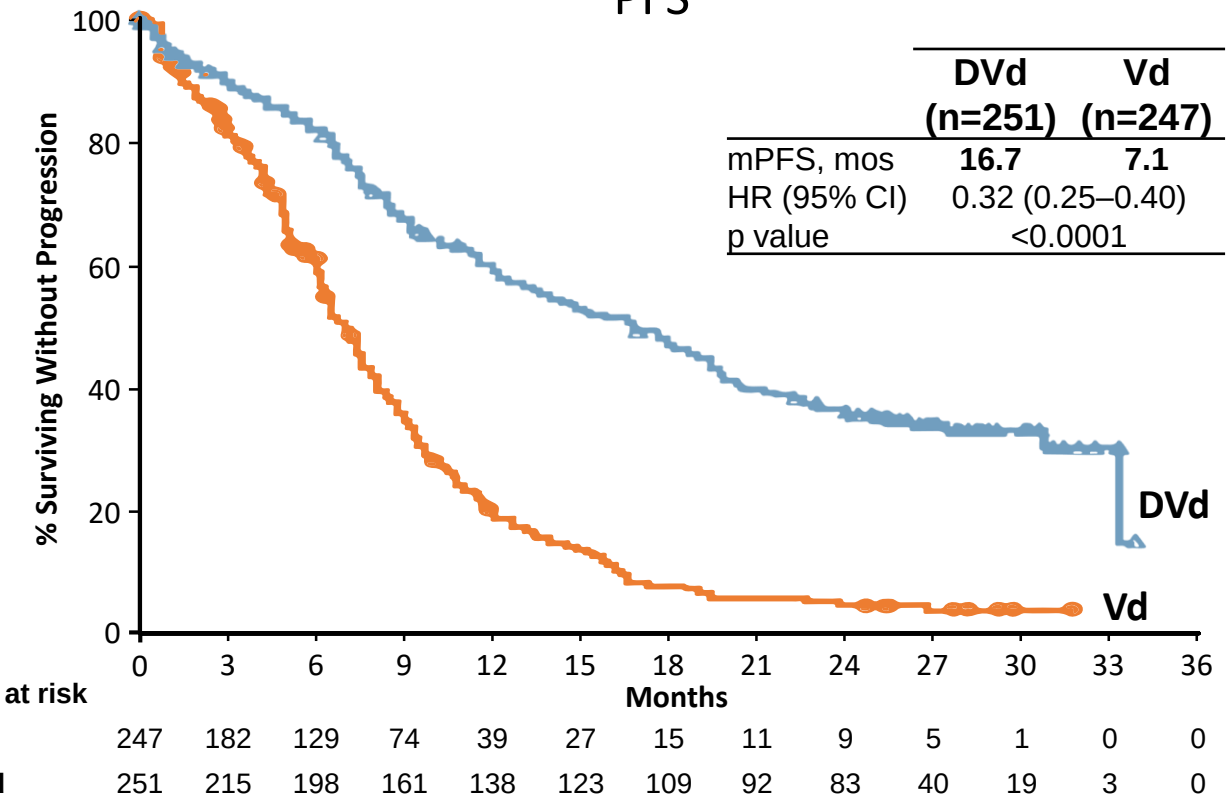
hrs = hours; IRR = infusion-related reaction; Wks = weeks.

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

DVd and DRd Regimens for Relapsed Myeloma

CASTOR Clinical Trial: MM Pts With 1 Prior Therapy

PFS

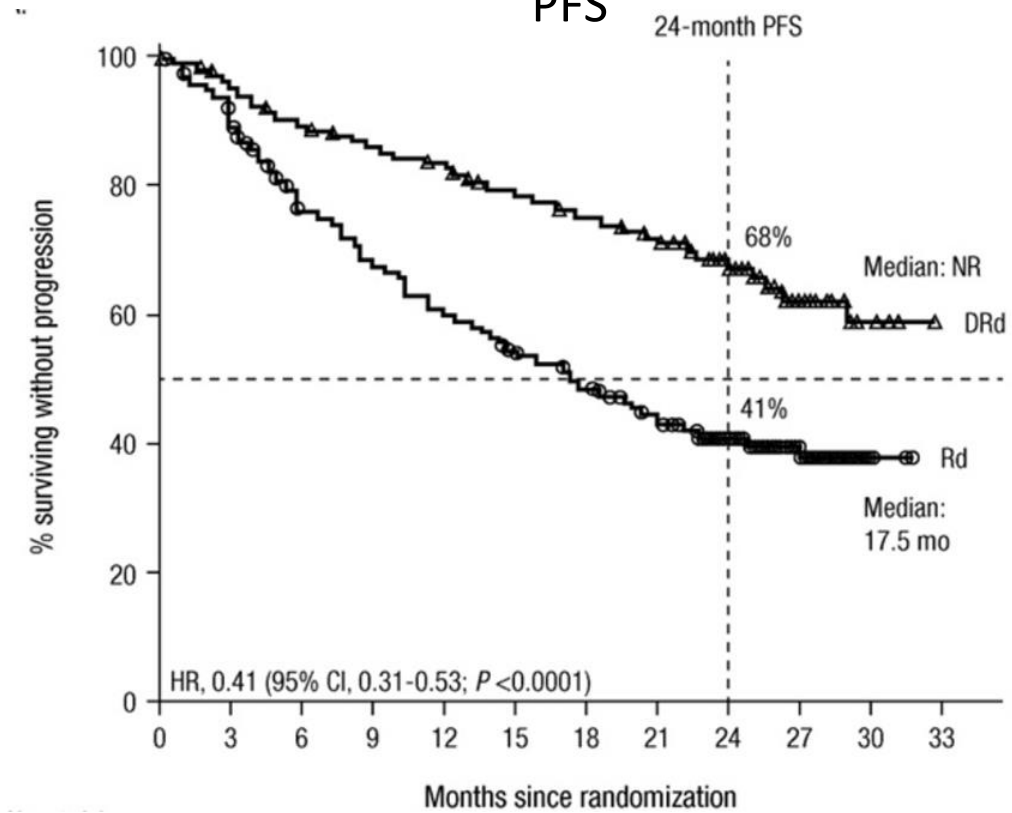


	DVd (n=251)	Vd (n=247)
mPFS, mos	**16.7**	**7.1**
HR (95% CI)	0.32 (0.25–0.40)	
p value	<0.0001	

No. at risk													
Vd	247	182	129	74	39	27	15	11	9	5	1	0	0
Dvd	251	215	198	161	138	123	109	92	83	40	19	3	0

Pollux Clinical Trial: MM Pts With 1 Prior Therapy

PFS

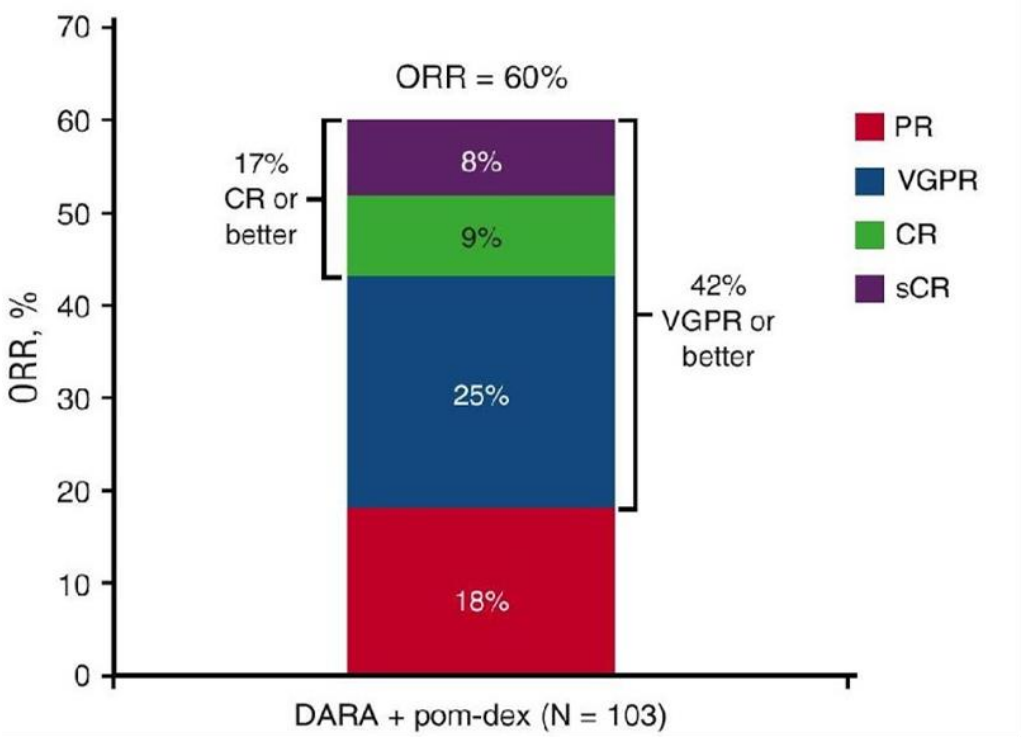


CI = confidence interval; dex = dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone; HR = hazard ratio; Mos = months; NR = not reached; PFS = progression-free survival; Rd = lenalidomide-dexamethasone; Vd = bortezomib-dexamethasone.

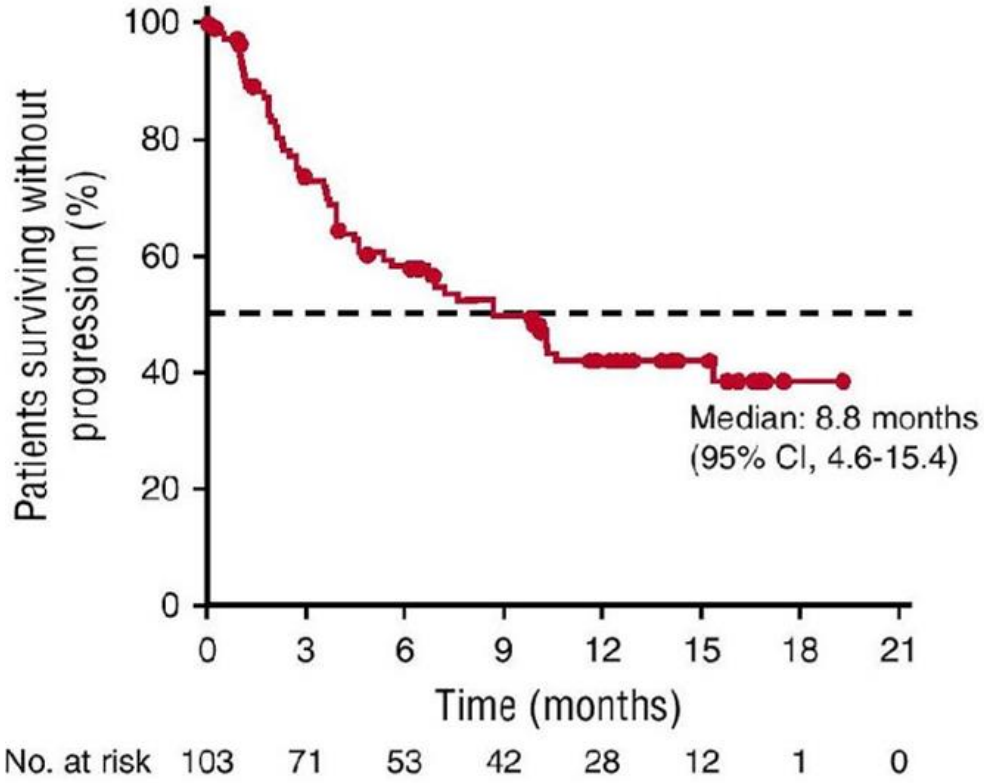
Spencer A, et al. *Blood* 2017;130:3145. Dimopoulous MA, et al. ASH 2017. Abstract 739.

DPd Regimen for Relapsed Myeloma

Response in MM Pts With ≥2 Prior Therapies



PFS in MM Pts With ≥2 Prior Therapies



CR = complete response; DARA = daratumumab; dex = dexamethasone; DPd = daratumumab pomalidomide dexamethasone; ORR = overall response rate; PFS = progression-free survival; pom = pomalidomide; sCR = stringent complete response; VGPR = very good partial response.

Chari A, et al. *Blood* 2017;130:974-981.

DARA Administration Options Under Investigation

90-Min Daratumumab Rapid Infusion

- AFTER first 2 doses of DARA as standard infusion rates pts eligible
- Pts with prior IRR NOT excluded

Daratumumab Accelerated Infusion
- 20% of the dose over the first 30 minutes
- Remaining 80% over 60 minutes

- 28 pts treated with rapid infusion
  - 1 AE: 1 pt with grade 2 hypertension; paused DARA for diuretic then resumed
  - No grade 3+ IRRs
- Conclusion: DARA accelerated infusion is feasible and well tolerated; now standard practice at the author's institution

AE = adverse event; DARA = daratumumab; IRR = infusion-related reaction.
Barr H, et al. *Blood*. 2017;130:1889.

Subcutaneous Daratumumab

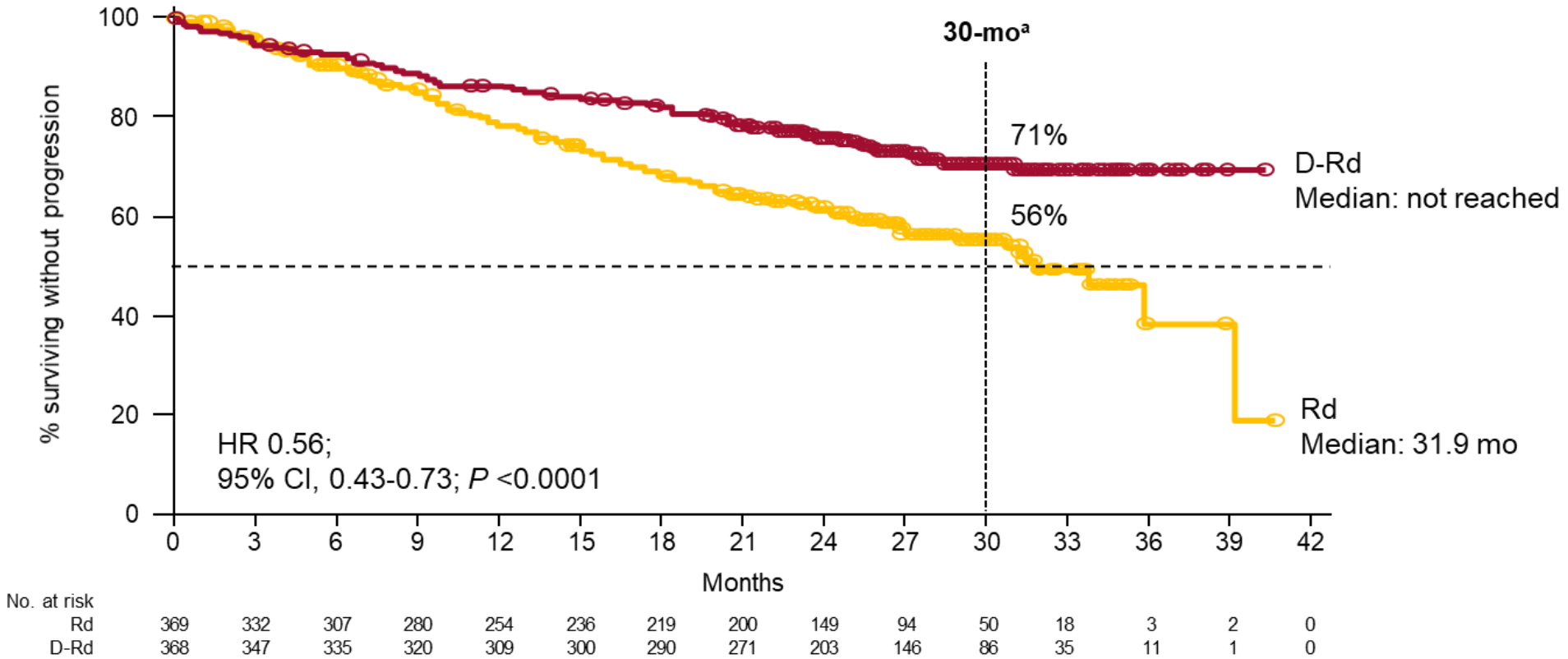
- Relapsed or refractory MM (≥ 2 prior therapies); two regimens

Daratumumab 1200 mg rHuPH20 30,000 U 20 min, n = 8	Daratumumab 1800 mg rHuPH20 45,000 U 30 min, n = 45
ORR = 25%	ORR = 38%

- No new safety signals
  - IRRs were grade 1 or 2 in the 1899 mg
  - 1 grade 3 IRR in 1200 mg group
  - All IRRs during the first infusion
- Conclusion: Subcutaneous daratumumab is well tolerated with similar efficacy to IV

Usmani SZ, et al. *Blood*. 2016;128 Abstract 1149.

Phase III MAIA: D-Rd vs Rd for Newly Diagnosed Pts With MM Who Are Transplant Ineligible



44% reduction in the risk of progression or death in patients treated with D-Rd

[a]Kaplan-Meier estimate.

D-RD = daratumumab lenalidomide dexamethasone; MM = multiple myeloma; Rd = lenalidomide.

Facon T, et al. ASH 2018. Abstract LBA-2.

CASE #2:

Aaron*

- After 3 months of D-Pd, zoledronic acid treatment:
  - Tolerating well
  - Managing glucose
  - Ca, Creatine normal
- Updated Survivorship Care Plan
  - Added current test results
  - Added current treatment plan
  - Reviewed patient education on renal health
  - Coordination with PCP for vaccinations and health screenings
- Health promotion; diet, exercise, lifestyle
- Support group

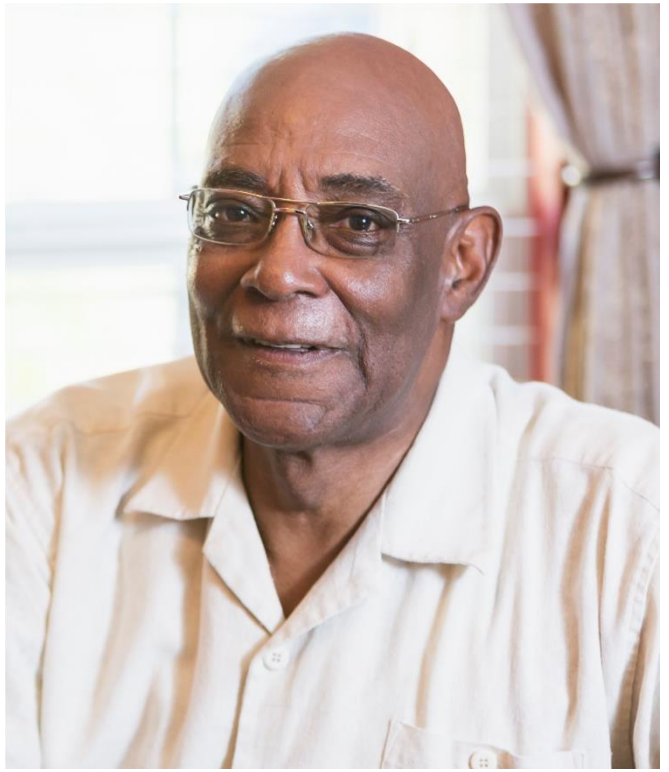
*HIPAA-compliant, stock photo (not actual patient).

Ca = calcium; D-Pd = daratumumab, pomalidomide, dexamethasone.

CASE #3:

James*

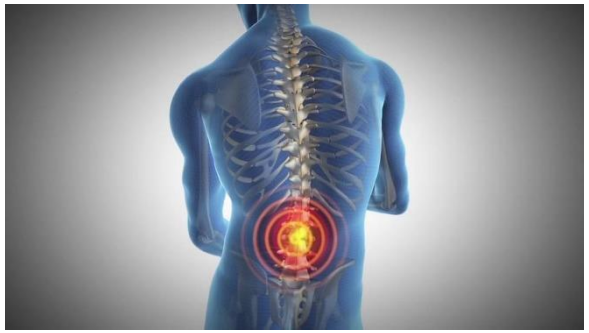
- Widowed store manager, 63 years old; helps his two daughters financially
- November 2013
  - Multiple myeloma diagnosed
  - VRd induction + ASCT + 2 yrs len maintenance
  - Standard risk: t(11;14)
- September 2018:
  - Leg pain
  - Skeletal survey: New lesions femur, ribs
  - No new genetic abnormalities
  - Creatine and Ca^{2+} elevated
- Considerations:
  - No cardiac history
  - Lives near clinic
- Shared decision-making: Considering IRd, KRd



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

ASCT = autologous stem cell transplantation; len = lenalidomide; VRd = bortezomib-lenalidomide-dexamethasone.

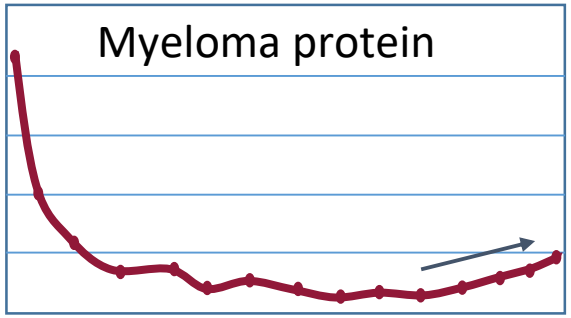
How Patients With Myeloma Relapse



Symptomatic

James

- New, worsening bone pain
- Increasing fatigue, anemia
- Next steps: Relapse workup, many therapy choices



Asymptomatic Biochemical Relapse

- Sequentially rising myeloma protein, free light chain
- No other symptoms
- Decisions: If, when, how to treat

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.

Ixazomib: Oral Proteasome Inhibitor

- Oral proteasome inhibitor
  - Indication: Patients with multiple myeloma who have received at least 1 prior therapy
  - In combination with Rd
- Administration
  - Oral capsule 1X per week; do not crush, 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.

NINLARO® (ixazomib) Prescribing Information. Faiman B, et al. *J Adv Pract Oncol.* 2016;7:45-52.

IRd: All Oral Regimen Dosing Calendar

Ixazomib dosing
28-day cycle

Recommended starting doses:

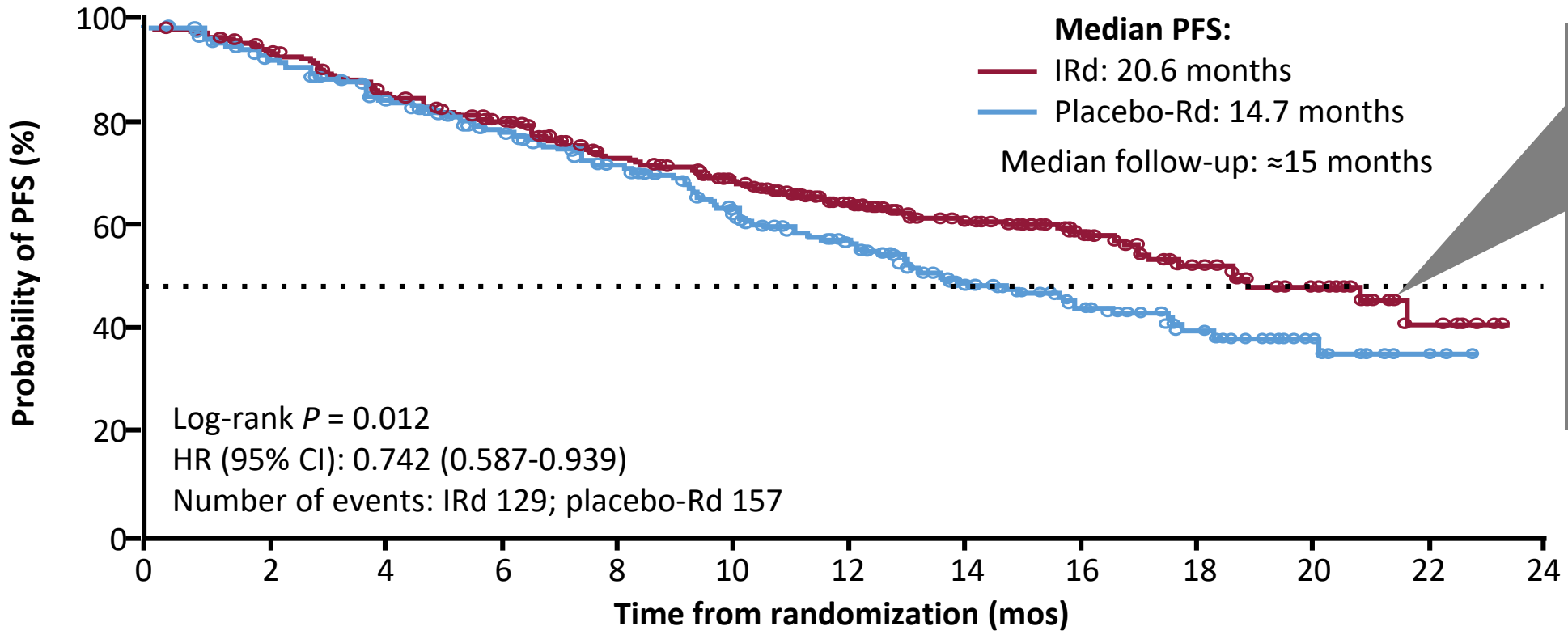
- Ixazomib 4 mg
- Lenalidomide 25 mg
- Dexamethasone 40 mg

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

IRd = ixazomib lenalidomide dexamethasone.

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; HR = hazard ratio; IRd = ixazomib-lenalidomide-dexamethasone; PFS = progression-free survival; Rd = lenalidomide-dexamethasone.

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

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
- Clinical pearls
  - Escalate dose
  - Dose-dependent 10- or 30-min infusion
  - Hydration but not over hydration
  - Premedication (dex)
  - Aspirin prophylaxis
  - Monitor blood counts, response
  - Monitor for infection
  - Herpes virus prophylaxis
  - Know cardiac and pulmonary status and optimize heart failure and blood pressure management
  - Diuretic (furosemide or torsemide) or inhalers if needed

New

Kd
20/70 mg/m²
once weekly
FDA approved

KRd
20/27 mg/m²

Kd
20/56 mg/m²

K monotherapy
20/27 mg/m²

dex = dexamethasone; IV = intravenous; K = carfilzomib; Kd = carfilzomib, dexamethasone; KRd = carfilzomib, lenalidomide, dexamethasone; len = lenalidomide; MM = multiple myeloma.

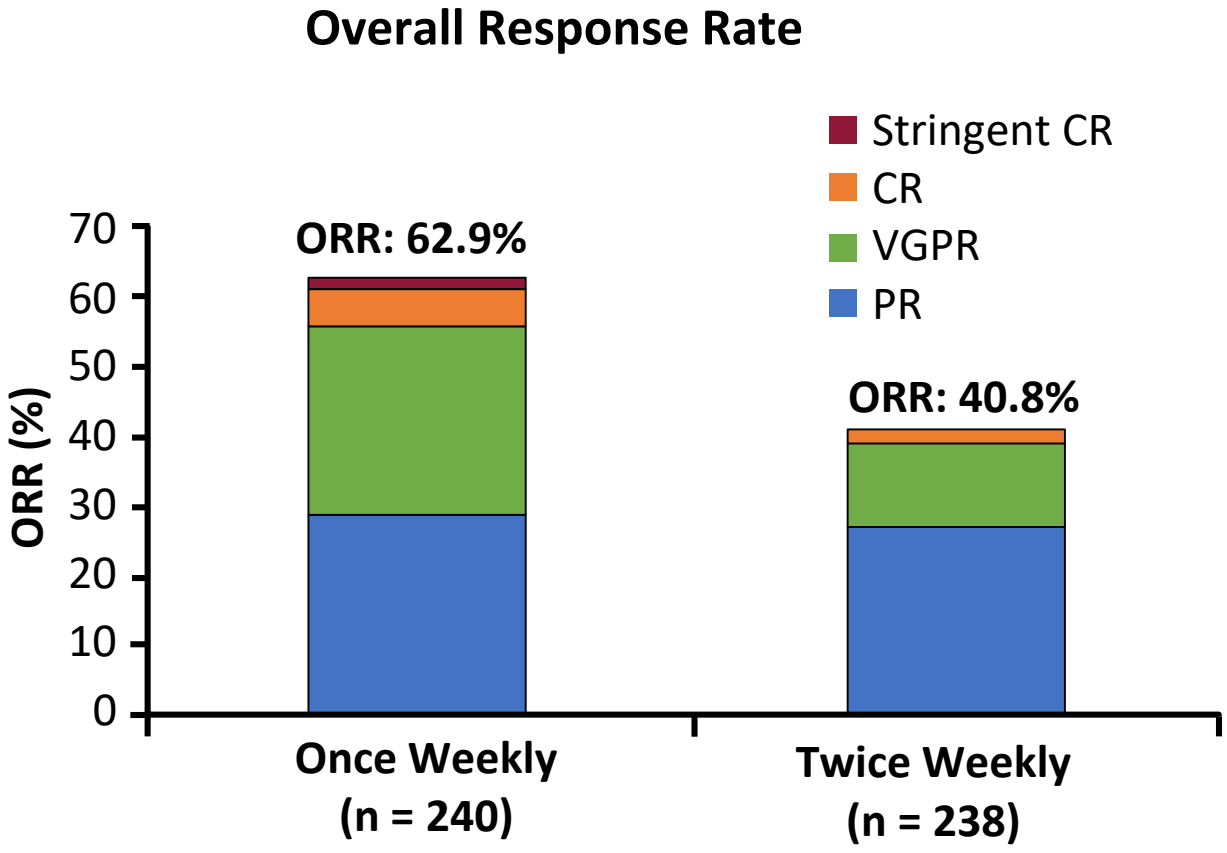
Stewart K, et al. *N Engl J Med.* 2015;372:142-152. Kyprolis® (carfilzomib) prescribing information.

New Once Weekly Carfilzomib Dosing in ARROW Clinical Trial

Patients with R/R MM
2-3 previous lines of therapy with IMiD and
PI exposure (no carfilzomib or oprozomib)
ECOG PS 0/1, and CrCl ≥ 30 mL/min
(N = 478)

Weekly Carfilzomib (70 mg/m²)* + dex (n = 240)

Twice Weekly Carfilzomib (27 mg/m²)* + dex (n = 238)



*After 20 mg/m² ramp up dose(s).

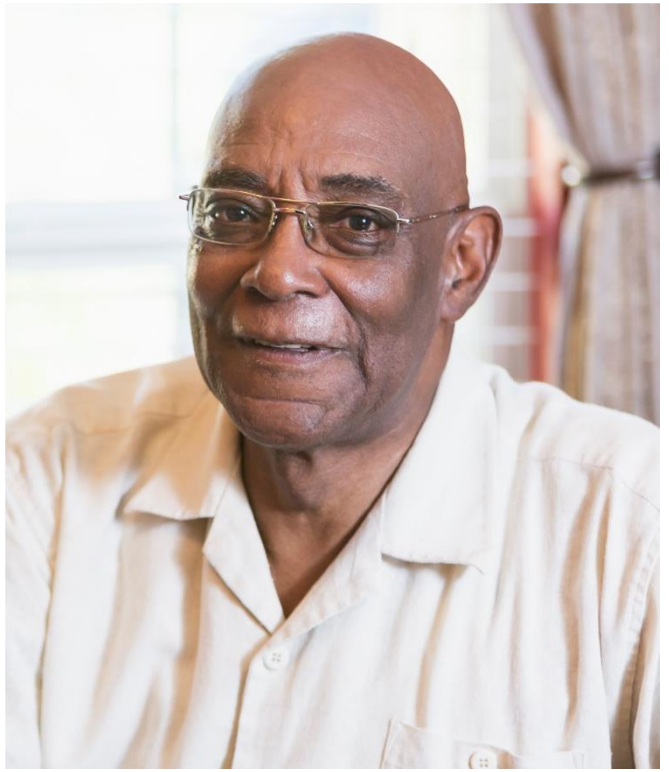
CrCl = creatinine clearance; CR = complete response; Dex = dexamethasone; MM = multiple myeloma; ORR = overall response rate; PR = partial response; R/R = relapse/refractory; VGPR = very good partial response.

Mateos MV, et al. ASCO 2018. Abstract 8000.

CASE #3:

James*

- Case Update
  - Considered options
  - IRd selected—all oral regimen
- After 4 cycles IRd
  - VGPR
  - Tolerating treatment well
  - Likes all oral regimen convenience



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

IRd = ixazomib lenalidomide dexamethasone; VGPR = very good partial response.

Drugs or Regimens in Development

Many myeloma drugs are in development

- Immuno-oncology approaches:
  - Vaccines approaches
  - Pembrolizumab
  - Nivolumab
  - **Isatuximab**
  - **CAR T-Cells**
  - SLAMF7 CAR T-Cells
  - GSK2857916
  - AMG 340
- Approved in other indications
  - **Venetoclax**
  - Ibrutinib
  - Bevacizumab
  - Ruxolitinib
- New myeloma targets / drugs
  - **Selinexor**
  - Filanesib / ARRY-520
  - Oprozomib

Combinations, Sequencing, Testing

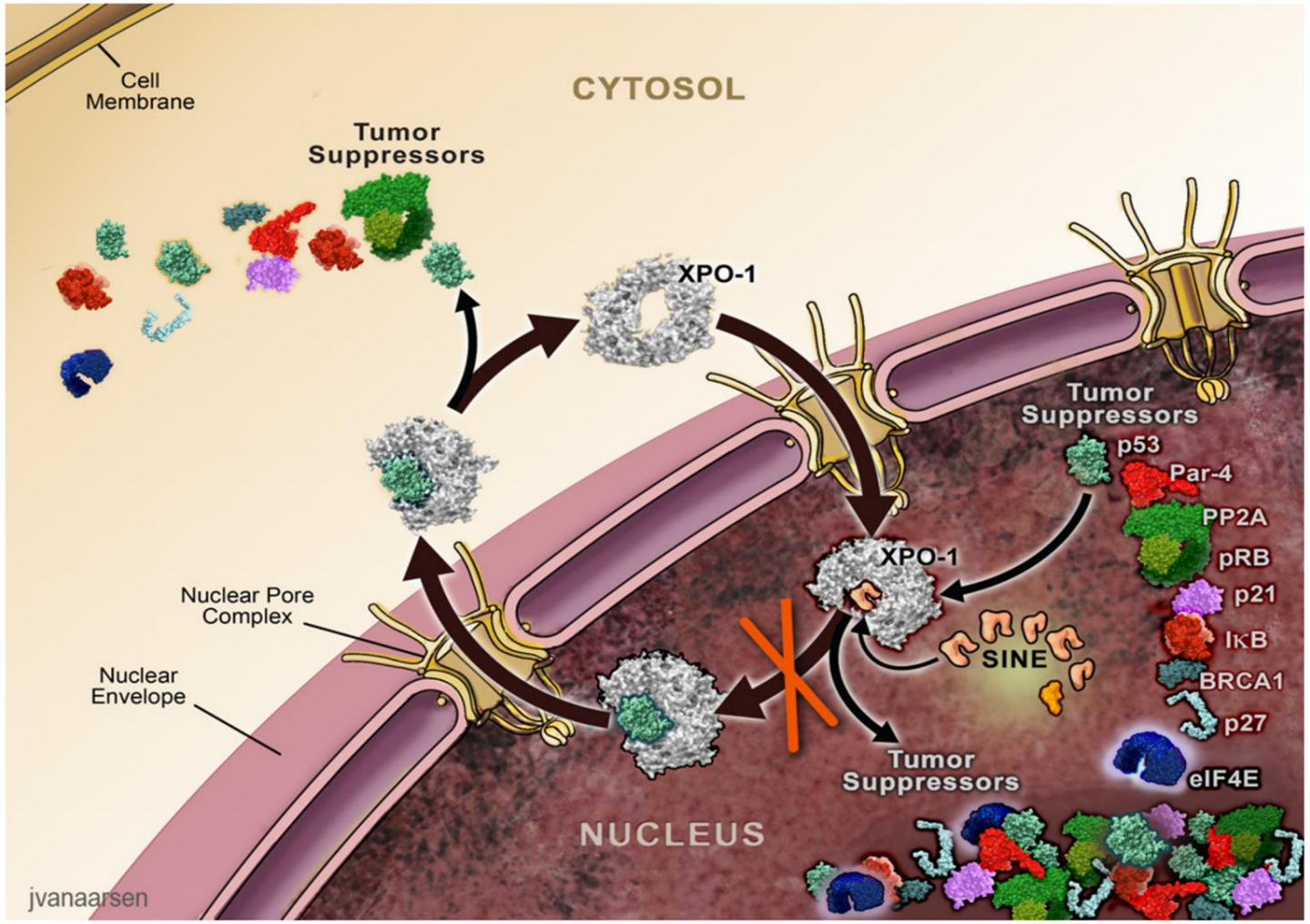
- First-line induction combinations
  - KRd, DVd, DRd
  - Many others
- Sequencing or timing of therapy
  - Early treatment (SMM)
  - New maintenance options
  - Role of transplantation (early, late)
- MRD testing

Watch for new data on myeloma therapies from ASCO June 2019

DRd = daratumumab-lenalidomide-dexamethasone; DVd = daratumumab-lenalidomide-dexamethasone; KRd = carfilzomib- lenalidomide-dexamethasone; SMM, smoldering multiple myeloma.

Clinical Trials.gov.

Selinexor: First-in-class, Oral Selective Inhibitor of Nuclear Export (SINE) Compound



Orphan Drug Designation by FDA

Fast Track Designation by FDA

Selinexor (KPT-330) is a covalent, oral selective inhibitor of nuclear export (SINE) that inhibits XPO1. By blocking tumor suppressor proteins (TSP) from being exported from the nucleus, selinexor forces nuclear restoration and reactivation of TSPs leading to selective induction of apoptosis of cancer cells

Chen C, et al. EHA 2014.

Selinexor Storm Part 2 Clinical Trial: 26.2% ORR in Heavily Pretreated Patients With MM

- MM patients with a **median of 7 prior treatment** regimens
  - ORR of 26.2%, including 2 stringent CRs
    - 2 pts with stringent CR (sCRs were MRD negative at 10^{-6} and 10^{-4})
    - 2 pts with previous PD after CAR T-cell therapy achieved PR
  - Median time to response was 1 month (range 1 to 14 weeks)
- Median OS: 8.6 mos
  - 15.6 mos in patients with ≥ MR vs 1.7 mos in patients with PD/NE
- Most commonly occurring grade ≥ 3 AEs were hematologic, GI-related, constitutional symptoms, and hyponatremia; typically responsive to dose modification and standard supportive care agents
- Investigators concluded that selinexor is a potential novel, oral treatment option for patients with MM who have exhausted all approved therapies

"The 26.2% ORR … in the STORM study is highly compelling and reinforces the potential of selinexor in this difficult to treat patient population."

CAR = chimeric antigen receptor; CR = complete response; MM = multiple myeloma; MR = minimum response; MRD = minimal residual disease; ORR = overall response rate; OS = overall survival; sCR = stringent complete response.

Chari A, et al. ASH Abstract 598. Karyopharm Press Release December 3, 2018. https://investors.karyopharm.com/node/11626/pdf accessed March 13, 2019.

Selinexor: Safety Profile

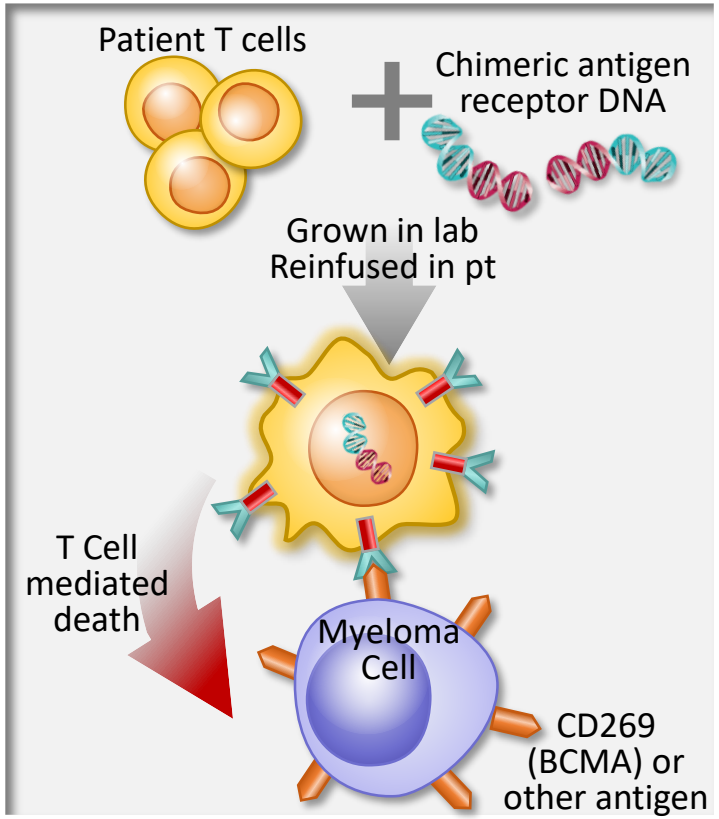
- **Most common treatment-related AEs were manageable with dose modifications and supportive care**
  - Cytopenias
  - Gastrointestinal and constitutional symptoms
  - Consistent with earlier studies (eg, Vogl et al. *J Clin Oncol*, 2018)
- **The most common non-hematologic treatment -related AEs (mostly Grade 1 and 2 events)**
  - Nausea (69%)
  - Fatigue (56%)
  - Anorexia (52%)
  - Weight loss (47%)
- **Most common Grade 3 and 4 treatment-related AEs**
  - Thrombocytopenia (54%)
  - Anemia (29%)
  - Neutropenia (19%)
  - Fatigue (19%)
- **No significant major organ toxicities were observed, and bleeding and infection rates were low**

AE = adverse event.

Chari A, et al. ASH Abstract 598. Karyopharm Press Release December 3, 2018. https://investors.karyopharm.com/node/11626/pdf accessed March 13, 2019.

New Ways to Target and Kill Myeloma Cells in Development

CAR-T Cell Therapy

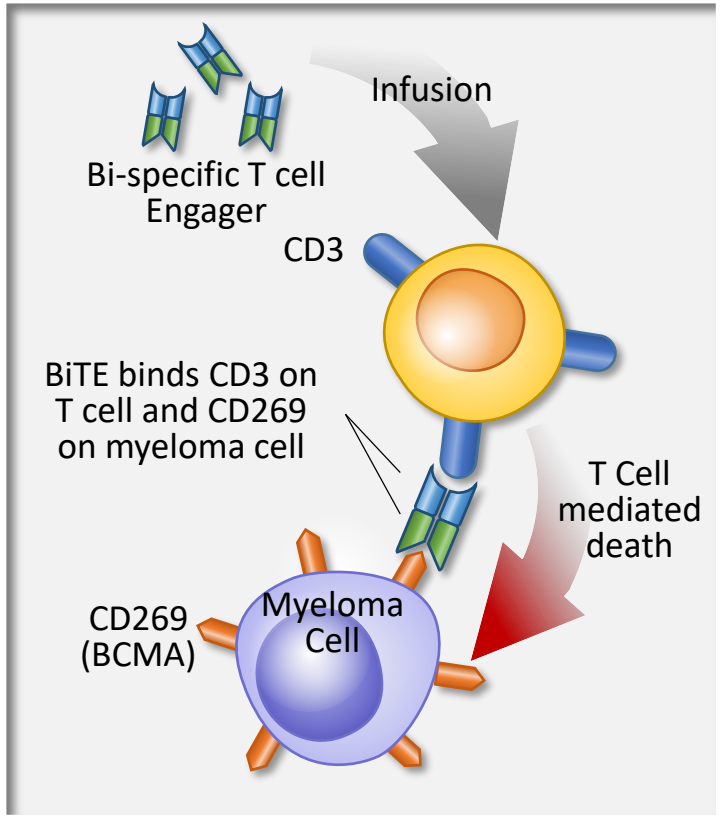


Examples: **bb2121, LCAR-B38M, MCARH171**

Raje NS, et al. ASH 2018. Abs #8007; Zhao W-H, et al. ASH 2018. Abs #955; Mailankody S, et al ASH 2018. Abs #959.

BCMA = B-cell maturation antigen.

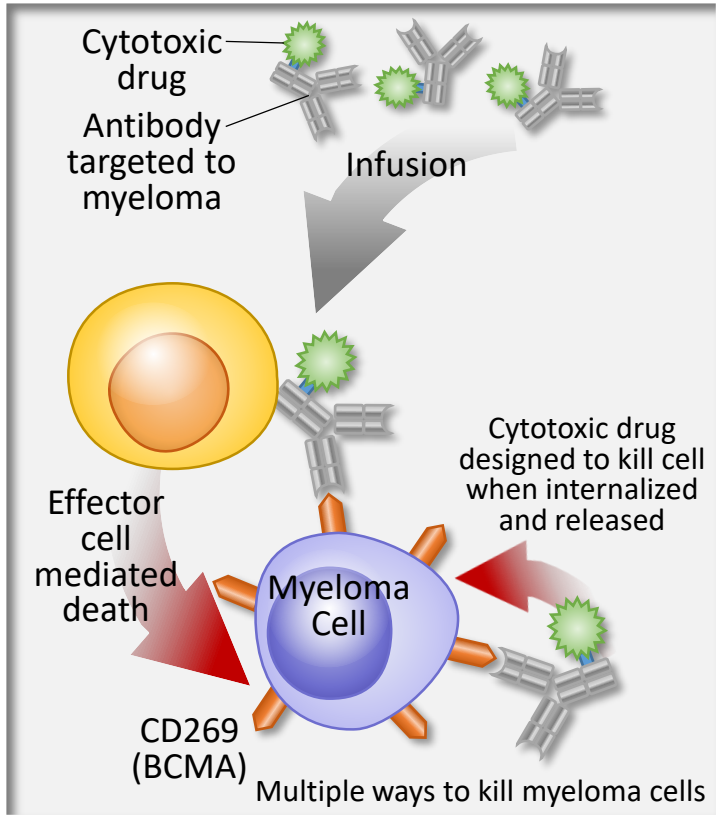
BiTE Antibody



Example: **AMG 420**

Topp MS, et al ASH 2018. Abstract #1010.

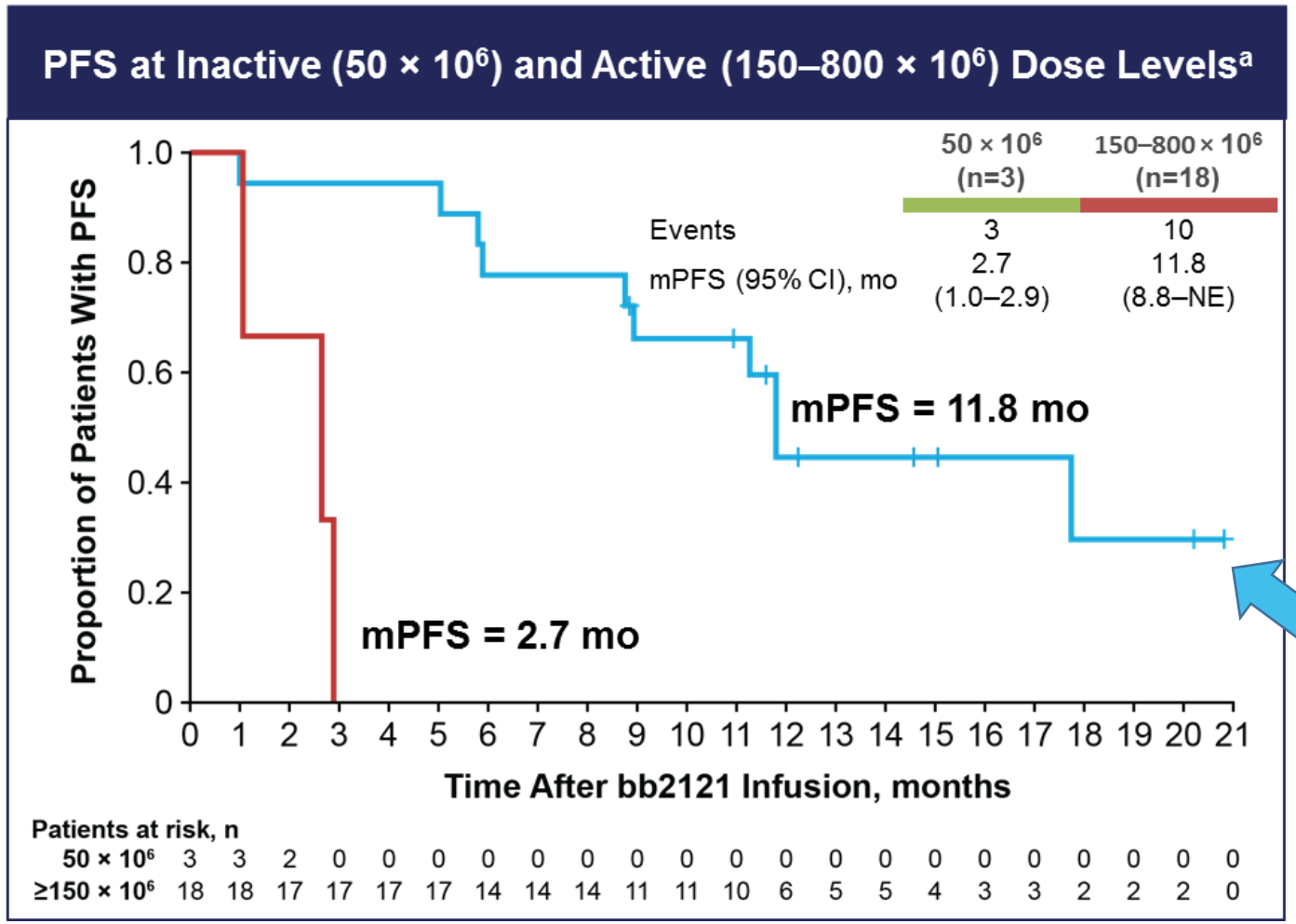
Drug-Antibody Conjugate



Example: **GSK2857916**

Trudel S, et al. *Lancet Oncol*. 2018;19(12):1641-1653.

CAR T Cell Clinical Trial in Myeloma



Bb2121 second-generation CAR T cell therapy targeting CD269 (BCMA)

- Phase I clinical trial
- 43 pts
- ≥3 prior lines of therapy including a proteasome inhibitor and an immunomodulatory agent, or were double refractory,
- ≥50% BCMA expression on plasma cells

Active dose had a median PFS of 11.8 months

CI = confidence interval; BCMA = B-cell maturation antigen, mPFS = median progression-free survival; PFS = progression-free survival

Raje NS, et al. ASCO 2018. Abstract #8007.

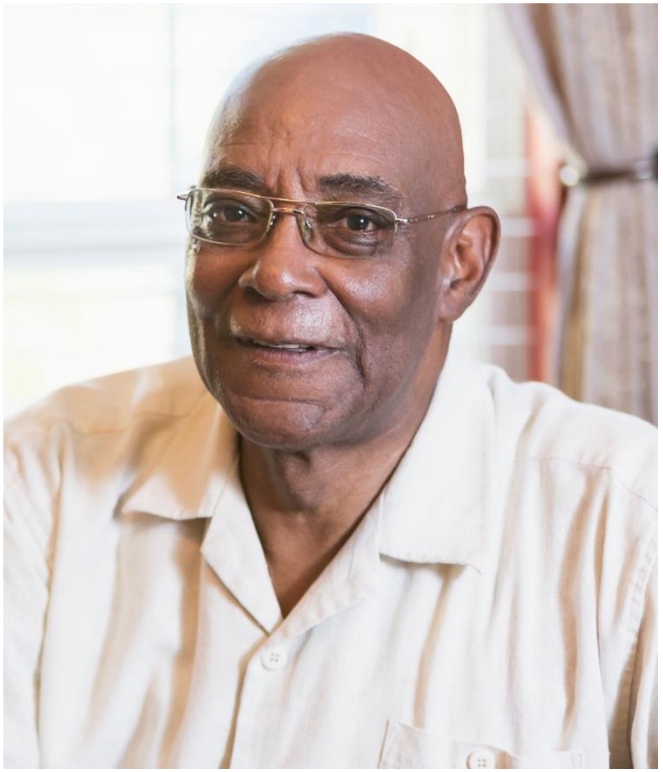
Nursing Implications of New Methods of Killing Myeloma Cells

- New drugs and drug classes mean HCPs need education
  - When and how to use
  - How to manage pts—new and potentially unfamiliar AEs
  - How to educate pts

Watch for

Watch for learning opportunities as new drugs for MM are approved

Thank You for Sharing in the Stories of Our Patients

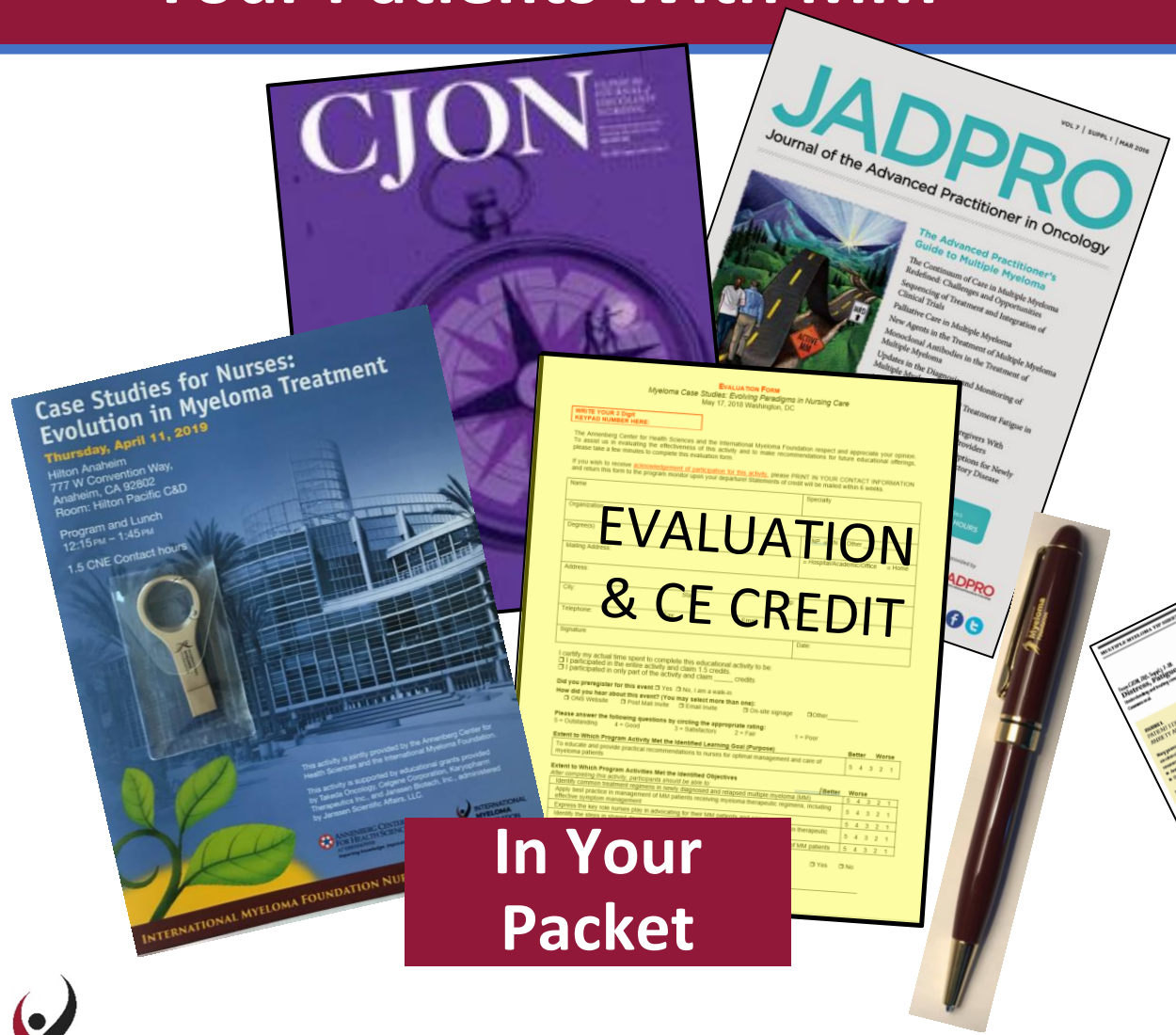


We Hope You Had an Enjoyable and Educational Time: Learning Objectives

As a result of this program, you learned to:

- Identify common treatment regimens in newly diagnosed and relapsed multiple myeloma
- Discuss nursing management of MM patients receiving myeloma therapeutic regimens, including effective symptom management
- Identify the steps in shared decision-making and strategies to support the patient's input in therapeutic decisions
- Discuss the importance of survivorship care plans and practical tools for long-term management and care of MM patients

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



And More

CE = continuing education; MM = multiple myeloma.

Thank You for Your Attendance and Participation

On behalf of the International Myeloma Foundation with the generous support from Celgene Corporation Takeda Oncology, Karyopharm, and Janssen Biotech, ***we thank you****.*

Faculty are available to answer questions.

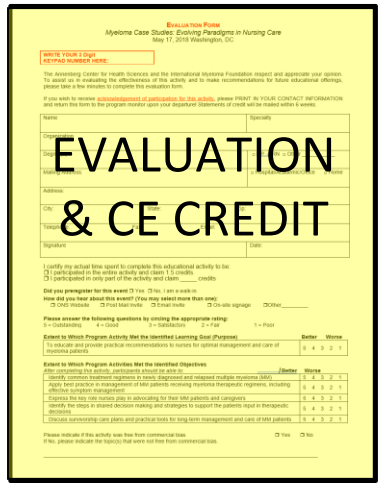
Please Contact IMF for Further Information and Resources:

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

TheIMF@myeloma.org

http://myeloma.org

Slides at
www.imf-ons.myeloma.org/ONS_2019.pdf



In box at exit or hand to staff

CE = continuing education.

Appendix Slides

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%	≥60%
Presence of MDE (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;356:2582-2590.
2. International Myeloma Working Group. *Br J Haematol.* 2003;121:749-757.
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 Oncol* 2014;15:e538-e548.

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®, EVOMELA®
	Cyclophosphamide	CTX, Cy, C	CYTOXAN®, NEOSAR®
Corticosteroid	Prednisone	pred, P	DELTASONE®
	Dexamethasone	D, d, dex, DXM	DECADRON®
Histone deacetylase inhibitor	Panobinostat	pano, F	FARYDAK®
Bone strengthener	Pamidronate	pmd	AREDIA®
	Zoledronic acid	Zol	ZOMETA®
	Denosumab	--	XGEVA®

Common/Important Side Effects of Myeloma Drugs (page 1 of 2)

	"Mides" Immunomodulatory drugs (IMIDS)			"Mibs" Proteasome Inhibitors		
	Thalomid® (thalidomide)	Revlimid® (lenalidomide)	Pomalyst® (pomalidomide)	Velcade® (bortezomib)	Kyprolis® (carfilzomib)	Ninlaro® (ixazomib)
Neuropathy (PN)	✔			✔*		
Thrombosis (DVT, PE)	✔ more with dex	✔ more with dex	✔ more with dex		✔	
Myelosuppression	✔ neutropenia	✔ anemia, neutropenia, thrombocytopenia	✔ neutropenia	✔ thrombocytopenia	✔ neutropenia, thrombocytopenia	✔ thrombocytopenia
Cardiopulmonary	✔ slow heart rate		✔ shortness of breath	✔ hypotension	✔ shortness of breath, other	
Fatigue, weakness	✔ (incl sedation)	✔	✔	✔	✔	✔ (incl sedation)
Renal	✔	✔	✔			
Rash	✔	✔	✔			
GI disturbance	✔ constipation	✔ diarrhea, constipation	✔ diarrhea, constipation	✔ nausea, vomiting, diarrhea	✔ nausea, vomiting, diarrhea, constipation	✔ diarrhea, constipation, nausea

*Subcutaneous administration reduces rates of PN

dex = dexamethasone; DVT = deep vein thrombosis; GI = gastrointestinal PE = pulmonary embolism; PN = peripheral neuropathy.

Prescribing Information: thalidomide, lenalidomide, pomalidomide, bortezomib, carfilzomib, ixazomib.

Common/Important Side Effects of Myeloma Drugs (page 2 of 2)

	"Mabs" Monoclonal Antibodies		HDAC inhibitor	Anthracycline	Alkylating Agents	
	Darzalex® (daratumumab)	Empliciti® (elotuzumab)	Farydak® (panobinostat)	Doxil® (liposomal doxorubicin)	Cytoxan® NEOSAR® (cyclophosphamide)	ALKERAN® EVOMELA® (melphalan)
Neuropathy (PN)						
Infusion reaction	✔	✔		✔ Acute infusion reactions	✔ hypersensitivity	✔ hypersensitivity
Myelosuppression	✔ neutropenia, thrombocytopenia		✔ neutropenia, thrombocytopenia	✔ neutropenia	✔ anemia, myelosuppression, immunosuppression	✔ severe bone marrow suppression
Cardiopulmonary			✔ arrythmias, ischemia		✔ myocarditis, arrythmias, pneumonitis	
Fatigue, weakness	✔	✔	✔	✔	✔	✔
Rash				✔	✔	
GI disturbance	✔ diarrhea	✔ diarrhea, nausea	✔ severe diarrhea, nausea, vomiting	✔ diarrhea, nausea, vomiting, constipation	✔ nausea, vomiting, diarrhea	✔ nausea, vomiting, diarrhea, oral mucositis

GI = gastrointestinal; PN = peripheral neuropathy.

Prescribing Information: daratumumab, elotuzumab, panobinostat, doxorubicin, cyclophosphamide, melphalan

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

AE = adverse event; PN = peripheral neuropathy; QD = daily; QOD = every other day; RVD = lenalidomide-bortezomib-dexamethasone; Tx = treatment; wk = week.

Palumbo A, et al. *Blood*. 2011;118:4519-4529. Palumbo A, et al. *Blood*. 2015;125:2068-2074. Ninlaro® (ixazomib) Prescribing Information. Pomalyst® (pomalidomide) Prescribing Information. O'Donnell EK, et al. *Br J Haematol*. *Br J Haematol.* 2018;182(2):222-230.

Nurses' Roles in Shared Decision-Making

Empower Patients

- Encourage participation in therapy decisions
- Encourage preparation for appointments (write down questions in advance, keep symptom diary)
- Adherence strategies (calendars, reminders, pill boxes, consistent schedule)

Inform Patients

- Educate pts to enable them to make informed decisions
- Be a trusted source of information for patients
- Point patients to reputable sources of information
- Provide strategies for symptom management, medication adherence

Advocate for Patients

- Discuss pt's goals and priorities
- Build consensus among pt and caregiver
- Advocate for best interest of the pt with the broader health care team
- Intercede to ensure pt's needs are being addressed

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, Hershman DL. *Am Soc Clin Oncol Educ Book.* 2013:271-276. Kurtin S, et al. *J Adv Pract Oncol.* 2016; (suppl 1):71-77.

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

Shared Decision-Making Benefits and Outcomes

Short-Term Benefits

- Increased confidence with treatment decisions
- Higher satisfaction with treatment decisions
- Enhanced trust in health care 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

Kane HL, et al. *CA Cancer J Clin*. 2014;64:377-388.

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	Calcium Level, Renal Status, Anemia, and Bone Lesions
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